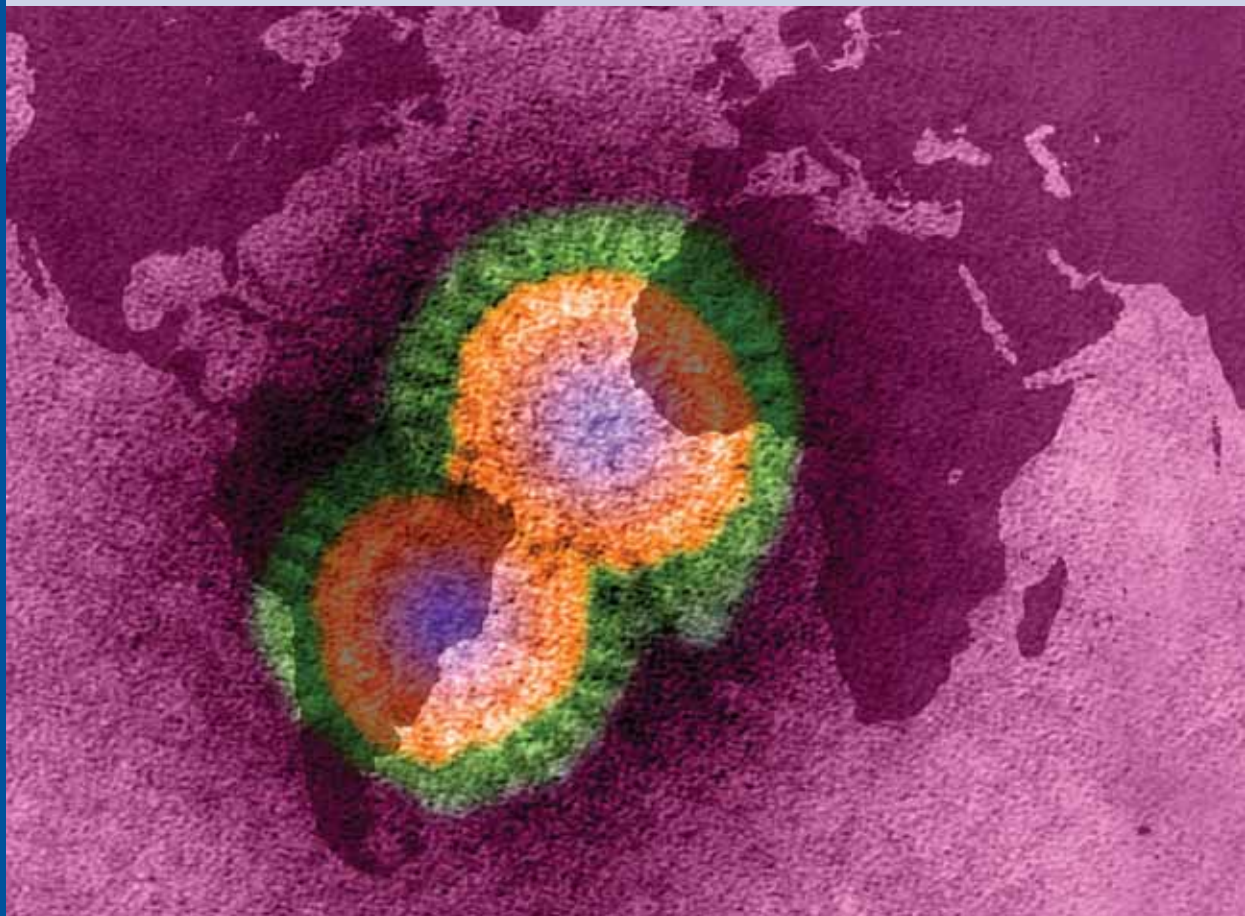


ISSUE REPORT

Germs Go Global:

WHY EMERGING INFECTIOUS
DISEASES ARE A THREAT TO AMERICA



OCTOBER 2008

PREVENTING EPIDEMICS.
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Trust for America's Health is a non-profit, non-partisan organization dedicated to saving lives and making disease prevention a national priority.

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Germs Go Global:

WHY EMERGING INFECTIOUS

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An Issue Brief from Trust for America's Health

Funded by a Grant from the de Beaumont Foundation

“ THE HEALTH OF U.S. CITIZENS IS INEXTRICABLY LINKED TO THE HEALTH OF OTHER PEOPLE IN OTHER PARTS OF THE WORLD: MICROORGANISMS CAN AND DO CROSS BORDERS EASILY AND OFTEN WITHOUT RECOGNITION.”¹

-- SCIENCE

OVERVIEW

Despite remarkable breakthroughs in medical research and advancements in immunization and treatments during the 20th century, infectious diseases are undergoing a global resurgence that threaten everyone's health.

Worldwide, infectious diseases are the leading killer of children and adolescents, and are one of the leading causes of death for adults. The range of infectious threats includes:

- The emergence of new infectious diseases, severe acute respiratory syndrome (SARS) and the H5N1 avian influenza virus;
- The resurgence of known infectious diseases, such as measles and pertussis (whooping cough);
- The persistence and spread of certain “neglected” infectious diseases, like dengue fever;
- The potential deliberate use of deadly bioterrorism agents, such as smallpox virus or anthrax; and
- The growing rise and spread of antimicrobial resistance has led to the development of resistant pathogens and allowed many diseases formerly treatable with drugs, like tuberculosis (TB) and malaria to resurge and take hold with new vigor.

The impact of emerging infectious diseases in developing countries is well known and well documented. But these diseases can also

impact Americans, with far-reaching consequences for the U.S. public health system, the delivery of medical care, and the economy. According to a National Intelligence Estimate, “newly emerging and re-emerging infectious diseases, many of which are likely to continue to originate overseas, will continue to kill at least 170,000 Americans annually. Many more could perish during a severe influenza pandemic or yet-unknown disease.”²

Intelligence analysts argue that “newly emerging and re-emerging infectious diseases will pose a rising global health threat and will complicate U.S. and global security over the next 20 years. These diseases will endanger U.S. citizens at home and abroad, threaten U.S. armed forces deployed overseas, and exacerbate social and political instability in key countries and regions in which the U.S. has significant interests.”³

Federal support for identifying, preventing, containing, and treating emerging infectious diseases varies widely. The U.S. government has invested significantly in the pursuit of drugs and vaccines that could counter an intentional biological attack. For example, the Strategic National Stockpile (SNS) has enough smallpox vaccine to protect every man, woman, and child in America and over 41 million treatment regimens for anthrax.⁴ Along with vaccine manufacturers, the federal government has invested heavily in developing new vaccine technologies

for influenza and vaccines that are effective against the H5N1 avian influenza virus. In the past few years, stockpiles of antiviral medications and vaccines that may be deployed during a pandemic flu outbreak have been added to the SNS.

On the other hand, many other emerging and re-emerging diseases have received far less attention. In the U.S., the private sector research and development pipeline for most emerging infectious diseases is stagnant or non-existent. Lack of action is fostered by a common view that many of these diseases are limited to the developing world, and that vaccine development and treatment options are not seen as profitable for U.S. pharmaceutical firms. Companies have found that the market for new antibiotics, medications, and vaccines for many infectious diseases is not as profitable as developing drugs to treat chronic conditions like high cholesterol. Therefore, diagnostics and treatment are outdated for infectious diseases like TB and *Staphylococcus aureus* (often referred to as “staph”). According to the U.S. Food and Drug Administration (FDA), “developing products targeted for ... less common diseases, prevalent third world diseases, prevention indications, or individualized therapy is becoming increasingly challenging.”

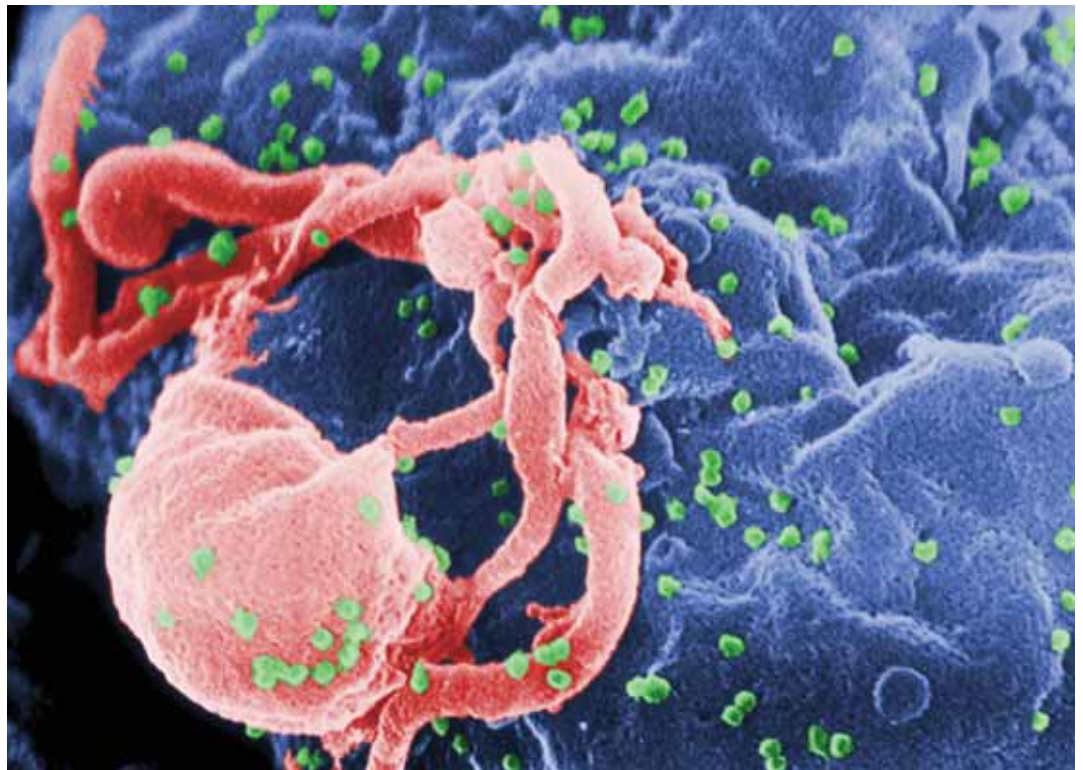
The U.S. government should lead efforts to detect and conquer emerging infectious diseases with the same energy it devoted to

tackling polio in this country during the last century. Americans need and deserve a national game plan to protect them from the wide range of infectious diseases that threaten their well-being.

Policymakers must start thinking of U.S. contributions to prevent, treat, and cure emerging infectious diseases as a national health imperative rather than as international good-will gestures. Leaders also must recognize that efforts to address biodefense and emerging infections are mutually supportive and that compartmentalizing these efforts is arbitrary and counterproductive. The response to emerging, re-emerging, and deliberately-introduced infectious diseases requires a well-funded federal effort; coordination with international initiatives; and incentives that stimulate breakthroughs in research, surveillance, next-generation diagnostics, treatments, and vaccines.

This issue brief examines what is currently known about a range of emerging infectious diseases and why they are potential threats to Americans. It also reviews the tools -- surveillance, diagnostics, vaccines, and therapeutics -- that exist or are in development and explores government incentives for enhancing them. Finally, it recommends increased action to protect the nation from deadly and debilitating infectious diseases.

Scanning electron micrograph of HIV-1 budding from cultured lymphocyte.



U.S. INVESTMENTS IN INFECTIOUS DISEASE CONTROL IN OTHER COUNTRIES PAY OFF

The U.S. cannot protect the health of its citizens without addressing infectious disease problems that are occurring elsewhere in the world. Helping other countries to control disease outbreaks prevents those diseases from spreading to the U.S., saving lives and dollars.

Smallpox

The global eradication of smallpox in 1980, with support from the U.S. Department of Health and Human Services and the U.S. Agency for International Development proved to be a prudent economic investment for the nation's health. In 1968, the U.S. spent \$92.8 million on smallpox vaccinations and revaccinations for Americans, or about \$6.50 per vaccination.⁶

The U.S. spent a total of \$32 million over a 10-year period in the global campaign to eradicate smallpox -- the first and only infectious disease to be eradicated through human intervention.⁷ For all developed countries, the economic benefits of contributing to the WHO global smallpox eradication program were substantial because costs associated with smallpox vaccine preparation and administration, medical care, and quarantine were eliminated. The U.S., the largest donor to the WHO effort, is estimated to save the total of all its contributions to the smallpox eradication effort every 26 days.⁸

Over time, these savings are impressive. According to a General Accounting Office (GAO) report, *Infectious Diseases: Soundness of World Health Organization Estimates for Eradication or Elimination*, the cumulative savings from smallpox eradication for the U.S. was \$17 billion through April 1998.⁹

TB

A study published in the *New England Journal of Medicine* in September 2005 found that U.S.-funded efforts to expand TB control programs in Mexico, Haiti, and the Dominican Republic could reduce TB-related morbidity and mortality among migrants to the U.S. and produce net cost savings for the federal government.¹⁰ The research team predicted the number of cases, deaths and costs using the traditional U.S. approach of screening immigrants and refugees for TB using chest X-rays obtained before or on arrival and subsequent treatment when detected, with expected outcomes if the U.S.-funded TB diagnosis and treatment programs in the home country.

Particularly striking were the findings regarding Mexico, which is the single largest source of immigrants to the U.S. The study found that if the U.S. government spent \$35 million to strengthen Mexican TB control, there would be a net savings of \$108 million for the federal government over 20 years.¹¹

The study also predicted that there would be 2,591 fewer TB cases in the U.S., and 349 fewer TB-related deaths over the same time period, than if the current approach were continued. And these figures do not even account for the fact that preventing these cases will prevent transmission of TB from immigrants to other U.S. citizens.

Similar U.S. government assistance for TB control in Haiti and the Dominican Republic would also lead to long-term savings. A \$9.4 million investment to expand TB diagnosis and treatment programs in these Caribbean nations would result in a net saving for the U.S. of \$20 million over a 20-year period.¹²

I. WHAT ARE EMERGING AND RE-EMERGING INFECTIOUS DISEASES?

In 1992, the Institute of Medicine (IOM) issued a landmark report, *Emerging Infections: Microbial Threats to Health in the United States*, which defined the concept of emerging and re-emerging infections. It identified factors contributing to disease emergence and re-emergence, and emphasized current and future challenges posed by infectious diseases. The report broadly defined **emerging infections** as new, re-emerging, or drug-resistant infections whose incidence in humans has increased within the past 2 decades or whose incidence threatens to increase in the near future.¹³ Recognition of an emerging disease occurs when the disease is identified in humans or another species for the first time or because links between an infectious agent and a chronic disease or a syndrome have only recently been identified.¹⁴

In 1994, the U.S. Centers for Disease Control and Prevention (CDC) issued a strategic plan emphasizing surveillance, research, and prevention activities necessary to maintain a strong defense against infectious diseases that affect, or threaten to affect, the public's health. It has become a roadmap for governmental infectious disease prevention and control. Plan updates and progress reports have been issued periodically.¹⁵

HIV/AIDS is an example of an emerging infectious disease that sparked a worldwide pandemic. Globally, in 2007, nearly 33 million people were reported to be living with HIV.¹⁶ More than 980,000 cases of AIDS have been reported in the U.S. since it was first reported in this country in 1981. Many more Americans are infected with the virus but do not have disease manifestations. Nearly 30 years after emerging as a deadly infectious disease, there is still no vaccine or cure for HIV. While a combination of pharmaceutical interventions, when used correctly, can mitigate the effects of the disease and allow those infected to live many years with HIV, its cost to society -- in terms of health care costs and quality of life -- is enormous.

Other new diseases recognized in the past few decades include SARS, hepatitis C, H5N1 avian influenza viruses, Lyme disease, and Legionnaire's disease.¹⁷

Re-emerging or resurging infectious diseases are also of growing concern to health

experts. For example, in the past 2 decades, countries in the Americas, Southeast Asia, and Western Pacific have witnessed a resurgence of dengue fever and its most serious manifestation, dengue haemorrhagic fever.¹⁸ This past year, Brazil reported its first outbreak of yellow fever in urban areas since the 1940s.¹⁹

Malaria, nearly eliminated in the U.S., is rampant in developing countries, particularly in sub-Saharan Africa and South Asia. In 2003, the most recent year for which there are reliable data, there were 408 million malaria cases worldwide and 1.2 million deaths. No deaths were reported in the U.S., although there have been sporadic cases reported.²⁰

More than one-third of the global population is infected with TB and TB disease remains one of the world's leading causes of disease and death. In 2006, there were 14.4 million people living with active TB worldwide and approximately 2 million people die from the disease annually. The U.S. accounted for 9,842 of those cases in 2006.²¹

TB disease is usually treated with a regimen of drugs taken for 6 months to 2 years depending on the type of infection. It is imperative that people who have TB disease finish the course of medicine, and take the drugs exactly as prescribed. If they stop taking the drugs too soon or do not take the drugs correctly, they can become ill again and the infection may become more drug resistant.²²

There is a growing concern among public health officials about a continuum of drug-resistant TB infections, which means that the TB bacteria can no longer be killed by commonly used antibiotics. As a result, the drug-resistant forms of the disease are more difficult to treat than ordinary TB and require as much as 2 years of multidrug treatment, or more in extreme cases.²³

Recently, several U.S. states experienced measles outbreaks, which is particularly troubling because transmission of the disease was thought to be largely eliminated thanks to immunization. More than 130 cases have been reported in the U.S. so far this year, which constitutes the largest number since 2001. At least 15 patients, including 4 children have been hospitalized. In

the decade before the measles vaccination program began, an estimated 3-4 million persons in the U.S. were infected each year. Of these, 400-500 died, 48,000 were hospitalized, and another 1,000 developed chronic disability from measles encephalitis.²⁴ Worldwide, 20 million cases of measles still occur each year, and the disease is a signifi-

cant cause of vaccine-preventable death among children. In 2005, 311,000 children under age 5 died from the disease globally.²⁵

Additional information on several of the world's deadliest infectious diseases can be found in Appendix A. Descriptions of animal-borne and foodborne diseases can be found in Appendix B.

TABLE 1: Leading Infectious Causes of Death Worldwide, 2002

Cause	Rank	Estimated Number of Deaths
Respiratory infections	1	3,871,000
HIV/AIDS	2	2,866,000
Diarrheal diseases	3	2,001,000
Tuberculosis	4	1,644,000
Malaria	5	1,224,000
Measles	6	645,000
Pertussis	7	285,000
Tetanus	8	282,000
Meningitis	9	173,000
Syphilis	10	167,000

Source: WHO 2004 World Health Report

The potential **deliberate use of pathogens as agents of bioterrorism** is of special concern in the post-9/11 world. CDC classifies biological agents that could be used for an intentional bioattack into 3 categories.

- Category A, or “High-Priority Agents,” is considered the most dangerous and includes: Anthrax, botulism, plague, smallpox, tularemia, and viral hemorrhagic fevers (e.g., Ebola, Marburg).
- Category B, or “Second-highest Priority Agents,” includes food safety threats (e.g., *Salmonella* and *E. coli*), ricin toxin, Typhus fever, and viral encephalitis, among others.
- Category C, or “Third-highest Priority Agents” include emerging pathogens that could be engineered for mass dissemina-

tion in the future because of availability; ease of production and dissemination; and potential for high morbidity and mortality rates and major health impact. Hantavirus is an example of a Category C agent.²⁶

Developing effective medical countermeasures against deliberately emerging diseases has become a national priority. Congress and the Bush Administration have taken measures to encourage the stockpiling of vaccines and medications to counter deliberately emerging infectious diseases. Project BioShield and the Biomedical Advanced Research and Development Authority (BARDA) were created to stimulate private sector investment with direct federal support for product development.

ANTHRAX AS A BIOLOGICAL WEAPON

Anthrax is a potentially lethal infection caused by the bacterium *Bacillus anthracis*. Outside of a host, this bacterium normally resides as a spore -- a hardy, dormant cell that may become active (germinate) in the right conditions. Anthrax generally affects large grazing animals, but it can also infect humans who handle products of infected animals. However, deliberate exposure to aerosolized anthrax spores also is a highly effective means of transmission.²⁷

That is why anthrax is considered by many to be the ideal bioweapon. It is extremely stable and can be stored almost indefinitely as a dry powder. The costs of producing anthrax material are relatively low and knowledge about production is widely available and does not require high degrees of technology. According to the U.S. Department of Defense (DOD), anthrax is easy to weaponize and can be loaded, in a freeze-dried condition, in munitions or disseminated as an aerosol with crude sprayers.²⁸ Currently, detection of this silent, invisible killer is limited. In 1999, CDC classified anthrax as a Category A bioterrorism agent, which means it poses the highest level of threat to national security. However, unlike some other Category A agents (e.g. smallpox), anthrax does not spread from person to person, thus limiting the risk to those directly exposed in an attack.²⁹

Historically, numerous nations have experimented with anthrax as a biological weapon, including the U.S. offensive biological weapons program that was disbanded in 1969.³⁰ The worst documented outbreak of inhalation anthrax in humans occurred in Russia in 1979, when anthrax spores were accidentally released from a military biological weapons facility near the town of Sverdlovsk, killing at least 66 people. In the fall of 2001, lethal anthrax bacteria were spread deliberately through the U.S. Postal Service. Seventeen people became ill, and 5 died.

SMALLPOX AND BIOTERRORISM

Although the World Health Organization (WHO) declared that smallpox was eradicated in 1980, this contagious and deadly infectious disease caused by the *Variola major* virus, remains high on the list of possible bioterror threats.

The last naturally occurring case of smallpox was reported in 1977. Currently, there is no evidence of naturally occurring smallpox transmission anywhere in the world. Although a worldwide immunization program eradicated smallpox disease decades ago, small quantities of smallpox virus officially still exist in research laboratories in Atlanta, Georgia, and in Novosibirsk, Russia.³¹ There is a fear there may be other unknown sources of smallpox virus that could fall into the hands of terrorists.

In January 2003, the Bush Administration declared smallpox the “number one bio-threat facing the country” and made planning for an attack a top priority.³² The Administration launched a national smallpox vaccination initiative with the goal of immunizing 500,000 health care workers in 30 days and 10 million emergency response personnel within a year. Immunization rates fell well-below that target level with approximately 40,000 people actually vaccinated. The plan faced obstacles, including unexpected side effects, worker compensation issues, and liability concerns that precluded its full implementation.³³

NEGLECTED TROPICAL DISEASES

Recently, neglected tropical diseases have garnered increasing international attention. The leaders of Canada, France, Germany, Italy, Japan, Russia, the United Kingdom, and the U.S. met at the G8 Summit in Japan in July 2008. Japan's Prime Minister, Yasuo Fukuda, summarized their position on neglected tropical diseases:

"We ... agreed to support the control or elimination of neglected tropical diseases (NTDs) to reach at least 75 percent of the people with NTDs. We also discussed the timeframe to provide US\$ 60 billion to fight infectious diseases and strengthen health, and agreed to do so over 5 years, while some countries will provide additional resources for health systems including water."³⁴

Health officials estimate that one billion people -- one sixth of the world's population -- suffer from one or more neglected tropical disease. Extreme poverty, war and civil conflicts, and natural disasters aggravate conditions that are conducive to the spread of these diseases. Lack of comprehensive surveillance, unreliable statistics, and the diseases' obscure names contribute to their low profile and status among global public health priorities.

WHO considers the following to be neglected tropical diseases: Buruli ulcer, dengue/dengue haemorrhagic fever, dracunculiasis (guinea-worm disease), fascioliasis, human African trypanosomiasis (sleeping sickness), leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis, trachoma, and yaws.³⁵

2. FACTORS CONTRIBUTING TO THE EMERGENCE OF INFECTIOUS DISEASES

Emerging and re-emerging infectious diseases pose serious threats to the health of the American people. In 2003, the IOM issued *Microbial Threats to Health: Emergence, Detection, and Response*, an important follow up to the 1992 IOM report on emerging infectious diseases. The 2003 IOM report assessed the threats of emerging infectious diseases to the U.S. and warned:

"While dramatic advances in science and medicine have enabled us to make great strides in our struggle to prevent and control infectious diseases, we cannot fall prey to an illusory

complacency ... Infectious diseases unknown in this country just a decade ago, such as West Nile encephalitis and hantavirus pulmonary syndrome, have emerged to kill hundreds of Americans -- and the long-term consequences for survivors of the initial illnesses are as yet unknown. Other known diseases, including measles, multidrug-resistant tuberculosis, and even malaria, have been imported and transmitted within the United States in the last 10 years... Compounding the threat posed by these infectious diseases is the continuing increase in antimicrobial resistance."³⁶

TABLE II: FACTORS OF EMERGENCE

- | | |
|---|---------------------------------------|
| ■ Microbial adaptation and change (i.e., drug resistance) | ■ International travel and commerce |
| ■ Human susceptibility to infection | ■ Technology and industry |
| ■ Climate and weather | ■ Breakdown of public health measures |
| ■ Changing ecosystems | ■ Poverty and social inequality |
| ■ Human demographics and behavior | ■ War and famine |
| ■ Economic development and land use | ■ Lack of political will |
| | ■ Intent to harm |

Source: 2003 IOM Report: *Microbial Threats to Health: Emergence, Detection, and Response*.

Antimicrobial (Drug) Resistance

“ IN THEIR ONGOING WAR AGAINST ANTIBIOTICS, THE BACTERIA SEEM TO BE WINNING, AND THE DRUG PIPELINE IS VERGING ON EMPTY...THE LAST DECADE HAS SEEN THE INEXORABLE PROLIFERATION OF A HOST OF ANTIBIOTIC-RESISTANT BACTERIA, OR BAD BUGS, NOT JUST MRSA BUT OTHER INSIDIOUS PLAYERS AS WELL.”³⁷

-- SCIENCE

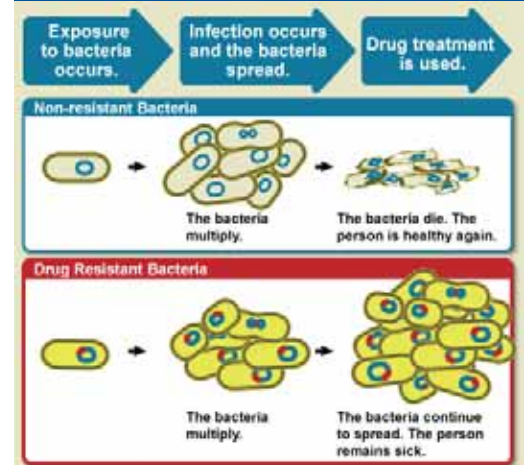
Antimicrobial resistance is a serious patient safety and public health issue. According to the National Institute of Allergy and Infectious Diseases (NIAID), “antimicrobial drug resistance is the ability of a microbe to grow in the presence of a chemical that would normally kill it or limit its growth.”³⁸ Disease-causing microbes that have become hard to treat with antibiotic drugs include *E. coli*, *Salmonella*, *Staphylococcus aureus*, and those causing TB, gonorrhea, and malaria, among others. People infected with antimicrobial-resistant organisms are more likely to have longer hospital stays and may require more complicated treatment.

A class of drug resistant bacteria known as “gram-negative” is particularly hard to treat. One strain, *acinetobacter baumannii*, has threatened the lives, limbs, and organs of hundreds of U.S. forces fighting in Iraq and Afghanistan. According to DOD documents, more than 250 patients at U.S. military hospitals were infected with a highly resistant strain of *acinetobacter* between 2003 and 2005, with 7 deaths as of June 2006, linked to *acinetobacter*-related complications.³⁹

Antimicrobial resistance is exacerbated by the overuse and misuse of antibiotics in people and animals, the lack of rapid diagnostic tests

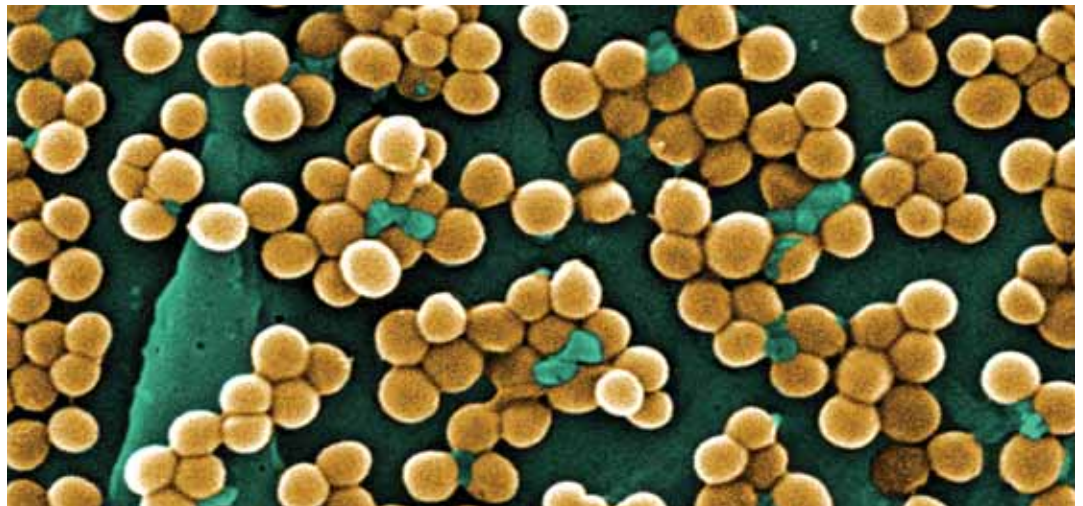
that can identify infectious agents, poor infection control in health care and community settings, and poor hand hygiene. The use of antibiotics in agriculture and aquaculture also contributes significantly to antimicrobial resistance.⁴⁰ Preventing infection and decreasing inappropriate antibiotic use are important strategies for controlling resistance.

Difference Between Non-Drug Resistant And Drug Resistant Bacteria



Source: National Institute of Allergy and Infectious Diseases, www.niaid.nih.gov

2005 colorized scanning electron micrograph (SEM) depicts numerous clumps of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteria. Methicillin-resistant *Staphylococcus aureus* infections, e.g., bloodstream, pneumonia, bone infections, occur most frequently among persons in hospitals and health-care facilities, including nursing homes, and dialysis centers.



MRSA

Methicillin-resistant *Staphylococcus aureus* (MRSA) infection is caused by *Staphylococcus aureus* bacterium. Often called “staph,” this organism is a common cause of serious skin, soft tissue, and bloodstream infections. The advent of antibiotics revolutionized the treatment of staph infections, greatly reducing morbidity and mortality. MRSA is a strain of staph that is resistant to broad-spectrum antibiotics commonly used to treat it. MRSA is a growing cause of fatal staph infections,⁴¹ causing potentially life-threatening infections in bones, joints, surgical wounds, the bloodstream, heart valves, and lungs.⁴²

In the past, most invasive MRSA infections occurred in hospitals or other health care settings, such as nursing homes and dialysis centers. This is known as health care-associated MRSA, or HA-MRSA. Older adults and people with weakened immune systems are at most risk of HA-MRSA.⁴³

More recently, community-associated MRSA, or CA-MRSA, has become increasingly responsible for serious skin and soft tissue infections and for a serious form of pneumonia among previously healthy persons.⁴⁴ The deaths of 2 previously healthy school children in October 2007 -- one in Virginia and the other in New York -- have significantly increased public awareness about this serious public health concern. CA-MRSA rates continue to rise at an alarming rate, now accounting for more than half of community-acquired staff infections in many communities.⁴⁵

Both HA- and CA-MRSA infections are painful, difficult to treat, and cost the U.S. health care system many billions of dollars annually. While both types of MRSA still respond to a few medications, intravenous *vancomycin* is the mainstay for treating severe MRSA infections and there are growing concerns that this medication may be losing its effectiveness. Some U.S. hospitals report seeing strains of MRSA that are less easily killed by *vancomycin*, and 7 cases of complete resistance were reported in this country between 2000-2006.⁴⁶

Globalization

Globalization, the worldwide movement toward economic, financial, trade, and communications integration, has impacted public health significantly. Technology and economic interdependence allow diseases to spread globally at rapid speeds. Experts believe that the increase in international travel and commerce, including the increasingly global nature of food handling, processing, and sales contribute to the spread of emerging infectious diseases.⁴⁷ Increased global trade has also brought more and more people into contact with zoonosis – diseases that originated in animals before jumping to humans. For example, in 2003, the monkeypox virus entered the U.S. through imported Gambian giant rats sold in the nation’s under-regulated exotic pet trade. The rats infected pet prairie dogs, which passed the virus along to humans.⁴⁸ International smuggling of birds, brought into the U.S. without undergoing inspection and/or quarantine, is of particular concern to public health experts who worry that it may be a pathway for the H5N1 “bird flu” virus to enter the country.

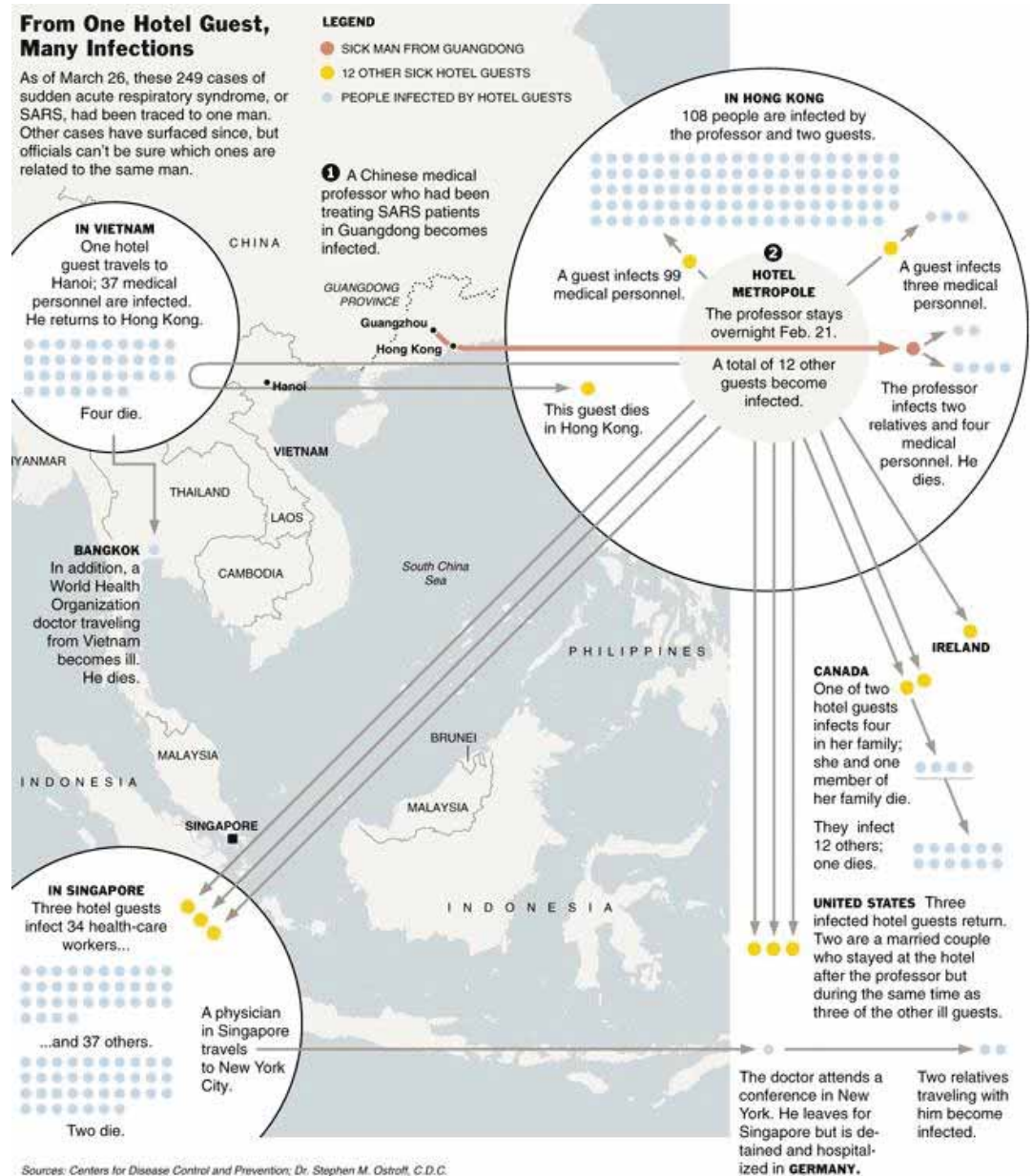
Lower cost and efficient means of international transportation allow people to travel to more remote places and potential exposure to more infectious diseases. And the close proximity of passengers on passenger planes, trains, and cruise ships over the course of many hours puts people at risk for higher levels of exposure. If a person contracts a disease abroad, their symptoms may not emerge until they return home, having exposed others to the infection during their travels. In addition, planes and ships can themselves become breeding grounds for infectious diseases.

The 2002-2003 SARS outbreak spread quickly around the globe due to international travel. SARS is caused by a new strain of *coronavirus*, the same family of viruses that frequently cause the common cold. This contagious and sometimes fatal respiratory illness first appeared in China in November 2002. Within 6 weeks, SARS had spread worldwide, transmitted around the globe by unsuspecting travelers. According to CDC, 8,098 people were infected and 774 died of the disease.⁴⁹

SARS represented the first severe, newly emergent infectious disease of the 21st century.⁵⁰ It illustrated just how quickly infection can spread in a highly mobile and interconnected world. SARS was contained and controlled because public health authorities in the communities most affected mounted a rapid and effective response.

SARS also demonstrated the economic consequences of an emerging infectious disease in closely interdependent and highly mobile world. Apart from the direct costs of intensive medical care and disease control interventions, SARS caused widespread social dis-

ruption and economic losses. Schools, hospitals, and some borders were closed and thousands of people were placed in quarantine. International travel to affected areas fell sharply by 50 - 70 percent. Hotel occupancy dropped by more than 60 percent. Businesses, particularly in tourism-related areas, failed. According to a study by Morgan Stanley, the Asia-Pacific region's economy lost nearly \$40 billion due to SARS.⁵¹ The World Bank found that the East Asian region's GDP fell by 2 percent in the second quarter of 2003.⁵² Toronto experienced a 13.4 percent drop in tourism in 2003.⁵³



Environmental Factors

Geophysical phenomena such as shifts in temperature, wind, and rainfall patterns can precipitate the appearance of new diseases in new places. Weather and climate affect different diseases in different ways. For example, diseases transmitted by mosquitoes, such as dengue fever, Rift Valley fever, and yellow fever are associated with warm weather (additional information on these diseases can be found in Appendix B) and experts believe that an El Niño occurrence (a fluctuation of the ocean-atmosphere system in the tropical Pacific having important consequences for weather around the globe), may be a factor in the resurgence of malaria and cholera.⁵⁴ On the other hand, influenza becomes epidemic primarily during cool weather. Meningococcal meningitis is associated with dry environments, while cryptosporidiosis outbreaks are associated with heavy rainfall, which can overwhelm sewage treatment plants or cause lakes, rivers and streams to become contaminated by runoff which contains waste from infected animals.

Climate changes in North America are believed to be responsible for the growing populations of 2 new species of mosquitoes, including Asian tiger mosquitoes, in the continental U.S. These insects, which are believed to be successful bearers, or “vectors,” of diseases like LaCrosse encephalitis, yellow fever, dengue fever, and West Nile virus, now infest more than 30 states.⁵⁵

Large scale climatic change may also have an effect on the timing of migration of wild birds, which in turn can impact the movement of other species such as ticks and lice. Wild birds are important to public health because they can be infected by a number of microbes that can then be transmitted to humans. In addition, birds migrating across national and intercontinental borders can become long-range carriers of any bacteria, virus, parasite, or drug-resistant organism they harbor.⁵⁶ Wild birds are believed to be key to the rapid spread of West Nile virus across the entire country just 3 years after the first case was identified in New York in 1999. Similarly, migratory birds are being closely observed by human health and veterinary health officials as they monitor the spread of the H5N1 avian influenza virus worldwide.⁵⁷

Deforestation and reforestation also can be factors in the spread and prevalence of certain emerging infectious diseases. Globally,



rates of deforestation have grown significantly since the beginning of the 20th century. Driven by rapidly increasing human population numbers, large areas of tropical and temperate forests, as well as prairies, grasslands, and wetlands, have been converted to agricultural and ranching uses. The result has been an upsurge of certain infectious diseases, as the relationships between humans and disease vectors (carriers) shift. Deforestation, with subsequent changes in land use and human settlement patterns, has coincided with increased malaria prevalence in Africa, Asia, and Latin America.⁵⁸ Conversely, reforestation in the Northeastern and the upper Midwest regions of the U.S. has promoted an increase in the population of the white-tailed deer, an important host for the ticks that carry Lyme disease.⁵⁹

Social Inequities, Geopolitical Events, and Human Behavior

A number of societal factors contribute to the emergence and re-emergence of infectious disease. Poverty, lack of access to health care, poor sanitation, unsafe water, and a lack of proper hygiene all contribute to the expanding impact of infectious diseases.

Overcrowded and poor living conditions make people living in poverty especially vulnerable to communicable diseases such as TB and cholera. Limited access to health care and medicine can render otherwise treatable conditions such as malaria and TB fatal for those living in poverty. Urban decay and squalid living conditions and the presence of vermin also contribute to the spread of infections, such as plague. Meanwhile, contaminated water and inadequate sewage treatment systems in impoverished nations contribute to the spread of infectious diseases like cholera.⁶⁰

Poor nutrition and compromised immune systems are also key risk factors for several major diseases including lower respiratory infections, TB, and measles. There is increasing evidence that suggests that malnutrition is the underlying reason for increased susceptibility to infectious diseases especially in children. At the same time, infections, especially those associated

with diarrhea, can lead to malnutrition in young children, so that diarrheal illness is both a cause and an effect of malnutrition.⁶¹

War and civil strife generally result in a breakdown of domestic stability, food and water shortages, and destruction of the medical infrastructure, including existing vaccination programs. Refugee camps often are crowded and dirty, with little or no access to medical care or protection from disease transmission.⁶²

High-risk behaviors continue to be an important factor in the transmission of some infectious diseases. Sexual behavior and use of intravenous drugs continue to be primary modes of HIV transmission, and public health efforts over the last few decades have demonstrated how difficult such behaviors are to change. In developing nations, ignorance of preventive measures and the absence of social agencies to teach the avoidance of risky behaviors exacerbate the problem. Once diagnosed with a particular disease, failure to comply with prescribed treatment regimens is another factor of transmission. The emergence of drug-resistant TB can be attributed in large part to poor patient compliance with therapy.⁶³

PARASITIC DISEASES AND POVERTY IN THE U.S.

Parasitic diseases are rare in the U.S. However, these diseases have been found in certain low-income communities. Researchers find at-risk populations to include “people of color living in the Mississippi Delta and elsewhere in the American South, in disadvantaged urban areas, and in the U.S.-Mexico borderlands, as well as in certain immigrant populations and disadvantaged white populations living in Appalachia.”⁶⁴ Natural disasters, compounded by poverty, can also lead to spikes in these diseases, as was the case post-Hurricane Katrina along the Gulf Coast.

Some of the top exiting parasitic threats currently in the U.S. include:

- *Ascariasis* -- the most common worm infection in humans. It is caused by a parasitic worm that lives in the intestine, and infected just under 4 million people in 1974 according to the last survey, in the South and Appalachia.
- *Toxocariasis* -- a roundworm parasite transmitted in dog droppings. It has the potential to cause intestinal illness and blindness, according to the CDC, and infect up to 14 percent of the U.S. population. So far, this parasite has infected up to 2.8 million poor black children in inner cities, the South and Appalachia.⁶⁵
- *Strongyloidiasis* -- caused by a threadworm that lives throughout the body and can cause hyper-immune reactions, and infects 68,000 to 100,000 people each year.
- *Cysticercosis* -- associated with the pork tapeworm.
- *Giardiasis* -- diarrheal illness caused by a one-celled parasite.

Not all of these diseases are life-threatening, but they can lead to symptoms and complications that make the lives of people in poverty even harder. Chronic conditions that can develop from these diseases include asthma, epilepsy, diarrhea, fever and heart disease, which can adversely affect child development and hearing, as well as professional and financial stability.

3. IMPACT OF EMERGING INFECTIOUS DISEASES AT HOME

Emerging infectious diseases already pose a domestic health crisis.

West Nile virus is now endemic in the U.S. American troops are returning from Iraq and Afghanistan with highly drug resistant bacterial infections. Increasingly, locker rooms and gymnasiums are sources of staph infections. A heretofore unknown pathogen -- SARS -- emerged, causing illness, death, and economic mayhem. Public health officials remain on high alert for the first sign that the deadly H5N1 avian influenza virus has breached U.S. borders. An American citizen thought to have XDR-TB exposed the vulnerability of the U.S. public health system. Deadly foodborne disease outbreaks from domestic and imported agricultural products

are increasingly commonplace. And, the U.S. has experienced its first deliberate and lethal attack using a biological agent as a weapon.

Emerging and re-emerging infectious diseases pose risks for all Americans. For example, if a severe influenza outbreak were to occur, the U.S. government estimates that as many as 90 million Americans could become sick and 2 million might die.⁶⁶ The consequences of a bioterror attack involving smallpox or anthrax are almost unfathomable.

While U.S. public health officials must be prepared for such scenarios, they remain hypothetical. There are, however, a number of emerging and re-emerging infections that are real threats to the health of Americans as well as the U.S. economy today.

High Prevalence Rates and High Costs

There are 1.2 million people living with HIV/AIDS in the U.S., including more than 440,000 with AIDS.⁶⁷ There are an estimated 56,300 new cases of HIV diagnosed in this country every year.⁶⁸ Nearly 566,000 Americans have died of AIDS since 1981.⁶⁹ African Americans accounted for 49 percent of new HIV infections diagnosed in the U.S. in 2006, although they comprise only 13.8 percent of the population. The HIV infection rate among African Americans is 7 times higher than the rate among whites. The infection rate among Latinos is 3 times higher than the rate among whites.⁷⁰

As devastating as the health consequences of this infectious disease may be, the costs of treating HIV/AIDS are equally staggering. The annual per-patient medical expenses associated with doctor appointments, laboratory tests, and drugs to prevent or treat HIV-related opportunistic infections average from \$18,000 - \$20,000, with even higher costs for those with more advanced HIV-related illness. These costs do not include those related to lost productivity.

The costs to the American taxpayer are also high. In Fiscal Year 2007, total federal spending on HIV/AIDS-related medical care, research, prevention, and other activities in the U.S. was \$23.3 billion.⁷¹ Additionally, during the same time period, the share of state-Medicaid spending on AIDS was estimated to be \$5.5 billion and states reported spending \$294 million on their AIDS Drug Assistance Programs.⁷²

The MRSA numbers are alarming too. A 2007 CDC-supported study published in the *Journal*

of the American Medical Association estimated that MRSA infects more than 94,000 people and kills nearly 19,000 annually nationwide.⁷³ That makes it the sixth leading cause of death in the U.S. MRSA-specific studies suggest that the additional cost of treating an antibiotic-resistant staph infection versus one that is not resistant range from a minimum of \$3,000 to more than \$35,000 per case. In 2005, such infections cost the health care system (patients and hospitals) an extra \$830 million to \$9.7 billion, before taking into account indirect costs related to patient pain, illness, and time spent in the hospital.⁷⁴

Hepatitis C is a liver disease caused by HCV and is transmitted through blood or other body fluids. These infections sometimes result in an acute illness, but most often become a chronic condition that can lead to cirrhosis of the liver and liver cancer.

In 2006, there were an estimated 19,000 new hepatitis C virus infections in the U.S. and an estimated 3.2 million Americans have chronic hepatitis C virus infection. Approximately 8,000-10,000 people die every year from hepatitis C related liver disease.⁷⁵ It is the leading cause of cirrhosis and liver cancer and the most common reason for liver transplantation in the U. S.

According to the American Liver Foundation, medical expenditures for people with hepatitis C are estimated to be \$15 billion annually. The projected direct and indirect costs of hepatitis C will be \$85 billion for the years 2010-2019, as the number of people chronically infected will likely continue to increase.⁷⁶

HEPATITIS C OUTBREAK IN LAS VEGAS

In February 2008, CDC investigators responded to a request from the Nevada health officials to help investigate 3 cases of hepatitis C (HCV) in people who had undergone procedures at the same Las Vegas endoscopy clinic. Three additional cases were identified later. During the investigation of the clinic, where routine colonoscopies were performed, health officials found that the re-use of syringes was the likely cause of transmission. Forty-thousand people were then notified that they might have been exposed to HIV and HCV, in what a federal health official called the largest notification of its kind in U.S. history.⁷⁷ The clinic was subsequently shut down by city officials.

Infections Making a Comeback

In addition to emerging infections, Americans also are increasingly at risk from re-emerging infectious diseases. For example, after seeing a decline in TB cases in the U.S. over the last decade, this contagious airborne disease could be on an upswing

Of particular concern is the number of cases of drug-resistant TB found in foreign-born individuals now residing in the U.S. According to a study conducted by CDC researchers, 57 percent of all TB cases in the U.S. were among foreign-born individuals in 2006.⁷⁸ Approximately 10 percent of drug-resistant TB infec-

tions occurred among immigrants, refugees, and foreign visitors, compared with a little more than 4 percent of U.S.-born residents with active TB infection.⁷⁹

Additional information on latent TB and active TB infection can be found in Appendix A.

Other infectious diseases, once thought to be under control, have experienced recent outbreaks in the U.S. They include pertussis (especially among adolescents), mumps, and measles, all of which are vaccine-preventable.

AN INTERNATIONAL TB SCARE

The threats posed by XDR-TB garnered public attention in May 2007, when Andrew Speaker, a U.S. citizen with drug-resistant tuberculosis, led public health officials on a trans-Atlantic chase.

The incident began when Speaker flew to Europe on a commercial airline for his wedding and honeymoon. He was aware that he had an active case of drug-resistant TB, but it was not until he was out of the U.S. that tests suggested he had XDR-TB. CDC officials tracked Speaker down in Rome and asked him to turn himself into Italian health officials. Instead, he and his wife flew commercially to Prague, then on to Montreal, and drove by car back into the U.S. Speaker claims he took these actions because CDC indicated that he would be held in Italian quarantine for up to 2 years.

Out of concern that Speaker could have infected fellow travelers with the disease, health officials advised anyone who flew with him on the trans-Atlantic flights to be tested. Subsequently, Speaker was treated at the National Jewish Medical and Research Center in Denver, where it was announced that Speaker's earlier diagnosis was incorrect and that he instead had the more treatable MDR-TB. CDC later confirmed this diagnosis.

The incident raised serious questions about the effectiveness and timeliness of TB testing, U.S. border security, and the practicality of international restrictions on travel by people with infectious diseases. A Congressional investigation into the incident found significant security gaps, heightening concern about vulnerability to potential cases of pandemic influenza or smallpox.

DENGUE FEVER NIPPING AT OUR BORDERS

Dengue fever is a flu-like illness that can be painful and debilitating and is sometimes referred to as “break bone” fever that is transmitted by mosquitoes. The more severe dengue hemorrhagic fever and dengue shock syndromes can be fatal.⁸⁰

Most common in tropical and subtropical regions, public health experts believe that dengue is one of the world’s most important re-emerging diseases. Worldwide, 50 to 100 million cases of dengue infection occur each year. This includes 100 to 200 cases in the U.S., mostly in people who have recently traveled abroad. Many more cases likely go unreported because some health care providers do not recognize the disease.

Mosquitoes that can transmit the illness have been found in 36 U.S. states and are of particular concern along the U.S.-Mexico border and in Puerto Rico.⁸¹ In 2001, there was a dengue fever epidemic in Hawaii that sickened at least 120 people.⁸²

Food-Related Infectious Diseases on the Rise

“FOODBORNE ILLNESSES ARE DEFINED AS DISEASES, USUALLY EITHER INFECTIOUS OR TOXIC IN NATURE, CAUSED BY AGENTS THAT ENTER THE BODY THROUGH THE INGESTION OF FOOD. EVERY PERSON IS AT RISK OF FOODBORNE ILLNESS.”⁸³

-- WORLD HEALTH ORGANIZATION

Infectious diseases transmitted by foods have become a major public health concern in recent years. It seems that hardly a month goes by without the report of a foodborne illness outbreak in the U.S.

Approximately 76 million Americans -- nearly one-quarter of the U.S. population -- are sickened by foodborne disease each year. Of these, an estimated 325,000 are hospitalized and 5,000 die. Medical costs and lost productivity due to foodborne illnesses are estimated to cost \$44 billion annually.⁸⁴ Major outbreaks can also contribute to significant economic losses in the agriculture and food retail industries.⁸⁵

Several new foodborne pathogens have emerged over the last few decades. *E. coli* O157:H7 was first identified in 1982 during

an outbreak of bloody diarrhea traced to hamburgers from a fast-food chain.⁸⁶ *Cyclospora* emerged in 1992 as a foodborne pathogen, and was later traced to outbreaks in the U.S. from imported Guatemalan raspberries.⁸⁷ In March 2008, melons imported from Honduras caused *Salmonella* infections in 16 states; and beginning in April 2008, a *Salmonella* outbreak, thought to be associated with jalapeño and Serrano peppers imported from Mexico, sickened at least 1,400 Americans in 43 states.⁸⁸ In 2007, the U.S. Department of Agriculture issued 20 separate meat recalls due to potential *E. coli* contamination, and in February 2008, the department issued its largest beef recall in history -- 143 million pounds of beef -- from a California meatpacking company.⁸⁹

“I, for the life of me, cannot understand why the terrorists have not attacked our food supply, because it is so easy to do.”

-- FORMER U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES SECRETARY, TOMMY THOMPSON, DECEMBER 2004.

Agroterrorism is the “deliberate introduction of an animal or plant disease with the goal of generating fear, causing economic losses, and/or undermining stability.”⁹⁰

The deliberate contamination of our nation’s food supply is a serious threat that could have a quick, widespread impact. In January 2004, the Bush Administration responded to this very real threat with *Homeland Security Presidential Directive/HSPD- 9*, “Defense of United States Agriculture and Food.”⁹¹ This directive calls for a coordinated national approach to countering threats to the food supply.

4. THE NEED TO IMPROVE INFECTIOUS DISEASE PREVENTION

Scientists worldwide -- government and academic, together with their industry partners and international collaborators -- have made great strides in understanding emerging and re-emerging infectious diseases. Many of these discoveries have resulted in novel diagnostics, anti-infective therapy, and vaccines. Yet, much remains to be done. The U.S. can,

and should, improve and expand its diagnostic and disease surveillance capabilities, and dramatically increase its investment in developing new treatments and vaccines. Scientists also need to better understand mechanisms of drug resistance and develop new ways to circumvent this growing public health threat.

Surveillance

Disease surveillance is defined as the “systematic collection and analysis of data and the provision of information which leads to action to prevent and control a disease, usually of an infectious nature.”⁹² The primary purpose of disease surveillance is to predict, observe, and minimize harm caused by outbreaks, pandemics, and pandemic situations, as well as to better understand what factors might contribute to the spread of the disease. In the U.S., state and local health departments, in collaboration with CDC, are responsible for disease surveillance. The National Electronic Disease Surveillance System (NEDSS), a component of the Public Health Information Network (PHIN), is a CDC-led initiative that was developed to integrate and standardize the tracking of infectious diseases at the local level. Additionally, BioSense, another component of PHIN, collects syndromic surveillance, like patients’ symptoms, quantities and types of prescriptions, and emergency room visits to alert health officials to possible disease outbreaks or health emergencies.

The U.S. government also implements or participates in more than 25 specialized systems for monitoring diseases. The networks include the Global Emerging Infectious Diseases Sentinel Network, also known as GeoSentinel; EMERGENCY ID NET; the Foodborne Diseases Active Surveillance Network (FoodNet); the Active Bacterial Core Surveillance System; the National Respiratory and Enteric Virus Surveillance System; the National Tuberculosis Genotyping and Surveillance Network; and the National Influenza Surveillance Systems, among others.

Despite this proliferation of networks, the overall system of disease surveillance in the U.S. has not developed into a robust, coordinated capability. Consider for example, the delay in identifying the source of the

2008 multi-state foodborne outbreak, which initially implicated tomatoes before identifying the source as peppers. Or consider the possibility of a domestic outbreak of a new strain of influenza virus.

That is why CDC should make it a priority to ensure that every state and local health department in the U.S. is part of a 21st-century disease surveillance system that is interoperable among jurisdictions and agencies to ensure rapid information sharing. Surveillance systems should be able to detect and characterize known infectious disease outbreaks, new syndromes (e.g., SARS in 2003), or a bioterrorist attack. Plans should ensure adequate laboratory surveillance of influenza and other infectious diseases, as well as testing for pathogens such as *E. coli* and XDR-TB.

Furthermore, CDC should consider how health information technology (HIT) can be mobilized far more effectively to improve surveillance capability and overall public health preparedness. When coordinated, HIT systems can facilitate data exchange among public health partners and facilitate the management of data from health care delivery facilities, laboratories, and health agencies.

At the same time the U.S. needs to be a leader in efforts designed to accurately assess the burden of infectious diseases in developing countries, detect the emergence of new microbial threats, and direct global prevention and control efforts. The nation’s endorsement and subsequent compliance with the 2005 revisions to the International Health Regulations (IHR), which encourage nations to work together to take preventive measures against, as well as detect, report on, and respond to, public health emergencies of international concern, is a step in the right direction.

Most traditional global disease surveillance programs target only specific diseases (e.g., influenza or polio) and the infrastructure and support is relatively weak for the more difficult task of tracking emerging and re-emerging infectious diseases. This is especially true in developing countries, where scarce human and material resources may not support even routine surveillance tasks, such as the recording of births and deaths. Recent international initiatives to expand capacity for the detection and surveillance of HIV/AIDS and avian influenza have not been broadened to enable a look at all major

infectious disease threats. Many public health officials support expansion of these existing systems because infectious diseases – often of animal origin – are a major cause of morbidity and mortality in poorer populations, and such environments frequently serve as incubators for emerging pathogens.⁹³

The U.S. should enhance its commitment to the 2005 IHR revisions by increasing support for CDC's Coordinating Office for Global Health, including expanding the number of its Global Disease Detection Centers. Similarly, DOD and NIH should expand and increase overseas program sites and research.

INTERNATIONAL HEALTH REGULATIONS (2005)

The International Health Regulations (2005) (IHR) govern the roles of WHO and 194 nations (Member States) with respect to disease outbreaks and other public health events with international impact. The regulations update the previous version of the IHR, which was adopted in 1969. They are designed to prevent and protect against the international spread of diseases while minimizing interference with world travel and trade.

The revised IHR, which became effective in 2007, gives WHO clearer authority to recommend to its Member States measures that will help contain the international spread of disease, including public health actions at ports, airports, and land borders, and on means of transport that involve international travel. The revised regulations include a list of 4 diseases -- smallpox, polio, SARS, and human cases of new subtypes of human influenza -- that Member States must immediately report to WHO. The U.S. government began complying with the revised IHR on July 18, 2007.⁹⁴

Diagnostics

New rapid diagnostic tests are needed across the spectrum of emerging infectious diseases. Many existing diagnostic tools are outdated and difficult to use. For example, the standard test for diagnosing active TB in most of the world is smear microscopy, generally of sputum sample. Quality samples are hard to obtain; moreover, this test is over 100 years old and is only 50 percent accurate, and cannot determine drug susceptibility. Failure to quickly and accurately detect infections, such as TB, can be deadly and costly. There is more opportunity for an infection to spread that longer that it goes undetected. In addition, the infection is more likely to be treated with a broad spectrum drug, which increases the risk for resistance and adverse outcomes.

A focus on point-of-care testing is particularly important. Developments in nanotechnology have the potential to improve sensitivity and specificity of point-of-care, hand-held diagnostics over time and at a potential cost-savings over current technology. This type of diagnostic tool would be particularly useful during an influenza pandemic.

The next generation of effective diagnostic tools needs to be made available worldwide for use by a workforce that has been adequately trained in their use. Also, given that 35 of the most recent emerging diseases, including avian influenza, monkeypox, West Nile Virus and SARS, have been zoonotic (animal-borne) in origin,⁹⁶ updated diagnostic tools to improve disease detection in animals should also be a priority.

CLINICAL TRIALS FOR NEW ANTIBIOTICS ARE CHALLENGING

A clinical trial is the scientifically controlled study of the safety and effectiveness of a drug or vaccine, using consenting human subjects.

Clinical trials for new antibiotics are complicated and time consuming. Finding enough patients to enroll in clinical trials of new drugs to treat resistant pathogens is not easy. For many resistant pathogens, there are no rapid diagnostic tests available to help researchers to identify patients who would be eligible for their studies. By contrast, when enrolling patients in a clinical trial to test a new cancer drug, researchers know from the start whether a specific patient has the specific type of cancer they are targeting. With antibiotic clinical trials, that is not necessarily the case. As one industry consultant explained, in order to test a drug that is intended to treat resistant strains, “You have to wait for epidemics to break out in hospital wards, and you can’t predict when that will happen. It may take 5 years to complete a clinical study.”⁹⁷ That is one of the reasons that the need for new rapid diagnostics to detect drug resistant bacteria infections is particularly acute.

Treatment

While dramatic advances in science and medicine have enabled scientists, medical practitioners, and public health officials to make great strides in the struggle to control and treat infectious diseases, there is a significant amount of research, development, and testing that remains to be done.

Once considered “miracle drugs,” antibiotics successfully treat a range of bacterial infections, such as strep throat, ear infections, urinary tract infections, and pulmonary infections. However, overconfidence in existing antibiotics, over-reliance on them, disincentives for industry to develop new antibiotics (because a drug that takes decades to develop might be useful clinically for only a few years), lack of sufficient diagnostic tools, and competition from more highly profitable opportunities for pharmaceutical development and sale of medicines to treat chronic diseases, has resulted in a lag in the production of new classes of antibiotics. According to the Infectious Diseases Society of America, “the end result of the decline in antibiotic discovery research is that U.S. Food and Drug Administration (FDA) is approving few new antibiotics. Since 1998, only 12 new antibiotics have been approved, 2 of which are truly novel (i.e., defined as having a new target of

action, with no cross-resistance with other antibiotics). In 2002, among 89 new medicines emerging on the market, none was an antibiotic.”⁹⁹ This trajectory needs to change.

The development of new, improved therapies to treat drug resistant bacterial infections, as well as for influenza and other viruses is essential. According to FDA, because of rising costs, innovators often concentrate their efforts on products with potentially high market return. Developing countermeasures and medicines targeted for important public health needs (e.g., drug resistance, counterterrorism), less common diseases, diseases prevalent in the developing world, or individualized therapy is becoming increasingly challenging.¹⁰⁰ That is why additional incentives may be necessary to foster the development of treatment medications for those diseases that do not represent large market opportunities but have high rates of morbidity and mortality. The threat of certain drug resistance and viruses as agents of biological terrorism emphasizes the increased need for the development of new countermeasures, as well as broad-spectrum antibiotics, antivirals, and immunomodulators, especially for those agents for which there are no vaccines.¹⁰¹

Vaccines

The success of vaccines in preventing infectious diseases has been profound. The childhood diseases of diphtheria, tetanus, and polio are relatively rare in the developed world and are controlled in many developing countries. Smallpox, one of the most horrific killers in human history, was eradicated through the employment of an effective vaccine. However, despite some progress and the dedication of scientists worldwide, there still are no highly effective vaccines available to prevent 3 of the world's largest killers: HIV/AIDS, TB, and malaria. And, a large proportion of the world's children do not have access to currently-available, highly effective vaccines.

As science and medicine progress, sometimes at lightening speed, opportunities for major breakthroughs in vaccine development are very promising. Scientists have made significant advances in genomics, immunology, and biotechnology, including discoveries in reverse genetics methods for faster development of influenza vaccines and for new vaccines such as Gardasil and Cervarix, which protect against certain types of the human papillomavirus (HPV) infection that can cause cervical cancer in girls and young women.

Vaccine development and production is complex and is dictated by a set of variables, including the translation of basic research into the development of effective vaccines, regulatory requirements, liability concerns, and market forces, which include market disincentives for developing new vaccine

production methods and a pricing structure that may not adequately compensate industry for development costs in the years immediately following licensure.¹⁰²

Cultural obstacles, religious and ethical concerns, and misinformation about the safety and efficacy of vaccines can impact market size and increase the likelihood of vaccine-preventable diseases in those who are not immunized. For example, of the 95 patients who contracted measles during the 2008 outbreak in the U.S. and were eligible for vaccination (over 12 months of age), 63 were unvaccinated because of their or their parents' philosophical or religious beliefs.¹⁰³

The U.S. must continue to modernize its approach to vaccine production and delivery, increase domestic capacity to manufacture vaccines, and recognize that it has a responsibility to help assure that all the people of the world have access to vaccines. This is both a moral responsibility and a practical necessity; in a highly interdependent world, mitigating the impact of any infectious disease pandemic requires that all corners of the globe are protected equally. As part of this effort, the U.S. government must coordinate activities between the public and private sectors, and with academia. To effectively harness the scientific expertise potentially available for this endeavor, vaccine development and modernization efforts must be open and transparent to ensure that experts from government, industry, and academia from around the world have access to vital information.

New Technology

Geographers are contributing to the fight against emerging infectious diseases by turning satellite imaging and global positioning systems into tools to help prevent infection. In the early 2000s, scientists predicted an outbreak of the mosquito-borne Rift Valley fever in Kenya by using these devices. Scientists at the Goddard Earth Sciences and Technology Center and at the Walter Reed Army Institute of Research have discovered that outbreaks of Rift Valley fever follow sudden floods triggered by El Niño and a similar (yet lesser-known) climate disturbance called the "Indian Ocean Dipole." Using weather satellites to track sea

surface temperature patterns in the Indian and Pacific oceans, scientists now believe they have found a way to predict outbreaks up to 5 months in advance. By predicting the likely onset of an outbreak, the geographers prompted local public health officials to implement prevention strategies.¹⁰⁴

Hantavirus outbreaks in the U.S. Southwest could also be monitored in this way. The virus is carried by deer mice and can kill people who have been exposed to it. Like Rift Valley fever, Hantavirus is correlated with rainfall, so the same kind of bioclimatic rhythms can be used to predict an outbreak.¹⁰⁵

5. FINANCIAL INCENTIVES ARE CRITICAL

If the demand for new diagnostics, therapeutics and vaccines to combat emerging infections is so urgent, why has industry not answered the call? The answer requires a closer look at market forces and business strategy.

The development of new medical technologies is a long and expensive process. Pharmaceutical industry standards for new drug development are a good example. These standards predict, on average, a 10-year development period from drug discovery to licensure at a price tag around \$1 billion.¹⁰⁶ A significant proportion of the time and funding required comes in advanced development. In addition, the expected failure rate is high; only 10 percent of candidate drugs in Phase I trials ever make it to licensure.¹⁰⁷

In order to maintain profitability in a highly competitive market, pharmaceutical and biotechnology companies must minimize the risk of development while maximizing the reward (profit) potential for products. Risk is minimized by spreading it among multiple drug candidates, pursuing class analogs similar to already successful products, and utilizing existing and proven systems for developing and manufacturing. Reward is maximized by targeting diseases with proven high returns. Generally drugs treating chronic and highly prevalent diseases create the best sales opportunities.

Unfortunately, most countermeasures for emerging infectious diseases present an unfavorable risk-reward balance for industry. NIAID funding has strengthened the academic research base for emerging infectious diseases and has produced promising candi-

date drugs. But these are still few for each disease, and success may rest on the fate of one or 2 products. New types of products also require new delivery systems (e.g., “gene gun” system for administering DNA vaccines) and new production systems (e.g., cell-based production systems for influenza vaccine) that carry their own development risks and costs. Finally, many emerging diseases are currently uncommon in the U.S. or are treated with short-course therapy, thus creating a small market for their sales.

When a large pharmaceutical or biotechnology company is faced with the choice of pursuing a new drug for TB or the next multi-billion dollar statin, shareholders are much less interested in altruism than in a wise investment that minimizes opportunity costs. As a result, a significant proportion of product development for biodefense or emerging infectious diseases rests with small companies. Many of these are supported by venture capital, and they lack institutional experience of carrying a product from discovery to licensure.

Advocates, policymakers, pharmaceutical companies, and researchers debate ways in which research and development of vaccines, treatments and diagnostic tools can be accelerated, but most agree that a combination of initiatives is needed to fight emerging infectious diseases. No one-size-fits-all approach will spur adequate investment in biomedical research and development on emerging infectious diseases. Different medications, vaccines, diagnostic tools, and surveillance systems have different market potential and require varying levels of up-front investment.

Public-Private Partnerships

Public-private partnerships are proving to be effective in the search for new vaccines and drugs. Treatments for dengue fever, malaria, and MDR-TB are under development through the Novartis Institute for Tropical Diseases, a public-private partnership involving the Swiss-based Novartis pharmaceutical company and the Singapore Economic Development Board.¹⁰⁸ Working with public and private research laboratories worldwide, the Global Alliance for TB Drug Development is committed to accelerating the discovery and development of new TB drugs that will shorten treatment, be effective against susceptible and resistant

strains, be compatible with antiretroviral therapies for those HIV-TB patients currently on such therapies, and improve treatment of latent infection.¹⁰⁹ The GAVI Alliance’s (formerly the Global Alliance for Vaccines) Accelerated Development and Introduction Plans (ADIPs) have promoted research and “negotiation with the pharmaceutical and public health sectors to achieve rapid, successful introduction of the pneumococcal and rotavirus vaccines.”¹¹⁰ Proponents of public-private partnership urge greater support of initiatives that involve small-scale commercial endeavors.

A massive infusion of philanthropic funds is also stimulating investment in research and development for vaccines and medicines, professional training, and public education efforts. The Bill and Melinda Gates Foundation is spearheading large global health initiatives, including support for the

Global Fund to Fight AIDS, Malaria and Tuberculosis. Former President Bill Clinton is supporting the Sabin Vaccine Institute's "Stop Neglected Tropical Disease Campaign."¹¹¹ British Prime Minister Gordon Brown recently committed his nation to buying 20 million mosquito nets for malaria-ravaged nations.

U.S. Government Programs to Spur Investment

The U.S. government has several measures already in place to encourage private sector investment for the development of vaccines, medicines and diagnostics. In addition to the specific measures described below, researchers

may be able to take advantage of existing programs that are well established. For instance, the far-reaching global HIV vaccine trial infrastructure may be a useful model for testing tuberculosis treatments or vaccines.

Orphan Drug Act

The Orphan Drug Act (P.L. 97-414, as amended) includes various incentives that have stimulated a considerable amount of interest in the development of orphan drug and biological products. The incentives include tax credits for clinical research undertaken by a sponsor to generate required data for marketing approval, and 7 years of marketing exclusivity for a designated drug or biological product approved by FDA.

For the purposes of the Act, an "orphan drug" is one that would treat or prevent a rare disease or condition that affects fewer than 200,000 persons in the U.S., or that may affect more than 200,000 persons in the U.S., but for which there is no reasonable expectation that the cost of developing and producing the drug would be recovered from its U.S. sales.¹¹²

Project BioShield and BARDA

In 2004, Congress passed the Project BioShield Act to jump-start the nation's ability to develop, purchase, and deploy cutting-edge countermeasures against a bioterrorism attack. The law also granted the federal government new authority to expedite research and development on the most promising and time-sensitive medicines to defend against bioterror. Congress authorized \$5.6 billion for Project BioShield over 10 years so that the government could purchase and stockpile vaccines and drugs to fight anthrax, smallpox, and other potential agents of bioterror. However, funding for Project BioShield has been significantly lower than the level authorized. For example, the program was authorized at \$1.07 billion for Fiscal Years 2006-08, but received an appropriation of only \$102 million in Fiscal Year 2008.

In signing the bill into law, President Bush acknowledged the vital role that the private sector plays in biodefense efforts by taking risks to bring new treatments to the market. He said, "By acting as a willing buyer for the best new medical technologies, the government ensures that our drug stockpile remains safe, effective, and advanced. The federal government and our medical pro-

fessionals are working together to meet the threat of bioterrorism -- we're making the American people more secure."¹¹³

In 2006, Congress enacted the Pandemic and All-Hazards Preparedness Act (PAHPA), which in part, directed HHS to establish the Biomedical Advanced Research and Development Authority, or BARDA, and authorized funding of advanced development of medical countermeasures, such as vaccines, drugs, and diagnostic tools for public health emergencies affecting national security.¹¹⁴

BARDA is the umbrella organization within the Office of the Assistant Secretary for Preparedness and Response at HHS that provides an integrated, systematic approach to the development and purchase of the medical countermeasures, treatments, and diagnostic tools for public health medical emergencies. Upon its creation, BARDA assumed responsibility for 2 existing separate, but complementary projects: The Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) and Project BioShield.

There is some expectation among researchers and government officials that the establishment of BARDA and its over-

sight of Project BioShield may improve the chances of success during the development phase of countermeasures. According to the Congressional Research Service, “one of BARDA’s roles is to support the advanced research and development of promising countermeasures. In theory, funding this part of the development process through

such a dedicated mechanism could allow countermeasures to further mature through the development process longer before competing for a Project BioShield contract. This could reduce the risk that a countermeasure will fail while under a Project BioShield contract.”¹¹⁵

Priority Review Voucher for Neglected Tropical Diseases

In September 2007, Congress approved an amendment sponsored by Senators Sam Brownback (R-KS) and Sherrod Brown (D-OH) to the Food and Drug Administration Revitalization Act, which created a transferable voucher to “encourage treatments for tropical diseases.”¹¹⁶ The amendment allows the sponsor of a newly approved drug or vaccine, which prevents or treats an eligible tropical or neglected disease, to receive a priority review voucher, which can then be applied to another product.

Priority review reduces the time it takes FDA to assess a product submitted for approval from an average of 18 months to “no longer” than 6 months. The company obtaining the voucher can use it for another human drug submission, affording an opportunity to get that product to market many months sooner. Alternatively, the

owner of the voucher can sell it to another company on the open market.¹¹⁷ New drugs or treatments for neglected tropical diseases may also qualify for market exclusivity and tax credits under the Orphan Drug Act.

Unlike many other incentive mechanisms, the voucher program does not require any up-front financial outlays by governments or donors, and no budgetary provisions are required. However, some worry that while developing new drugs and treatments is a crucial step to alleviating the burden of tropical diseases, the voucher program does not guarantee that producers will make new treatments available in sufficient quantities or at prices that will be affordable to individuals.¹¹⁸ Vouchers, which are not universally supported by medical experts or the pharmaceutical industry, could be worth as much as \$500 million according to some estimates.¹¹⁹

Strategies to Address Antimicrobial Resistance (STAAR) Act

Introduced in 2007 by Senators Sherrod Brown (D-OH) and Orrin Hatch (R-UT) and Representatives Jim Matheson (D-UT) and Michael Ferguson (R-NJ), the STAAR Act is designed to enhance the U.S. ability to respond to the antimicrobial resistance problem. The bill would provide comprehensive strategies to strengthen federal antimicrobial resistance surveillance, prevention and control, and research efforts. The legislation would authorize new funding and strengthen coordination within

HHS agencies as well as across multiple federal departments, including Agriculture, Veterans Affairs, Labor, and Defense, as well as the Environmental Protection Agency.

The STAAR Act would also provide new opportunities to address the global antimicrobial resistance problem. The STAAR Act includes a comprehensive set of specific actions to avoid a public health crisis that is taking and/or debilitating the lives of hundreds of thousands of Americans annually.¹²⁰

6. RECOMMENDATIONS

The magnitude and urgency of addressing emerging and resurging diseases demand renewed attention, dedication, and sustained resources to ensure the health and safety of the nation and of the world.

U.S. policy makers must abandon a point of view that emerging infectious diseases in the developing world are a back-burner concern for Americans. And the nation's commitment to eliminating these diseases, or mitigating their impact on global mortality and morbidity, can no longer be based on international goodwill alone. Emerging and re-emerging diseases, especially those related to potential bioterror threats, are a matter of national security.

Trust for America's Health (TFAH) recommends the following actions, many of which mirror those made by the Board on Global Health and the IOM in their 2003 report, *Microbial Threats to Health: Emergence, Detection, and Response*.¹²¹

1. U.S. federal, state, and local governments should allocate the necessary resources to build and sustain the nation's public health capacity to respond to emerging diseases that are naturally occurring or intentional.

The nation's public health capacity must be enhanced to respond quickly to emerging disease threats and to monitor infectious disease trends. Prevention and control capacity should be expanded at the local, state, and national levels and be executed by an adequately trained and competent workforce. Examples include enhancing surveillance (medical, veterinary, and entomological [related to insects]); augmenting laboratory facilities; building epidemiological, statistical, and communication skills among the workforce; and implementing information and logistical systems to ensure the rapid utility and sharing of information among the public, industry, health care facilities, and all levels of government.

2. The U.S. should further its leadership role in enhancing the global capacity to respond, control, and eliminate infectious disease threats.

The U.S. should continue efforts to coordinate with key international agencies such as WHO, with active communication, collabora-

tion, and coordination with industry, academia, private organizations, and foundations. Additional investments should take the form of financial and technical assistance, operational research, enhanced surveillance, and efforts to share both knowledge and best public health practices across national boundaries. The U.S. should exert its leadership in setting global goals for elimination or eradication of diseases where this is possible, such as malaria and tuberculosis. In addition, the President should appoint a distinguished public health official to a new high-level position responsible for coordinating the U.S. effort and for serving as a point of contact for public, private, and public-private efforts.

3. The U.S. should enhance its leadership role in promoting the implementation of a comprehensive system of surveillance for global infectious diseases that builds on the current global capacity of infectious disease monitoring.

This multinational effort will require regional and global coordination, expertise, and financial resources from participating nations. A comprehensive system is needed to accurately assess the burden of infectious diseases in developing countries, detect the emergence of new threats, and direct prevention and control efforts. Sustainable progress in these efforts will require health agencies to broaden partnerships to include philanthropic foundations and international institutions such as the World Bank and the United Nations. At the same time, infectious disease surveillance systems in developed nations will require sustained investments to strengthen their capacity and make them more effective, accurate, and timely.

4. The U.S. government should develop a comprehensive, multi-year, government-wide research agenda for emerging infectious disease prevention and control in collaboration with state and local public health partners, academia, and industry.

This agenda should be designed to investigate the role of genetic, biological, social, economic, political, ecological, and physical environmental factors in the emergence of infectious diseases in the U.S. and throughout the world. This agenda should also include the development and assessment of

public health measures to address emerging and re-emerging diseases, including the intentional use of biological agents. The research agenda should be flexible enough to permit rapid assessment of new and emerging threats, and should be rigorously reevaluated every 5 years to ensure that it is addressing areas of highest priority.

Components of the research agenda should include:

- **A national vaccine strategy for protecting the U.S. population from emerging and re-emerging infectious diseases.** The federal government should explore innovative mechanisms, such as cooperative agreements between government and industry or consortia of government, industry, and academia, to accelerate research and development efforts.
- **A national strategy for developing new antimicrobials, as well as producing an adequate supply of approved antimicrobials.** This strategy should include plans for stockpiling and distributing antibiotics, antivirals, and antitoxins for naturally occurring or intentionally introduced disease threats.
- **A national strategy to better understand the mechanisms of antibiotic resistance and to develop and evaluate interventions to prevent and control resistance in human, animal and agricultural environments.**
- **A national strategy for developing new rapid, cost-effective sensitive diagnostics to identify targeted pathogens, ensure appropriate use of existing antimicrobials in the clinical setting, and reduce the cost of clinical trials for new antimicrobials thereby serving as an incentive for greater industry research and development.** Development of rapid, point-of-care diagnostic tests for TB, including drug-resistant TB; health care associated bacterial infections; and various strains of the influenza virus, should be priorities.
- **Research on innovative systems of surveillance that capitalize on advances in health information technology.** Integration of electronic medical records into public health surveillance systems should be pursued.
- **Research on vector control.** The development of safe and effective pesticides and repellents, as well as strategies for pro-

longing the use of existing pesticides is paramount in the absence of vaccines to prevent most vector-borne diseases.

5. The U.S. government, professional health organizations, academia, health care delivery systems, and industry should expand efforts to decrease the inappropriate use of antimicrobials in human medicine, agriculture and aquaculture through:

- Expanded outreach and better education of health care providers, veterinarians, drug dispensers, the food industry, and the general public on the inherent dangers associated with the inappropriate use of antimicrobials.
- Increased use of diagnostic tests, as well as the development and use of rapid diagnostic tests, to determine the nature of the infection and drug sensitivity, thereby ensuring a more appropriate use of antibiotics.

6. The U.S. government should work with academia, private organizations, and foundations to recruit, retain, and train public health professionals capable of identifying, verifying, preventing, controlling, and treating emerging infectious diseases.

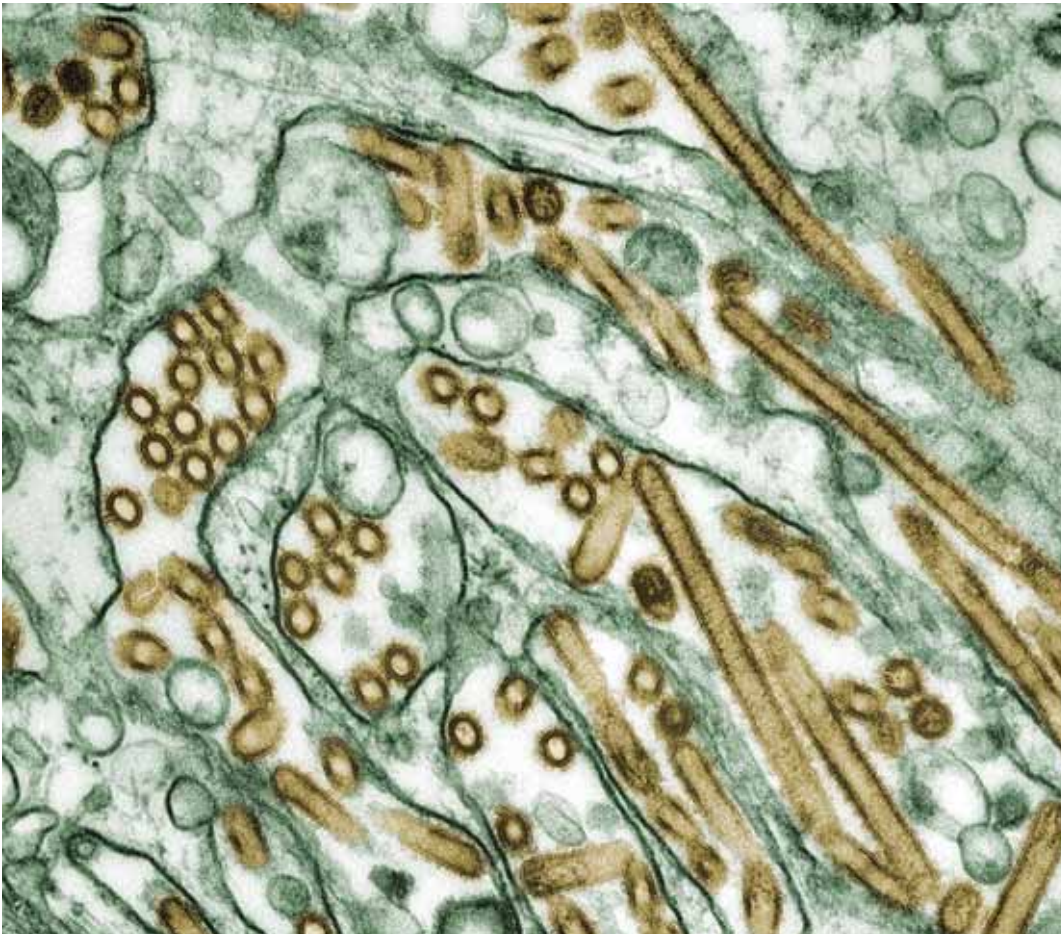
- Training should combine field and laboratory approaches to infectious disease prevention, diagnosis, and control. Federal agencies should develop these programs in close collaboration with state and local public health partners and academic centers and should include an educational, hands-on experience at state and local public health departments.

7. The U.S. government should support intensified public health education efforts to prevent the spread of infectious diseases.

- The U.S. should launch public education campaigns on hand hygiene and cough etiquette, as well as the importance of complying with the recommended schedule of childhood and adult vaccines, including seasonal influenza vaccines. Additionally, disseminating information to the general public about the appropriate use of antibiotics should be a priority for the nation's public health departments.

8. The U.S. Congress should:

- Amend the Orphan Drug Act to explicitly address infectious diseases like MRSA, or create a parallel incentive system to address the unique concerns in this area. Specially tailored incentives are needed to spur the development of new antimicrobials, vaccines, and diagnostics.
- Fully fund BARDA, which was authorized at \$1.07 billion for Fiscal Years 2006-08, but was funded in Fiscal Year 2008 at \$102.1 million.
- Enact the Strategies to Address Antimicrobial Resistance (STAAR) Act to strengthen the U.S. response to the increasing antimicrobial resistance crisis through enhanced coordination, leadership, research, prevention and control, and surveillance.
- Request a professional judgment budget for a comprehensive, multi-year, government-wide research agenda for emerging infectious disease prevention and control and fully fund it. For example, according to the professional judgment of senior NIH researchers, a \$50 million investment in TB research could have a significant impact on disease control and mitigation globally, including vaccine development.
- Enhance appropriations for ongoing emerging infectious disease programs at NIH, CDC, DOD, the Department of Agriculture, and the Department of Homeland Security.
- Increase appropriations for global surveillance efforts, including an increase in funding to \$45 million for the CDC's Global Disease Detection program, which was funded at \$31 million in Fiscal Year 2008.
- In light of the threat emerging and re-emerging diseases pose to Americans, Congress should fully fund CDC's programs to support state and local public health departments' all-hazards preparedness activities. At a minimum, funding should be restored to the Fiscal Year 2005 level of \$919 million. In Fiscal Year 2008, programs to upgrade the capacity of state and local public health departments were funded at \$746 million.



Colorized transmission electron micrograph of Avian influenza A H5N1 viruses (seen in gold) grown in MDCK cells (seen in green).

APPENDIX A: THE WORLD'S DEADLIEST INFECTIOUS DISEASES

Many of the global efforts to reduce the burden of infectious diseases are concentrated on HIV/AIDS, TB, and malaria. Combined, these 3 diseases account for approximately 500 mil-

lion or more illnesses a year and at least 6 million deaths.¹²² Also, hepatitis C (HCV) infections are pervasive worldwide -- an estimated 200 million people have the virus.

Human Immunodeficiency Virus (HIV) Acquired Immunodeficiency Syndrome (AIDS)

AIDS is a chronic, life-threatening condition caused by the human immunodeficiency virus (HIV). By damaging or destroying the cells of the body's immune system, HIV interferes with the ability to effectively fight off viruses, bacteria, and fungi that cause disease. This makes individuals with HIV more susceptible to certain types of cancers and to opportunistic infections that the body would normally resist, such as pneumonia, TB, and meningitis.¹²³ The virus itself is known as HIV. The term acquired immunodeficiency syndrome (AIDS) is used to mean the later stages of an HIV infection.

An individual can become infected with HIV in several ways, including unprotected sex; transfusion of infected blood; transmission through needle sharing or accidental needle sticks; re-use of syringes in a medical setting, especially where the medical infrastructure is lacking; or transmission from mother to child during pregnancy, delivery, or through breast feeding. In rare cases, the virus may be transmitted through organ or tissue transplants or unsterilized dental or surgical equipment.¹²⁴

In the nearly 3 decades since the first reports of the disease, AIDS has become a global pandemic. Worldwide, an estimated 38.6 million people are living with HIV, nearly half of them women and girls between the ages of 15 and 24. And though the spread of the virus has slowed in some countries, it has escalated or remained steady in others. In 2007, more than 2.7 million people were newly infected with HIV; 25 million have died of AIDS since the pandemic began, 2 million in 2007 alone.¹²⁵

Despite improved treatments and better access to care for people in the hardest-hit parts of the world, most experts agree that the pandemic is still in the early stages. With a vaccine probably years away, the best hope

for stemming the spread of HIV is to focus on prevention, treatment, and education.

The U.S. commitment to the global battle against HIV/AIDS has been impressive. In 2003, President Bush launched the President's Emergency Plan for AIDS Relief (PEPFAR), committing \$15 billion over 5 years to combat global HIV/AIDS -- the largest international health initiative in history to fight a single disease. In July 2008, the U.S. Congress reauthorized PEPFAR and increased its funding level to \$39 billion over the next 5 years.¹²⁶ In addition, the new law provides funding to fight the diseases that complicate HIV/AIDS. It commits \$4 billion to fight tuberculosis -- which is the leading killer of Africans living with HIV -- and pledges an additional \$5 billion to combat malaria.

According to the White House, PEPFAR has already helped bring life-saving treatments to millions of people worldwide. For example, at the end of Fiscal Year 2007, PEPFAR was supporting life-saving antiretroviral treatment for approximately 1.7 million people living with HIV/AIDS in the 15 focus countries in Sub-Saharan Africa, Asia, and the Caribbean. When the President announced PEPFAR in 2003, only 50,000 people in all of sub-Saharan Africa were receiving treatment. PEPFAR has also supported treatment and care for nearly 7 million people, including millions of orphans and vulnerable children. At the signing of the PEPFAR reauthorization, President Bush observed that the initiative had allowed nearly 200,000 children in Africa to be born HIV-free.¹²⁷

There are 1.2 million people living with HIV/AIDS in the U.S., including more than 440,000 with AIDS.¹²⁸ There are an estimated 56,300 new cases of HIV diagnosed in this country every year.¹²⁹ Nearly 566,000 Americans have died of AIDS since 1981.¹³⁰

Hepatitis C (HCV)

Hepatitis C is a contagious liver disease that ranges in severity from a mild illness lasting a few weeks to a serious, lifelong illness. It results from infection with the hepatitis C virus (HCV), which is spread primarily through contact with the blood of an infected person. Hepatitis C can be either “acute” or “chronic.”

Acute hepatitis C virus infection is a short-term illness that occurs within the first 6 months after someone is exposed to the hepatitis C virus. Approximately 75 to 85 percent of people who become infected with hepatitis C virus develop chronic infection.

Chronic hepatitis C virus infection is a long-term illness that occurs when the hepatitis C virus remains in a person’s body. HCV can last a lifetime and lead to serious liver problems, including cirrhosis (scarring of the liver) or liver cancer.

People can become infected with the hepatitis C virus by:

- Sharing needles, syringes, or other equipment to inject drugs.
- Exposure to needle stick injuries in healthcare settings.
- Exposure to unclean tattooing or body-piercing instruments.
- Being born to a mother who has hepatitis C.

Less commonly, a person can also get hepatitis C virus infection through:

- Sharing personal care items that may have come in contact with another person’s blood, such as razors or toothbrushes.
- Having sexual contact with a person infected with the hepatitis C virus.¹³¹

Globally, 200 million people, or more than 3 percent of the world’s population are infected with HCV.¹³² CDC estimates that 3.2 million Americans have chronic HCV infection, and approximately 10,000 die each year from HCV liver disease.¹³³

Malaria

Although malaria has been virtually eliminated in developed nations with temperate climates, it is still prevalent in tropical and subtropical countries in Africa, Asia, the Middle East, South America, and Central America. Evolving strains of drug-resistant parasites and insecticide-resistant mosquitoes continue to make this emerging infectious disease a global health threat.

Malaria is caused by a single-celled parasite from the genus *Plasmodium* and is typically transmitted to humans by mosquitoes. Malaria can also be transmitted through blood transfusions, organ transplants, or contaminated needles or syringes. “Congenital” malaria refers to the transmission from a mother to her fetus before or during childbirth.¹³⁴

A malaria infection is generally characterized by recurrent attacks, each of which has 3 stages – chills, followed by fever, and then sweating. Along with chills, the person is likely to have headache, malaise, fatigue, muscular pains, occasional nausea, vomiting, and diarrhea. Within an hour or 2 of the initial symptoms, the body temperature rises, and the skin feels hot and dry. Subsequently, as the body temperature falls, a drenching sweat begins.¹³⁵

Doctors can treat malaria effectively with several medications, which are known collectively as “antimalarial drugs.” However, there is increasing worry about drug-resistant parasites that have rendered some of these medicines ineffective.

QUICK FACTS ON MALARIA

- More than 40 percent of the world’s population lives in areas where there is a risk of contracting malaria.
- A child dies of malaria every 30 seconds.
- More than one million people die of malaria every year, mostly infants, young children, and pregnant women; most of them live in Africa.
- Approximately 300-500 million cases of clinical malaria occur each year.
- Malaria accounts for at least \$12 billion in economic losses each year in Africa, and a reduction in annual economic growth estimated at 1.3 percent.

Source: World Health Organization

Tuberculosis (TB)

Tuberculosis has plagued mankind for centuries. Today, despite advances in treatment, TB is a global pandemic, fueled by the spread of HIV/AIDS, poverty, a lack of health services, and the emergence of drug-resistant strains of the bacterium that causes the disease.¹³⁶

Every year, about 9 million people develop active TB disease, and TB kills nearly 2 million people worldwide. The infection is common -- about one-third of the human population is infected with TB, with one new infection occurring every second.¹³⁷

TB is a contagious airborne disease caused by infection with *Mycobacterium tuberculosis*. TB typically affects the lungs; however it also may affect any other organ of the body, such as the brain, the kidneys, or the spine.

There is a difference between latent TB infection and active TB disease, which makes people sick and can be spread to others. One-third of the world's population has the TB bacterium in their bodies, and they are considered to have a TB infection. Those who do not get sick are known to have latent TB infection, which is not contagious. TB bacteria can remain in this dormant state for months, years, and even decades without increasing in number and without making the person sick. Most people with latent TB infection will test positive on the tuberculin skin test, or their chest X-ray will show signs of latent TB, but will not develop active TB disease, may never get sick, may never show any symptoms, and may never spread the bacteria to others.¹³⁸

However, approximately one in 10 people infected with TB bacteria develop active TB disease. When an individual develops active TB, it means the TB bacteria are multiplying and attacking the lung(s) or other parts of the body. Symptoms of active disease include cough, loss of weight and appetite, fever, chills, and night sweats as well as symptoms from the specific organ or system that is affected; for example, coughing up blood or sputum in TB of the lungs or bone pain if the bacteria have invaded the bones.¹³⁹ TB germs spread when a person infected with active TB disease in the lungs or throat coughs or sneezes.¹⁴⁰ People with active TB disease are most likely to spread it to people they spend time with every day. This includes family members, friends, and coworkers.

People with weakened or compromised immune systems -- individuals with HIV disease, those receiving chemotherapy, pregnant women -- are at a much greater risk for developing active TB disease. When these people breathe in TB bacteria, the bacteria settle in the lungs and start growing because the individual's immune system cannot fight the bacteria. In these people, TB disease may develop within days or weeks after the infection. In 2006, CDC reported 9,842 cases of active TB in the U.S.¹⁴¹

The most common method for detecting TB infection is a tuberculin skin test, which is performed by injecting a small amount of tuberculin antigen under the skin in the lower part of the arm. A person given the tuberculin skin test must return within 48 to 72 hours to have a trained health care professional look for a reaction on the arm. A positive tuberculin skin test only indicates that a person has been infected with TB germs. It does not confirm that the individual has progressed to active TB disease. The presence of symptoms and additional tests, such as a chest x-ray and a sample of sputum, are needed to determine whether the individual has active TB disease.¹⁴²

TB disease usually can be cured with prompt and appropriate treatment, but it remains a major cause of death and disability in the world. It is usually treated with a regimen of drugs taken for 6 months to 2 years depending on the type of infection. It is imperative that people who have TB disease finish the medicine, and take the drugs exactly as prescribed. If they stop taking the drugs too soon or do not take the drugs correctly, they can become ill again and the infection may become more drug resistant.¹⁴³

Public health officials are particularly concerned about 2 forms of TB disease that are drug resistant. According to NIAID, multidrug-Resistant Tuberculosis (MDR-TB) is a form of drug-resistant TB in which the TB bacteria can no longer be killed by at least the 2 best antibiotics, isoniazid (INH) and rifampin (RIF), commonly used to cure TB. As a result, this form of the disease is more difficult to treat than ordinary TB and requires up to 2 years of multidrug treatment. Extensively drug-resistant tuberculosis (XDR-TB) is a less common form of multidrug-resistant TB in which the TB bacteria have changed enough to circum-

vent not only INH and RIF, but also most of the alternative drugs used against MDR-TB. These second-line drugs include any fluoroquinolone, and at least one of the other 3 injectable anti-TB drugs: amikacin, kanamycin, or capreomycin. As a result, XDR-TB generally needs at least 2 years of extensive drug treatment and is very challenging to treat.¹⁴⁴

Susceptibility testing for TB is time-consuming, resource-intensive, and not well-validated. Few laboratories are able to conduct the tests, which dramatically complicates the ability of public health officials to determine whether a patient is infected with the standard variety TB, MDR-TB, or XDR-TB.

MILLENNIUM DECLARATION AND MILLENNIUM DEVELOPMENT GOALS

Since their adoption by 189 nations in September 2000, the Millennium Declaration and the Millennium Development Goals (MDGs) have become a universal framework for development and a means for developing countries and their development partners to work together in pursuit of shared commitments to reduce poverty and hunger, and to tackle major health issues, gender inequality, lack of education, lack of access to clean water and environmental degradation. Together, the 8 MDGs represents a compact that recognizes the contribution that developed countries can make through trade, development assistance, debt relief, access to essential medicines, and technology transfer.

Goal 6 is directly related to infectious diseases. The following lists the targeted outcomes for the goal and how progress will be measured.

GOAL 6: Combat HIV/AIDS, Malaria & Other Diseases

Target 6A: By 2015, halt and begin to reverse the spread of HIV/AIDS.

- HIV prevalence among population aged 15-24 years
- Condom use at last high-risk sexual encounter
- Proportion of population aged 15-24 years with comprehensive correct knowledge of HIV/AIDS
- Ratio of school attendance of orphans to school attendance of non-orphans aged 10-14 years

Target 6B: Achieve, by 2010, universal access to treatment for HIV/AIDS for all those who need it.

- Proportion of population with advanced HIV infection with access to antiretroviral drugs

Target 6C: By 2015, halt and begin to reverse the incidence of malaria and other major diseases.

- Incidence and death rates associated with malaria
- Proportion of children under 5 sleeping under insecticide-treated bednets
- Proportion of children under 5 with fever who are treated with appropriate anti-malarial drugs
- Incidence, prevalence, and death rates associated with tuberculosis
- Proportion of tuberculosis cases detected and cured under directly observed treatment short course

Source: United Nations Development Programme.

APPENDIX B: EMERGING INFECTIOUS DISEASE THREATS TO THE U.S.

ANIMAL-BORNE DISEASES

Bolstering defenses against emerging human infections of animal origin, also known as zoonoses or zoonotic diseases, is crucial to improving global public health. More than 35 of the most recent emerging diseases, including H5N1 avian influenza, monkeypox, West Nile virus, and SARS, have been zoonotic in origin.¹⁴⁵

The link between animal and human health is not novel and has been studied for centuries. In 1967, a landmark study undertaken by the United Nation's Food and Agriculture Organization and WHO documented more than 150 zoonotic diseases. By 2000, more than 200 diseases occurring in humans were known to be transmitted through animals. Experts believe that the increased emer-

gence of zoonotic diseases worldwide can be attributed to population displacement, urbanization and crowding, deforestation, and globalization of the food supply.¹⁴⁶

The following are descriptions of emerging or re-emerging zoonotic diseases that are endangering or may endanger the health of Americans. CDC, NIAID, and WHO have thorough and accessible information on the symptoms, transmission, treatments (if any), and epidemiology of these and many other animal-borne diseases, including yellow fever, hantaviruses, Japanese encephalitis virus, and rabies. Anthrax and SARS, which are described in earlier sections, also are considered zoonotic diseases.

Avian Influenza in Humans

Most Americans have had some experience with seasonal influenza, a respiratory illness that strikes annually. Seasonal flu is not a benign illness -- it kills an average of 36,000 and hospitalizes over 200,000 people in the U.S. every year.¹⁴⁷ Most experts generally regard it as a manageable public health problem, since many people have some form of immunity, and a new vaccine is available each year.

Fears about pandemic influenza have intensified in recent years with the emergence of a deadly strain of avian (bird) influenza. Avian influenza is an infection caused by avian influenza (flu) viruses. One such virus, influenza A, subtype H5N1, has scientists and public health officials especially concerned. H5N1 originated in Asia, but has spread through Europe, Africa, and the Middle East, with cases in birds reported as far north as England and human cases reported as far south as Nigeria.

H5N1 has led to the deaths of hundreds of millions of wild and domestic birds and as of August 15, 2008, 243 human fatalities.¹⁴⁸ Currently, however, bird flu remains difficult for humans to contract. Most people who have developed symptoms have had close contact with sick birds, though in a few cases, bird flu has been transmitted from one person to another.¹⁴⁹

Health officials are concerned that a major bird flu outbreak could occur in humans if the

H5N1 virus mutates into a form that can spread more easily from person to person. The grimmest scenario would be a global outbreak to rival the flu pandemic of 1918 and 1919, which claimed millions of lives worldwide.

Because the H5N1 virus does not commonly infect humans, there is little or no immune protection against it in the human population. At present, 2 antiviral medicines used to treat seasonal influenza -- oseltamivir (Tamiflu) and zanamivir (Relenza) -- may be treatment options should an H5N1 or another influenza virus spark a pandemic.¹⁵⁰ However, there remains uncertainty about their utility in a pandemic: Access may be limited, resistance may develop, and additional barriers may prevent the rapid administration after the onset of symptoms necessary for optimal benefit.

In April 2007, FDA approved the first human vaccine to prevent infection from one strain of H5N1 bird flu virus. This vaccine is not available to the public, but the U.S. government is stockpiling it and may distribute it if it is closely matched to the influenza virus that sparks the next pandemic. Additional research and clinical trials are being supported by NIAID and vaccine manufacturers, including studies on the use of an adjuvant -- something that helps a vaccine provoke stronger immunity in the human body -- in candidate H5N1 vaccines.¹⁵¹ Adjuvants also are important because they can extend the available vaccine supply.

H5N1 viruses, however, are not the only pandemic influenza threat. Other influenza A viruses that have jumped from animals to cause illness in people include swine H1N1

viruses and avian H7N2, H7N3, and H9N2, highlighting the need for continued vigilance in monitoring for influenza viruses with the potential to cause a pandemic.

Lyme Disease

Lyme disease (*borreliosis*) is the most prevalent tick-borne infectious disease in the U.S. The disease is caused by a spiral-shaped bacterium, *Borrelia burgdorferi*, and transmitted to humans by the bite of the black-legged tick. Typical symptoms include fever, headache, fatigue, and a characteristic skin rash. The telltale rash starts as a small red spot at the site of the tick bite and expands over time, forming a circular or oval-shaped rash.

As infection spreads, rashes can appear at different sites on the body. It is often accompanied by symptoms such as fever, headache, stiff neck, body aches, and fatigue. If left untreated, infection can spread to joints, the heart, and the nervous

system. About 10 to 20 percent of untreated people develop chronic arthritis.¹⁵⁵

Lyme disease can also affect the nervous system, causing such symptoms as stiff neck, Bell's palsy, and numbness in the limbs. Less commonly, untreated people can develop heart problems, hepatitis, and severe fatigue.¹⁵⁶

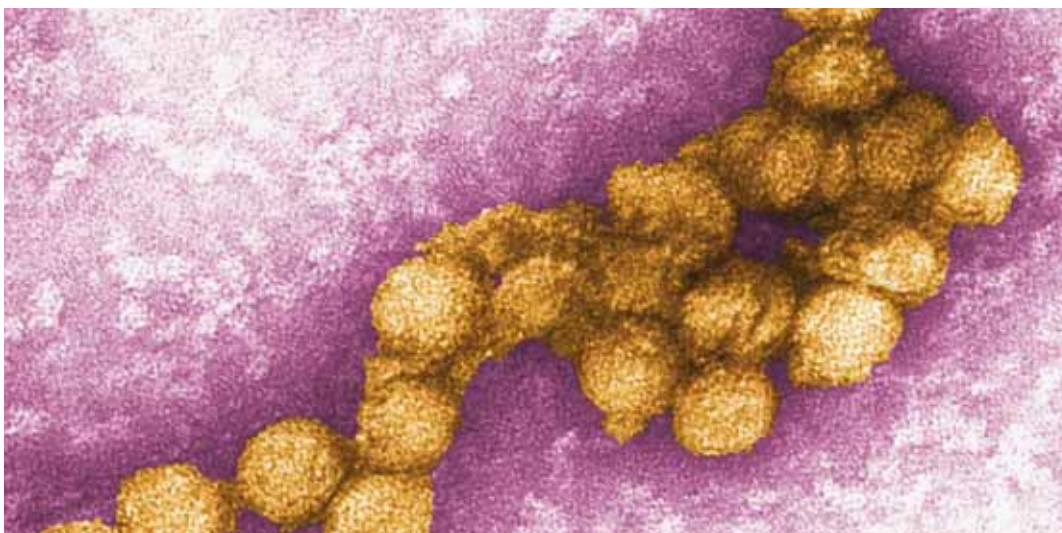
According to CDC, in 2006, there were 19,931 cases of Lyme disease reported in the U.S., yielding a national average of 8.2 cases per 100,000 persons. In the 10 states where Lyme disease is most common, the average was 30.2 cases per 100,000 persons.¹⁵⁷ The disease continues to spread geographically and increases in intensity in areas in which it had already been found.

Rift Valley Fever

Rift Valley Fever (RVF) is a serious, fever-causing viral disease that affects domestic animals (such as cattle, buffalo, sheep, and goats) and humans. RVF is most commonly associated with mosquito-borne epidemics during periods of unusually heavy rainfall. Generally found in regions of eastern and southern Africa where sheep and cattle are raised, a RVF outbreak was reported in Saudi Arabia in 2000 and subsequently in Yemen.

Bites from infected mosquitoes are generally the means of transmission of RVF to humans, although people can also get the disease if they are exposed to the blood, body fluids, or

tissues of infected animals. Individuals with RVF typically have either no symptoms or a mild illness associated with fever and liver abnormalities. Patients who develop symptoms usually experience fever, generalized weakness, back pain, dizziness, and extreme weight loss at the onset of the illness. However, in some patients the illness can progress to hemorrhagic fever (which can lead to shock or hemorrhage), encephalitis (inflammation of the brain, which can lead to headaches, coma, or seizures), or ocular disease (including blindness). Typically, patients recover within 2 days to one week after onset of illness.¹⁵⁸



This is a transmission electron micrograph (TEM) of the West Nile virus (WNV).

West Nile Virus

West Nile Virus (WNV) first emerged in the Western Hemisphere in 1999 in the New York City area and spread rapidly throughout the U.S. The virus is transmitted to humans by mosquitoes.

In general, most human infections are mild, causing fever, headache, and body aches, often accompanied by a skin rash and swollen lymph glands. If the virus crosses the blood-brain barrier, however, it can cause life-threatening conditions that include inflam-

mation of the brain and spinal cord.¹⁵⁹ In 2007, CDC reported 3,630 cases of WNV in the U.S. and 124 deaths from the disease.¹⁶⁰

Licensed WNV vaccines exist for horses, but there are no specific vaccines or treatments for human WNV disease. According to NIAID, “Faced with a potentially deadly illness spreading quickly across the U.S., scientists and public health officials have accelerated research on developing tools to prevent and treat WNV disease.”¹⁶¹

THE ONE HEALTH INITIATIVE

The One Health Initiative, designed to foster greater collaboration between physicians and veterinarians, is a direct response to increasing concerns about the threat of emerging diseases worldwide and the significant threats such outbreaks pose to the health of humans and domesticated animals.

Created in July 2007, a major goal of One Health is the integration of educational systems within and among medical schools, veterinary schools, and schools of public health. The cross-disciplinary project will promote increased research on cross-species disease transmission and the integration of human, veterinary, and wildlife disease surveillance and control systems. The initiative also will encourage comparative research on diseases affecting both humans and animals, including diabetes, cancer, autoimmune disorders, and obesity.¹⁶²

FOODBORNE ILLNESSES

Foodborne disease is caused by consuming contaminated foods or beverages. According to CDC, more than 250 different foodborne diseases have been identified.¹⁶³ Most of these diseases are infections, caused by a variety of bacteria, viruses, and parasites that can be foodborne. Other diseases are poisonings, caused by harmful toxins or chemicals that

have contaminated the food, for example, poisonous mushrooms. These different diseases have various symptoms, and although they are often referred to as “food poisoning,” there is not a single “syndrome” that constitutes foodborne illness. However, nausea, vomiting, abdominal cramps, and diarrhea are common symptoms in many foodborne illnesses.¹⁶⁴

Botulism

Botulinum toxins are the most poisonous substances known to humans. They are derived from bacteria called *Clostridium botulinum*. The toxins affect the nerves and, if untreated, can cause paralysis and respiratory failure. Exposure to the toxins can be fatal.¹⁶⁵

Foodborne botulism is caused by eating foods that contain botulism toxin. Although deadly, botulism is not contagious.¹⁶⁶ Signs and symptoms include difficulty swallowing or speaking, facial weakness, double vision, trouble breathing, nausea, vomiting and abdominal cramps and paralysis. Symptoms usually begin

within 18 to 36 hours after eating contaminated food, but can occur in as few as 6 hours or as long as 10 days afterward.¹⁶⁷

Of particular concern to public health officials are ongoing attempts by a number of countries to develop these toxins into bioweapons. This poses a major threat because of its lethality and relative ease of production.

A supply of antitoxin against botulism is maintained by CDC. The antitoxin is effective in reducing the severity of symptoms if administered early in the course of the disease.¹⁶⁸

E. coli O157:H7

The *Escherichia coli* (*E. coli*) group of bacteria includes numerous strains and most are harmless. However, in 1982, scientists identified the first harmful foodborne strain of *E. coli* in the U.S. -- O157:H7, which lives in the intestines of ruminants, sheds in their feces, and is a leading cause of foodborne illness in this country. Most often, people are exposed to the *E. coli* bacteria through food or water, especially from undercooked ground beef and contaminated raw vegetables or unpasteurized apple cider. In the U.S., about 75,000 people each year become ill after being infected with *E. coli* O157:H7.¹⁶⁹

The main symptoms of *E. coli* O157:H7 are diarrhea, which may range from mild and watery to severe and bloody, and abdominal cramping, pain, or tenderness. Some people also may have a low-grade fever and others experience nausea or vomiting. Approximately 5 to 10 percent of people who are diagnosed

with *E. coli* infections develop a potentially life-threatening complication known as hemolytic uremic syndrome (HUS). Symptoms include decreased frequency of urination, extreme fatigue, and pallor. People with HUS should be hospitalized because their kidneys may stop working and they may develop other serious problems. Most persons with HUS recover within a few weeks, but some suffer permanent damage or die.¹⁷⁰

For most people with an *E. coli* infection, the best treatment option is to rest and drink plenty of fluids to help with dehydration and fatigue. People are advised to avoid taking anti-diarrheal medications, which can slow the digestive system down, making it more difficult to get rid of the toxins. According to CDC, antibiotics should not be used to treat this infection. There is no evidence that treatment with antibiotics is helpful, and taking antibiotics may increase the risk of HUS.¹⁷¹

Salmonella

Salmonellosis, or *Salmonella* infection, is one of the most common bacterial infections of the intestinal tract. *Salmonella* typically live in the intestines of animals and humans and are shed through feces, where the bacteria remain highly contagious. Humans become infected most frequently through the ingestion of contaminated food sources, such as poultry, meat, raw dairy products, and chicken eggs. *Salmonella* can survive for months in water, ice, sewage, and frozen meat.¹⁷²

Typically, people with *Salmonella* infection develop diarrhea, fever and abdominal cramps within 12 to 72 hours. Signs and symptoms of *Salmonella* infection generally last 4 to 7 days. Most healthy people recover without specific treatment.¹⁷³

In some cases, diarrhea can cause severe fluid loss, requiring prompt medical attention to

avoid circulatory collapse. Life-threatening complications may also develop should the infection spread beyond the intestines. In most otherwise healthy people, diarrhea and abdominal pains subside within several days to 2 weeks without specific treatment.

An antibiotic-resistant strain of *S. typhimurium*, first found in the United Kingdom and then in the U.S., poses a major public health threat because it is resistant to several antibiotics normally used to treat people with *Salmonella* disease.¹⁷⁴

Salmonella may occur in small, contained outbreaks in the general population or in large outbreaks in hospitals, restaurants, or institutions housing children or the elderly. Every year, CDC receives reports of 40,000 cases of *Salmonellosis* in the U.S.¹⁷⁵

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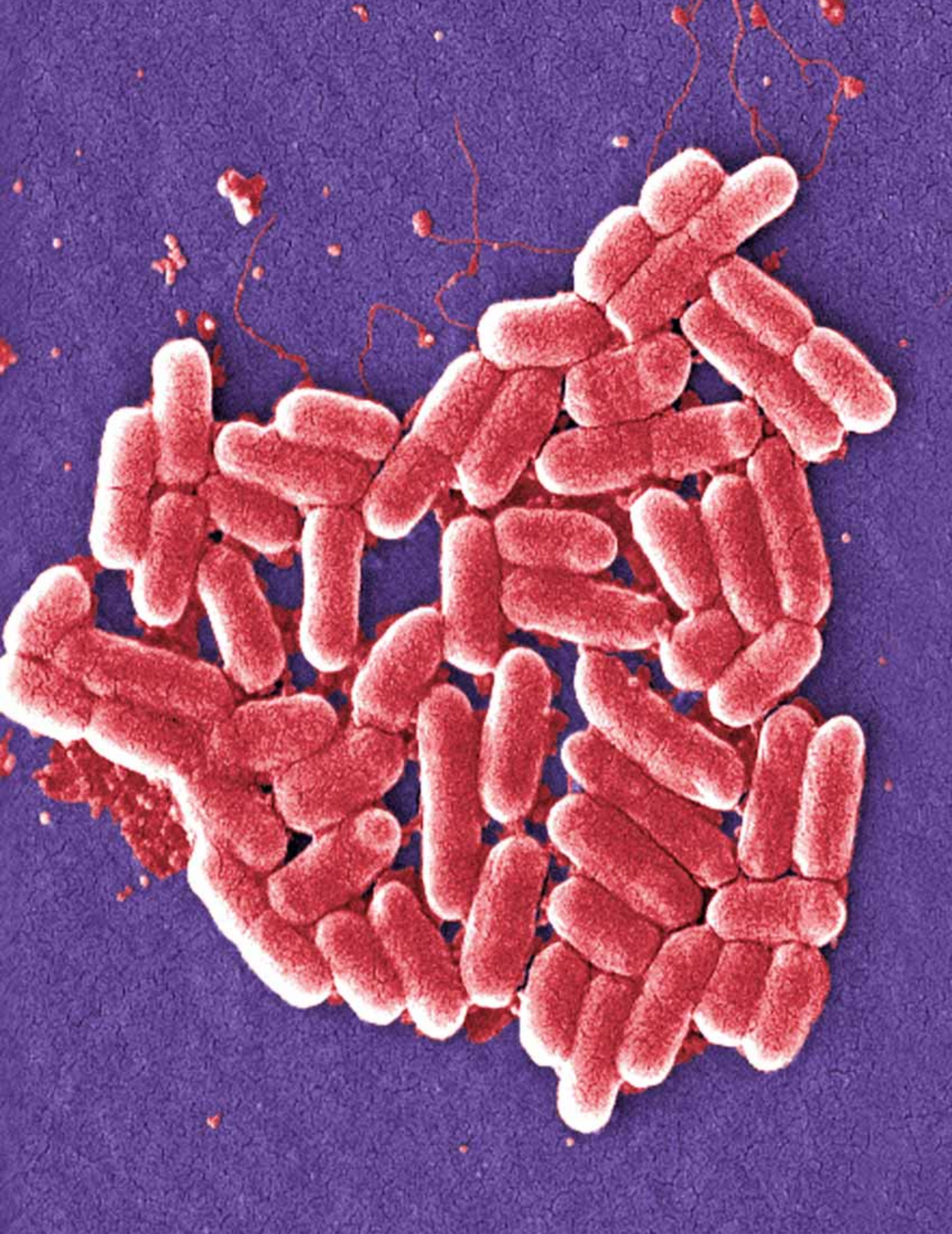
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