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Emerging new technologies in clinical virology

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In the recent past, the discovery of the viral aetiology of several human diseases, and major advances in our knowledge of the steps of the viral life cycle, and the natural history, pathogenesis and chemotherapy of viral diseases, have led to the development of powerful assays for the diagnosis of these diseases. Indeed, almost all central hospitals and healthcare facilities in western countries have an active viral diagnostic laboratory. The above process, however, took several decades, and is far from being complete, with new methods and techniques currently being developed for the diagnosis, monitoring and characterization of viral infections, and new and unexpected issues on the topic being generated.

When the concept of 'diagnosis of viral infection' was introduced, the major emphasis was placed on the isolation of viruses and on 'conventional' serological tests. From the very beginning, however, it was clear that virus isolation was expensive and, above all, time-consuming, and that serological tests required sera collected ≥10 days from the onset of infection: in both cases, the tests frequently provided a diagnosis in retrospect.

Later, the clinical virology laboratory benefited from other, more modern, techniques, such as electron microscopy, immunofluorescence, radioimmunoassay, and ELISAs. As well as detecting antibodies to the viruses, some of these methods were adapted to detect viruses directly in clinical specimens. This yielded more rapid results, and a diagnosis could sometimes be established on the day when the clinical sample was collected, making the assays clinically useful.

More recently, dramatic advances in molecular techniques have revolutionized the diagnosis of viral infections, together with several other biomedical disciplines. The different molecular techniques, known and utilized only in specialized laboratories for decades, found application in clinical virology laboratories. This represented a breakthrough whose impact, to my mind, is still ongoing. Foremost has been the development of PCR and, later, real-time PCR, which are highly sensitive, specific, reproducible, relatively inexpensive and easy to automate molecular technologies. Additionally, gene sequencing technology has now matured into a modern technique that is able to yield results in a reasonable time at reasonable cost. Thus, it is today possible to determine the specific virus that the patient is harbouring, sequence it, and measure its viral load in biological samples in a matter of few days. This allows the clinician to monitor the infection or to evaluate the efficacy of an antiviral treatment in, to quote an over-used term, real-time. In special circumstances, such as human immunodeficiency virus, hepatitis B virus and hepatitis C virus infections, or viral infections in transplanted patients, virological surveillance by sensitive and quantitative molecular methods has become an essential part of the diagnostic routine, because the timely detection and monitoring of virus copy numbers are prerequisites for successful preemptive and therapeutic treatment approaches.

For the above reasons, concept and significance of viral diagnosis and inherent processes have changed in many instances and along the years. The clinical virologist not only has to identify the virus whose infection is associated with definite symptoms, but must also provide insights to clinicians to help them define the course of infection, its prognosis, and eventually the efficacy of therapy.

As stated before, the evolution of the viral diagnosis process is far from complete. We are witnessing a burgeoning development of impressive new diagnostic technologies, and innovations are appearing in the field.

This theme section aims to describe and discuss only some of these new technologies, in the belief that, if properly and carefully utilized, they could soon become part of the virology laboratory routine to assist the clinician in the modern and cautious management of patients with viral infections.

The technologies that are rapidly entering the field include the new techniques based on multiplex RT-PCR amplifications followed by microarray analysis. This new assay has already been applied in clinical virology laboratories for various viral infections caused by definite viruses [1,2], and has the potential of rapidly detecting and identifying viruses directly in clinical specimens, including typing and subtyping of a broad panel of common and newly discovered human viral pathogens. Some of the reagents have found rapid applications and have become commercially available, but the wide-scale application of the technology in clinical virology

laboratories merits awareness and attention. The latter arguments are the main topic of the review by Andreoletti's group [3] in this issue.

Major advances in nucleic acid sequencing technologies, often referred to as 'next-generation sequencing', have produced an outright revolution, providing a new opportunity for the diagnosis of viral infections. This process has already been applied at the diagnostic level for some viral infections, leading to the discovery of new viruses, sequencing of the whole viral genomes present in clinical specimens and/or the detection of minor viral variants that may have clinical relevance, which were previously not possible with conventional methods [4,5]. In this issue, Capobianchi *et al.* [6] discuss what is currently known about the possibility of wider application of next-generation sequencing in clinical virology laboratories.

'Omics' technologies, such as genomics and transcriptomics, have greatly enhanced the systematic evaluation of gene expression. Despite their usefulness, the limitations of genomics and transcriptomics approaches are well known, and this is also true in clinical virology. For instance, virus–host interactions cannot be easily predicted by genomics and transcriptomics, as gene mutations and mRNA expression levels often do not necessarily mirror the actual situation in terms of mature and functional proteins, owing to the possibility of post-translational regulation. In light of the above considerations, the major advances in mass spectrometry-based proteomics technologies may provide a unique tool for structural and functional analysis of the effectors of biological functions, and this may find useful applications in virology, shedding more light on host–virus interactions. At present, this approach has been applied to viral infections in some cases [7–9], but, in my opinion, it has the possibility of wide application, especially in clinical situations where knowledge of the pathogenetic mechanism of the viral infection may help in disease management. These aspects are addressed in this issue by Tripodi's group [10], who mainly discuss the potential of mass spectrometry proteomics in viral infections, focusing essentially on hepatitis C virus infection.

Irrespective of the type of new technique addressed, the quality of diagnostic results is of paramount importance. Indeed, for the future, there is a pivotal need to concentrate on the issue of ensuring quality results in terms of accuracy. As logistic factors sometimes prevent the institutional entities operating in parallel with the rapid acquisition of new technical knowledge, other approaches can be used. The above topics are discussed in the review by Ieven *et al.* [11] in this issue.

The theme section does not tackle another, to my mind, very important issue. The clinical virology laboratory is, and in the immediate future will be increasingly, able to provide an enormous amount of detailed data on the characterization of the patient harbouring viruses and, eventually, the effectors of the mechanism of pathogenesis and recovery from the infection. The leading task is to translate all of these new findings into the patient's clinical management, in an attempt to monitor the infections and readily predict the efficacy of an antiviral treatment or give a reasonable prognosis. This necessarily entails a reappraisal of and an emphasis on the role of the clinical virologist, who has to work alongside clinicians to manage patients and their treatment. This means that communication between laboratory personnel and clinicians (which, for logistic reasons, large hospitals might lack) is vital to ensure that the diagnostic process is carried out properly.

Trasparency Declaration

There are no conflicts of interest to declare.

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