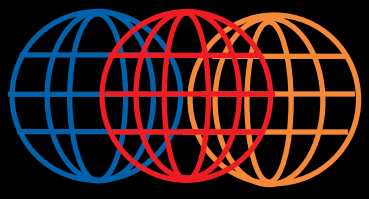
INFECTIOUS DISEASES

THE GLOBAL FIGHT



GLOBAL ISSUES

NOVEMBER 1996
Volume 1, Number 17

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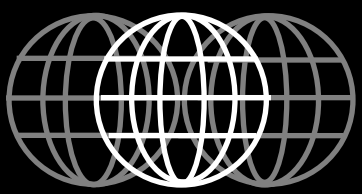

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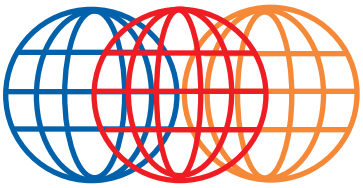

INFECTIOUS DISEASES

THE GLOBAL FIGHT

Infectious diseases are the single most common cause of death worldwide, 40 years after the introduction of antibiotics. In the United States only heart disease and cancer kill more people. This month, through interviews and in-depth reports, we present the views of a variety of medical and public-health authorities on the problems and issues surrounding infectious diseases. While experts believe that the threat will continue and may even intensify in coming years, they also report that scientists are developing better ways to treat and prevent many infectious diseases that afflict people around the world.

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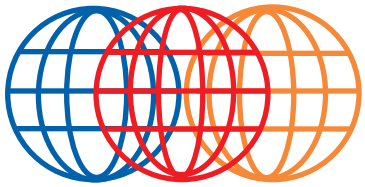

INFECTIOUS DISEASES: THE GLOBAL FIGHT

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GLOBAL ISSUES
Electronic Journals of the U.S. Information Agency
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USIA's electronic journals, published and transmitted worldwide at two-week intervals, examine major issues facing the United States and the international community, and inform foreign publics about the United States. The journals — ECONOMIC PERSPECTIVES, GLOBAL ISSUES, ISSUES OF DEMOCRACY, U.S. FOREIGN POLICY AGENDA, and U.S. SOCIETY AND VALUES — provide analysis, commentary, and background information in their thematic areas. French and Spanish language versions appear one week after the English. The opinions expressed in the journals do not necessarily reflect the views or policies of the U.S. Government. Articles may be reproduced and translated unless there are specific copyright restrictions cited on the articles. Current or back issues of the journals can be found on the U.S. Information Service (USIS) Home Page on the World Wide Web at "http://www.usia.gov/journals/journals.htm". They are available in several electronic formats to facilitate viewing on-line, transferring, downloading, and printing. Comments are welcome at your local USIS office or at the editorial offices — Editor, Global Issues (I/TGIC), U.S. Information Agency, 301 4th Street SW, Washington, D.C. 20547, United States of America. You may also communicate via email to *ejglobal@USIA.gov*.

Here To Stay

An interview with Dr. David Satcher, director, U.S. Centers for Disease Control and Prevention

A family physician who became the first African-American director of the leading U.S. public health agency, the Centers for Disease Control and Prevention (CDC), Dr. Satcher is confident that we will conquer polio, measles, and guinea worm in the next 20 years, but he warns that we have to reinforce the capability to deal with new diseases and those that are becoming resistant to current treatment.

Though progress against infectious and chronic diseases is being made on many fronts, deadly bacteria and viruses — not to mention some unhealthy lifestyles — will bedevil humankind for a long time to come. Satcher was interviewed by Contributing Editor Jerry Stilkind.

Question: How serious is the problem of new and reemerging infectious diseases around the world, particularly in the developing countries?

Satcher: When the Institute of Medicine (a congressionally chartered research organization) defined emerging infectious diseases in 1992, it included new diseases that had developed in the past two decades, and old diseases that are increasing in number or becoming drug resistant.

When you define it that way, malaria stands out in Africa because of its resistance to chloroquine. We are seeing a resurgence of malaria in many places in Africa. We are seeing a lot of children coming into the hospital after their parents have attempted to treat them with chloroquine at home, and these kids often come in with cerebral malaria, which is the worst kind. So the whole issue of drug-resistant malaria represents what we consider to be part of an emerging infection.

Then there is Ebola in Africa. Ebola was first recognized in 1976. Before 1976, we had never heard of or seen Ebola. Then we had cases in the Sudan and in Zaire and sporadic outbreaks since, including the 1995 outbreak in Zaire and the recent outbreak in Gabon. It's a severe, deadly virus, killing over 80 percent of the people who are infected, according to some studies.

If you were to ask me, however, what is the major emerging infectious disease throughout the world, I would say the human immunodeficiency virus (HIV) that causes AIDS. AIDS was first defined as an epidemic in 1981. The virus was discovered in the early 1980s. We now project that, by the year 2000, there may be as many as 40 million people infected with the AIDS virus.

While the area that has been the most severely affected up to this point has been Africa, the area where the virus is most dramatically spreading is Southeast Asia and India. AIDS is, without question, the premier emerging infectious disease.

Q: Not long after you became director of the Centers for Disease Control (CDC) four years ago, you said that the United States and other countries had become complacent about infectious diseases, that we had neglected to maintain the resources to detect disease outbreaks and to respond quickly with diagnosis and treatment. Around the world, has the situation gotten better or worse since then?

Satcher: Throughout the world there was an attitude for a while that we were making such great progress against infectious diseases that we could become less vigilant. In a hearing before Congress in 1969, the U.S. Surgeon General said, "It's actually time to close the book on infectious diseases."

That attitude pervaded Europe, also, although maybe not to the same extent. But all over the world we're now seeing a major effort to regroup and to deal with the problem of emerging infectious diseases.

I attended a European conference in Madrid last year to deal with the problem of emerging infectious diseases. People are being trained. Laboratories are being rejuvenated. So I think there is a realization that infectious diseases are here to stay, that microorganisms have a way of surviving — they mutate, they adapt, they emerge. I think we've learned that lesson now, and I think all over the world there is an attempt to gear up to deal with that.

Q: How, then, is the CDC and other U.S. agencies working with other countries to fight these problems around the world?

Satcher: I would say our major partner in terms of global response to emerging infectious diseases is still the World Health Organization (WHO). The CDC has a long history of cooperation with WHO. We have 23 collaborating infectious disease centers. These centers have expertise in diseases all over the world. WHO will call upon certain centers when they run into various problems.

I chaired a task force on emerging infectious diseases, which was established under the aegis of a committee of President Clinton's National Science and Technology Council. The task force included about 20 different federal agencies, such as State, Agriculture, Commerce, the U.S. Agency for International Development, the National Institutes of Health, and the Food and Drug Administration. We prepared a report called "Infectious Diseases — A Global Health Threat," and submitted it to President Clinton. Three months ago, he approved it.

It directs this country to help develop a system of global surveillance and response to infectious diseases. That includes strengthening domestic surveillance and also playing a prevention role globally. The president recommended that CDC be given more authority and resources to carry out this mission.

Q: After the Ebola virus broke out in Zaire in 1995, didn't some CDC people go there to try to figure out what it was and what was happening?

Satcher: Yes. We sent a team of people over there. At first, the blood samples were sent to Belgium. But it was determined, because of the possibility of the virus being Ebola, that CDC probably was the only place where they could be safely handled and quickly diagnosed. They were sent to us and we made the diagnosis within, I think, one day or so that it was Ebola and that it was very similar to the Ebola of 1976.

Q: Is early detection crucial in emerging diseases?

Satcher: Early detection is critical in the control of emerging infectious diseases. I can give you an example. The E. coli 0157-H7, which recently affected Japan, comes from eating undercooked ground beef. We had an outbreak in this country in 1993 in which about 500 people were infected at a restaurant chain in the Pacific Northwest. A few children died.

We now know that outbreaks occurred in various parts of the country in the early 1980s but were not immediately recognized. Had they been, we probably could have prevented some of the outbreaks that took place later.

Q: Should we expect further nasty surprises like AIDS and Ebola in the future?

Satcher: We should expect it and we should prepare for it because of the ability of microorganisms to mutate, adapt, and change to survive, and to become resistant to antibiotics. But especially because they're always evolving. That means periodically you're going to have a new virus, a new bacterium that we haven't seen before. Or we could have a virus that's been there all along living in a monkey or some other animal, and then, for some reason, it mutates and becomes virulent to human beings.

Q: A recent report by researchers from Harvard University, the World Bank, and WHO says the kind of chronic ailments that now dominate the developed world — heart disease, strokes, for example — will become dominant in the developing countries as they progress economically. Would you agree with that assessment?

Satcher: I would agree in part. I think they were trying to emphasize the growing threat of chronic disease injuries as causes of death, and I agree with that. However, I don't believe that you can take from that that there should be any diminishing of our effort to control infectious disease.

For example, in this country there has been a 58 percent increase in deaths from infectious diseases just since 1980. So even in this country, where chronic diseases have been the leading cause of death for some years now — I mean heart disease, stroke, cancer — deaths from infectious diseases have still gone up. So, infectious diseases are here with us for some time to come.

Q: Do you agree with the report, "The Global Burden of Disease," that one reason that chronic diseases will rise sharply in developing countries is because poverty, hunger, and malnutrition, and the infectious diseases related to those conditions, will sharply decline in the future?

Satcher: I don't think we're going to see the end of poverty or the decline of it as rapidly as we would like. But it is true that many of the tobacco companies in this country are now marketing their products to developing countries, so you see more smoking in a lot of those countries and, without question, that means more heart disease and more cancer.

In addition, the study implies that there are going to be richer diets, higher in cholesterol, less physical activity as people become more sedentary, and that all of those things are going to lead to more chronic diseases. So I think there are several factors at work here.

Q: Do you see smoking, then, in places where smoking is heavy, such as China and Russia, causing a great deal more death and disability?

Satcher: More than any other thing that's happening in those countries, smoking is probably going to have the greatest impact on mortality in the future. Now there are about three million people a year who die from smoking in the world, and in 20 years we project there will be at least 10 million deaths a year.

And when I say from smoking, I'm talking about heart disease, cancer, respiratory illnesses, and even things that we didn't know were associated with smoking before, like sudden infant death syndrome and asthma.

Q: Do you also have projections on infectious diseases in the next 20 years?

Satcher: No, that's a little bit more difficult, because infectious diseases are much less predictable. After all, who could have predicted 20 years ago that HIV would be a leading cause of death around the world. There are two forces at work with infectious diseases. We are improving our vaccines. We're making a lot of progress against vaccine-preventable diseases. We think we will be able to eradicate polio around the world by the year 2000. We've already eradicated it in the Western Hemisphere. We haven't had a case of naturally occurring polio in the United States since 1979, and in the Western Hemisphere since 1991. So we are now projecting that, by the year 2000 or shortly thereafter, we should be able to eradicate polio in the world.

I was in China recently and we've had a major polio vaccine effort there the past four years. Well, the last case of naturally occurring polio in China was September 1994. And that's a massive country. Yet, using the immunization base, we've been able to get control of that, and we will hopefully do the same thing in India. Some major efforts are scheduled to take place there in the next few months.

So we're making a lot of progress with infectious diseases when it comes to vaccine-preventable diseases. On the other hand, we have these other forces that are working against us, like drug resistant microorganisms and people moving to cities. That means people are crowding into smaller and smaller areas, which gives rise to new infections. So there are counterbalancing forces, and it's very hard to predict which of these forces will get the upper hand over the next 20 years.

Q: Will developing countries need more financial help for the newer vaccines, which are usually more expensive than older ones?

Satcher: They're getting quite a bit of help from the United States right now. We funded a great amount of the polio vaccine in China, for example. The United States has spent at least $20 million a year to purchase polio vaccines for the global eradication program, plus we are providing the technical support with our laboratories and disease control experts.

But it's not all altruistic, you know. Once we've eradicated polio, we won't have to immunize against polio in this country. That will save us almost $250 million a year. It cost us $32 million over a 10-year period to eradicate smallpox. The United States saves that much every 26 days by not having to immunize against smallpox, or to have quarantines against it.

Q: What other diseases do you think will soon be eradicated?

Satcher: After polio we think that measles will be next. There is also currently the guinea worm eradication program that we think is going to be successful very soon, maybe by the year 2000. Guinea worm does not affect as many places as polio. There are only a few countries left that have major problems with guinea worm, but we think it's going to be eradicated. We think that yellow fever eradication is in the future.

Q: What are your priorities in health care? Where do you think we should do more than we are now doing?

Satcher: This is a country that spends 1,000,000 million dollars a year on its health system, most of it for tertiary care, that is, last stage care, when people are on their dying bed, in many cases.

But we only spend about 1 percent of our health budget for the prevention of illness. I think that's the wrong way to approach a health system. I think we ought to be spending more on the front end to prevent things, as opposed to spending it on the back end to try to treat things after they occur. I think this country ought to be investing more in public health and population-based prevention. Our budget has been going up for emerging infectious diseases. It has also increased in areas like breast and cervical cancer screening.

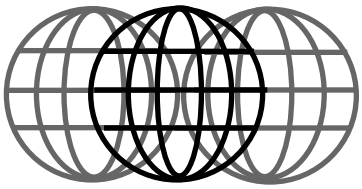
Q: What kind of prevention programs would you like to see expanded?

Satcher: I would like to see programs that deal with water cleanliness and clean air; I'd like to see programs that deal with immunizations and human behavior; and I'd like to see programs in the schools teaching kids health education. Many children develop the behaviors that are going to lead to chronic diseases while they're teenagers.

About 85 to 90 percent of new smokers today begin smoking before they're old enough to make that decision. The same thing with sexual behavior. By the time they graduate from secondary school, over 70 percent of our teenagers are sexually active, and many of them have had three and four partners. And you ask them, "Since you're sexually active, what kind of protection do you use?" And 50 percent of them don't use any, for the most part. So these are people at risk for AIDS, and we are seeing the results of that, in terms of this disease. We've made some progress, but there's so much more to do in that area.

I don't think there is a state in the union that now requires physical education from grades kindergarten through 12. I think we pay a price, because with physical activity alone we can prevent about 50 percent of the cardiovascular disease deaths in this country; 30 percent of diabetes from even developing; and a lot of the hypertension. So I think we ought to be investing in areas like that — nutrition, physical activity, smoking cessation, sex education — all those areas that are going to make such a difference in the future health of people.

Jerry Stilkind writes on global issues for the United States Information Agency



New Drugs, New Vaccines, New Diseases

An interview with Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases (NIAID).

Dr. Anthony Fauci, one of the America's leading AIDS researchers, says basic research is providing new weapons to protect man against the onslaught of infectious diseases. At the same time, advances in molecular biology are fueling the development of a new generation of vaccines to prevent and possibly eradicate a legion of deadly diseases ranging from tuberculosis to AIDS. Dr. Fauci was interviewed by Managing Editor Jim Fuller.

Question: Outbreaks of infectious diseases are on the upswing. Would you discuss some of these diseases and why they are cause for concern?

Fauci: If you just look worldwide at the infections that have caused major devastation, tuberculosis certainly is one. Although we can treat tuberculosis in the United States, it still accounts for about three million deaths annually worldwide. People tend not to think of tuberculosis as being necessarily that important. But it's the leading infectious killer of adults in the world today.

Malaria has been, for decades if not centuries, a major killer, and it still is, killing between one and two million people a year. The victims are mostly developing-country babies, particularly African babies.

Then, if you look cumulatively at all of the tropical diseases that are parasitic, helminthic-type diseases — schistosomiasis, filariasis, and so on — if you put them all together in a package you have a major burden of disease that has an enormous impact physically, socially, and economically on developing countries.

And then there are other infections that are very important killers. For example, pneumococcal pneumonia in certain African countries is still a very important source of infection. There's the constant burden of influenza each year that generally goes unnoticed, and then, every few years, you have a blip on the curve of excess deaths associated with influenza.

And last but not least, you have the human immunodeficiency virus (HIV) that causes AIDS. By the year 2000, at least 30 or 40 million people are going to be infected, if not more, and that's still a major epidemic that's out of control.

We also need to worry about the constant emergence and re-emergence of antibiotic and antimicrobial resistant organisms, which are as big a threat as pending epidemics from new microbes. The fact is that microbes that we traditionally should have under very good control, all of a sudden are emerging into rather resistant strains. And that goes for everything from tuberculosis to staphylococcus and streptococcus infections. So there are still a significant number of infections that are accounting for a really unacceptable disease burden throughout the world.

Q: How significant is the threat from the Ebola virus that broke out in Zaire last year and more recently in Gabon?

Fauci: Ebola is scary and you can't be complacent about it. But the thing about Ebola that would prevent it from being a raging epidemic is the same thing that prevented it from being a raging epidemic in Zaire — and that is that it is virtually only spread by people when they are grossly symptomatic.

So the fact that you can quarantine someone and keep them away from contact with others is a very effective way of curtailing the epidemic.

That's unlike other diseases like influenza, where I could feel fine and cough on someone — and it could be nothing more than clearing my throat — and I could give that person influenza. Or a sexually transmitted disease like HIV where a person can be infective for 10 or 15 years and could conceivably infect others during that long period of time.

With Ebola, the window for an infected person being able to transmit it is very well-defined, so it is unlikely that you're going to have a raging epidemic that would involve hundreds of thousands of people. That's not impossible, but unlikely.

Q: What role has basic research played in the battle against infectious diseases?

Fauci: There are several ways to prepare for the threat of emerging and re-emerging microbes. One of them is more appropriate for the Centers for Disease Control (CDC), and another falls much more under the National Institutes of Health (NIH). Together they complement each other very well.

For example, the whole question of monitoring disease and being able to detect the emergence of an epidemic in its earliest stages falls under the broad category of surveillance and epidemiology, which the CDC does very well. But what NIH does is to keep the basic research matrix — the foundation of molecular biology, microbiology, vaccinology — and other types of research at the highest level of sophistication so when a microbe does emerge, you'll be able to jump on it.

A classic example of that was the basic research that went into the tumor viruses back in the early 1970s, when researchers discovered the reverse transcriptase enzymes and Robert Gallo discovered HTLV-1 as a cause of human T-cell lymphoma, Type 1. That, in and of itself, provided the tools that were necessary to be able to recognize HIV as a new disease. That's because, if you didn't have the reverse transcriptase assay, you would never be able to identify this new virus that was characterized by the reverse transcriptase enzyme — the enzyme HIV uses when it first infects a cell.

If we weren't supporting basic biomedical research in microbiology and virology in the early and mid-1970s, even though we didn't know consciously that we were preparing for the AIDS epidemic then, we wouldn't be nearly as far ahead as we are right now in the development of diagnostic tests, several drugs, and on our way to a vaccine.

So as far as what we can do now in 1996 to prepare for the great epidemic that may occur in the year 2010, it's more a matter of what we're doing to make sure that our basic research base in microbiology, immunology, antimicrobials, and vaccinology is at the very highest level.

Q: How are we working with researchers in other parts of the world to deal with these health threats?

Fauci: There's a whole wide range of cooperation and collaboration. For example, we have foreign investigators who train in the United States and then go back to their own countries. NIAID also funds tropical disease units in the United States that work on problems applicable to developing countries. And we have units within the foreign countries that are collaborating with foreign investigators.

For example, we have very close collaborations in Uganda, Haiti, and Brazil. We're supporting fundamental basic research that's right at the brim of the rain forest in Brazil, right in the middle of the jungle in Uganda, and right in the inner cities of Haiti — all places where new microbes emerge. We also are doing research in Thailand and South Africa and other nations. So the research effort is very integrated with foreign countries.

Q: Are there new generations of vaccines being developed to prevent and possibly eradicate some of these diseases?

Fauci: Yes. A typical example of a new generation vaccine is the very important success story in the past two years with the development of an acellular pertussis vaccine that is much less toxic than the one we've successfully used for several decades. Pertussis - whooping cough - is an extremely contagious disease that causes about 350,000 deaths worldwide each year.

Because of the concern over toxicities in pertussis vaccine — it's more of a concern than a

reality — several countries, including Italy, Sweden, and others, have actually loosened the requirement for a pertussis vaccination. This has led to the re-emergence of new epidemics of pertussis in those countries.

In collaboration with some foreign governments and pharmaceutical companies, we played a major role in the developing and testing of the new acellular pertussis vaccine, which doesn't contain those components of the pertussis bacteria that are toxic. In vaccine trials it has proven not only to be safer, but even more effective than earlier pertussis vaccines. These results mark important progress toward the eventual goal of developing acellular combination vaccines that can protect children against numerous diseases with a minimum of vaccine shots and side effects.

There's also a new technique called DNA immunization where you take the DNA from a disease-causing microbe and inject it into a person's muscle, their fibroblast. The proteins of the microbe then express themselves and are recognized in a way that induces a much more robust and long-lasting immune response.

These vaccines would be applicable to all diseases — the same ones that we prevent right now as well as new ones. I would imagine that over the next 10 to 20 years that all of our vaccines are going to be replaced by the new generation of DNA vaccines. It's very likely.

Q: What about transgenic plants that might lead to the development of "edible" vaccines? In preliminary studies, such plants have been used to immunize mice against hepatitis B and E. coli toxin.

Fauci: We can now genetically engineer plants to express proteins that are immunizing agents for a particular disease. For example, you can put the gene of a particular microbe — hepatitis, pertussis, polio — into a plant and grow these things in unlimited quantities. If they prove safe and effective, such plants could allow us to vaccinate large populations at minimal cost. If you could make a very good vaccine for practically nothing, it would help make those vaccines available to developing countries.

It's just another example of the extraordinary power of molecular biology. We now have the capability of genetically manipulating cells, animals, and plants so you can code them to make a whole bunch of proteins that are used as vaccines.

Q: What would you say is the good news and the bad news about AIDS? Have we turned the corner on this deadly epidemic?

Fauci: It's one of those complicated issues. If you're talking about acceleration of new cases, then the Western developed countries, like the United States, Canada, and those in Western Europe, have certainly plateaued in total numbers. Even though the level of that plateau is unacceptable, it's still not as accelerated as it was just a few years ago.

But in regions like Sub-Saharan Africa and Asia, particularly India and Thailand, it is still accelerating. And particularly in Asia, it's going to accelerate even more. That's the bad news.

Also, the bad news is that we may start to be getting a little complacent, and not appreciating that the demography of the epidemic — particularly in the United States — is changing a bit. It's becoming more of a disease that involves heterosexual women, and the children of infected mothers.

Q: What about the reports of positive results when using combinations of drugs to treat AIDS? Some researchers have raised the tantalizing hope that combination therapy can eliminate HIV from patients.

Fauci: There have been extraordinary advances over the past few years, not only in our understanding of what we call the pathogenesis of HIV disease — or how the virus destroys the body's immune system — but also with the development of a series of drugs that are now used in combinations, particularly combinations that include protease inhibitors. These combination therapies are having a profound impact on the level of virus in the body, to the point where we now have much more potent control over virus replication. And that's beginning to show a significant impact on clinical outcomes.

The thing we don't know is how good the news is going to be. We know that what we have now with drug therapy is better than anything

that we've had up to now. We're not sure whether this is going to translate into something that truly will bring the disease under control, being able to treat it like a chronic manageable disease, or whether we're going to run into one of the perennial problems with microbes — the cumulative toxicities of the drugs or the emergence of microbial resistance.

Q: Is there good news to report with regard to the situation with AIDS in developing countries?

Fauci: Certainly. The developing countries are already showing that education and behavioral modification are having an impact. There are a couple of classic examples of that. One of them is in Thailand. At one time, the rate of infection among military recruits, particularly in northern Thailand, was a disaster with 15 to 18 percent of them infected. The government, together with the non-governmental organizations and the military, began a crash education campaign regarding prostitutes and the use of condoms. In the past couple of years they have brought that infection rate down from high double digits to just a few percent in new military recruits.

We're also starting to see that behavioral modification in some segments of the Sub-Saharan African population is having an effect. So clearly, education and prevention are important.

However, when you look at the global picture, particularly developing countries, you need a vaccine to put the disease under the kinds of control that we now have with smallpox and polio.

Q: Are we anywhere close to developing an AIDS vaccine?

Fauci: We certainly are making good scientific progress in developing a vaccine, but I would be reluctant to say we're close.

We are making step-by-step progress in getting better vaccine candidates. Over the past few years, the accumulation of data on second-generation vaccines are indicating a broader spectrum of responses, suggesting that they will ultimately be more effective than the earlier ones.

Q: Can we expect diseases like AIDS to occur more frequently in the future?

Fauci: I wouldn't say necessarily more frequently. The emergence of the AIDS epidemic is not out of line with what has been happening for the entire history of mankind. You look back at the extraordinary flu epidemic of 1918 that was even more devastating than HIV, and before that, smallpox, and before that the plague and tuberculosis and cholera.

We're going to have the emergence of new diseases. Even if it isn't any worse, you're still going to see another AIDS epidemic with a different microbe, and maybe a totally different type of disease. I'm positive that's going to emerge at sometime.

Dr. Richard Crause, a former director of the NIAID, in his book, "The Restless Tide," describes how man lives in a microbial sea of bacteria, viruses, and parasites. Some of these microbes cause diseases that are in constant evolution and de-evolution, moving back and forth over decades and centuries. So in the history of mankind, there is a constant battle between the human species and microbes.

Jim Fuller writes on science, technology and other global issues for the United States Information Agency

Attacking the Root Causes of Disease

By J. Brian Atwood
Administrator, U.S. Agency for International Development

The U.S. Agency for International Development marshals a wide variety of tools and resources to strengthen public health systems around the world and to combat the global spread of infectious diseases.

Like characters in a spy novel, infectious disease agents often travel across national borders incognito, secretly endangering everyone who comes in contact with them and threatening the stability of nations. Public attention focuses on frightening new pathogens like Ebola and "mad cow disease," but old infectious diseases once controlled by antibiotics or insect-spraying programs are also making news. At a time when people and cargoes that can harbor disease cross oceans and continents in a matter of hours, the emergence of deadly new diseases and reemergence of old killers are a global concern.

The U.S. Agency for International Development has long fought infectious disease in the developing world, providing assistance in health research and health care delivery in over 40 developing countries. USAID is the lead U.S. agency in support of international health and has a key role in responding to emerging diseases. USAID's budgetary portion of the U.S. government's emerging disease-fighting effort was $295 million in fiscal year 1996.

In June 1996, a presidential directive on emerging infectious diseases recognized USAID's leading role in long-term efforts to address root causes of emerging and reemerging diseases in developing countries. The document calls for strengthened surveillance, response, and research activities within the United States and in cooperation with other countries to attack these diseases.

HOW DO INFECTIOUS DISEASES SPREAD?

Epidemics are not always caused by new organisms. Known diseases can spread to new places or to people who are not immune. Changing ecological and climatic conditions or land uses can increase human exposure to "vectors" — insects, rodents, or other animals that carry the diseases. As more and more people in developing countries move from rural areas into crowded urban areas with inadequate housing, sanitation, or health systems, conditions are ripe for the development and spread of emerging diseases.

Malaria, tuberculosis, gonorrhea, and pneumonia are reemerging as major health problems because disease organisms develop resistance to drugs and because insect vectors become resistant to pesticides. Health systems must be able to recognize "unusual events" that may signal the presence of new or reemerging diseases, and be capable of quick, appropriate responses.

USAID PREVENTIVE PROGRAMS

In developing countries, infectious diseases are the major risk of serious disability (morbidity). Chronic, disabling diseases deter self-sufficiency and economic progress. New and reemerging diseases with the greatest economic impact in developing countries are HIV AIDS, malaria, and tuberculosis.

Rather than create programs to combat specific diseases, a constantly moving target, USAID increases the ability of health systems to recognize, prevent, and treat infectious diseases through improved training, budget management, pharmaceuticals, logistics, and communications. Assistance is also directed to developing epidemiological skills and disease control, and

to fostering of immunization, health education, and risk-behavior modification.

Effective in-country epidemiological surveillance systems are crucial, yet very difficult to create and sustain. Special surveillance systems for rare diseases may not be practical over the long term. USAID helps developing countries establish systems that can detect unusual events and provide information to guide appropriate action against infectious disease outbreaks.

Health systems are only one weapon in the fight against emerging infectious diseases. There is growing evidence that complex issues of human behavior, economic development, and the environment contribute to the emergence and spread of diseases. USAID programs in these areas address such problems as population pressure; poor use of land, water and plant life; and poor nutrition.

HIV AIDS

Since 1986, USAID has been a global leader in fighting the HIV AIDS epidemic by focusing on reducing the spread of the virus and lessening its social and economic impact. This strategy prevents the emergence and reemergence of other diseases, like tuberculosis. USAID spends about $120 million a year on HIV AIDS prevention and mitigation programs designed to build local capacity to combat the disease and its consequences.

In many developing countries, women are as likely as men to contract HIV AIDS. Therefore including local women in the design and implementation of efforts to reduce the disease is essential. Other key programs include increasing the availability of condoms, promoting changes in behavior, and improving services to control other diseases that increase the chance of contracting HIV AIDS.

ANTIBIOTIC RESISTANCE

Over time, all bacteria will develop some degree of resistance to antibiotics. This makes it certain that severe problems will occur in the future from drug-resistant bacteria.

USAID is especially concerned about antibiotic-resistant diseases that threaten children in developing countries and that pose increasing risks to developed countries. USAID gives high priority to childhood diseases caused by pneumococcal bacteria (pneumonia), as well as pneumonia and meningitis caused by hemophilus bacteria, and dysentery caused by shigella bacteria.

RESEARCH

USAID research on infectious diseases in developing countries focuses on three areas:

❒ reducing common childhood illnesses such as diarrhea, malaria, pneumonia, and vaccine-preventable diseases through better means of prevention, supportive care, and the rational use of antimicrobial drugs;

❒ reducing high reproductive morbidity and mortality through the appropriate treatment and prevention of sexually transmitted diseases; and

❒ reducing the transmission of HIV AIDS.

COORDINATION WITH PARTNERS

USAID collaborates with other U.S. partners through formal agreements and coordinating arrangements. Multilateral activities include substantial financial and technical contributions to the programs of the World Health Organization (WHO) to control HIV AIDS, tuberculosis, and antibiotic resistance. USAID also fosters international support for regional infectious disease surveillance activities based at the International Center for Diarrheal Disease Research in Dhaka, Bangladesh.

The agency also devotes resources to international emergency issues. Our Office of Foreign Disaster Assistance responds to natural and man-made disasters, and we have made substantial commitments to controlling epidemics such as cholera and diphtheria, and to the operations of U.S. and international agencies dealing with outbreaks of new viral infections such as the Ebola virus.

USAID field operations in developing countries will continue to develop local capacity for monitoring and controlling infectious diseases. Our primary contribution will be to continue to attack the root causes and conditions that foster infectious diseases.

COMMENTARY

A Paradise for Pathogens—Almost Everywhere

By Judith Randal

As a new millennium approaches, diseases like smallpox and polio seem to be on their way out, but a crowded world and less effective antibiotics are allowing an array of other deadly diseases to take their place.

As recently as the 1950s, eight million people a year died of smallpox that permanently scarred millions more. No longer. Thanks to an immunization campaign the World Health Organization launched in 1967 that reached into the remotest corners of the globe, there hasn't been a new case of smallpox anywhere since 1978. Indeed, so successful was the campaign that even the need for immunization has disappeared. That, by itself, has saved thousands of millions of dollars' worth of health care costs.

Still, smallpox is the only infectious illness ever to have become extinct. As a new millennium approaches, heart disease, cancer, and stroke are the major killers of the elderly, but viruses, bacteria, and parasites are relentlessly claiming more than 16 million lives a year worldwide, and in many countries — particularly poor ones — they are the leading cause of death in children and young adults.

There has been, to be sure, some recent progress — notably the virtual eradication of polio in the Western Hemisphere because of an aggressive immunization program largely privately funded by Rotary International. However, the situation as a whole has not changed for the better and the potential for the spread of deadly organisms is, by most experts' reckoning, getting worse.

One of the more alarming indicators of the problem is the waning effectiveness of antibiotics, which first became evident 30 years ago in New Guinea, but has gone global since.

"Antibiotics never did work against viruses, but we used to be able to count on them for most other kinds of infections," says Dr. Gail Cassell, professor of microbiology at the University of Alabama in Birmingham. "Now — whether it is tuberculosis, bacterial pneumonia, strep or staph infections, or any of many others — the chances that they will respond to antibiotics grow slimmer almost by the day."

Every antibiotic, sooner or later, becomes the victim of its own success.

The reason these drugs lose their clout is that fewer and fewer germs are susceptible to them the more they are used. As Cassell puts it, "every antibiotic, sooner or later, becomes the victim of its own success." To make matters worse, she says, "microbes owe their resistance to antibiotics to packets of genetic material that different strains — and even different species — of germs can swap among themselves. This has made it that much harder to develop new antibiotics fast enough to stay ahead of the curve."

Among the many other reasons for the growing threat of infectious illness is that the world has become increasingly crowded. The more people there are the more targets pathogens can aim at. The earth's population — 2,500 million only 50 years ago — is 6,000 million now and still rising. The impacts on the environment

alone, it turns out, can have devastating public health effects. For example, deforestation to make way for new settlements and to accommodate agriculture, logging, and other pursuits has ex- panded opportunities for people to be exposed both to exotic organisms — such as the deadly Ebola and Lassa fever viruses, first identified, respectively, in Zaire and Nigeria — and to more familiar ones. The increase of malaria in Brazil, which is largely due to mining the Amazon jungle for gold, is a typical case in point. Malaria, in fact, is a particular concern because Plasmodium falciparum, the severest form of the illness, has become increas-ingly resistant to available drugs. There is no vaccine for it.

Population growth has, besides, fueled the growth of cities. Dr. Donald Henderson, who led the campaign to eradicate smallpox and now teaches at the Johns Hopkins University School of Public Health in Baltimore, is fond of reminding his students that the only two cities that had as many as 7.5 million people in 1950 were New York and London. "Now, there are 30," he says, "and seven of those are well on the way to becoming twice that size or more."

Pathogens find refugee facilities, slums, and homeless shelters almost as much to their liking as hospitals.

Especially troubling to Henderson is that most of the new megacities are in countries whose governments cannot afford to tackle the lack of sanitation, overcrowding, dearth of clean water, and other infection-friendly conditions that beset the burgeoning numbers of their urban poor. On top of that, he notes, modern civil wars in Asia, Africa, and the former Yugoslavia have compounded the problem by creating tens of millions of displaced persons and refugees who often spend months and even years in squalid camps that — like the shanty settlements of many super cities — are a paradise for pathogens.

As a single example, there have been serious outbreaks of cholera among the 500,000 or so Rwandans who fled to neighboring Zaire to escape ethnic conflict at home. And with the spread of that conflict into Zaire itself, the number of refugees has swelled to more than a million and the risk of pestilence has grown apace. Though there is a cholera vaccine, it is not very effective. Besides, most vaccines, including this one, require refrigerated storage, which is scarce in central Africa.

Says Henderson: "Our experience with smallpox and with the Ebola and Lassa fever viruses taught us that, in the less developed world at least, disease organisms are most readily spread by the exposures staff and visitors get to them in hospitals and then take with them into the community. Indeed, it's reasonable to suppose that was how AIDS originally took hold. But it is equally apparent that pathogens find refugee facilities, slums, and places in the industrialized world like homeless shelters almost as much to their liking as hospitals."

Still, at a time when any part of the world can be reached from any other in no more than 36 hours, it would be naive to blame the growing threat of infectious illness only on environmental degradation, hospitals, and the conditions that confront slum dwellers, refugees, and homeless persons. The consequent enormous increase in international travel and the expansion of international commerce also bear a share of the responsibility.

In 1986, for instance, tiger mosquitoes — a species that can carry the virus for dengue fever as well as several viruses that cause encephalitis — turned up in tires that had been shipped to the United States from Southeast Asia. More recently, cases of malaria among airport personnel in London and New York were traced to mosquitoes that had hitchhiked from the tropics on commercial jets.

Not always, however, is the problem the importation of pathogens into places that are not their natural habitat. Instead, the culprit is sometimes the introduction of technology that allows them to flourish in that habitat as never before. For example, the enormous increase in Egypt of schistosomiasis followed the completion of the huge Aswan hydroelectric dam on the upper Nile river in 1968. Schistosomiasis is a parasitic disease transmitted to people by contact with freshwater snails. The Aswan dam, by creating Lake Nasser and slowing the river's flow rates, caused the snail population to explode downstream. The problem has yet

to be solved either in Egypt or elsewhere — in Sudan and Ghana, for example — where large power dams have also been built.

Moreover, what such dams have done for schistosomiasis, they seem to have also done for a mosquito-borne viral illness. Rift Valley fever was once almost exclusively a livestock scourge. Since the completion of the Aswan dam, Egypt has, for the first time, had human epidemics of the disease as well. Other countries with enormous dams and a similar experience include Senegal, Mauritania, and Madagascar.

While all this may suggest that only changes in technology that alter the landscape can have such repercussions — and then only in countries where there is little modern infrastructure — there is ample evidence to the contrary.

England has learned to its sorrow, for example, that cattle fed a protein derived from sheep — rather than their natural, entirely plant-based diet — can put people who eat beef produced in this way at risk of getting an invariably fatal neurologic illness called Creutzfeldt-Jacob disease. The consequent economic loss has been staggering. Hundreds of thousands of British cattle raised on the protein have had to be destroyed because they developed a similar illness — bovine spongiform encephalitis, popularly known as "mad cow disease" — and millions more fed the protein have been slaughtered because of near iron-clad proof that an infectious agent to which sheep are susceptible is fundamentally to blame.

Nor are changes in farming practices the only ones that can pose foodborne threats. So, it has turned out, can changes in distribution and marketing patterns, as was illustrated by a 1993 outbreak of Escherichia coli 0157:H7 infection that was first identified in the U.S. Pacific Northwest, but ultimately was found to have involved 21 states. Since all the people these bacteria afflicted — some of them fatally — had eaten hamburgers at outlets of fast food restaurant chains, that part of the outbreak was no mystery. What public health investigators also needed to know, however, was exactly where the contaminated meat had come from. They were to discover that they could not get a definitive answer because the meat used for the hamburgers had come not only from a half dozen or so states, but at least two and possibly more countries in addition to the United States.

It would, the public health community agrees, be bad enough if beef were the only commodity that was worrisome on this score. But the dimensions of the problem are far greater because more and more of the world's groceries — from meat, poultry, fish, and other seafood to fruits, vegetables, dairy products, baked goods, and even bottled water — are being bought, sold, processed, and distributed at great distances from where they or some of their ingredients originated.

Cases of malaria in London and New York were traced to mosquitoes that had hitchhiked from the tropics on commercial jets.

Given the globalization of the marketplace and the myriad opportunities it has created for many kinds of infectious contamination at every step of the way, not even the richest country has the means or other resources to keep abreast of them all.

Then, too, there are other concerns. Among them is the impact of changes in the weather. No one had any idea, for example, why, in 1993, there should have been an outbreak of hantavirus in the southwestern United States. In so far as was known, this airborne virus — which attacks the lungs and can be lethal — had never been there before.

By putting several pieces of circumstantial evidence together, the problem was traced to a very heavy snow melt, followed by a lot of rain — both after several years of severe drought. More specifically, deer mice turned out to be a natural reservoir for hantavirus and the indigenous deer mouse population had exploded because the abundance of water in their environment had produced a bumper crop of pine nuts, their favorite food. Forced by their greater numbers to expand their territory, these rodents — which are not made ill by hantavirus — exposed humans to it when they released it in their urine and feces and the releases found their way into the dust particles that the victims inhaled.

On the other hand, the story of morbilli virus is indicative of how perplexing, though fascinating,

the study of infectious pathogens can be. Morbilli virus — likely a family of viruses — seems to have evolved from the same virus that causes distemper in dogs. Since human settlements, with their dogs, have closed in on the borders of Tanzania's Serengeti National Park, that may explain the deaths of a third of the park's lions from this infection. Less obvious, however, are the deaths from morbilli of wild seals and porpoises in several parts of the world and the equine morbilli in Australia that has not only killed the horses infected, but two of their trainers besides.

Not so long ago medicine was so confident of the weapons in its infection-fighting arsenal — the drugs and vaccines — that its mandarins proclaimed that it was time for the research community to focus all its energies on the degenerative diseases of aging and other non-communicable disorders. The advent of AIDS in the early 1980s and its global spread since have shaken that complacency. Rather, the take home lesson is one that is preached by Dr. Stephen Morse, the virologist who coined the term "emerging infections" and — after a long career at Rockefeller University in New York City — has recently moved to the federal government's Defense Advanced Research Projects Agency in suburban Washington.

Morse's view is this: that we ignore at our peril the ability of viruses, bacteria, and parasites to exploit changing circumstances on their own behalf. These days, he has plenty of company in that belief.

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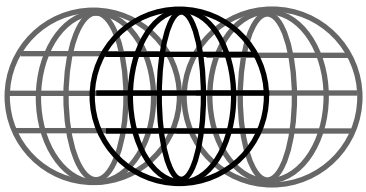

The Return of Infectious Disease

By Laurie Garrett

The Darwinian law of natural selection is alive and well in the world of bacteria and viruses, which means big headaches for scientists trying to control the spread of infectious diseases.

THE POST-ANTIBIOTIC ERA

Since World War II, public health strategy has focused on the eradication of microbes. Using powerful medical weaponry developed during the postwar period — antibiotics, antimalarials, and vaccines — political and scientific leaders in the United States and around the world pursued a military-style campaign to obliterate viral, bacterial, and parasitic enemies. The goal was nothing less than pushing humanity through what was termed the "health transition," leaving the age of infectious disease permanently behind. By the turn of the century, it was thought, most of the world's population would live long lives ended only by the "chronics" — cancer, heart disease, and Alzheimer's.

The optimism culminated in 1978 when the member states of the United Nations signed the "Health for All, 2000" accord. The agreement set ambitious goals for the eradication of disease, predicting that even the poorest nations would undergo a health transition before the millennium, with life expectancies rising markedly. It was certainly reasonable in 1978 to take a rosy view of Homo Sapiens' ancient struggle with the microbes; antibiotics, pesticides, chloroquine and other powerful antimicrobials, vaccines, and striking improvements in water treatment and food preparation technologies had provided what seemed an imposing armamentarium. The year before, the World Health Organization (WHO) had announced that the last known case of smallpox had been tracked down in Ethiopia and cured.

The grandiose optimism rested on two false assumptions: that microbes were biologically stationary targets and that diseases could be geographically sequestered. Each contributed to the smug sense of immunity from infectious diseases that characterized health professionals in North America and Europe. Anything but stationary, microbes and the insects, rodents, and other animals that transmit them are in a constant state of biological flux and evolution. Darwin noted that certain genetic mutations allow plants and animals to better adapt to environmental conditions and so produce more offspring; this process of natural selection, he argued, was the mechanism of evolution. Less than a decade after the U.S. military first supplied penicillin to its field physicians in the Pacific theater, geneticist Joshua Lederberg demonstrated that natural selection was operating in the bacterial world. Strains of staphylococcus and streptococcus that happened to carry genes for resistance to the drugs arose and flourished where drug-susceptible strains had been driven out. Use of antibiotics was selecting for ever-more-resistant bugs.

More recently scientists have witnessed an alarming mechanism of microbial adaptation and change — one less dependent on random inherited genetic advantage. The genetic blueprints of some microbes contain DNA and RNA codes that command mutation under stress, offer escapes from antibiotics and other drugs, marshal collective behaviors conducive to group survival, and allow the microbes and their progeny to scour their environments for potentially useful genetic material. Such material is present in stable rings or pieces of DNA and RNA, known as plasmids and transposons, that move freely among microorganisms, even jumping between species of bacteria, fungi, and parasites. Some plasmids carry the genes for resistance to five or more different families of antibiotics, or dozens

of individual drugs. Others confer greater powers of infectivity, virulence, resistance to disinfectants or chlorine, even such subtly important characteristics as the ability to tolerate higher temperatures or more acidic conditions. Microbes have appeared that can grow on a bar of soap, swim unabashed in bleach, and ignore doses of penicillin logarithmically larger than those effective in 1950.

In the microbial soup, then, is a vast, constantly changing lending library of genetic material that offers humanity's minute predators myriad ways to outmaneuver the drug arsenal. And the arsenal, large as it might seem, is limited. In 1994 the Food and Drug Administration licensed only three new antimicrobial drugs, two of them for the treatment of AIDS and none an antibacterial. Research and development has ground to a near halt now that the easy approaches to killing viruses, bacteria, fungi, and parasites — those that mimic the ways competing microbes kill one another in their endless tiny battles throughout the human gastrointestinal tract — have been exploited. Researchers have run out of ideas for countering many microbial scourges, and the lack of profitability has stifled the development of drugs to combat organisms that are currently found predominantly in poor countries. "The pipeline is dry. We really have a global crisis," James Hughes, director of the National Center for Infectious Diseases at the Centers for Disease Control and Prevention (CDC) in Atlanta, said recently.

DISEASE WITHOUT BORDERS

During the 1960s, 1970s, and 1980s, the World Bank and the International Monetary Fund devised investment policies based on the assumption that economic modernization should come first and improved health would naturally follow. Today the World Bank recognizes that a nation in which more than 10 percent of the working-age population is chronically ill cannot be expected to reach higher levels of development without investment in health infrastructure. Furthermore, the bank acknowledges that few societies spend health care dollars effectively for the poor, among whom the potential for the outbreak of infectious disease is greatest. Most of the achievements in infectious disease control have resulted from grand international efforts such as the expanded program for childhood immunization mounted by the U.N. Children's Emergency Fund and WHO's smallpox eradication drive. At the local level, particularly in politically unstable poor countries, few genuine successes can be cited.

Geographic sequestration was crucial in all postwar health planning, but diseases can no longer be expected to remain in their country or region of origin. Even before commercial air travel, swine flu in 1918-19 managed to circumnavigate the planet five times in 18 months, killing 22 million people, 500,000 in the United States. How many more victims could a similarly lethal strain of influenza claim in 1996, when some 500 million passengers will board airline flights?

Every day one million people cross an international border. One million a week travel between the industrial and developing worlds. And as people move, unwanted microbial hitchhikers tag along. In the 19th century most diseases and infections that travelers carried manifested themselves during the long sea voyages that were the primary means of covering great distances. Recognizing the symptoms, the authorities at ports of entry could quarantine contagious individuals or take other action. In the age of jet travel, however, a person incubating a disease such as Ebola can board a plane, travel 12,000 miles, pass unnoticed through customs and immigration, take a domestic carrier to a remote destination, and still not develop symptoms for several days, infecting many other people before his condition is noticeable.

Surveillance at airports has proved grossly inadequate and is often biologically irrational, given that incubation periods for many incurable contagious diseases may exceed 21 days. And when a recent traveler's symptoms become apparent, days or weeks after his journey, the task of identifying fellow passengers, locating them, and bringing them to the authorities for medical examination is costly and sometimes impossible.

The British and U.S. governments both spent millions of dollars in 1976 trying to track down 522 people exposed during a flight from Sierra Leone to Washington, D.C., to a Peace Corps volunteer infected with the Lassa virus,

an organism that produces gruesome hemorrhagic disease in its victims. The U.S. government eventually tracked down 505 passengers, scattered over 21 states; British Airways and the British government located 95, some of whom were also on the U.S. list. None tested positive for the virus.

In the fall of 1994 the New York City Department of Health and the U.S. Immigration and Naturalization Service took steps to prevent plague-infected passengers from India from disembarking at New York's John F. Kennedy International Airport. All airport and federal personnel who had direct contact with passengers were trained to recognize symptoms of Yersinia pestis infection. Potential plague carriers were, if possible, to be identified while still on the tarmac, so fellow passengers could be examined. Of 10 putative carriers identified in New York, only two were discovered at the airport; the majority had long since entered the community. Fortunately, none of the 10 proved to have plague. Health authorities came away with the lesson that airport-based screening is expensive and does not work.

Humanity is on the move worldwide, fleeing impoverishment, religious and ethnic intolerance, and high-intensity localized warfare that targets civilians. People are abandoning their homes for new destinations on an unprecedented scale, both in terms of absolute numbers and as a percentage of population. In 1994 at least 110 million people immigrated, another 30 million moved from rural to urban areas within their own country, and 23 million more were displaced by war or social unrest, according to the U.N. High Commissioner for Refugees and the Worldwatch Institute. This human mobility affords microbes greatly increased opportunities for movement.

THE CITY AS VECTOR

Population expansion raises the statistical probability that pathogens will be transmitted, whether from person to person or vector — insect, rodent, or other — to person. Human density is rising rapidly worldwide. Seven countries now have overall population densities exceeding 2,000 people per square mile, and 43 have densities greater than 500 people per square mile. (The U.S. average, by contrast, is 74.)

High density need not doom a nation to epidemics and unusual outbreaks of disease if sewage and water systems, housing, and public health provisions are adequate. The Netherlands, for example, with 1,180 people per square mile, ranks among the top 20 countries for good health and life expectancy. But the areas in which density is increasing most are not those capable of providing such infrastructural support. They are, rather, the poorest on earth. Even countries with low overall density may have cities that have become focuses for extraordinary overpopulation, from the point of view of public health. Some of these urban agglomerations have only one toilet for every 750 or more people.

Most people on the move around the world come to burgeoning metropolises like India's Surat (where pneumonic plague struck in 1994) and Zaire's Kikwit (site of the 1995 Ebola epidemic) that offer few fundamental amenities. These new centers of urbanization typically lack sewage systems, paved roads, housing, safe drinking water, medical facilities, and schools adequate to serve even the most affluent residents. They are squalid sites of destitution where hundreds of thousands live much as they would in poor villages, yet so jammed together as to ensure astronomical transmission rates for airborne, waterborne, sexually transmitted, and contact-transmission microbes.

But such centers are often only staging areas for the waves of impoverished people that are drawn there. The next stop is a megacity with a population of ten million or more. In the 19th century only two cities on earth — London and New York — even approached that size. Five years from now there will be 24 megacities, most in poor developing countries — Sao Paulo, Calcutta, Bombay, Istanbul, Bangkok, Tehran, Jakarta, Cairo, Mexico City, Karachi, and the like. There the woes of cities like Surat are magnified many times over. Yet even the developing world's megacities are way stations for those who most aggressively seek a better life. All paths ultimately lead these people — and the microbes they may carry — to the United States, Canada, and Western Europe.

Urbanization and global migration propel radical changes in human behavior as well as in the ecological relationship between microbes and

humans. Almost invariably in large cities, sex industries arise and multiple-partner sex becomes more common, prompting rapid increases in sexually transmitted diseases. Black market access to antimicrobials is greater in urban centers, leading to overuse or outright misuse of the precious drugs and the emergence of resistant bacteria and parasites. Intravenous drug abusers' practice of sharing syringes is a ready vehicle for the transmission of microbes. Underfunded urban health facilities often become unhygienic centers for the dissemination of disease rather than its control.

THE EMBLEMATIC NEW DISEASE

All these factors played out dramatically during the 1980s, allowing an obscure organism to amplify and spread to the point that WHO estimates it has infected a cumulative total of 30 million people and become endemic to every country in the world. Genetic studies of the human immunodeficiency virus (HIV) that causes AIDS indicate that it is probably more than a century old, yet HIV infected perhaps less than .001 percent of the world population until the mid-1970s. Then the virus surged because of sweeping social changes: African urbanization; American and European intravenous drug use and homosexual bathhouse activity; the Uganda-Tanzania war of 1977-79, in which rape was used as a tool of ethnic cleansing; and the growth of the American blood products industry and the international marketing of its contaminated goods. Government denial and societal prejudice everywhere in the world led to inappropriate public health interventions or plain inaction, further abetting HIV transmission and slowing research for treatment or a cure.

The estimated direct (medical) and indirect (loss of productive labor force and family-impact) costs of the disease are expected to top $500,000 million by the year 2000, according to the Global AIDS Policy Coalition at Harvard University. The U.S. Agency for International Development predicts that by then some 11 percent of children under 15 in sub-Saharan Africa will be AIDS orphans, and that infant mortality will soar fivefold in some African and Asian nations, due to the loss of parental care among children orphaned by AIDS and its most common opportunistic infection, tuberculosis. Life expectancy in the African and Asian nations hit hardest by AIDS will plummet to an astonishing low of 25 years by 2010, the agency forecasts.

Medical experts now recognize that any microbe, including ones previously unknown to science, can take similar advantage of conditions in human society, going from isolated cases camouflaged by generally high levels of disease to become a global threat. Furthermore, old organisms, aided by mankind's misuse of disinfectants and drugs, can take on new, more lethal forms.

A White House-appointed interagency working group on emerging and reemerging infectious diseases estimates that at least 29 previously unknown diseases have appeared since 1973 and 20 well-known ones have reemerged, often in new drug-resistant or deadlier forms. According to the group, total direct and indirect costs of infectious disease in the United States in 1993 were more than $120,000 million; combined federal, state, and municipal government expenditures that year for infectious disease control were only $74.2 million (neither figure includes AIDS, other sexually transmitted diseases, or tuberculosis).

THE REAL THREAT OF BIOWARFARE

The world was lucky in the September 1994 pneumonic plague epidemic in Surat. Independent studies in the United States, France, and Russia revealed that the bacterial strain that caused the outbreak was unusually weak, and although the precise figures for plague cases and deaths remain a matter of debate, the numbers certainly fall below 200. Yet the epidemic vividly illustrated three crucial national security issues in disease emergence: human mobility, transparency, and tensions between states up to and including the threat of biological warfare.

When word got out that an airborne disease was loose in the city, some 500,000 residents of Surat boarded trains and within 48 hours dispersed to every corner of the subcontinent. Had the microbe that caused the plague been a virus or drug-resistant bacterium, the world would have witnessed an immediate Asian pandemic. As it was, the epidemic sparked a global panic that cost the Indian economy a minimum of $2,000

million in lost sales and losses on the Bombay stock market, predominantly the result of international boycotts of Indian goods and travelers.

As the number of countries banning trade with India mounted that fall, the Hindi-language press insisted that there was no plague, accusing Pakistan of a smear campaign aimed at bringing India's economy to its knees. After international scientific investigations concluded that Yersinia pestis had indeed been the culprit in this bona fide epidemic, attention turned to the bacteria's origin. By last June several Indian scientists claimed to have evidence that the bacteria in Surat had been genetically engineered for biowarfare purposes. Though no credible evidence exists to support it, and Indian government authorities vigorously deny such claims, the charge is almost impossible to disprove, particularly in a region rife with military and political tensions of long standing.

Even when allegations of biological warfare are not flying, it is often exceedingly difficult to obtain accurate information about outbreaks of disease, patricularly from countries dependent on foreign investment or tourism or both. Transparency is a common problem, though there is usually no suggestion of covert action or malevolent intent, many countries are reluctant to disclose complete information about contagious illness. For example, nearly every country initially denied or covered up the presence of the HIV virus within its borders. Even now, at least 10 nations known to be in the midst of HIV epidemics refuse to cooperate with WHO, deliberately obfuscating incidence reports or declining to provide any statistics....

The specter of biological warfare having raised its head, Brad Roberts of the Center for Strategic and International Studies is particularly concerned that the New Tier nations — developing states such as China, Iran, and Iraq that possess technological know-how but lack an organized civil society that might put some restraints on its use — might be tempted to employ bioweapons. The Federation of American Scientists has sought, so far in vain, a scientific solution to the acute weaknesses of verification and enforcement provisions in the 1972 Biological Weapons Convention, which most of the world's nations have signed.

That treaty's flaws, and the very real possibility of bioweapons use, stand in sharp focus today. Iraq's threat in 1990-91 to use biological weapons in the Persian Gulf conflict found allied forces in the region virtually powerless to respond — the weapons existence was not verified in a timely manner, the only available countermeasure was a vaccine against one type of organism, and protective gear and equipment failed to stand up to windblown sand. Last June the U.N. Security Council concluded that Iraqi stocks of bioweaponry might have been replenished after the Gulf War settlement.

More alarming were the actions of the Aum Shinrikyo cult in Japan in early 1995. In addition to releasing toxic sarin gas in the Tokyo subway on March 18, cult members were preparing vast quantities of Clostridium difficile bacterial spores for terrorist use. Though rarely fatal, clostridium infections often worsen as a result of improper antibiotic use, and long bouts of bloody diarrhea can lead to dangerous colon inflammations. Clostridium was a good choice for biological terrorism: the spores can survive for months and may be spread with any aerosol device, and even slight exposure can make vulnerable people (particularly children and the elderly) sick enough to cost a crowded society like Japan hundreds of millions of dollars for hospitalizations and lost productivity.

The U.S. Office of Technology Assessment has calculated what it would take to produce a spectacular terrorist bioweapon: 100 kilograms of a lethal sporulating organism such as anthrax spread over Washington, D.C., by a crop duster could cause well over two million deaths. Enough anthrax spores to kill five or six million people could be loaded into a taxi and pumped out its tailpipe as it meandered through Manhattan. Vulnerability to terrorist attacks, as well as to the natural emergence of disease, increase with population density.

A WORLD AT RISK

A 1995 WHO survey of global capacity to identify and respond to threats from emerging disease reached troubling conclusions. Only six laboratories in the world, the study found, met security and safety standards that would make them suitable sites for research on the world's

deadliest microbes, including those that cause Ebola, Marburg, and Lassa fever. Local political instability threaten to compromise the security of the two labs in Russia, and budget cuts threaten to do the same to the two in the United States (the army's facility at Fort Detrick and the CDC in Atlanta) and the one in Britain. In another survey, WHO sent samples of hantaviruses (such as Sin Nombre, which caused the 1993 outbreak in New Mexico) and organisms that cause dengue, yellow fever, malaria, and other diseases to the world's 35 leading disease-monitoring facilities. Only one — the CDC — correctly identified all the organisms; most got fewer than half right.

Convinced that newly emerging diseases, whether natural or engineered, could endanger national security, the CDC requested $125 million from Congress in 1994 to bolster what it termed a grossly inadequate system of surveillance and response; it received $7.3 million. After two years of inquiry by a panel of experts, the Institute of Medicine, a division of the National Academy of Sciences, declared the situation a crisis.

Today's reality is best reflected in New York City's battle with tuberculosis. Control of the W-strain of the disease — which first appeared in the city in 1991-92, is resistant to every available drug, and kills half its victims — has already cost more than $1,000 million. Despite such spending, there were 3,000 TB cases in the city in 1994, some of which were the W-strain. According to the Surgeon General's annual reports from the 1970s and 1980s, tuberculosis was supposed to be eradicated from the United States by 2000. During the Bush administration the CDC told state authorities they could safely lower their fiscal commitments to TB control because victory was imminent. Now public health officials are fighting to get levels down to where they were in 1985 — a far cry from elimination. New York's crisis is a result of both immigration pressure (some cases originated overseas) and the collapse of the local public health infrastructure.

National preparedness has further eroded over the past five years in the face of budgetary constraints. Just as WHO cannot intercede in an epidemic unless it receives an invitation from the afflicted country, the CDC may not enter a U.S. state without a request from the state government. The U.S. system rests on an increasingly shaky network of disease surveillance and response by states and territories. A 1992 survey for the CDC showed that 12 states had no one on staff to monitor microbial contamination of local food and water; 67 percent of the states and territories had less than one employee monitoring the food and water of every one million residents. And only a handful of stateswere monitoring hospitals for the appearance of unusual or drug-resistant microbes.

State capacity rests on county and municipal public health, and there too weaknesses are acute. In October, dengue hemorrhagic fever, which had been creeping steadily northward from Brazil over the past eight years, with devastating results, struck in Texas. Most Texas counties had slashed their mosquito control budgets and were ill prepared to combat the aggressive Tiger mosquitoes from Southeast Asia that carry the virus. In Los Angeles County that month, a $2,000 million budget shortfall drove officials to close all but 10 of the 45 public health clinics and to attempt to sell four of the county's six public hospitals. Congress is contemplating enormous cuts in Medicare and Medicaid spending, which the American Public Health Association predicts would result in a widespread increase in infectious disease.

PRESCRIPTION FOR NATIONAL HEALTH

Bolstering research capacity, enhancing disease surveillance capabilities, revitalizing sagging basic public health systems, rationing powerful drugs to avoid the emergence of drug-resistant organisms, and improving infection control practices at hospitals are only stopgap measures. National security warrants bolder steps.

One priority is finding scientifically valid ways to use polymerase chain reaction (popularly known as DNA fingerprinting), field investigations, chemical and biological export records, and local legal instruments to track the development of new or reemergent lethal organisms, whether natural or bioweapons. The effort should focus not only on microbes directly dangerous to humans, but on those that could pose major threats to crops or livestock.

Most emerging diseases are first detected by health providers working at the primary-care level. Currently there is no system, even in the United States, whereby the providers can notify relevant authorities and be assured that their alarm will be investigated promptly. In much of the world, the notifiers' reward is penalties levied against them, primarily because states want to hush up the problem. But Internet access is improving worldwide, and a small investment would give physicians an electronic highway to international health authorities that bypassed government roadblocks and obfuscation.

Only three diseases — cholera, plague, and yellow fever — are subject to international regulation, permitting U.N. and national authorities to interfere as necessary in the global traffic of goods and persons to stave off cross-border epidemics. The World Health Assembly, the legislative arm of WHO, recommended at its 1995 annual meeting in Geneva that the United Nations consider both expanding the list of regulated diseases and finding new ways to monitor the broad movement of disease. The Ebola outbreak in Kikwit demonstrated that a team of international scientists can be mobilized to swiftly contain a remote, localized epidemic caused by known nonairborne agents.

Were a major epidemic to imperil the United States, the Office of Emergency Preparedness and the National Disaster Medical System (part of the Department of Health and Human Services) would be at the helm. The office has 4,200 private-sector doctors and nurses throughout the 50 states who are at its disposal and committed to rapid mobilization in case of emergency. The system is sound but should be bolstered. Participants should be supplied with protective suits, respirators, mobile containment laboratories, and adequate local isolation facilities.

As for potential threats from biological weapons, the U.S. Department of Energy has identified serious lapses in Russian and Ukrainian compliance with the Biological Weapons Convention. Large stockpiles of bioweapons are believed to remain, and employees of the Soviet program for biological warfare are still on the state payroll. Arsenals are also thought to exist in other nations, although intelligence on this is weak. The location and destruction of such weapons is a critical priority. Meanwhile, scientists in the United States and Europe are identifying the genes in bacteria and viruses that code for virulence and modes of transmission. Better understanding of the genetic mechanisms will allow scientists to manipulate existing organisms, endowing them with dangerous capabilities. It would seem prudent for the United States and the international community to examine that potential now and consider options for the control of such research or its fruits.

To guard against the proliferation of blood-associated diseases, the blood and animal exports industries must be closely regulated, plasma donors must be screened for infections, and an internationally acceptable watchdog agency must be designated to monitor reports of the appearance of new forms of such diseases. The export of research animals played a role in a serious incident in Germany in which vaccine workers were infected with the Marburg virus and in an Ebola scare in Virginia in which imported monkeys died from the disease.

Nobel laureate Joshua Lederberg of Rockefeller University has characterized the solutions to the threat of disease emergence as multitudinous, largely straightforward and commonsensical, and international in scope; "the bad news," he says, "is they will cost money."

Budgets, particularly for health care, are being cut at all levels of government. Dustin Hoffman made more money last year playing a disease control scientist in the movie *Outbreak* than the combined annual budgets for the U.S. National Center for Infectious Diseases and the U.S. Program on AIDS/HIV.

Laurie Garrett, a medical and science reporter for Newsday, *is the author of* The Coming Plague: Newly Emerging Diseases in a World Out of Balance. *This article appeared in the January/February 1996 issue of* Foreign Affairs.

INFORMATION

Plan of Action

By James W. LeDuc

The World Health Organization has a strategic plan to aid countries around the world in detecting and controlling emerging infectious diseases.

Recent outbreaks of infectious diseases have clearly demonstrated that the concerns raised in the Institute of Medicine report, "Emerging Infections," are more than theoretical. Whether due to diseases previously unknown to medical science, such as Hantavirus pulmonary syndrome or the Morbillivirus pneumonia of horses, or the return of known scourges like plague, cholera, and tuberculosis, infectious diseases are in a state of flux globally.

The causes for this resurgence are many and complex and include overcrowded cities where population growth has outpaced supplies of clean water and adequate housing; increases in national and international travel; changes in food handling, shipping, and processing; and the concurrent deterioration of traditional public health activities such as surveillance and diagnostic laboratories needed to quickly recognize emerging problems.

The net result is that national health has become an international challenge. Infectious diseases do not respect international boundaries; consequently, an outbreak of disease anywhere must now be perceived as a threat to most countries, and especially those that serve as major hubs of international travel.

Clearly the problem is global in perspective and requires global leadership in response. Toward that end, the World Health Organization (WHO) is in the process of developing a strategy to strengthen and coordinate its response to emerging infectious diseases.

The WHO is uniquely positioned for this global response effort because it has both the mandate and the networks to enable countries of the world to intensify their efforts against emerging diseases in a coordinated manner. The WHO can advise countries, particularly in the developing world, on effective ways to intensify national efforts to detect and control emerging diseases, since it maintains ongoing relationships with health ministries throughout the world.

Through several collaborating networks, the WHO interacts with centers around the world, many of which are at the cutting edge of research and analysis of specific disease and health issues. Through these collaborating centers the WHO can mobilize the best scientific and medical experts to assist in emergency response activities or to serve on expert committees and study groups. The WHO also has the responsibility to collect and publish epidemiological data from around the world and to implement the international health regulations.

All of these activities are conducted through an organizational structure that ensures cost sharing among all the 190 member states of WHO. Each dollar contributed by the United States to the regular WHO budget is matched by $3 pooled from other member countries.

Based on the mandate given by these 190 member states at its annual World Health Assembly in May 1995, the WHO has developed a strategy to strengthen and coordinate its response to emerging infectious diseases. A

new division, established on October 1, 1995, will provide a focal point for the WHO's intensified efforts in the surveillance and control of emerging and other communicable diseases.

PRIORITIES OF ACTION

Two international meetings have been held in Geneva (April 1994 and January 1995) to define the areas where the WHO could best contribute to the challenge of emerging infectious diseases and to consider the organizational framework best suited to facilitate the activities.

Four major goals were adopted: strengthen global surveillance of infectious diseases; rebuild the international infrastructure necessary to recognize, report, and respond to emerging and resurgent infectious diseases; foster applied research; and enhance the international capacity for infectious disease prevention and control.

The strategy is consistent with the plan developed by the U.S. Centers for Disease Control and Prevention (CDC), "Addressing Emerging Infectious Disease Threats: A Prevention Strategy for the United States," but international in perspective. Specific tasks were suggested for each goal.

1. Strengthen Global Surveillance

We are expanding, as necessary, the existing networks of the WHO collaborating centers that might be used to assist in surveillance efforts to recognize and help respond to outbreaks and emerging problems.

Several specific targets have been identified for early action: influenza, exotic virus diseases, antimicrobial resistance, and foodborne pathogens. Some of these networks are already well developed and have proven their worth.

For example, the influenza network, comprising more than 200 laboratories around the world, serves to isolate and characterize influenza viruses in circulation. These results are then forwarded to one of three WHO collaborating centers (located in Atlanta, London, and Melbourne) where isolates are further characterized genetically and antigenically and the global results summarized. Each February, representatives of the three centers meet at WHO headquarters in Geneva to decide on the composition of the influenza vaccine. This system has proven to be quite successful in matching the vaccine produced to the major influenza strains in circulation each year.

The emerging diseases initiative is also being closely linked with the campaigns for global eradication of polio and for elimination of measles from the Americas, making maximum use of existing networks of collaborating laboratories in the Americas and those being established elsewhere.

2. Strengthen International Infrastructure

Laboratory capabilities are being surveyed by the WHO, with special attention being paid to the availability of diagnostic reagents, equipment, and adequate staff trained in the skills necessary to accomplish laboratory diagnosis of infectious diseases.

We hope that each country eventually will have the capability to diagnose commonly occurring infections and locally link specific etiologies with the clinical diseases seen. For now, we are concentrating on the WHO collaborating centers to ensure that they are able to provide assistance through a regional referral system where problem samples may be sent for more complex analysis or confirmation of preliminary results.

Communications are also being improved, especially through greater use of the Internet, so that information reliably flows between diagnostic laboratories and national and international health officials.

3. Applied Research

We are attempting to make greater practical use of the biotechnological revolution now under way. Areas most likely to benefit from these advances include enhanced diagnostics using expressed noninfectious antigens for rapid and inexpensive serological tests, better epidemiological tools to genetically pinpoint infecting organisms, and improved control interventions, such as ensuring that bacterial pathogens are sensitive to the antibiotics prescribed.

These benefits will be especially valuable for diseases found primarily in the developing world, where there is little or no economic impetus for commercial development, but where significant public health threats exist.

4. Strengthen Prevention and Control

Using the information resulting from implementation of the above recommendations, we hope to improve infectious disease prevention and control activities. Most problems are not likely to be manageable through vaccination alone; consequently, practical public health steps must be defined and instituted to resolve them.

For example, addressing antimicrobial resistance, combating zoonotic diseases, and attacking foodborne parasites will all require practical interventions at the local level. Having adequately equipped national or regional laboratories with well-trained staff and access to the appropriate diagnostic reagents will be essential to accurately define emerging problems, and experienced epidemiologists and other public health officials will be crucial to coordinate interventions. The networks now being developed should help to facilitate access to these resources.

PROGRAM IMPLEMENTATION

Many recent examples of emerging diseases have been viral in nature, especially arboviruses and hemorrhagic fever viruses: Hantavirus pulmonary syndrome and Ebola virus infection are but two examples. Indeed, the virus laboratory is often called into service when a disease of unknown etiology is encountered.

The WHO has a network of 36 laboratories in 27 countries specializing in these viruses, which includes the CDC Special Pathogens Branch and the Division of Vectorborne Infectious Diseases. These laboratories were selected or their technical expertise and special capabilities and often serve as national reference centers for virus diseases.

We recently surveyed these laboratories to determine their technical capabilities and discovered that they were generally quite well equipped, had ready access to clinically ill patients, and in most cases either were directly or indirectly associated with the national ministries of health or were independent university centers. We were concerned to learn, however, that most lacked the reagents necessary to diagnose many common viral diseases. For example, dengue and yellow fever are increasingly important, widely distributed virus diseases, yet one-third or more of the laboratories in the network lacked the reagents necessary to diagnose these diseases. With less common diseases, like Ebola, only about a quarter of the laboratories had the reagents needed to make the diagnosis.

The overall pattern that emerged was one of a network of laboratories generally well prepared to diagnose diseases common to their own geographical area, but often not able to recognize common pathogens present in other parts of the world. To resolve this and other shortcomings, we have begun a program to provide diagnostic reagents and training to these and other virus laboratories internationally.

For example, in June 1995, we hosted a workshop in Nairobi, Kenya, to train virologists from six sub-Saharan nations in laboratory confirmation of yellow fever and other arthropod-borne viruses and hemorrhagic fevers. We are including similar training in a series of ongoing polio laboratory workshops, and we are attempting to produce large quantities of diagnostic reagents for these "exotic" virus diseases.

Antimicrobial resistance is another area of growing international concern. Bacterial pathogens develop resistance to antimicrobials after wide usage, and there is a need to have a reliable method of monitoring this problem.

To do this, a computer program has been developed, WHONET, which is designed for use in microbiological laboratories to facilitate the local management of antibiotic sensitivity test results from routine clinical isolates. Both quantitative and qualitative results may be stored and examined, and the resulting database aids local hospitals in defining their antimicrobial resistance problems. A universal file system is used, so that any laboratory can analyze its own as well as other laboratories' data. The accumulated data may also be periodically reported to a central facility where it may be summarized for local, national, and regional trend analysis.

Currently more than 200 hospitals and labor-atories use WHONET, and we plan to expand this coverage and make greater use of the accumulated test results as the program on emerging infectious diseases develops. The CDC is playing a critical role in implementing this project by providing essential quality control and proficiency testing for contributing laboratories.

Of equal importance with the monitoring of antimicrobial resistance is the development of simple methods for analyzing the derived data and, in particular, guidelines for modifying antimicrobial drug use policies. This is complicated by the fact that the correlation between laboratory-determined resistance and therapeutic effect varies considerably between required organism and drug combinations.

Clear guidance is needed on when to make changes in the antimicrobials recommended for specific diseases, especially as this will often entail changing to more expensive regimens. Strategies must also be developed for limiting the emergence of antimicrobial resistance through effectively applied policies. These will need to be supported with appropriate research. Monitoring of antimicrobial resistance is of limited value unless the action related to it is clearly defined.

CONCLUSIONS

Emerging infectious diseases and the increase in antibiotic resistance are worldwide problems requiring global leadership in their solutions. The WHO is developing a multifaceted strategy making use of existing resources and technical expertise.

The strategy is fully complementary to the U.S. plan developed by CDC and to the recommendations made by the 17 U.S. government agencies as part of the National Science and Technology Council Committee on International Science, Engineering and Technology (CISET) working group on emerging and reemerging infectious diseases.

The WHO strategy uses the existing international health infrastructure as a base to improve global surveillance, enhance capacity of local and national public health laboratories, foster applied research to address practical problems, and improve infectious disease prevention and control.

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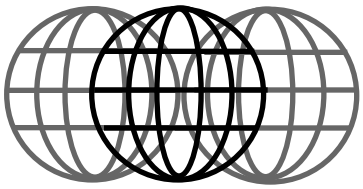

The Threat of Emerging Infections

Emerging infections, which include newly discovered pathogens as well as new forms of older infectious agents, have a variety of causes, some still shrouded in mystery. Most produce the typical symptoms of acute infection —fever, headache, malaise, vomiting, and diarrhea. Some have no known treatment or cure. The following list includes some of the better-known emerging infections:

VIRAL

DENGUE

Causes of Emergence:
Poor mosquito control; increased urbanization in tropics; increased air travel.
Mode of Transmission:
Bite of infected mosquito (primarily Aedes aegypti).
Symptoms:
Hemorrhagic fever; eruptions similar to measles.
Treatment/Prevention:
No specific treatment; analgesic and sedative agents; mosquito control.

FILOVIRUSES (Ebola, Marburg)

Causes of Emergence:
Natural host still unknown; studies underway in forests of Cote D'Ivoire to identify reservoir in which the Ebola virus hides; in Europe and the United States, virus-infected monkeys shipped from developing countries via air.
Mode of Transmission:
Direct contact with infected blood, organs, secretions, and semen.
Symptoms:
Sudden fever, diarrhea, vomiting, massive hemorrhaging.
Treatment/Prevention:
No specific therapy, but convalescent serum may be helpful. No cure.

HANTAVIRUSES

Causes of Emergence:
Environmental changes increasing exposure to rodent hosts.
Mode of Transmission:
Inhalation of aerosolized rodent urine and feces.
Symptoms:
Abdominal pain, hemorrhagic fever, kidney failure.
Treatment/Prevention:
No specific therapy; ribavirin (an antiviral drug) may help.

HEPATITIS B

Causes of Emergence:
Probably increased sexual activity and intravenous drug abuse; transfusion (before 1978).
Mode of Transmission:
Contact with saliva, semen, blood, or vaginal fluids of an infected person; mode of transmission to children not known.
Symptoms:
Nausea, vomiting, jaundice; chronic infection leads to hepatocellular carcinoma and cirrhosis.
Treatment/Prevention:
A vaccine for use in preventing hepatitis B was licensed in the United States in 1981

HEPATITIS C

Causes of Emergence:
Recognition through molecular virology applications; blood transfusion practices following World War II.
Mode of Transmission:
Exposure to contaminated blood or plasma; sexual transmission.
Symptoms:
Nausea, vomiting, jaundice; chronic infection leads to hepatocellular carcinoma and cirrhosis.
Treatment/Prevention:
The drug interferon alpha-2b used to treat chronic hepatitis C. Only 10 to 15 percent of patients experience long-term remission.

HUMAN IMMUNODEFICIENCY VIRUS (HIV AIDS)

Causes of Emergence:
Travel, migration to cities. Sexual transmission, use of contaminated needles, transfusions.
Mode of Transmission:
Sexual contact with or exposure to blood or tissues of an infected person.
Symptoms:
AIDS; severe immune system dysfunction, opportunistic infections.
Treatment/Prevention:
Several antiviral drugs can slow progression; other drugs are used to treat opportunistic infections from immunosuppression.

INFLUENZA

Causes of Emergence:
Natural hosts, such as pigs and ducks, may facilitate rapid genetic changes, causing periodic epidemics.
Mode of Transmission:
Airborne, highly contagious, especially in crowded, enclosed spaces.
Symptoms:
Sore throat, fever, headache, cough, malaise.
Treatment/Prevention:
Immunization; rest and liquids are usually adequate; some drugs such as amantadine can shorten illness.

LASSA FEVER

Causes of Emergence:
Rapid urbanization in squalid conditions bringing humans in contact with rodent hosts.
Mode of Transmission:
Contact with urine or feces of infected rodents.
Symptoms:
Fever, malaise, headache, sometimes shock, seizures.
Treatment/Prevention:
No specific therapy is known. Ribavarin, ventilation, and dialysis sometimes needed.

MEASLES

Causes of Emergence:
Deterioration of public health infrastructure supporting immunization.
Mode of Transmission:
Airborne; direct contact with respiratory secretions of infected persons.
Symptoms:
Fever, conjunctivitis, cough, red blotchy rash.
Treatment/Prevention:
Children who have not had measles should be immunized with live attenuated measles vaccine at 12 months of age. Inactivated vaccine produces short-lived protection.

RIFT VALLEY FEVER

Causes of Emergence:
Dam construction, irrigation, facilitating spread of mosquito vector (carrier); importation of infected mosquitoes or animals.
Mode of Transmission:
Bite of an infective mosquito.
Symptoms:
Abrupt onset of fever, severe fever complications in survivors, with visual and nerve damage.
Treatment/Prevention:
Mosquito control and vaccination.

ROTAVIRUS

Causes of Emergence:
Increased recognition; infects 90 percent of humans by age of 3, regardless of hygiene standards.
Mode of Transmission:
Handshaking, drinking from an infected person's glass, playing with toys that are contaminated.
Symptoms:
Diarrhea, vomiting, dehydration, and low-grade fever.
Treatment/Prevention:
Replace fluids with a substance that contains both water and salt. There is no medication to cure it. Vaccines under development.

YELLOW FEVER

Causes of Emergence:
Lack of effective mosquito control and widespread vaccination; urbanization in tropics; increased air travel.
Mode of Transmission:
Bite of an infective mosquito (Aedes aegypti).
Symptoms:
Fever, headache, muscle pain, nausea, and vomiting.
Treatment/Prevention:
No specific therapy. Absolute rest; cool, well-ventilated room; liquid diet; vitamin K and calcium gluconate for hemorrhagic tendency; analgesics for pain.

BACTERIAL

CHOLERA

Causes of Emergence:
Recent epidemic in South America introduced from Asia by ship; spread by travel and inadequate water chlorination; poor sanitation.
Mode of Transmission:
Ingestion of water contaminated with feces of infected persons; ingestion of food exposed to contaminated water.
Symptoms:
Severe diarrhea, rapid dehydration.
Treatment/Prevention:
Recent strains resistant to several antibiotics.

ESCHERICHIA COLI 0157:H7 (E. coli)

Causes of Emergence:
Contamination of meat during butchering process; spread by poor handling and inadequate cooking. Likely due to development of new pathogen.
Mode of Transmission:
Ingestion of contaminated food, especially undercooked beef and raw milk.
Symptoms:
Hemolytic uremic syndrome, hemorrhagic colitis.
Treatment/Prevention:
Oral or intravenous replacement of fluids.

LEGIONNAIRES' DISEASE (Legionella)

Causes of Emergence:
Legionella bacterium widely distributed in environment; found in creeks and ponds, hot and cold water taps, hot water tanks, and air-conditioning systems.
Mode of Transmission:
Air-cooling systems, water supplies.
Symptoms:
Fever, headache, confusion, pneumonia.
Treatment/Prevention:
Antibiotics such as erythromycin and rifampicin appear to be effective.

LYME DISEASE

Causes of Emergence:
Increase in deer and human populations in wooded areas.
Mode of Transmission:
Bite of infective deer (Ixodes) tick.
Symptoms:
Fatigue, headache, rash, fever, arthritis, neurologic and cardiac abnormalities.
Treatment/Prevention:
Oral or intravenous antibiotics.

STREPTOCOCCUS INFECTIONS (Group A)

Causes of Emergence:
Change in virulence of the bacteria; possibly mutation.
Mode of Transmission:
Direct contact with infected persons or carriers; sometimes ingestion of contaminated foods.
Symptoms:
Necrotizing fasciitis, streptococcal toxic shock.
Treatment/Prevention:
Antibiotics.

TUBERCULOSIS

Causes of Emergence:
Increase in immunosuppressed population, improper treatment exposing more people to disease.
Mode of Transmission:
Exposure to sputum droplets exhaled through a cough or sneeze of a person with active disease.
Symptoms:
Cough, weight loss, lung lesions; infection can spread beyond lungs to other organs.
Treatment/Prevention:
Combination of antibiotics for at least six months.

TYPHOID

Causes of Emergence:
Spread of typhoid bacillus.
Mode of Transmission:
Infected water or milk supplies. Human carriers, particularly food handlers, may be responsible for spread of infection.
Symptoms:
Fever, headache, abdominal pain.
Treatment/Prevention:
General care, isolation, disinfection of all discharges. Inoculation with vaccine containing killed Salmonella typhi.

PARASITIC

CRYPTOSPORIDIUM AND OTHER WATERBORNE PATHOGENS

Causes of Emergence:
Protozoan-contaminated surface water; development near watershed areas; immunosuppression.
Mode of Transmission:
Fecal-oral, person-to-person.
Symptoms:
Diarrhea, vomiting, usually lasts less than 30 days.
Treatment/Prevention:
Fluid/electrolyte replacement.

MALARIA

Causes of Emergence:
Migration and travel to mosquito-infested areas; urbanization; changing parasite biology; environmental changes; drug resistance.
Mode of Transmission:
Bite of infective Anopheles mosquito.
Symptoms:
Fever, headache, can cause respiratory and renal failure.
Treatment/Prevention:
Chloroquine, but some forms may be resistant to most drugs.

Source: Information gathered from Emerging Infectious Diseases, *January-March 1995; and 1992 Institute of Medicine report, "Emerging Infections: Microbial Threats to Health in the United States."*

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EDITORIAL: TUBERCULOSIS CONTROL IN RESOURCE-POOR SETTINGS WITH HIGH RATES OF HIV INFECTION
American Journal of Public Health, vol. 86, no. 8, August 1996, pp. 1071+

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JAMA: Journal of the American Medical Association, vol. 274, no. 10, September 13, 1995, p. 786

Article Alert

Abstracts of a few recent articles on the global aspects of infectious diseases.

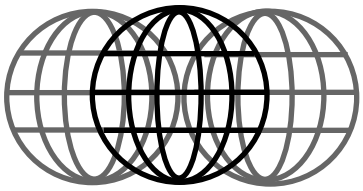
Chow, Jack C.
HEALTH AND INTERNATIONAL SECURITY
The Washington Quarterly, vol. 19, no. 2, Spring 1996, pp. 63-77
The author examines the connection between conflict, disease, and instability in the Post-Cold War era. Health has never been defined as an element of national and international security, but Chow believes that "any future consideration of international security as it affects American interests must consider health-based threats."

De Cock, Kevin M.
EDITORIAL: TUBERCULOSIS CONTROL IN RESOURCE–POOR SETTINGS WITH HIGH RATES OF HIV INFECTION
American Journal of Public Health, vol. 86, no. 8, August 1996, pp. 1071-1073
This editorial describes efforts to control tuberculosis in developing countries. The strategies of the Global Tuberculosis Programme of the World Health Organization and the International Union Against Tuberculosis and Lung Disease are discussed.

Garrett, Laurie
COVERING OUR "FINAL PREDATORS"
IPI Report, August/September 1996, pp. 5-6
Laurie Garrett, a reporter for Newsday who won the Pulitzer Prize in 1996 for her coverage of the Ebola outbreak in Zaire, is critical of the way reporters cover epidemics. She describes the way the world's media handled the Ebola epidemic in May 1995. Most of the reporters, according to Garrett, were not science-trained, did not take precautions against contamination, and showed little compassion towards the patients. Also, Garrett urges better preparation for the reporters covering epidemics.

Stoeckle, Mark Y. and R. Gordon Douglas, Jr.
INFECTIOUS DISEASES
JAMA: Journal of the American Medical Association, vol. 275, no. 123, June 19, 1996, pp. 1816-1817
The authors discuss the worldwide dissemination of antibiotic-resistant bacteria. The unanticipated outbreak of Ebola virus in 1995 illustrates the unpredictable nature of infectious diseases. The establishment of new global and national surveillance systems helps to identify the factors involved in the emergence and reemergence of infectious diseases.

A more comprehensive Article Alert is offered on the international home page of the U.S. Information Agency:http://www.usia.gov/admin/001/wwwhapub.html



Internet Sites

USIS assumes no responsibility for the content and availability of the resources listed below

CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)
The CDC promotes health and quality of life by trying to prevent and control disease, injury, and disability. Its elements include an International Health Program Office and a National Center for Infectious Diseases.
http://www.cdc.gov

CDC NATIONAL AIDS CLEARINGHOUSE
Reference specialists at the Clearinghouse can provide information and materials on HIV and AIDS over the phone Monday-Friday, 1400 to 2400 GMT, except holidays at 301-217-0023. They can be reached by fax at 301-738-6616 or by writing CDC National AIDS Clearinghouse, Post Office Box 6003, Rockville, MD 20849-6003.
http://cdcnac.aspensys.com

EMERGING INFECTIOUS DISEASES
A journal published on the World Wide Web by the National Center for Infectious Diseases, a division of the CDC. It aims to promote the recognition of new and reemerging infectious diseases and to better understand the factors involved in disease emergence, prevention, and elimination. Its scope is international and is written for professionals.
http://www.cdc.gov/ncidod/EID/eid.htm

NATIONAL CENTER FOR INFECTIOUS DISEASES (NCID)
CDC created the NCID in 1981 to support surveillance, research, prevention efforts, and training in combating infectious diseases. Its mandate is broad — the control of traditional, new, and reemerging infectious diseases in the United States and around the world.
http://www.cdc.gov/ncidod/ncid.htm

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
A division of the National Institutes of Health (NIH), the allergy and infectious diseases institute is a major support for scientists trying to understand, treat, and prevent the many infectious, immunologic, and allergic diseases around the world. Some of the main areas of research are AIDS, tuberculosis, tropical diseases, and intestinal diseases.
http://www.niaid.nih.gov

NATIONAL INSTITUTES OF HEALTH (NIH)
It started the one-room Laboratory of Hygiene in 1887 and has grown to be one of the world's leading biomedical research centers. The goal of the NIH is to initiate research that will lead to better health for everyone in the world. To do that, it conducts research in its own laboratories and supports non-federal scientists throughout the country and overseas.
http://www.nih.gov

U.S. NATIONAL LIBRARY OF MEDICINE
The library advances medical and public health knowledge through the collection, dissemination, and exchange of information from around the world. It has easy-to-use software for searching its databases. Although the library is open to the general public, it's target audience is the health professional.
http://www.nlm.nih.gov

WORLD HEALTH ORGANIZATION (WHO)
WHO acts as the directing and co-ordinating authority on international health work, helps governments to strengthen health services, and gives technical assistance and, in emergencies, aid if requested by governments.
http://www.who.ch