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Strengthening Global Preparedness for Defense against Infectious Disease Threats

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By their very nature, infectious diseases have the potential to spread internationally. Throughout most of human history, isolation and quarantine were the only measures available for protection. As a result, the course of human history was frequently altered by epidemics that swept unchecked across continents, claiming more lives and creating more social devastation than wars.

With the development of vaccines and the discovery, during the previous century, of potent classes of antimicrobial drugs, humanity could, for the first time in history, prevent many infectious diseases and cure many others. The risk that epidemics might again sweep across continents seemed remote. The defenses were in place, the threat was considered under control, and the world relaxed its guard.

The magnitude of the problem

The microbial world is complex, dynamic, and constantly evolving. Microbes proliferate rapidly, mutate frequently, and adapt with relative ease to new environments and hosts. They will also eventually develop resistance to the drugs used to treat them. Numerous factors, including those linked to human activities, can accelerate and amplify these natural phenomena, as has happened in recent years. Moreover, when a complacent world relaxes its vigilance and lets down its defenses, the consequences can be dramatic as well as rapid. Microbes are quick to exploit new opportunities to spread, adapt, and resist.

As a result of several recent trends, the world now finds itself in a situation where epidemics are again spreading around the globe unchecked, but this time at unprecedented speed. New or newly recognized diseases are being reported at the rate of approximately one per year. AIDS emerged as an important infectious disease in the early 1980s and is now entrenched on a scale that threatens global security. Other emerging diseases, such as Ebola haemorrhagic fever and new variant Creutzfeld-Jakob disease, illustrate the severe damage caused by lethal new agents that cannot currently be curbed by vaccines or drugs. In 1997 and 1999, when influenza viruses previously confined, respectively, to birds and swine suddenly appeared in humans, experts voiced fears of a pandemic on the scale of the deadly Spanish Flu of 1918, which some believe was caused by an avian virus that first crossed the species barrier to swine before jumping to humans. Altogether, over 30 new infectious diseases have emerged over the past 25 years.

The phenomenal recent increase in global travel and trade has given microbes multiple opportunities to spread around the global in novel ways and with unprecedented speed. Microbes can incubate in apparently healthy travellers, hide in food, animals, or cargo, or be carried by insects stowed away in the cabin and luggage holds of jets or in the pots of exotic plants. In the UK alone, 1,128 cases of malaria were imported into the country by travellers in 2000. Cases of "airport malaria", in persons who live or work near international airports yet have not travelled, are detected regularly in cities such as London, Paris, Brussels, Geneva, and Oslo as well as in the United States and Canada. In just the past two years, unexpected outbreaks of relatively new or previously rare diseases have taken populations on every continent by surprise. Legionellosis and leptospirosis in Australia, Lassa fever, yellow fever, hantavirus, listeriosis, and new variant CJD in Europe, and yellow fever, West Nile fever, cryptococcosis, and *E. coli* O157 in the US are just some examples. In the face of such highly mobile, microscopic, and easily disguised threats, national borders are porous. An outbreak anywhere in the world must now be considered a threat everywhere else.

Once an infectious disease, or the insects and animals that carry it, invades a new country or continent, it can prove difficult – if not impossible – to control. This has been the case with West Nile fever, which made its initial appearance on the American continent in 1999 and is now firmly entrenched and spreading, and with Rift Valley fever, which crossed the Red Sea from East Africa to the Arabian peninsula for the first time in 2000. The aggressive tiger mosquito, capable of spreading dengue, yellow fever, LaCrosse encephalitis, and other diseases, and able to breed in any container large enough to hold water, entered the US in a shipment of used tires in 1985 and has since spread to 25 states.

Apart from the need to cope with the emergence and spread of new diseases, public health infrastructures are further burdened by the dramatic resurgence of older epidemic-prone diseases such as malaria, dengue, tuberculosis, cholera, and yellow fever. Cholera, for example, is now causing epidemics in parts of Latin America where it had previously been quiescent for over 100 years. The global spread of dengue, which began in Southeast Asia in the 1950s, has intensified dramatically, showing a four-fold increase with unprecedented numbers of its deadly haemorrhagic form. On 23 August 2001, Venezuela's president declared the country's current dengue epidemic, with more than double the number of cases seen in the previous year and over 600 cases of its potentially lethal form, a national emergency.

The costs can be enormous. In recent years, wealthy nations have been stunned by outbreaks of foodborne disease causing economic losses in the billions of dollars. Some experts place losses associated with the emergence of mad cow disease in Europe at close to $38 billion. In New York in the early 1990s, the emergence of multidrug-resistant tuberculosis, with a death rate of up to 80%, incurred costs associated with the failure to prevent its spread estimated at over $1 billion. In the Russian Federation, the re-emergence of tuberculosis, including multidrug-resistant forms, is estimated to have cost over $4 billion in 1999 alone. Initial costs associated with cases of West Nile fever in New York have been placed at almost $100 million.

The spectre of a "post-antibiotic" era

As yet another especially serious and costly problem, resistance to inexpensive and effective antimicrobial drugs is emerging and spreading at an alarming rate. The bacterial infections which contribute most to human disease are also those in which emerging resistance is of most concern: diarrhoeal diseases such as dysentery, respiratory tract infections, including common pneumonia and multidrug-resistant tuberculosis, sexually transmitted infections such as gonorrhoea, and a host of hospital-acquired infections that are notoriously difficult and expensive to treat. Among the other major infectious diseases, the development of resistance to drugs commonly used to treat malaria is of particular concern, as is the emerging resistance to anti-HIV drugs.

The development of resistance is a natural phenomenon that occurs, sooner or later, with every antimicrobial. In the past, medicine and science were able to stay ahead through the discovery of potent new classes of antimicrobials, a process that flourished from 1930–1970 and has since slowed markedly, partly because of misplaced confidence that infectious diseases had been conquered, at least in the industrialized world. In just the past few decades, the emergence of resistant microbes has been greatly accelerated due to several concurrent trends. These have worked to increase the number of infections and thus expand both the need for antimicrobials and the opportunities for their misuse. Important trends include urbanization with its associated overcrowding and poor sanitation; pollution, environmental degradation and changing weather patterns, which can affect the incidence and distribution of infectious diseases and the habitats of the insects and animals that carry them; and a growing proportion of elderly people needing hospital-based treatments and thus at risk of exposure to highly resistant pathogens found in hospitals.

Additional trends include the resurgence of malaria and tuberculosis, causing millions of infections each year, and the AIDS epidemic, which has greatly enlarged the population of immunocompromised patients at risk of opportunistic infections and thus in need of treatment. Moreover, the enhanced food requirements of an expanding world population have led to the widespread routine use of antimicrobials as growth promoters or preventive agents in food-producing animals and poultry flocks. In North America and Europe, an estimated 50% in tonnage of all antimicrobial production is used for these purposes. Such practices have contributed to a rise in resistant microbes which can be transmitted from animals to humans.

The associated costs are high. For example, treatment costs for tuberculosis can vary between $15 and $40 per person to achieve a complete cure, whereas treatment costs for multidrug-resistant tuberculosis can be up to $3,000 per person. Most alarming of all are microbes that have accumulated resistance genes to virtually all currently available drugs and have the potential to cause untreatable infections, thus raising the spectre of a post-antibiotic era. Even if the pharmaceutical industry steps up efforts to develop new drugs immediately, current trends suggest that some diseases may have no effective therapies within the next ten years. Moreover, if current trends continue, many important medical and surgical procedures, including cancer chemotherapy, bone marrow and organ transplantation, and hip and other joint replacements, could no longer be undertaken out of fear that the associated compromise of immune function might place patients at risk of acquiring an untreatable and ultimately fatal infection. Opportunistic infections in AIDS patients would likewise be untreatable.

The need for global solutions

Antimicrobial resistance is a global problem requiring a global solution. No single nation, however effective it is at containing resistance within its borders, can protect itself from the importation of resistant pathogens. The enormous growth of global trade and travel means that a resistant microbe can spread from its place of origin to almost anywhere else in the world within 24 hours.

Taken together, the threats posed by emerging and re-emerging infectious diseases, and by the emergence and spread of antimicrobial resistance are serious, steadily growing, and universally costly. Their nature is inherently global, with causes related to the world’s growing

interconnectedness, and with consequences that must be addressed by global solutions, ideally aimed at prevention.

WHO's capacity for alert and response

As an international health agency with over 50 years of experience, the World Health Organization is well placed to gather global disease intelligence and coordinate the rapid, multifaceted response needed to contain outbreaks quickly and prevent their international spread.

- **Privileged access.** WHO staff, consultants, and expert advisers have privileged access to all countries. This privilege allows WHO, in the interest of safeguarding international health, to transcend the prevailing political reality in which access to critical expertise might be denied because of one country's political relationship with others. On many occasions, the Organization's ability to secure laissez-passer status has proved decisive in getting international experts quickly and smoothly into countries where, for diplomatic reasons, entrance might otherwise be delayed if not denied. This ability to obtain privileged status is extended to all of the many security-cleared partners who may be needed to mount an effective international response.

- **Geographical resources.** WHO has unique and permanently positioned geographical resources. These include six regional offices and an additional 141 country offices, located within or in close proximity to ministries of health, and concentrated in areas where epidemics are most frequent and new diseases are most likely to emerge. Although the size of these offices varies according to the disease situation in the country concerned, all offices are staffed with medical experts and often with epidemiologists, and all have the essential logistic equipment, including vehicles and local communications, needed for the prompt on-the-scene investigation of a suspected outbreak. When outbreaks occur, country offices facilitate the arrival of international assistance by arranging flights, customs and immigration clearance, and accommodations. All offices are now linked electronically to WHO and thus to its global network of institutional resources and collaborators.

- **Collaborating centres.** WHO's disease control activities are supported by a network of over 250 laboratories and institutions formally designated as WHO Collaborating Centres. These centres provide the expertise and facilities needed to conduct field investigations, handle dangerous pathogens, test samples, identify unknown agents, and confirm the diagnosis of cases. Many additional laboratories and public health institutes also collaborate with

WHO on a regular basis. The ability to draw assistance from top experts and facilities is vital given the fact that most previously unknown and highly lethal diseases, including Ebola and other viral haemorrhagic fevers, tend to emerge in those countries that lack the requisite laboratory and epidemiological capacity to detect an unusual disease event and identify its causative agent. Apart from its close working relationships with its Collaborating Centres, WHO draws considerable technical support from public health agencies in WHO member states. Such collaboration with leading, international experts and institutes lends added authority to WHO's efforts to identify and track outbreaks accurately and keep the world reliably informed.

- **Surveillance networks.** WHO coordinates a large number of electronic "detective" systems and databases for keeping experts alert to changes in the volatile infectious disease situation. These networks, most of which now operate in real time, keep watch over disease-related events ranging from new strains of influenza virus, through outbreaks of salmonellosis and dengue, to the emergence of drug-resistant pathogens. Most of these networks also include quality assurance and training components to ensure that data submitted from all parts of the world are comparable and conform to established standards. The oldest of these, FluNet, was established over 50 years ago and has served as the prototype for the design and implementation of subsequent systems. It now draws support from 110 collaborating laboratories in 84 countries. The sensitivity of FluNet has recently proved vital in the early detection of cases where influenza virus strains have crossed the species barrier from animals, such as swine and poultry, to infect humans.

These surveillance networks all operate within the framework of the International Health Regulations, which provide the only international legally-binding instrument, implemented by WHO, governing the reporting of epidemic-prone diseases and the application of measures to prevent their spread.

- **Welcomed assistance.** WHO is politically neutral, and often greatly needed in the developing world. Ministries of health in such countries have repeatedly gone on record to state their reliance upon WHO as their single most important source of authoritative advice and technical assistance, particularly in matters pertaining to the control of infectious diseases. As a result, direct assistance from WHO to control infectious diseases is frequently requested and warmly welcomed with the best support the country can offer.

- **Deep experience.** WHO has over 50 years of experience in coordinating the field operations needed to control infectious diseases. Current campaigns, which include global initiatives aimed at eradicating or eliminating eight diseases, build on the epidemiological approaches and logistic infrastructure that contributed to the successful global eradication of smallpox. These mechanisms, which have been refined over time, have proved robust and effective even under difficult conditions. The successful containment of the largest recorded outbreak of Ebola, which began in Uganda in October 2000, was coordinated by WHO and involved over 500 local staff and volunteers, supported by some 120 international staff from 22 institutions and agencies. WHO coordinated the considerable efforts and logistics needed for the identification and confirmation of 425 cases and the surveillance of approximately 5,600 contacts in an area in which 70% of the population was internally displaced because of civil disturbances. As part of the drive to eradicate polio, mass immunization campaigns have been successfully conducted in the midst of complex emergencies and considerable civil unrest, with WHO's partners providing strong and needed support.

The framework for disease surveillance and response:

A three-pronged approach

As WHO maintains only a small number of staff at its headquarters in Geneva and its six regional offices, the framework for global disease surveillance and response is based on the use of a large number of partners, including government agencies, non-governmental organizations, the private sector, and industry. Such partnerships allow WHO to magnify the impact of its efforts considerably.

The framework relies on a three-pronged approach, with different strategies for combatting known risks and unexpected events, and for improving both global and national preparedness.

- **Containing known risks.** Epidemic-prone diseases, such as cholera, dengue, influenza, measles, meningitis, shigellosis, and yellow fever, and foodborne diseases pose a constant threat to human populations. They are well adapted to transmission in human populations either directly from person to person, through transmission by insects and other disease vectors, or by contamination of the environment or food. These diseases are generally well understood and, in most cases, effective measures are available for their control.

WHO maintains numerous programmes for the monitoring and control of these well-known and almost constant risks to public health. Disease-

specific networks of partners help WHO mount a rapid response when outbreaks occur, at times following a breakdown in standard public health control measures in the country concerned. Established protocols, based on extensive experience, facilitate prompt, coordinated action. For some of these infections, such as epidemic meningitis, influenza, and yellow fever, WHO also collaborates with researchers and industry to anticipate future outbreaks and ensure that adequate emergency vaccine supplies are available when needed. Other known risks monitored by WHO include those caused by foodborne diseases and the emergence and spread of drug resistance.

- **Responding to the unexpected.** Unexpected or unusual disease events can be caused by previously unknown infectious agents, agents that have crossed the species barrier from animals to humans, agents appearing in a new geographical area, and agents that may be deliberately engineered and introduced by acts of bioterrorism. Novel pathogens are usually poorly understood in terms of their source and mechanisms of transmission, and many have the potential to cause large outbreaks. Fortunately, some of these pathogens are not well adapted to human populations and lack the potential for sustained, epidemic spread. As experiences with the AIDS epidemic have demonstrated, however, sustained epidemic spread is a distinct possibility that can have a major impact on societies and economies as well as on the life expectancies of countries. While novel pathogens may not always cause major outbreaks, they are often associated with high death rates, as they are poorly understood as they emerge, and initial prevention or treatment strategies are absent or ineffective. Examples include hantavirus infections, Ebola and, most recently, Nipah virus.

WHO has recently established innovative mechanisms for responding to previously unknown diseases and unexpected or unusual disease events. These mechanisms take full advantage of the powerful new opportunities for heightened vigilance and rapid response that have been created by the widespread use of electronic communications. To heighten vigilance, WHO takes advantage of a semi-automatic electronic system, developed for WHO by Health Canada, that continuously and systematically crawls Web sites, news wires, public health email services, electronic discussion groups, including the US-based Pro-MED, and local online newspapers for rumours of outbreaks. In this way, WHO is able to scan the world for informal news that gives cause for suspecting an unusual disease event. A WHO team responsible for outbreak verification investigates suspicious reports each morning to determine whether they pose a threat of international health concern. When appropriate, WHO uses its technical and geographical

resources to verify the presence of an outbreak. Since 1998, WHO has used this system to verify over 800 outbreaks of potential international importance.

To ensure that heightened vigilance is accompanied by a rapid response, WHO enlarged and formalized its procedures for outbreak detection, verification, and response in April 2000, when the Global Outbreak Alert and Response Network was formed. The Network draws together 72 existing networks, many operating under WHO's responsibility, others maintained by national governments or regional nongovernmental organizations . The Network reports and verifies information, on a daily basis, from a wide range of formal sources, including ministries of health, national institutes of public health, government and military health facilities and laboratories, and nongovernmental organizations, such as the Red Cross, having a strong presence in epidemic-prone countries. When an outbreak is judged to require international assistance, as agreed upon in confidential consultation with the affected country and with experts in the Network, WHO uses the latest electronic communication tools to coordinate quick and appropriate assistance. Since early 2000, the network has launched effective international responses in Afghanistan, Bangladesh, Egypt, Ethiopia, Kosovo, Saudi Arabia, Sierra Leone, Sudan, Uganda, and Yemen.

The work of coordinating large-scale international assistance, which can involve many agencies from many nations, is facilitated by operational protocols, developed by WHO, which set out standardized procedures for the alert and verification process, communications, coordination of the response, emergency evacuation, research, evaluation, monitoring, and relations with the media. WHO has also issued guidelines for the behaviour of foreign nationals during and after field operations in the host country. By setting out a chain of command, and imposing order on the containment response, such protocols help protect against the very real risk that samples of a lethal pathogen might be collected for later provision to a terrorist group.

- **Improving preparedness.** WHO conducts a number of activities aimed at helping countries strengthen their laboratory and epidemiological capacity and take advantage of new tools such as HealthMap (an interactive information and mapping system), and remote sensing data from NASA and other satellites. WHO suppors the Training Programmes in Epidemiology and Public Health Interventions network (TEPHINET), another global network utilized by the Global Outbreak Alert and Response Network, which seeks, through shared resources and expertise, to enhance the effectiveness of national training programmes. In February 2001, WHO opened a new office in Lyon, France, to provide two-year specialized training for epidemiologists and laboratory specialists from developing countries where the epidemic risk

is greatest. The training, which includes a six-week course in Lyon, is followed by specially tailored field work and support in the home country, supervised by Lyon-based staff. In so doing, the new programme is working to strengthen disease detection and response activities in those countries where epidemics and unexpected disease events are most likely to occur.

As another example, a working group on long-term preparedness for outbreak response was recently established to help ensure that the energy and resources that are provided to a country for the investigation and containment of an outbreak do not vanish after containment, but are instead harnessed in the form of long-term technical assistance. During 1998 and 1999 major epidemics, including outbreaks of haemorrhagic fever, cholera, and meningitis, caused a significant increase in morbidity and mortality in southern Sudan and necessitated major international assistance. In 1999, a WHO-coordinated international team responding to an outbreak of relapsing fever set up an Early Warning and Response Network (EWARN) in partnership with nongovernmental organizations present in the field. With support from several sources, EWARN has been expanded to cover seven diseases and a wide geographical area, and now ensures that epidemics are rapidly detected and investigated while responses are launched quickly using prepositioned materials. This international partnership in the field has already saved thousands of lives and is sustained by systematic capacity building among the local communities.

Capacity building for national epidemic detection and response is far more cost-effective than mounting an international response. During the Ebola outbreak in Uganda, containment activities left behind permanent improvements in the form of isolation wards at two hospitals in Gulu district, a community-based early warning surveillance and response system for priority infectious diseases, and sustained improvements in civil administration through the establishment of a community registry of births and deaths. In June 2001, a new focus of three suspected cases of haemorrhagic fever was detected by local staff within three days of onset, patients were immediately isolated in the recently established ward, and specimens were despatched for testing at the WHO Collaborating Centre in South Africa, where results fortunately proved negative. In this case, strengthened national capacity made it possible to defend global health security through local vigilance, without the need for costly international assistance.

Preparedness for a bioterrorist attack

WHO will soon be issuing an updated edition of its standard guide to health aspects of chemical and biological weapons, initially published in 1970. In view of the devastating impact on civilian populations that use of such weapons could have, the guide urges governments to prepare response plans as an integral part of existing national emergency plans. The strengthening of public health infrastructure, particularly for surveillance and response, is singled out as a major contribution to preparedness. The establishment of routine, sensitive, and near real time disease surveillance systems enhances preparedness for deliberate as well as natural outbreaks. National systems are important as experience has shown that many region-wide and global systems are inadequately sensitive to pick up local outbreaks quickly.

National surveillance systems need to be in place well in advance of possible intentional use of a biological weapon, as adequate data on the prevalence of background diseases are needed to aid recognition of an unusual and possibly deliberately caused disease. Moreover, the epidemiological techniques needed to investigate deliberate and natural outbreaks are the same. Since many of the agents that can be used as bioweapons cause disease in animals, countries also need to establish mechanisms for the routine exchange of information between the public health and veterinary sectors.

Within the context of its outbreak alert and response activities, WHO has developed protocols for containing outbreaks of diseases, such as anthrax and viral haemorrhagic fevers, which could result from the intentional use of biological agents. As part of its official mandate for dealing with smallpox-related issues in the post-eradication era, WHO is responsible for ensuring the security of the remaining stocks of smallpox virus and overseeing their final fate.

A more proactive role for WHO

Traditionally, one of the main factors undermining the effectiveness of infectious disease surveillance has been the reluctance of countries to report outbreaks due to fear of the negative impact this news would have on travel, trade, and tourism. This traditional reluctance is now beginning to change. In line with the growth of electronic media, approximately 65% of the world’s first news about infectious disease events during the past four years has come not from official country notifications but from informal sources, including press reports and the Internet. Transparency about outbreaks and prompt reporting have therefore become increasingly important: unverified rumours of an outbreak or unusual disease can have a

negative impact on travel and trade in the country and its neighbours even though the rumour may be totally unjustified or grossly exaggerated.

In May 2001, the World Health Assembly, the supreme governing body of WHO, adopted by consensus a resolution on global health security that considerably strengthens WHO's capacity to act in response to outbreaks and epidemics. WHO is now in a position to investigate and verify rumoured outbreaks even prior to receipt of an official notification from the government of the country concerned. Though WHO continues to confer, in confidence, with governments and secure their agreement to mount an international response, this strengthened capacity allows WHO to act with unprecedented speed.

In the new order of the electronic era, countries are increasingly aware of the advantages of prompt outbreak reporting and official verification, accompanied by prompt international aid when needed, and prompt advice from WHO to the international community concerning the associated risks and the realistic need for restrictions on travel and trade. For example, during the Ebola outbreak in Uganda, WHO was informed as soon as the first suspected cases were detected, and a WHO-coordinated investigative team was on the spot within 24 hours. Throughout the five-month long epidemic, WHO issued 42 updated reports on the epidemic via its Web site. The country's borders were never closed.

During the May debate that preceded adoption of the resolution on global health security, delegations from developing countries repeatedly urged WHO to help them strengthen the laboratory and epidemiological capacities needed to detect outbreaks quickly, identify their cause, monitor their spread, and introduce containment measures. Both the need to act and the will to do so are present. The risks are known, immediate, alarming, and relevant to every country in the world. WHO and its many partners and member states know what needs to be done.

Mechanisms for monitoring and containing these risks exist, but need to be strengthened. Above all, the multiple threats posed by infectious diseases – whether well known or unexpected – have global causes and consequences that can only be addressed through global solutions. Strengthening of national capacities and public health infrastructures represents one of the surest, most sustainable, and most cost-effective measures for preventing the international spread of diseases and thus defending global health security for the benefit of all.

Conclusions

The resurgence of infectious diseases and the emergence and spread of antimicrobial resistance have unleashed threats whose magnitude is almost certain to grow. Epidemics are again sweeping across continents. The tools needed to control emerging diseases are, in many cases, non-existent. The control of re-emerging and epidemic-prone diseases likewise suffers from the spread of resistance to inexpensive first-choice drugs. Nonetheless, today's world is better equipped to protect itself, through preventive measures, than in the past, when isolation and quarantine comprised the sole measures for control. Aided by powerful electronic communication tools, key defense strategies now include early alert, through sensitive global networks for real-time outbreak detection and verification, and rapid national and international responses once outbreaks are confirmed. The strengthening of infrastructure in epidemic-prone countries is vital to the successful and cost-effective implementation of both strategies.

In a world that is now closely interrelated in matters of health as well as in economics and trade, defense against the threats posed by infectious diseases requires a collaborative, multifaceted, global response. WHO continues to track the evolving infectious disease situation, sound the alarm when needed, share expertise, and mount the kind of response needed to protect us all from the consequences of epidemics, whatever and wherever their origin might be.