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Role of the microbiology laboratory in infectious disease surveillance, alert and response

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ABSTRACT

Surveillance is usually defined as the ongoing and systematic collection, analysis and interpretation of health data essential to the planning, implementation and evaluation of public health practice. During recent years, most of these programmes have been developed in the field of antimicrobial resistance and nosocomial infections, but efforts have also been made in other areas. Recent experiences of emerging microbial threats, including severe acute respiratory syndrome and new influenza variants affecting humans, the re-emergence of infectious disease problems and the possibility of bioterrorism have evidenced the need for implementation of infectious disease surveillance programmes. Clinical microbiology laboratories play a pivotal role in these programmes. They have the first opportunity to detect these problems and should participate in the design of reporting strategies and dissemination of this information. Policies for the flow of data to national and international authorities should be established using passive surveillance strategies. However, active surveillance programmes taking advantage of new methodologies, including virtual tools and mathematical programs, should be the goal for early detection of unusual patterns of microbial pathogens, outbreaks and healthcare-associated infections. In addition, early implementation of response strategies should be designed and performed with the cooperation of microbiology laboratories, and intervention and response protocols should be defined with the participation of clinical microbiologists.

Keywords Active surveillance, clinical microbiology laboratory

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INTRODUCTION

Surveillance is commonly defined as the 'ongoing and systematic collection, analysis and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with timely dissemination of these data to those who need to know; the final link of the surveillance chain being the application of these data to the control and prevention of human disease and injury' [1,2]. During recent years, most of these programmes in the area of infectious diseases have been developed in the field of antimicrobial resistance and nosocomial infections, but efforts have also been made in other areas [3].

A non-exhaustive list of areas of interest and research in infectious disease surveillance is presented in Table 1.

The clear importance of the participation of clinical microbiology laboratories and microbiologists has been established in resistance and infection surveillance programmes and has been considered as a model for other areas of research [4]. These fields represent an opportunity for the implementation of microbiology techniques and research projects [5,6]. Interestingly, in resistance and nosocomial surveillance programmes, microbiologists are widely accepted and integrated into the core decision and control teams. Moreover, these programmes provide an example of effective feedback, achieved by the participation and integration of professionals.

Different publications address the importance of the microbiologist and laboratories in infection and antimicrobial resistance control programmes in the nosocomial setting [5, 7–9]. More recently, this experience has been applied to community-

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Table 1. Areas of interest and research in infectious disease surveillance

Antimicrobial resistance and multiresistant pathogens
Food-borne and water-borne diseases
Vector-borne and zoonotic diseases
Chronic diseases caused by infectious agents
Diseases transmitted through blood transfusions
Vaccination and consequences of infecting agents
Diseases of pregnant women and newborns
Diseases of travellers, immigrants and refugees
Terrorism-associated infectious disease pathogens
New emerging and re-emerging pathogens

acquired infections, and several surveillance programmes have been implemented [10]. In these programmes, quantification of resistance is commonly used for guidance in antimicrobial use, research and education programmes, and design of intervention strategies for the control of antimicrobial resistance, and this also has a clear impact on new antimicrobial development and licensing strategies. In all these programmes, microbiologists are essential partners. It has been recommended that this experience be applied to other areas of infectious disease surveillance.

Recent experience of emerging microbial threats, including the severe acute respiratory syndrome (SARS) and new influenza A virus variants affecting humans, the re-emergence of infectious disease problems and the possibility of bioterrorism have demonstrated the need for implementation of infectious disease surveillance programmes. Clinical microbiology laboratories play a pivotal role in these programmes, as they are first in line for the detection of emerging problems and consequently should participate in the design of reporting strategies, dissemination of information and intervention programmes.

MICROBIOLOGY LABORATORY: TOWARDS A NEW SCENARIO?

In the last decade, new organisational models for microbiology laboratories have emerged, due to drastic changes in healthcare systems and the emergence of microbial threats in infectious diseases. The former have been deeply analysed [11] and are related to changes in patient demographics, technical developments and changes in the workforce. In addition, the objective of healthcare cost containment has had a drastic influence on

this situation [12,13]. As a result, most microbiology laboratories have changed their organisational structures or may be required to do so in the near future. Externalisation of the microbiology assistance in central laboratories belonging to the private sector has been accomplished in some countries [14]. Also, consolidation is an attractive way for microbiology laboratory survival [14]. In some cases, routine microbiology processes such as serology or urine screening are concentrated in a core laboratory, which can provide a rapid-response at a low cost. Most of these core laboratories have emerged from biochemistry and haematology laboratories, due to the necessity of incorporating automatable processes in a rapid-response and cost-effective structure. Redundant instruments capable of multiple analyses are eliminated, and those remaining are concentrated in a core laboratory. Nowadays, core laboratories, including microbiology and immunology processes, have a horizontal organisational model (Fig. 1). Theoretically, with this organisation, microbiology processes are under the supervision of senior clinical microbiologists. An inherent advantage is that non-repetitive microbiology techniques can be developed in specific microbiology laboratories. This may consolidate microbiology laboratories. They can improve techniques in the field, including molecular techniques, implementing traditional microbiology-based techniques, and restoring the consultation role of the clinical microbiologist [13]. This has led to the active participation of microbiologists in nosocomial

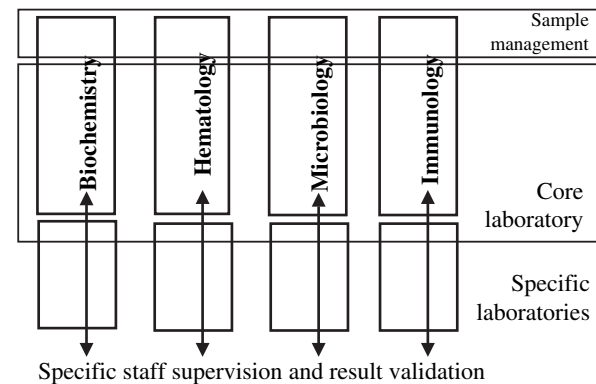


Fig. 1. Core laboratory structure with a horizontal model organization. Automation systems, technologies, management of patient samples. Quality control protocols are common but supervision of the results is performed by different staff.

infection management. In some European countries, microbiologists are considered essential for the control of nosocomial infections. Microbiology surveillance studies, educational interventions, recommendations for the control of nosocomial infection, audits and feedback initiatives are developed with the active participation of the microbiologist.

It is worth noting that organisational models of microbiology laboratories may drastically affect infectious disease surveillance. The emergence of West Nile viruses in the USA has shown the need for the maintenance and revitalisation of microbiology laboratories [14]. The experience gained with emerging viral infections, including Ebola and influenza A viruses, and particularly with SARS, has revealed that microbiology laboratories might act as sentinels of emerging infectious disease threats [16]. Rapid alert to outbreak situations may be accelerated with microbiology laboratories integrated into national and supra-national global surveillance programmes. Open cooperation with international networks has been essential for the design of control strategies. In addition, the application of new molecular diagnostic techniques and the involvement of basic research microbiology laboratories have been effective in resolving new microbiological threats (e.g., the SARS experience).

ALERT AND RESPONSE OF MICROBIOLOGY LABORATORIES IN INFECTIOUS DISEASE SURVEILLANCE PROGRAMMES

The alert and response of microbiology laboratories in infectious disease surveillance programmes should be performed with the implementation of natural workflows in microbiology laboratories. Some of these processes can be developed in cooperation with research laboratories if this activity is not integrated in the same laboratory (Fig. 2). Natural workflow of microbiology laboratory includes: (1) specimen management, (2) specimen processing (methods), and (3) results and data flow.

Specimen management

Specimen management is essential for accurate work in the clinical laboratory. It has been

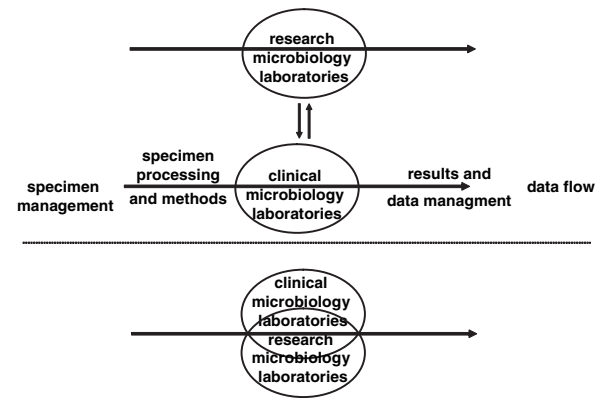


Fig. 2. Work flow of microbiology laboratories, integration of research laboratories and processes that can be implemented for infectious diseases surveillance in these laboratories.

recognised that appropriate collection and handling are essential for the diagnosis of infectious diseases and also for infectious disease surveillance [17]. Specimen selection criteria, collection procedures, labelling, transport conditions and storage criteria should be established with the participation of the clinical microbiologist. All these processes should be performed under adequate biosafety conditions capable of protecting laboratory workers.

Nowadays, transport of biological material to different laboratories or from healthcare facilities to a laboratory is a common feature of healthcare systems. Moreover, in infectious disease surveillance networks, transportation of biological samples, including patients' material and viable microorganisms, to a central laboratory is a common practice. These materials should be adequately packed, not only to protect transport handlers, but also to prevent specimen deterioration and avoid the spread of infectious agents. In addition, labelling should be performed according to national and international regulations. Although these processes are bureaucratic and time-consuming, microbiologists should be familiar with these procedures, particularly when samples are sent for processing in a central laboratory.

Specimen processing and methods

Microbiology laboratories must implement rapid techniques, including immunoassay, microscopy and molecular testing [13]. New molecular methods have been developed during the last two

decades and have recently been introduced in clinical laboratories as a consequence of automation and the development of techniques that are easier to perform. Clinical microbiologists should become familiar with molecular techniques and incorporate these in the normal microbiology routine. The introduction of rapid response in some laboratory areas has demonstrated clinical and economic benefits for healthcare systems, particularly in antimicrobial susceptibility testing and virology [18,19].

Molecular techniques have had a direct impact on rapid response and infectious disease surveillance. They have been shown to be essential for the identification of emerging pathogens and for understanding their population structure. They are also useful for characterising virulence determinants and the genes participating in antimicrobial resistance. During outbreaks, they are essential tools for tracking the spread of microbial pathogens and for evaluation of intervention strategies [6,20]. The results of a large number of researchers have shown the advantages of molecular techniques in infectious disease surveillance, including local studies and international networks, not only in the nosocomial setting but also in the community. Molecular techniques also have the advantage of being useful for researching genetic determinants without culturing organisms, thus allowing a more rapid laboratory response.

Results and data management

Most of the infectious disease surveillance networks have based their strategies on the management of results generated by microbiology laboratories [21–23]. The different experiences at local and international levels have increased the efficiency of this process. The clinical laboratory should ensure sufficient internal data management resources and a substantial database storage capacity, as well as adequately developed computing equipment and protocols. Internal microbiology software should permit the automatic alert of unusual results, and detection of increased trends and accumulation of cases. These systems must be flexible and accessible to other computing systems in order that microbiology data can be integrated in regional, national and international databases. Again, experience in this area is based on resistance surveillance with the active participation of microbiologists.

ROLE OF THE MICROBIOLOGIST AND CLINICAL MICROBIOLOGY LABORATORIES IN PASSIVE, ACTIVE AND VIRTUAL SURVEILLANCE

Surveillance programmes have made apparent the importance of microbiology laboratories for public health action in infectious diseases [24]. The strategies of traditional systems (passive surveillance), which have been used on national and international levels, were based on detecting problems through the systematic routine analysis of all microbiological data. These systems are time-consuming and do not require personnel trained in infectious diseases or infection control. Alert is commonly performed with a paper-based system and requires a prolonged period of time for response.

The alternative to passive surveillance is the active surveillance system, which targets infectious disease problems and thresholds that have been previously established. Trained professionals, including clinical microbiologists and epidemiologists, actively participate in surveillance, and information is more rapidly processed. Recently, there has been an increase in international use of sentinel laboratories to improve upon traditional systems [23]; unreported infectious disease problems have been detected, and additional information obtained by global surveillance networks has been provided.

Active surveillance systems are now augmented by the inclusion of new computing technologies and the use of mathematical models. This novel strategy, also called 'virtual surveillance', is one of the most attractive options to optimise available laboratory information and can be developed with the active participation of specifically trained clinical microbiologists to provide real-time information. Nowadays, virtual surveillance should be the goal for early detection of unusual patterns of microbial pathogens and healthcare-associated infections [25].

Recent experience has demonstrated the advantages of surveillance systems that employ electronic laboratory-based reporting systems. They are frequently promoted to improve data quality and efficiency of collection, but they are essential for outbreak detection. In this sense, the availability of internet access permits rapid feedback and

even interactive interventions for the exchange of interpretation and action plans. In the Pennsylvania experience, which covered a large population area [20], several laboratories implemented their computing systems and connected them to the regional healthcare electronic information system. Automatic reporting was found to be more effective than the conventional system, reducing the time needed for a paper-based report (median, 5 days), to a median of 1 day for an electronic report. Similar systems have now been developed in some European countries [22]. Features include the use of a flexible algorithm for daily analysis of data and presentation of signals on the internet for interpretation by health professionals. These systems are designed to complement, but not replace, conventional methods, as they receive reports from sources other than laboratories (e.g., clinician-based surveillance of notifiable diseases). Electronic/laboratory-based surveillance will allow early implementation of response and control strategies. Moreover, electronic reporting is highly sensitive and specific, with a low rate of false-positive and false-negative results.

ADVANTAGES OF MICROBIOLOGY LABORATORY PARTICIPATION IN INFECTIOUS DISEASE SURVEILLANCE

The participation of routine microbiology laboratories in surveillance has clear advantages for infectious disease surveillance. Technical methodologies and reporting of results can lead to better analysis, and all the information can be centralised, particularly when laboratory computing systems are connected to regional, national and supra-national systems. Automatic 'expert systems' can thus be developed to augment the analysis of surveillance data, and automatic alerts can be centralised for response strategies. Microbiology laboratories and microbiology resources may also facilitate temporal and spatial analysis of surveillance data, which would ensure the complete collection of notifiable diseases, as well as the detection of changing patterns.

CONCLUSION

In conclusion, infectious disease surveillance requires the active participation of microbiology

laboratories, in which new methodologies and robust information technologies should be implemented in order to guarantee early detection of outbreaks. Early response strategies should be designed with the cooperation of microbiology laboratories, in which the efforts of clinical and research microbiologists should be coordinated.

REFERENCES

1. Teutsch SM, Thacker SB. Planning a public health surveillance system. *Epidemiol Bull* 1995; **16**: 1–6.
2. Thacker SB. Surveillance. In: Gregg MB, ed. *Field Epidemiology*. Oxford: Oxford University Press, 1996; 16–32.
3. Pinner RW, Rebmann CA, Schuchat A, Hughes JM. Disease surveillance and the academic, clinical, and public health communities. *Emerg Infect Dis* 2003; **9**: 781–7.
4. Peterson LR, Hamilton JD, Baron EJ *et al.* Role of clinical microbiology laboratories in the management and control of infectious diseases and the delivery of health care. *Clin Infect Dis* 2001; **32**: 605–11.
5. Peterson LR, Noskin GA. New technology for detecting multidrug-resistant pathogens in the clinical microbiology laboratory. *Emerg Infect Dis* 2001; **7**: 306–11.
6. van Belkum A. High-throughput epidemiologic typing in clinical microbiology. *Clin Microbiol Infect* 2003; **9**: 86–100.
7. Pfaller MA, Herwaldt LA. The clinical microbiology laboratory and infection control: emerging pathogens, antimicrobial resistance, and new technology. *Clin Infect Dis* 1997; **25**: 858–70.
8. Struelens MJ. Multidisciplinary antimicrobial management teams: the way forward to control antimicrobial resistance in hospitals. *Curr Opin Infect Dis* 2003; **16**: 305–7.
9. Nicolas-Chanoine M-H. Future needs – diagnostic services. *Clin Microbiol Infect* 2000; **6**: 423–5.
10. Felmingham D, Feldman C, Hryniewicz W *et al.* Surveillance of resistance in bacteria causing community-acquired respiratory tract infections. *Clin Microbiol Infect* 2002; **8**(Suppl 2): 12–42.
11. Rose NR. *Microbiology in the changing world of health care management*. Washington: American Academy of Microbiology, 1998.
12. Robinson A, Marcon M, Mortensen JE *et al.* Controversies affecting the future practice of clinical microbiology. *J Clin Microbiol* 1999; **37**: 883–9.
13. Raoult D, Fournier PE, Drancourt M. What does the future hold for clinical microbiology? *Nat Rev Microbiol* 2004; **2**: 151–9.
14. McDade JE, Hausler WJ Jr. Modernization of public health laboratories in a privatization atmosphere. *J Clin Microbiol* 1998; **36**: 609–13.
15. Fine A, Layton M. Lessons from the West Nile viral encephalitis outbreak in New York City, 1999: implications for bioterrorism preparedness. *Clin Infect Dis* 2001; **32**: 277–82.
16. Kuiken T, Fouchier R, Rimmelzwaan G, Osterhaus A. Emerging viral infections in a rapidly changing world. *Curr Opin Biotechnol* 2003; **14**: 641–6.
17. Reisner BS, Woods GL, Thomson RB, Larone DH, Garcia LS, Shimizu RY. Specimen processing. In: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Tenover RH, eds. *Manual*

- of *Clinical Microbiology*, 7th edn. Washington, DC: American Society for Microbiology, 1999; 65–104.
18. Barenfanger J, Short MA, Groesch AA. Improved antimicrobial interventions have benefits. *J Clin Microbiol* 2001; **39**: 2823–8.
 19. Barenfanger J, Drake C, Leon N, Mueller T, Trout T. Clinical and financial benefits of rapid detection of respiratory viruses: an outcomes study. *J Clin Microbiol* 2000; **38**: 2824–8.
 20. Hasnain SE. Molecular epidemiology of infectious diseases: a case for increased surveillance. *Bull WHO* 2003; **81**: 474.
 21. Panackal AA, M'ikanatha NM, Tsui FC *et al.* Automatic electronic laboratory-based reporting of notifiable infectious diseases at a large health system. *Emerg Infect Dis* 2002; **8**: 685–91.
 22. Widdowson MA, Bosman A, van Straten E *et al.* Automated, laboratory-based system using the Internet for disease outbreak detection, the Netherlands. *Emerg Infect Dis* 2003; **9**: 1046–52.
 23. Arita I, Nakane M, Kojima K, Yoshihara N, Nakano T, El-Gohary A. Role of a sentinel surveillance system in the context of global surveillance of infectious diseases. *Lancet Infect Dis* 2004; **4**: 171–7.
 24. Peterson LR, Brossette SE. Hunting health care-associated infections from the clinical microbiology laboratory: passive, active, and virtual surveillance. *J Clin Microbiol* 2002; **40**: 1–4.
 25. Peterson LR, Hacek DM, Rolland D, Brossette SE. Detection of a community infection outbreak with virtual surveillance. *Lancet* 2003; **362**: 1587–8.