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Journal of Clinical Virology 40 Suppl. 1 (2007) S58–S60

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Respiratory virus panels for global surveillance of emerging infectious diseases

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Keywords: Diagnostic assays; Multiplex; Infectious Disease Surveillance

1. Introduction

The success in dealing with SARS can partially be attributed to detection of a unique disease within an established healthcare system, international efforts to contain the spread of disease, and rapid identification of a newly emerging pathogen using advanced molecular techniques. Despite this success, the outbreak exposed several weaknesses in the established surveillance networks and demonstrated the potential social and economic toll infectious disease outbreaks can exert, even in developed countries. SARS was a slow-spreading virus with low communicability and a long incubation period, yet it spread to 29 countries in five continents over a period of a few weeks, infecting over 8000 patients with 774 fatalities (Poon et al., 2004). In contrast, influenza has a shorter incubation period, higher infectiousness rate than SARS and annually kills tens of thousands of persons. Global attention is now focused on the increasing number of influenza A H5N1 outbreaks in poultry and humans, as well as increased infections of humans with other avian influenza viruses (Wong and Yuen, 2006). Although no clear evidence of efficient human-to-human transmission of avian influenza has as yet been reported, the increased number of confirmed influenza A H5N1 in family clusters raises concerns that sustained human-to-human transmission will soon emerge (Gilsdorf et al., 2006; Kandun et al., 2006).

The SARS epidemic in 2002, *Streptococcus suis* outbreaks in China in 2005 (Ye et al., 2006), and the current spread of influenza A H5N1 around the world are examples that highlight the need for global engagement on regional disease outbreaks, especially in resource-poor countries where the burden of disease is highest (Lopez et al., 2006). Sustained global investment is needed to improve the capacity in many developing countries to detect endemic, epidemic and newly emerging pathogens. Accurate determination of agent-specific regional disease burden will help guide the allocation of limited resources for use in existing prevention modalities, provide crucial information for vaccine development, and assist public health authorities to establish directed vaccination programs and other public health prevention strategies. Since agent-specific disease burden estimates will likely vary based on regional conditions, it is important to establish the different geographic and epidemiological profiles in order to establish priorities for prevention strategies.

2. Dilemmas in identifying viral pathogens in respiratory samples

Public health laboratories (PHLs), which form the foundation of the global surveillance network, are faced with some key dilemmas with respect to the identification of viral pathogens in respiratory samples. We believe that many of these problems might be addressed through the selective use of some of the newly available commercial respiratory viral panels (RVPs). The newest of these RVPs allows for the sensitive and specific detection of viral pathogens following extensive multiplexing of polymerase chain reaction (PCR) and reverse-transcriptase PCR (RT-PCR) reactions without the loss of sensitivity previously seen in other diagnostics systems (Li et al., 2007).

2.1. Dilemma 1 – How to deal with large numbers of patient samples?

During SARS our laboratory in Toronto faced surges of numbers in respiratory samples that were 5–10 times those normally encountered. During a normal respiratory virus

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season our PHL will also be required to identify a wide variety of respiratory viruses in tens of thousands of patient samples from respiratory virus outbreaks as well as sporadic cases of fever and respiratory illness. Thus, identification methods must be rapid, comprehensive and must conserve laboratory as well as human resources (Brown, 2006; Cheng et al., 2004). Although traditional methods of identification that use a combination of methods (i.e. culture, rapid antigen detection assays and low target number molecular assays) are often effective (Dunn et al., 2004; Zitterkopf et al., 2006) the combination of these techniques reduces the number of patient samples that can be tested at any one time, and also limits the sample volume available for further testing (Khanna et al., 2005).

2.2. Dilemma 2 – How to be a comprehensive reference laboratory?

Since the etiology of one-half to three-quarters of community-acquired pneumonia cases is unknown, new technologies to identify a wider variety of respiratory viruses are needed (Ewig et al., 2002; Fine et al., 1999; Garbino et al., 2002). The initial difficulties of culturing emerging avian influenza viruses (Brown, 2006) and common viruses such as human metapneumovirus (Scheltinga et al., 2005) indicate that PHLs must develop culture-independent diagnostic methods. Even though non-culture based methods (i.e. molecular diagnostics) are widely available for the identification of individual respiratory viral pathogens, methods for simultaneously screening for a wide array of pathogens are needed (Rachlin et al., 2005).

2.3. Dilemma 3 – How to prepare for emerging respiratory pathogens including pandemic influenza and bioterrorism agents?

The past decade has seen the emergence of several new respiratory viruses (Gillim-Ross and Subbarao, 2006). The spectre of these agents, including pandemic influenza and bioterrorism agents, means that PHLs will face increasing pressure to identify new agents as they emerge, and develop a capacity to separate highly pathogenic agents from less virulent seasonal respiratory viruses (Cirino et al., 2004). Extensively multiplexed PCR reactions may help PHLs identify a wide variety of agents without the use of Biosafety Level III laboratories. Molecular techniques will also allow PHLs to identify subtypes and strains of emerging respiratory viruses, and laboratory working groups for pandemic influenza now suggest that PHLs retain the ability to subtype and characterize influenza strains (i.e. resistance testing and virulence testing) using these techniques[1].

[1] http://www.phac-aspc.gc.ca/cpip-pclcpi/ann-c_e.html

3. Commercial respiratory virus panels as a solution to these dilemmas

We propose that the above dilemmas might be solved through the use of broad-spectrum commercially available respiratory virus panels which utilize extensively multiplex technologies. With proper planning, RVPs may be integrated into protocols that allow for large numbers of samples to be tested rapidly and economically (Brunstein and Thomas, 2006). The inclusion of "difficult to grow" viral pathogens in these panels will provide better data on their prevalence. RVPs can also be integrated into pandemic preparedness and bio-terrorism plans. Not only can they be used for the sub-typing of influenza viruses but they may be used during the early phases of a pandemic to differentiate between outbreaks caused by seasonal influenza or other pathogens and those caused by an emerging pandemic strain. The extensively multiplexed nature of newer RVPs might allow for the development of new tools for the diagnosis of pathogens used in biological warfare and bioterrorism.

4. Conclusions

We believe that the emergence of commercially available respiratory virus panels heralds a new era in public health microbiology. These tools will hopefully not only improve work flow but will also benefit clinical reporting, public health epidemiology and increase laboratory preparedness for pandemic influenza and other emerging pathogens.

5. Conflict of interest statement

None declared.

6. Acknowledgements

Dr. Brice would like to thank Jean-Paul Chretien and Shannon Putnam for their discussions and review of the manuscript. The opinions are the views of the author, and are not to be construed as official views of the Department of the Navy or the Department of Defense. Dr. Low's research is supported by Tm BioScience.

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