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EDITORIAL

Urine-based viral diagnostics: an innovation in waiting

During my professional lifetime, viral diagnostics have graduated from a cottage to a multinational biotechnical industry. This change has brought with it automation, standardisation, regulation and more accurate results that offer better support to clinicians than ever before.

The downside, however, has been deskilling within hospital laboratories, a narrowing of diagnostic range and a brake on responsiveness and in-house innovation. This loss of versatility may be most keenly felt by those who have to confront emergent infections and need laboratory support for the clinical and public health measures that must quickly be taken to deal with epidemic disease. In the past, it was rapidly possible to diagnose HIV infection once that virus had been discovered and then, successively and promptly, to diagnose SARS and the Middle East coronaviruses, influenza A H5N1 and Ebola viruses. But will, for instance, a new epidemic strain of influenza now be recognised as quickly or the extent of any other emergent infection be determined with the same responsiveness? These unforeseen challenges often have logistical, cultural, ethical and safety as well as technical aspects, and they require rapid, workable solutions. They make demands that "Big Diagnostics" may not meet in a sufficiently timely fashion.

The continuing epidemic of Ebola infection in three contiguous West African states in 2014/15 has pointed up the problems that the further erosion of diagnostic laboratories' versatility and bench skills may give rise to. The joint clinical and public health response to the epidemic has required polymerase chain reaction (PCR)-based assays, and as fast track vaccine development proceeds, it will need the development of serological tests. To evaluate candidate Ebola vaccines, regional laboratory diagnostic services will have to be maintained even as the epidemic subsides.

The success so far in bringing Ebola in West Africa under control has been due to the establishment of field laboratories where patients have been tested for Ebola infection and other infections excluded. These excellent interventions have been funded by partnerships between international charities and governmental and other donors, and have been based on the know-how of a few First World laboratories. Commercial diagnostics have so far only played a small part, though innovative start-up laboratories may increasingly do so in the future.

Where might such innovation lead? The recent announcement by its manufacturer of a low-tech Ebola antigen test, even one less accurate than PCR, points the way towards a more convenient laboratory diagnostic and so a quicker outbreak control in the future. An antigen test will be less sensitive than PCR and may imply a day or two's delay in diagnosis; but a point-of-care test that is better adapted to local conditions may prove the adage that the perfect (i.e. PCR) can sometimes be the enemy of the good.

The Ebola epidemic has involved repeated collections of venous blood samples, often with difficulty because of poor venous access and attendant safety considerations. In these circumstances, might more readily collected urine samples substitute for venous blood? Urinary viral diagnostics have so far only attracted intermittent attention, but urine samples can be self-collected, and procedures as sensitive as PCR can then be applied to them. In November 2014, the Centers for Disease Control and Prevention posted a method for the PCR detection of Ebola sequences applicable to urine samples [1].

A non-exhaustive trawl of the web reveals references to the application of PCR to urine samples for other diagnoses: measles; mumps; cytomegalovirus (CMV); human immunodeficiency virus (HIV); polyoma virus; adenovirus; middle east coronavirus; and dengue virus. Few of these publications give a definitive indication of clinical sensitivity, but they suggest that urine-based diagnostics might be useful in otherwise difficult circumstances even if not as immediately accurate as a blood sample. Given the

general high sensitivity of nucleic acid amplification procedures, a urine-based PCR might be expected to detect those viruses like mumps, CMV and polyoma that are readily isolated from urine in cell culture as well as other, blood-borne infections. It could be of value in signalling high viraemia and so in determining infection control procedures e.g. in Ebola and other currently emergent infections [2].

Detection of specific antibodies in urine samples has been reported in respect of HIV, measles and hepatitis viruses, often based on the capture of the specific antibody onto an anti-IgG and/or an IgM-coated surface and then adding a diagnostic enzyme label or virally coated particles [3]. This approach has proved surprisingly sensitive and has already been employed in the contexts of public health screening and epidemiological surveys to indicate recent or persistent infection. It may have clinical diagnostic value too.

In the short term, innovations like these are unlikely to yield profit for "Big Diagnostics", and so it is down to academic and other public laboratories to explore their applications. In an age of black box automation and laboratory machine minding, it is particularly important not to allow the diagnostic laboratory response to emergent infections to become dependent on, and so have to wait for, the appearance of a substantially profitable commercial opportunity. Emerging infections in the Developing World context need not-for-profit involvement and the maintenance of the skills that will support rapid *ad hoc* diagnostics. These skills should therefore remain part of technical training and be nurtured, and the innovatory spirit associated with them should not be allowed to wither.

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