Outbreak investigation and epidemiology - from practice to science - .
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CHAPTER 8

General discussion: The investigation and control of outbreaks requires improvement

8.1 INTRODUCTION

Recently, infectious diseases and outbreaks of infectious diseases are back on the top of the priority lists of politicians as an emerging threat for the stability of our society. Outbreaks of natural causes on one hand - like SARS-corona virus and closer to home Legionnaires' disease, meningococcal disease caused by serogroup C and avian flu (H7N7) - and the threat of bioterroristic outbreaks on the other hand - like anthrax and smallpox - have accelerated this uprise in attention. In this scope of (re)emerging threats with possible aggravating consequences for individuals, the community and possibly even humankind, we need a robust communicable disease control system in a clear public health infrastructure. An effective communicable disease control system is essential to protect the health status of our society. With these recent changes in infectious disease dynamics, the major question is 'Is our communicable disease control system able to cope with outbreaks? To know whether we are prepared for the worst-case scenario, we first have to learn from the control and epidemiology of less serious outbreaks. The topic of this general discussion is the lessons learned from outbreak investigation.
8.2 DETECTING SIGNALS IS ESSENTIAL FOR OUTBREAK RECOGNITION

Outbreak investigation always starts with the first step - recognizing a signal of one or more cases as an outbreak. Physicians, medical laboratories and institutions have the formal task to act as eyes and ears of the communicable disease infrastructure as is stated in the Communicable Disease Act. In practice, there is still a weak link between the Municipal Public Health Service (MHS - public health) and the health care system. Therefore, many (clusters of) infectious diseases are reported quite late or not at all (underreporting). This deficiency was also identified in the Canadian public health infrastructure after an analysis of their public health response to SARS. In the outbreaks described in this thesis, a school, a rehabilitation clinic and a nursing home noticed an unusual number of cases while the general practitioners did not notice any patient. Because even everyday infectious diseases are not notified in a proper way, the detection of emerging infectious disease threats are hampered even more.

Intrinsic to the problem, evidence of the present lack of detection of signals is hard to get. Yet, evidence for underreporting of notifiable disease can be estimated with a statistical technique known as ‘capture-recapture (CRC) analysis. CRC analysis has been used to assess the completeness of notification in the Netherlands. By using this method the percentage of completeness for notifiable diseases malaria and meningococcal disease was estimated about 60%. Underreporting of infectious disease clusters can be suggested by national surveys. In 2002, the National Institute of Public Health and the Environment (RIVM) conducted a national assessment on all notified gastro-intestinal outbreaks by all Dutch MHSs. Large differences in number of outbreaks reported were observed between MHS-regions when adjusted for regional population. It is likely that a major part of these outcome differences is due to differences in notification compliance. The most reported outbreaks were from our MHS (30/281; 11%) while our region is only the 17th in order of magnitude and is inhabited by only 3% of the Dutch population.

The MHS has to make every effort to create awareness among potential notifiers of their essential role in the communicable disease control infrastructure. The better the relationships between the MHS and physicians, microbiological laboratories and institutions are, the sooner and the more often signals reach the MHS. When the MHS is able to create a general awareness among the public that they can always contact the MHS in case of infectious disease questions and observations, many signals can be received from them too.

Therefore, I suggest some strategies for the MHS to increase regional commitment to infection control. With regard to general awareness, it is beneficial to inform local media frequently about infectious disease topics and make explicit the central role and expertise of the MHS in communicable disease control. With regard to formal notification partners it is conducive to set up written agreements about mandatory and voluntary notification, have personal contact, participate in educational programs, give feedback on notified cases,
show the benefits of notification, inform formal notifiers with useful infectious disease recommendations when it matters, organize or participate in meetings and seminars about infectious disease topics, initiate or participate in infectious disease research, use modern means of communication like e-mail and websites and be accessible and available for signals, questions and advice during 24-hours a day. Particularly regarding regional institutions, it is good for notification awareness to participate in infection prevention and hygiene committees, play a role in Legionella prevention policies and institution policies for puncture and bite accidents, and care for hepatitis B vaccination programs.

8.3 ACCESS TO A PUBLIC HEALTH LABORATORY IS ESSENTIAL FOR OUTBREAK INVESTIGATION

In an outbreak investigation, diagnostic assays are essential when taking outbreak control serious. Laboratory confirmation should be part of the case definition applied when investigation an outbreak and even in an earlier stage verifying a signal. It is necessary to test patients and potentially exposed persons (contacts) to map out the outbreak and draw convincing conclusions. After all, a diagnostic survey can result in identification of the cases, the asymptomatic cases, the immunes and the susceptible contacts. A relationship of close cooperation with a Regional Public Health Laboratory (PHL) and a proper arrangement to finance diagnostic assays is an essential precondition for outbreak investigations. In daily practice, there are difficulties with timely access to laboratory testing and laboratory results. This was also identified as a systemic deficiency after the analysis of the response to SARS by the Canadian public health system. Furthermore, low invasive diagnostic public health assays (e.g. with saliva) and specific molecular typing methods to verify epidemiological assumptions are not always easily available for outbreak investigations by the MHS.

The personal benefits of diagnostic tests in the scope of individual patient care over-rule invasiveness of procedures, but in infection control, invasive procedures can restrict the voluntary attendance to diagnostic assays. Because venepuncture is often considered to be an upsetting procedure in children and mentally disabled, less invasive diagnostic procedures, such as oral fluids tests, urine tests or thumb prick tests (capillary bleeding), which are currently hardly available in the Netherlands, would be valuable for the analysis of outbreaks. Although these low invasive assays may be less sensitive and specific, this drawback is not always a problem. Outbreak control and analysis needs a diagnosis in a group and a correct diagnosis in all individuals has a lower priority. Furthermore, the predictive value of a test under epidemic circumstances requires less sensitivity and specificity to judge on the cause of an outbreak, because the incidence in the tested group is often high.

The study of an outbreak of parvovirus B19 (chapter 3) demonstrated that the thumb prick was well tolerated and well accepted as a low-invasive method to collect blood samples
in primary school children during outbreaks. When oral fluid tests are available, these will even prevail. Other examples of low invasive investigations are the *Streptococcus pyogenes* classroom outbreak diagnosed with throat swabs depicted in chapter 4, a *Mycoplasma pneumoniae* outbreak in an institution for mentally disabled people studied with PCR on throat swabs, the usage of an influenza quick test on oral fluids in for instance an influenza outbreak in a nursing home or home for the elderly and also the fecal samples from Norovirus outbreak from chapter 5.

The complimentary nature of the epidemiological analytical and microbiological findings provides the evidence of an outbreak’s source, reinforced by the specific microbiological typing assays. Outbreaks confirmed with these techniques give evidence that is more convincing in establishing cause-effect relationships. In this thesis, we successfully used molecular typing assays. We used M-genotyping, T-serotyping and exotoxin-A-and-C-gene PCR on *Streptococcus pyogenes* in the classroom outbreak of scarlet fever (chapter 2), genotyping in the Norovirus Birmingham outbreak (chapter 5), the nosocomial *Legionella pneumophila* serogroup 1 outbreak (chapter 6) and the use of genotyping in meningococcal clusters as concluded in chapter 4. During the meticillin-resistant *Staphylococcus aureus* outbreak in a nursing home the phage typing and the mecA gene tests showed their value in convincingly assessing the spurious nature of the outbreak (chapter 7).

As CCDCs experience thresholds in initiating diagnostic assays, I suggest some strategies to fill in this deficiency in our communicable diseases control infrastructure. The government should enhance the public health laboratories (network with RIVM)) and make the link between MHS and laboratory more explicit. The epidemic response capacity must be improved by investing in centres of expertise in infectious disease research (public health) and outbreak investigation where public health laboratory (and RIVM), university and MHS operate together. In these centres, the availability of low-invasive assays and molecular typing techniques for outbreak investigations should be supported. The theoretical education and experience of the CCDCs should be improved regarding microbiological procedures and epidemiological investigations of outbreaks. The government should support the status of CCDCs for initiating diagnostic tests, which are paid by the health insurance companies or by a governmental budget.
8.4 REGIONAL OUTBREAK INVESTIGATIONS IS ESSENTIAL TO IMPROVE THE NATIONAL POLICY

Regional outbreak investigations are important in public health to identify the source, implement control measures and prevent future illness; in addition, they frequently yield new knowledge that may lead to amended national infection control policies. Infection dynamics change constantly over time and exactly in case of outbreaks, investigations can reveal new sources, new routes of transmission and new patterns of disease. An example of this is the death of a veterinarian by influenza N7H7 during the avian flu outbreak in the Netherlands in 2003. Even the mild consequences for humans (conjunctivitis) were not in line with the existent knowledge of influenza A viruses in birds. This thesis shows regional outbreak investigations that lead or can lead to adjustment of national policy.

The report of the *Legionella* outbreak from chapter 6 is the first to establish the clinical relevance of *Legionella* in the cold water supply of a health care institution, causing nosocomial infections. The suggestions about surveillance of intramural water systems on temperature and *Legionella* growth - cold and hot water - were implemented in the national policy for *Legionella* prevention accelerated by the public effects of the *Legionella* outbreak at the Flower show.10

Incorrect identification of MRSA is not restricted to the incident reported in chapter 7, as proficiency-testing programs have shown that MRSA has not always been reported accurately. This alleged outbreak prompted the IGZ to discuss the subject in a circular sent to the directors of health care facilities, microbiologists and laboratories. The IGZ emphasised the importance of standardised quality and interpretation of laboratory results by microbiological experts.

Chapter 3 illustrates the confirmation of an outbreak of parvovirus B19 in a primary school using IgM ELISA and PCR on blood samples collected by thumb prick. Unexpectedly, the results showed a considerable number of discrepancies in sample results demonstrating that maximum sensitivity of parvovirus testing would require both tests to be performed. These findings are implemented in a LCI-protocol on exanthemas in children. The RIVM has worked on a low invasive diagnostic panel for exanthemas using oral fluids, urine and thumb prick tissue paper samples for assessment of the diagnosis. A pilot-project in co-operation with several MHSs is now implemented to analyse school and day care centre exanthema outbreaks using this panel to assess measles, rubella and fifth disease.

The research on meningococcal clusters (chapter 4) confirmed present control policy. Secondary cases could not have been prevented by any other interventions than the present protocols on rifampicin prophylaxis for close contacts. Moreover, no effect on meningococcal prevention is expected when distributing rifampicin prophylaxis to other groups.

Chapter 5 demonstrated a recreational fountain as a novel source of Norovirus infection showing that not only drinking water, but also recreational water may be the source
of gastroenteritis outbreaks. This outcome may lead to amended infection control policies on quality of recreational water because recreational fountains are a popular attraction in playgrounds but also in public parks or town centres. Thereby, they are a potential risk for large groups of children.

Outbreak investigations can thus not only prevent illness in direct related persons but also indirect by a declining incidence of disease through adjusted infection control policies. The Advisory Council on Health Research (RGO) also noted the lack of infectious diseases research (related to public health) in their advice on knowledge infrastructure in communicable diseases. They conclude that the MHS is the ideal setting for research into the control of communicable diseases and should be stimulated strongly. They emphasise that there should be a guaranteed possibility of performing research within the MHS.
8.5 REFERENCES


