 10.1111/j.1469-0691.2007.01738.x

Are point-of-care (POC) virological tests what is needed?

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ABSTRACT

Point-of-care (POC) tests are becoming more available, although the way in which they should be used is currently undecided. Any 'laboratory'-based diagnosis of respiratory infections has three components: the specimen taken, the test used, and the interpretation of the results. Each of these components needs to be carefully addressed when using POC tests for the diagnosis of respiratory tract infections. Given the enthusiasm with which POC tests are being developed, it is likely that they will be used more and more widely. If so, the advantages and limitations of their use should be fully discussed and the implications recognised.

Keywords Diagnosis, influenza, point-of-care tests, respiratory tract infections, travellers

Clin Microbiol Infect 2007; **13**: 655–656

In this issue of CMI, Weitzel and colleagues from Berlin present data concerning the use of a point-of-care (POC) test for the detection of influenza A and B viruses [1]. This and other similar tests are intended to be used by clinicians at the bedside to allow patient management and treatment decisions to be made very rapidly, especially with respect to returning travellers who may be carrying, e.g., new pathogenic strains of pandemic influenza virus. The test evaluated by Weitzel *et al*. [1] shows adequate specificity (the positives were, except for a small number, correct with only one false-positive) for both viruses, but the sensitivity was low. Only about two-thirds of the individuals who were positive according to PCR assays or culture were positive according to the POC test. This is worrying if this and other similar tests (http://www.who.int/csr/disease/avian_influenza/guidelines/rapid_testing/en) are promoted for widespread use as front-line tests for identifying influenza in febrile travellers returning from foreign countries, which is an approach that has been recommended by the WHO (http://www.who.int/csr/disease/avian_influenza/guidelines/rapid_testing/en).

Any 'laboratory-based' diagnosis of respiratory infections, bedside or otherwise, has three components: the specimen taken from the patient; the test used; and the interpretation of the result of the test. All these components must be of a standard good enough for the task, but the quality of the specimen is crucial. A poorly taken specimen containing no or insufficient virus material cannot yield a positive result, even if the patient is, indeed, infected. Inevitably, such a specimen will give a false-negative result. Where the patient may be bringing a novel infection into a country or community, this is potentially disastrous and negates the purpose of using a POC test.

All diagnostic virologists are aware of the difficulties of getting good respiratory specimens. As few patients enjoy having swabs or aspirators inserted into their nose or nasopharynx, it is much, much easier to take a bad specimen than a good one. Missing from almost all tests, POC or traditional, is any form of marker to indicate whether the specimen contains sufficient material to make the result reliable, particularly when apparently negative results are obtained. Only immunofluorescence (IF) provides this vital feedback at present [2]—if there are no ciliated respiratory cells visible in the preparation examined in the microscope, the microscopist knows that the specimen is unsuitable, either because it has been inadequately taken or because it has been mishandled during preparation. POC tests have no such safeguard, and the poor sensitivity reported by Weitzel *et al*. [1] may have been caused, at least in part, by poor specimens having been taken. Tellingly, the authors comment that

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the positivity rate was higher with more floridly ill patients and with children, from both of whom it may have been easier to get a competent specimen.

This is not a transient problem. Diagnostic virologists know that getting good, consistent respiratory specimens is a battle that is never won. Non-virologists rarely understand the problem in detail, and the continuing successful collection of specimens at the bedside relies heavily on (often indignant) feedback from the laboratory. Moreover, no sooner is one set of nurses or junior doctors well-trained in how to collect a good specimen than staff rotation takes the situation back to square one. Commercially produced tests have not hitherto included a marker to assess specimen quality, and perhaps the manufacturers should be more aware of this deficiency. It does not matter how well the actual test performs if it does not tell the user that time is being wasted on a useless specimen, and that the ensuing result (if negative) cannot be relied upon.

Dipstick-type tests have been available to detect protein, sugar, haemoglobin, etc. in urine for many years. In contrast to respiratory tract specimens, urine is (comparatively speaking) easy to collect and much more standard than the respiratory equivalents—if it looks like and smells like urine, that is what it is likely to be. A swab, or even an aspirate, is not so informative, and the available quantity is much smaller. Bacteriological swabs are less critical because culture is relatively fast and can compensate better for a minimal specimen.

Another limitation of the specific POC test evaluated by Weitzel *et al*. [1] is that, at present, it detects only influenza A or B viruses; other viruses also cause very similar syndromes [3]. The ability to detect a different aetiological cause (because dual infections are generally rare, at least in adults) is more useful than a test that is simply negative for influenza. Not influenza virus? Then what is the patient suffering from? Any test that concentrates on one virus to the exclusion of others must give a biased perspective on virus diseases generally. It may not be influenza virus, but it could be SARS virus, an adenovirus, a parainfluenza virus, a respiratory syncytial virus, a metapneumovirus, or even measles virus. Not to mention a common cold virus.

Finally, there is the matter of interpreting (any and all) results and assessing new tests and variants of old tests. This is, or has been, the province of the professional virologist (http://www.rcpath.org/index.asp?PageID = 117). Training to become proficient takes time and experience; are those clinicians who might use POC tests willing to acquire a similar proficiency in virology, as well as in their own clinical specialty? In English, this is called 'keeping a dog and barking yourself'. Does it make sense? Both a positive result and a negative result need interpretation, and even positive results are not always significant [4–10]. This should be a task for an individual who is familiar not only with the test being used, and its limitations, but also with whatever other viruses are currently circulating in the community/world at large, as well as the medical details of the patient; in other words, someone who can put the result into a wider and proper context.

Given the enthusiasm with which POC tests are being developed, it is likely that they will be used more and more widely. If so, the advantages and limitations of their use should be fully discussed and the implications recognised.

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