

Collaboration: the key to investigations of emerging and re-emerging diseases

Douglas L. Hatch¹ and Imam Z. Imam²

العدوى المستجدة والمنبئة من مرقدتها : العمل المشترك هو مفتاح الاستقصاء
دوغلاس ل. هاتش ، وإمام زغلول إمام

خلاصة تحتاج الدول إلى فرق من أخصائيي الوبائيات ذوي الخبرة الميدانية العريضة للعمل مع أخصائيي المعالجة السريرية والمختبرات ، من أجل إجراء استقصاءات عاجلة وفعالة لفاشيات الأوبئة . وحتى يمكن التعرف على الفاشيات الناجمة عن هذه المشاكل المحتملة ، المستجدة أو المنبئة من مرقدتها ، يجب تعزيز نظم الترصد القائمة ، والتحقق من جودة معطياتها على نحو روتيني . فضلا عن ذلك ، فإن المسؤولين بوزارات الصحة وبالهيئات الدولية يحتاجون إلى بيئة علمية منفتحة يعملون فيها معاً . وخير بيئة يمكن فيها تصميم التدخلات وتدابير المكافحة الفعالة للحد من مغبة هذه المشكلات المستجدة في صحة الجماهير ، هي البيئة التي بسودها التعاون والعمل المشترك .

ABSTRACT Countries need teams of well trained epidemiologists with extensive field experience to work with clinicians and laboratory scientists to conduct prompt and effective outbreak investigations of epidemics. To identify these outbreaks of possible emerging or re-emerging problems, existing surveillance must be strengthened and the quality of data validated routinely. In addition, ministry of health officials and international agencies need an open, collaborative, scientific work environment. The best environment to design effective interventions and control measures to limit the impact of these newly identified problems on the public's health is one of cooperation and collaboration.

Les infections émergentes et réémergentes: la collaboration est essentielle pour leur investigation

RESUME Les pays ont besoin d'équipes d'épidémiologistes qualifiés possédant une vaste expérience sur le terrain pour collaborer avec les cliniciens et les spécialistes scientifiques de laboratoire afin de procéder à une investigation rapide et efficace des épidémies. Pour détecter ces flambées épidémiques de maladies émergentes ou réémergentes éventuelles, il faut renforcer la surveillance existante et valider systématiquement la qualité des données. En outre, les responsables des ministères de la santé et les organisations internationales ont besoin d'un milieu de travail scientifique ouvert et coopératif. La collaboration et la coopération constituent le cadre le plus propice pour concevoir des interventions et mesures de lutte efficaces visant à limiter l'impact sur la santé publique de ces problèmes nouvellement identifiés.

¹ US Centers for Disease Control and Prevention, Epidemiology Program Office/International Branch, CDC Adviser, Field Epidemiology Training Program, Cairo, Egypt.

² Senior Technical Adviser, Field Epidemiology Training Program, Cairo, Egypt.

Introduction

Since the early cholera investigations by John Snow in London during the mid-1800s [1], great progress has been made in the ability to identify new infectious agents and scientifically investigate disease outbreaks [2]. The global eradication of smallpox during the 1970s and subsequent success in many areas with reduction in the burden of disease due to poliomyelitis, diphtheria, tetanus, measles and pertussis has resulted mainly from widespread increases in immunization coverage and access to health services. The science of epidemiology has also played an important role in advances in investigations of outbreaks, assessment of vaccine efficacy and monitoring of disease trends. Laboratory support has been the foundation of both improving the sensitivity and quality of surveillance data and identifying the emergence of newly identified agents such as Ebola virus or the human immunodeficiency virus (HIV) [2].

Unfortunately, very few countries have developed the ability to coordinate sophisticated epidemiological assessments in a timely manner or support reference laboratories able to identify emerging or re-emerging infectious agents. Obstacles that can restrict a ministry of health from developing the capacity for prompt epidemiological investigations include competing priorities for funding, lack of practical epidemiological training for public health officials and inadequate laboratory infrastructure.

The present decade has brought with it new challenges with advances in travel opportunities, telephone communications, faxes, satellite links, sophisticated computers, the Internet and an increasingly open format for newspapers and publications responding to public concern about emerging infections.

This article will discuss some of the key issues surrounding outbreak investigations

and stress the need for professional interactions, equal division of responsibilities and international collaboration among those groups working in this important area of public health.

Reasons to conduct outbreak investigations

Epidemiology applied to fieldwork

Epidemiology remains an important tool for public health officials, because practical application of its principles often provides insight about current health problems. The use of epidemiology during outbreak investigations, for example, can often identify the cause of an epidemic and assist health personnel responsible for designing interventions to protect the public's health. When to conduct an outbreak investigation remains a key issue and is dependent upon many factors, including historical data about disease in the population, interpretation of trends over time, whether a disease is endemic, or whether there have been changes in surveillance results or activities. Reasons for conducting an outbreak investigation include determining the extent of the problem, finding the most appropriate control measures and allaying public concern. In addition investigations increase scientific knowledge and human resources development, and the information gleaned from them can be used to evaluate public health programmes. When a decision is made to conduct an investigation, communication, planning, personnel and approval are all necessary.

In addition to determining the actual extent of any problem being examined, outbreak investigations can provide important support for regional authorities requesting assistance with a problem they do not have the resources to examine carefully. Public or clinician concerns are important to address,

and these concerns may be heightened if media attention is focused on the issue. As a general rule, it is often advisable to promptly investigate possible outbreaks, both to address public concern and establish scientifically if an outbreak actually exists. Deciding whether an epidemic has begun is complicated, and requires careful consideration of many factors. During investigations, evidence can be gathered about the magnitude of the problem, whether this might represent a new infectious agent or perhaps a new pattern of antimicrobial drug resistance. Finally, since epidemics occur regularly in many countries, infrequent investigations are more likely to represent lack of capacity rather than lack of intention. An additional benefit to regular investigations is to establish a cadre of qualified field epidemiologists capable of functioning effectively should a major problem emerge.

Formulating a case definition

Early in an investigation, a case definition must be developed. Such a case definition requires information about time, place and person. Standardizing the characteristics of those persons affected by the outbreak is important in assisting investigators to discover possible exposure and risk factors in diseased and nondiseased persons. This standardization also helps investigators because there may be different clinical manifestations of the disease of interest (for example, fever and/or encephalitis), or cases may occur in multiple locations. A case definition is also useful to exclude other diseases not of interest. Understanding events preceding an epidemic in both the diseased and nondiseased is important in developing hypotheses about causative agents and mechanisms of disease transmission. The same information is also important in developing prompt and effective strategies for control. The case definition does not have to

be constant, but can be modified by investigators as necessary as more information about the case characteristics and illness under study becomes available.

Confirming the diagnosis

One of the principal reasons for having a strong public health laboratory infrastructure and well trained laboratory personnel is to maximize the ability to confirm a diagnosis during an outbreak. Proper sample collection is dependent upon many factors, including the need to have clinicians treating ill persons collect adequate specimens and the availability of media and containers for safe transportation of specimens. An additional concern is the possible susceptibility of health personnel and laboratory workers and the ability to use and availability of appropriate protective equipment or measures (such as gloves, masks and/or vaccination) necessary to prevent transmission to health workers. Laboratory expertise involves many fields, including bacteriology, virology, serological testing and histopathology, and not all centres will have capacity in all areas. Thus, intercountry and international collaboration when epidemics are encountered is likely to increase the technical quality of the response, increase the likelihood of maximizing the scientific knowledge resulting from these investigations and minimize any chance of endangering health workers.

For infectious agents that pose the highest risk to human health (for example, Ebola virus), sophisticated equipment and facilities are needed to safely process and handle potentially infected specimens. Such facilities are available only at so-called level 4 laboratories, which exist in only a few locations such as the US Centers for Disease Control and Prevention (Atlanta, USA) and the US Army Medical Research Institute of Infectious Diseases (USAMRIID at Fort

Detrick, Maryland) and the P4 level laboratories in Belgium and South Africa.

Working with local public health officials

Despite existing surveillance systems designed to provide timely and complete information to central decision-makers, the reality is that substantial underreporting is often a problem, even with priority diseases (such as cholera, yellow fever or haemorrhagic fever). Therefore, ministry of health officials need to be responsive to local officials who notify central departments about a suspected outbreak of an unusual disease in their area. This prompt response demonstrates to local officials central interest and will likely encourage additional intracountry collaboration, which will build the skills of both regional and national authorities. From the beginning of fieldwork on any outbreak, it is often useful to divide scientific responsibilities. The work is more likely to proceed in an efficient fashion if all the investigators, as well as local public health officials, understand from the beginning who is bearing what responsibility for the work. This can also minimize misunderstandings when the scientific data are collected and analysed. Finally, if an epidemic is developing, investigators need to keep senior officials fully informed.

Need for surveillance

Developing an infrastructure of accurate regional surveillance in countries is an essential component of good public health policy for many reasons. First, accurate surveillance data provide ongoing information about disease trends over time. Secondly, if reporting is prompt this may serve to identify outbreaks in the early stages of development. If surveillance data are linked to laboratory results, this can increase the likelihood that laboratories will contact interna-

tional agencies qualified to respond if an unusual outbreak were to occur. In addition, by using active surveillance, quality control and validation procedures, competent programme managers can identify weaknesses in existing surveillance systems at the regional or local level and take the necessary steps to correct these.

During an outbreak investigation one necessary step is to establish surveillance of the disease of interest if none exists, or strengthen any existing surveillance. Historically, feedback from these activities has provided epidemiologists and public health officials with the best opportunity to both understand how an outbreak is progressing and design the most effective control strategies. It is critically important, therefore, that background information and ongoing monitoring of reportable infectious diseases be as complete as possible. Clinicians and surveillance experts need to be vigilant for changes in disease trends or unusual clinical manifestations to be able to identify newly emerging or re-emerging problems. The importance of this monitoring is clearly demonstrated with the recent recognition of newly described pathogens or re-emerging diseases (such as *Escherichia coli* O157:H7 causing haemolytic uraemic syndrome, hantavirus causing adult respiratory distress syndrome or Rift Valley fever virus causing outbreaks in Egypt in 1977 and 1993) [2,3,4].

Resources available in the Eastern Mediterranean Region

The World Health Organization, in partnership with both developing and developed countries, has access to many technical resources that can be brought to bear on any public health threat important to countries in the Eastern Mediterranean Region. It is well

known that infectious diseases do not honour political boundaries, so the emergence of an infectious agent in one country of the Region is a potentially important public health threat to other countries. The strong technical support available from WHO and other international agencies is one of the most important mechanisms available to concerned public health officials trying to plan outbreak responses to infectious threats to the public's health in this area.

Importance of infrastructure development

Field epidemiology training programmes

The Eastern Mediterranean Region is unique in many ways, but one important aspect is the public's interest in improved child survival, immunizable disease control and the use of applied field epidemiology to address public health issues. For example, in 1993 the Ministry of Health in Egypt established a field epidemiology training programme, which is responsible for scientific investigations of the epidemiology of important public health issues [5]. Since inception, this programme has applied the principles of epidemiology to field investigations of a wide variety of topics in Egypt including the Rift Valley fever outbreak in 1993, acute poliomyelitis, acute viral hepatitis, neonatal tetanus, pulmonary tuberculosis and other topics [4,6-10]. This programme is similar to 15 field epidemiology training programmes functioning worldwide, including one in Saudi Arabia, operational since 1985. Other Ministry of Health departments, working with other governmental departments and the staff and faculty from university schools of public health, the International Clinical Epidemiology Network (INCLEN) and Public Health

Schools without Walls (a Rockefeller Foundation funded organization), have also played a critically important role in developing the epidemiological expertise and infrastructure capable of responding to infectious threats to the public's health.

Laboratory resources available to countries in the Eastern Mediterranean Region

Additional resources available in the Region for responding to surveillance and response to emerging infections includes central and public health laboratories in ministries of health. Pasteur Institutes (Algeria, Islamic Republic of Iran and Morocco), WHO collaborating centres (Egypt, Islamic Republic of Iran, Kuwait, Morocco, Qatar and Tunisia), the US Naval Medical Research Unit No. 3 (NAMRU-3, Cairo, Egypt), the US Agency for International Development (USAID) and National Institute for Allergies and Infectious Diseases (NIAID) Middle Eastern Regional Cooperation Programs or NIAID collaborations in infectious disease research (Egypt, Pakistan, Saudi Arabia, Sudan and United Arab Emirates). Because expertise in control measures is not limited to any one country, the World Health Organization is in a unique position to organize this collaboration and improve both the quality of planning adequate responses to these outbreaks and designing control measures.

Discussion and recommendations

The recent recognition of newly emerging diseases such as infection by Ebola virus in central Africa, *Vibrio cholerae* O139 in Asia and HIV worldwide highlights the threats that exist to the public's health due to newly recognized infections. Additional

challenges for public health officials result from the increased resistance of strains of *Mycobacterium tuberculosis*, *Staphylococcus aureus* and *Enterococci* to many antibiotics currently in use [2]. These events have occurred without a clear explanation, and a great deal of scientific research needs to be done both to better understand the causes and to prepare interventions to deal with these problems. The capacity of public health officials to respond to these issues is limited by the lack of availability of well trained field epidemiologists in many ministries of health, the inadequate financial and technical support for public health laboratories, the lack of intercountry and interagency coordination and the general poor quality of information available from many existing surveillance systems.

Health workers in all countries should understand the value of professional collaboration and the need to identify outbreaks in the early stages of development, of working with laboratory experts to collect proper specimens, and the importance of assistance from international agencies able to correctly identify drug resistance or newly emerging agents. Many of these agencies are also willing and able to assist in strengthening routine surveillance and routine laboratory capabilities in the absence of any epidemic. This strengthening would serve to prepare the public health infrastructure to better respond to any future emergency. In addition, public health planners and managers need to acknowledge that a key element in improving and protecting the public's health is based on the quality and timeliness of surveillance data reported to them by epidemiologists.

The World Health Organization, working closely with technical experts from many countries, is one of the leading resources available to technically support countries seeking to improve surveillance and identify new agents or new resistance patterns. In the future, the public sector will likely continue to be constrained by inadequate funding, weak existing surveillance, insufficient laboratory support, inadequate outbreak response and lack of epidemiological expertise. Only a concerted effort by forward-looking officials in each country is likely to facilitate building both an infrastructure capable of recognizing outbreaks and responding to them in an effective manner.

Given the public's increasing concern with family health and the possible impact of emerging and re-emerging infections, it is the strong belief of the authors that establishing a responsive ministry of health infrastructure capable of responding to outbreaks is likely to pay out many dividends both in the improvement of public health conditions and increased credibility of the public sector. Outbreak investigations by competent public health officials with field experience and trained in the principles of epidemiology remains the most likely framework for successfully identifying emerging infectious diseases and designing adequate responses. Responsible public health officials need to begin planning now with the World Health Organization and other international scientific organizations to assure professional collaboration and prompt responses to the infectious outbreaks that will likely pose substantial threats to the health of large segments of the population in the Eastern Mediterranean Region in the future.

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