Quality control and quality assurance for point of care (POC) diagnostic tests

Introduction

Point of care (POC) tests are those performed outside a central laboratory, using testing devices that are easily transportable to perform testing near where the patient is located [1]. POC testing is also known as near patient testing, patient self testing, rapid testing and bedside testing. This definition involves a wide range of types of POC testing which is summarised in Table 1.

Experience with blood-borne viruses (particularly HIV [7]) has made POC tests suitable for home use, such as the HIV OraQuick [licensed by the US FDA on 7 November 2002]. Thus, POC testing takes in a wide range of different testing algorithms, some of which are listed in Table 2.

The availability of POC tests to individuals in the community is often dependent upon ease of use. Moderately simple testing utilising incubation steps [8], has been superseded by card based immunochromatographic methods [9]. In turn, the availability of POC treatment for illnesses such as HIV [10] and influenza [11] have prompted decision-based algorithms for treatment, based upon comparison of POC testing versus treatment without testing.

Table 1. Types of POC tests

POC testing and their uses
Non-infectious agents
• Glucometers
• Blood gas monitors
• Pregnancy
• Cardiac monitors
Infection markers
• acute phase reactants [2]
• C-reactive protein [3]
Infectious agents [4-6]
• Influenza
• HIV
• STI
• Meningococcus

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Some POC testing algorithms overlap testing at the bedside and in the laboratory. For example, patient self testing using a glucometer or a HIV self-test is often combined with near patient testing by trained clinical professionals able to perform follow-up.

Testing in sexual health clinics for Chlamydia, on populations of patients who do not return for follow-up, has become of interest to governments and health professionals. Issues in relation to the need for informed consent for voluntary testing for HIV [12], difficulties with sensitivity and specificity of HIV POC tests [7, 10, 13] and the effects on clinical practice of rapid testing for common STI agents such as *Chlamydia trachomatis* [14], all need to be considered in relation to how such POC tests might be used.

POC testing for infectious diseases can be further subdivided into four categories as summarised in Table 3.

POC testing technologies are highly variable, e.g. POC tests utilising immunochromatography have been available for many years but it is only very recently that molecular diagnostic testing systems have been adapted to POC use [1]. The drivers for POC testing overlap with drivers for laboratory based testing but, in some cases, differ in emphasis. For example, cost is important to both, although POC testing costs are often driven at the consumer in the community, rather than laboratory.

Over the last 8-10 years, there have been moves for improved POC testing for respiratory agents. Algorithms for diagnosis of the major agents of children (respiratory syncytial virus) have been established for the use in paediatric emergency units [15] or for testing of influenza during epidemic seasons [9, 11]. The World Health Organization (WHO), as well as other global organisations and governments, have developed considerable interest in rapid testing for influenza with the threat of pandemic human influenza. Nineteen POC tests are listed on the review published in July 2005 by the WHO [available at http://

www.who.int/csr/disease/avian_influenza/guidelines/rapid_testing/en/index.html]. More tests are becoming available, particularly for highly pathogenic avian influenza (HPAI). Such assays will require significant quality control and quality assurance when introduced.

Assays for detection of viral gastroenteritis (adenovirus, rotavirus), detection of Cryptosporidium, Giardia, Entamoeba, and other agents of gastroenteritis have been available for some time. Faecal occult blood testing and testing for faecal white cells are well established in gastrointestinal practice, and yet very few of these fulfil the optimum features required for a good POC test (Table 4).

Quality control and quality assurance

Quality control (QC) is essentially establishing adequate performance characteristics (sensitivity, specificity, negative predictive value, positive predictive value, cross reactivity, etc.) of a given test kit. Quality assurance (QA) is determining the ongoing adequate performance of a test in analysis of clinical conditions.

QC for POC tests is reasonably straightforward, involving the comparison of new rapid tests against established methods such as viral culture, bacterial culture, nucleic acid tests and other reference standards in statistically adequate numbers of positive and negative analytes. As such, QC for POC tests can be performed, robust performance characteristics established, and the tests used [16]. QA, on the other hand, is an ongoing and lifelong assessment of test performance in real people at risk of infection.

QA of POC tests is more problematic, particularly if such tests are to be used by patients at their own bedside. QA assessment of such testing is further complicated by the use of newer collection methods [15] where the potential for error arises from technical issues associated with collection, POC testing, operator use, operator test interpretation, and the action taken by infected patients. For instance, there is enormous significance surrounding diagnoses of HIV or STI POC testing that can potentially create significant problems. On the other hand, POC testing using glucometers by patients with diabetes is well-established, reasonably accurate and, with suitable clinical backup, has had enormous positive impact upon the lives on diabetics worldwide.

Most models of POC testing for infectious agents involve the use of health professionals, either in the laboratory or in facilities closer to patients such as pharmacies, GPs or home delivered by nurse practitioners. These are models where POC testing is performed by adequately trained clinicians with appropriate knowledge of clinical and therapeutic implications of POC test results. Indeed, discussions of pharmacies that have introduced screening for Chlamydia with rapid PCR in the UK, have indicated strong community demand. Six thousand tests were performed by Boots Pharmacies in the UK during the first 3 months of such a programme [Kirkbride R, RCPA Update Meeting, Darling Harbour, Sydney 2006, personal communication]. Problems with such a system have become immediately evident. This includes the lack of consistent quality systems, problems with comparability of POC test results with those from routine diagnostic laboratories, lack of contact with clinicians able to prescribe therapy, and lack of regulation of such testing.

Indeed, such regularity and personal problems lead organisations involved in POC testing in the 1990s to strongly counsel "Point of care testing is not the panacea for all the ills of our current health care system, and the laboratory

Table 2. POC testing algorithms

Testing performed by	Example	Test type
Patient on his or her self		HIV, pregnancy, STI
Minimally laboratory qualified individual	Clinician	Wide range of different tests
Minimally laboratory trained staff	Clinician (nurse practitioner or GP)	Performing one or two tests on large numbers of patients
Laboratories	Scientific staff	Small numbers of specimens with rapid turnaround times
Bedside	Clinician	Test designed to direct further testing

Table 3. Types of POC tests for infectious diseases.

Purpose of rapid testing	Conditions	Example
Urgent therapy	Life threatening for patient	Meningococcal meningitis
Initiation of therapy	Patients at risk	HIV, MRSA, Influenza
Specific level of containment	Major threat of contagion	Tuberculosis, Bioterrorism
Appropriate treatment sought elsewhere	Patient follow-up unavailable	STI clinics, developing countries

must be part of validating which tests should be appropriately performed at the bedside" (www.ascls.org/position/point.asp).

It is evident that QA will be crucial to the use of POC tests in diagnosing infectious illness. Consistent with this, the Australian Government Department of Health and Ageing is closely involved in POC testing, including trials in general practice (HTTP://www.health.gov.au/).

Emerging issues

POC testing is now strongly entrenched. All POC testing models require support from the laboratory. POC testing is an opportunity for laboratories to demonstrate their capabilities through prioritising support for algorithms that allow management of such testing to optimise predictive ability, accuracy and quality of such testing [7, 10, 11].

The laboratories' roles continue to change from doing to managing tasks, from producing to monitoring test results, and from receiving requests for testing to providing clinicians with information regarding appropriate testing. POC will continue to emerge as an increasing part of this role, resulting in a need for ongoing education [17,18], new technologies [1, 8], and review of new groups of at-risk individuals with their own demographic characteristics [19].

Laboratory involvement must keep pace with changes in technologies and changes in assay use by a broader spectrum of the population. Our role as microbiologists is the most significant of any scientific or health professional group due to the clinical complexity attached to many POC testing for infections. This involves such diverse personal, community, governmental and scientific implications that it requires significant input from experienced laboratory professionals. It is our role to rise to the challenge for QC and QA that POC diagnostic tests provide.

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Table 4. Features of an ideal POC test.

Feature	Characteristics	Available?
Sensitivity	Highly sensitive – no false negatives ever	No, approaching 90% in some tests
Specificity	Highly specific	No, approaching 100% in some tests
Ease of use	Target population served	No, e.g. glucometers. Diabetics often have peripheral neuropathy and are elderly
Quality control	Adequate, easily measured	No, approaching for some tests e.g. glucometer, laboratory utilised influenza tests, HIV-1
Quality assurance	Adequate, monitored centrally	No, approaching for some tests e.g. cardiac testing
Clinical backup	Available for all conditions, particularly for critical illnesses	No, particular issues with infections eg. STI, HIV-1
Connectivity	Integration into higher level health care services	No, approaching for some tests e.g. cardiac testing, influenza POC tests in laboratory