



## Review Article

# POCT Tests - would they Meet the Goal of the Clinical Microbiology Laboratories

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## ABSTRACT

### Keywords

Point of care tests, Clinical microbiology laboratory

Clinical microbiology laboratories mainly rely on culture based techniques. These procedures have a long turnaround time and require highly trained laboratory staff. This problem can be overcome by point of care testing or near patient testing for in – patients in wards, outpatients in clinics or special functional areas of the hospital like emergency, operation theater, delivery room etc. Point of care testing is gaining prominence in the recent years. The tests available for point of care testing in microbiology are for detection of beta hemolytic *Streptococci*, *Peumococci*, HIV, malaria, filarial, dengue, leprosy, influenza and legionellae. Point of care tests not only are useful for diagnosis of diseases but also aid in disease monitoring and screening. Validation of POCT is important before implementing any POCT. Quality assurance is absolutely essential for POCT testing.

## Introduction

The clinical microbiology laboratory works with the primary goal of providing an aetiological diagnosis for patients suffering from infections and guiding the management of infections. The conventional culture based method continues to be mainstay procedures in achievement of its goal. The major limitation of these techniques is a long turnaround time. Time is required for processing of specimens, in vitro growth of microbes, their identification by biochemical tests and performing antibiotic susceptibility tests. All these procedures are labour intensive and require highly trained laboratory staff. In recent

years other nonculture methods of microbial identification, automated instrumentations and molecular techniques are available now – days. However these tests are not widely available and turnaround time is again a limitation because of the need to transport specimens to the laboratory, time required for processing of specimens and infrequent testing. Hence the smaller and more efficient technological wonders - the point of care devices have captured the attention of microbiologists because of their ease of use and enhanced capabilities.<sup>2</sup> Point of care testing (POCT) also known as near patient testing (NPT), addresses the problem of a

long turnaround time in laboratory medicine hence can improve the quality of patient care. POCT is defined as the analytical testing of clinical specimens beyond the confines of the laboratory or simply the provision of laboratory testing at the point where patient care is rendered, with measurement systems that are easy to operate, with therapeutic relevance in patients at risk of death, within departments for in –patients, in outpatient clinics or special functional areas like emergency, operation theater, delivery room, endoscopy unit and Interventional radiology by personnel who have in general had no detailed training as medical technical assistants and no experience in laboratory medicine.<sup>3</sup>

Other terms used to describe POCT are bedside testing, near-patient testing, ancillary testing, decentralized testing, and patient-focused testing. Now a day POCT is achieving greater prominence in health care delivery. This is due to changes in the delivery of health care, economic considerations and the movement toward a more “patient focused” approach to health care<sup>4</sup>.

## **History**

The first reported use of POCT is found in papyrus documents dating back to 1550 B.C., which depict Egyptian physicians using ants to determine glycosuria in patients suspected of having diabetes mellitus.

The concept of POCT is not a new concept. Since years, microscopy was used in gynaecology wards and clinics and STD clinics for the rapid diagnosis of gonorrhoea, *Trichomonas vaginalis* and yeast infection and bacterial vaginosis, similarly simple rapid dipstick urine analysis is used in the

general wards and clinics for presumptive diagnosis of urinary tract infection.<sup>5</sup>

## **Status of POCT in developing nations**

The status of POCT testing is still in the early stages in economically backward countries where many health care centres are not adequately equipped and the samples are outsourced for diagnosis to a distant place, which in turn leads to delays resulting in impaired patient care. Advanced laboratory facilities remain elusive for the rapid diagnosis of various infectious diseases; that could be helpful in initiating appropriate antimicrobial agents and thereby better patient care<sup>6</sup>. Developing countries that carry huge of the burden of HIV, Tuberculosis, Malaria and other infectious agents are not properly equipped to diagnose, manage and monitor progression and control their spread<sup>7</sup>

## **Point of care testing in microbiology**

Most common POCT tests done in microbiology are for Group A streptococcal pharyngitis, HIV, for Influenza, Tropical infections and Respiratory infections. The basic principle in most systems is the immunochromatographic test of a specific microbial antigen or antibody in the patient sample such as urine, swab, whole blood, using the ELISA principle.<sup>8</sup> The most common format of a POCT kit in microbiology is the antigen or antibody capture method using a lateral-flow immunochromatographic system. This is essentially an enzyme immunoassay and typically comprises a nitrocellulose strip embedded with complementary antibody or antigen to the protein of interest, conjugated to a colloidal metal or coloured dye. Test and control areas, each containing a suitable reagent to form an immunological complex, are usually contained within the strip and the

expected reaction produces a visual effect like a line or a cross. In some tests, the patient's specimen needs to be pretreated with detergent to release microbial antigens from cells, or be diluted before adding it to the test strip. In all cases, small volumes of sample are required and incubation is usually at room temperature for a short period of time like 10 minutes. Point-of-care test methods based on the detection of microbial nucleic acids in easily portable devices are also in development. If the price per test and the size of the equipment can be reduced to acceptable levels, molecular POCT methods have the potential to provide greater sensitivity and specificity than immunological assays.<sup>9</sup>

#### **POCT for detection of *Streptococci***

For beta-hemolyzing streptococci, POCT tests are available for directly detecting the antigens of group A streptococci and of group B streptococci<sup>10</sup>. The tests are based on the extraction of the C-antigen from the cell wall, followed by detection with an immunological reaction. If GAS is directly detected during the examination of a tonsillitis patient, it is then possible to decide whether antimicrobial therapy is necessary. Studies have shown that this can reduce the unnecessary use of antibiotics in pharyngitis by at least a quarter. Moreover, the sensitivity and specificity of these modern systems is now almost similar to culture which is the gold standard. Hence these systems especially the GAS rapid test was included by many medical societies in their recommendations and guidelines for tonsillitis as a routine diagnostic component. On the other hand, dispensing with culture excludes the possibility of testing for macrolide sensitivity, and macrolide resistance which is a growing problem. Group B streptococci (GBS) are important cause of neonatal infections. Although there

has been considerable progress in their diagnosis and treatment, GBS infections lead to high morbidity and mortality<sup>11</sup>. The most efficient strategy to reduce the frequency and severity of neonatal infection is currently thought to be culture detection of group B streptococci from rectovaginal screening swabs in weeks 35 to 37 of pregnancy and intrapartum chemoprophylaxis with ampicillin. If however culture screening is not possible because of a premature birth, there are a variety of EIA available for intrapartum screening. Moreover, the specificity of these tests is about 91% to 100% and that of culture is 89%. However, the sensitivity of the test is much poorer 11% to 79% when compared to culture which is 91%. This is not good enough in practice and is probably due to some pregnant women being colonized with a low bacterial inoculum. This is too low to be detected, but can nevertheless lead to infections. For this reason, routine use of the GBS rapid test is currently not recommended by specialty societies.<sup>12</sup>

#### **POCT for HIV detection**

Reversing and arresting the epidemic of HIV are a challenge for any country. Early diagnosis and rapid initiation of treatment remain a key strategy in the control of HIV. Technological advances in the form of low-cost rapid point-of-care tests have completely transformed the diagnosis and management of HIV, especially in resource limited settings, where health infrastructure is poor and timely access to medical care is a challenge. Point-of-care devices have proven to be easy to transport, operate, and maintain, and also lower-skilled staff is equally able to perform these tests as compared to trained laboratory technicians. Point-of-care tests allow rapid detection of HIV allowing for rapid initiation of therapy, monitoring of antiretroviral therapy and

drug toxicity, and detection of opportunistic infections and associated illnesses.<sup>13</sup> Bedside rapid tests to detect HIV antibodies are now an equivalent alternative to the conventional antibody screening tests, as their sensitivity (98% to 100%) and specificity (86% to 100%) are comparable to the values found with the enzyme immunoassays performed in the laboratory. They are particularly useful in areas with little access to laboratories, in people who are difficult to reach, for the critical period in which a decision has to be made about prophylaxis after exposure, and after a birth where the HIV status of the mother is uncertain. Even though the specificity is 86% to 100%, a rapid test can always in principle give a false positive result. Therefore it is essential that positive rapid test results should be confirmed by an alternate rapid test if resources are limited or by a conventional test e.g. Western blot.<sup>14</sup> Point-of-care testing of HIV refers to the practice undertaken by health care professionals of providing pretest counseling, posttest counseling, and a preliminary HIV antibody result at the time of testing outside a designated laboratory. The standard methods of HIV testing, enzyme linked immunosorbent assay or western blot with confirmatory testing using p24 antigen detection or viral nucleic acid detection can take several days for availability of results.<sup>15</sup> A significant proportion of individuals who agree to undergo HIV serologic testing do not return to the HIV testing site to receive their test results<sup>16,17,18</sup>. POC testing of HIV attempts to address delay in detection of HIV status by providing preliminary antibody results. POC tests can be most useful in resource limited settings or outreach settings where there is lack of well-trained laboratory technicians, poor physical infrastructure, extremes of climate, and lack of uninterrupted power supply, all of which impact the use of laboratory technologies.

Rapid HIVPOCT test kits deliver results within about 20 minutes of a specimen being taken; so, results are available within a single consultation. Rapid test devices are typically capillary flow tests for use on whole blood e.g., fingerprick, plasma, urine, or oral fluid<sup>19,20,21,22</sup>. They detect HIV antibodies against HIV 1 and 2 antigens produced by oligopeptide synthesis or recombinant DNA technology. Quick turnaround time, ease of sampling, performance and reading results, no requirement of cold chain, and specialized equipment make these tests highly suitable in resource limited settings. Since, oral fluid/saliva testing is more convenient, noninvasive and safe for laboratory workers, it can serve as an alternative for screening as well as surveillance purposes<sup>23</sup>. Oral fluid sampling for HIV could particularly benefit the uptake among children and injectable drug users who may have collapsed blood vessels. However, not all RTDs are usable at the point-of-care. Any HIV POC test approved for use is required to have sensitivity and specificity equivalent to HIV screening test kits approved for laboratory use.<sup>24</sup> Currently, seven FDA approved HIV RTDs are available in the market. The field has also advanced with the development of over-the-counter self-testing options for HIV and multiplexed platforms that allow for simultaneous detection of infections associated with HIV, such as hepatitis B and C and syphilis. Researchers believed that home testing could be valuable “in empowering individuals to manage their HIV risks; in helping couples to learn their partners’ HIV status before the initiation of sexual relations; and in addressing the three principal barriers to wider HIV-test acceptance: stigma, convenience, and privacy”.<sup>25</sup> FDA approved the OraQuick In-Home HIV Test, the first over-the-counter home use rapid HIV test kit to detect the presence of antibodies to HIV-1 and HIV-

<sup>26</sup>. Fourth generation HIV RTDs that detect both antigen and antibodies, ARCHITECT HIV Ag/Ab Combo Assay, Alere Determine HIV 1/2 Ag/Ab Combo assay are being developed. They allow for early detection of HIV infection, prior to the emergence of HIV antibodies, therefore reducing the window period of antibody detection. These tests, however, need validation and extensive performance evaluation in diverse field settings. When to Use the HIV POC Test Kits? POC testing of HIV is not designed for screening the general population; it is to be used to screen patients at high risk for HIV. The rapid turnaround time associated with its use can guide urgent decision making. This makes it suitable for use in targeted clinical scenarios where the immediate administration of antiretroviral drugs is recommended to reduce the risk of transmission or in cases where the patient's management may be altered by the availability of a reactive test result. In obstetric settings, testing pregnant women for HIV at the time of labor and delivery is the last opportunity for prevention of mother-to-child HIV transmission measures, particularly in settings where women do not receive adequate antenatal care. In India, many rural women present for delivery without any prior antenatal care. Those who do get antenatal care are not always tested for HIV, because of deficiencies in the provision of HIV testing and counseling services<sup>27</sup>. POC testing should be provided to women with risk factors for HIV infection. Access of a women with no recorded HIV status presenting in established labour to immediate HIV results improves the judicious use of antiretroviral prophylaxis.<sup>28</sup> In case of Blood and Body Fluid Exposure/Health Care Worker Occupational Exposure, knowledge of the source of the individual's HIV status during an evaluation of blood and body fluid exposure can help to determine more

precisely those situations where HIV prophylaxis might be useful. HIV POC testing of source individuals offers an opportunity to eliminate anxiety and the unnecessary use of post exposure prophylaxis in the exposed person. In acutely ill patients, it may be critical to have a rapid HIV diagnosis so that immediate and appropriate therapy or further diagnostic work-up can be provided, for example, a patient with risk factors for HIV who presents with pneumonia for which differential diagnosis would include *Pneumocystis jirovecii* pneumonia or patients undergoing hemodialysis. In patients attending sexually transmitted diseases clinics, POC testing is acceptable, feasible, and leads to timely entry of people with HIV positive tests into the health care facility.<sup>29</sup> Also among the STD clinic attendees presenting with genital ulcer, HIV reactivity was found to be statistically significant.<sup>30</sup>

There are many challenges in POC HIV testing, the first among them is counseling. POC HIV testing requires pre- and posttest counseling to be modified from the usual HIV counseling that accompanies standard HIV testing. However, in certain clinical situations may make detailed pretest counseling difficult, for example, rapid testing for pregnant women in labour, informed consent for testing is a minimum requirement. Informed consent is a process of communication that enables a person to make a reasonable and informed decision. In contrast to the situation in standard HIV testing, the health care workers in the POC setting assume responsibility for specimen collection, testing, and counseling of the patient. Adequate resources, appropriate training, and the implementation of quality assurance practices will be critical in ensuring the proper administration of the test and the correct interpretation of the test

result. Rapid HIV test kits must be licensed for use in the country. POCT devices are generally satisfactory for the detection of uncomplicated HIV infection or its absence but are less sensitive than lab-based ELISAs and automated systems for detecting early infections. Also specificity of RTDs is lower than conventional ELISAs although it can be improved by immediate repeat of all RTD positives.<sup>31</sup> Since these may not be reliable in the “window” period, appropriate repeat testing should be advised, no currently available RTDs incorporate HIV p24 antigen detection in contrast to the commonly used conventional combination ELISA laboratory tests which are more sensitive in early HIV infection. Ethical Implications also occur due to the use of POCTs. Ease of testing might lead to people being tested without their voluntary, specific, and informed consent. This is a particular risk where patients are anaesthetised (e.g., occupational exposure) or unable to communicate (e.g., woman in labour) or otherwise lack capacity to make decisions. Appropriate training on the use of kits, reading of results, and detection of errors, quality assurance, counseling, and regular assessment of staff who will be performing POC testing is required for providing HIV point-of-care testing. Tuberculosis is one of the most common opportunistic infection in developing countries Therefore, there will also be a need for rapid POC detection of opportunistic infections. Thus decentralization of laboratory services is required to detect the maximum possible number of HIV-positive patients and to put them on antiretroviral therapy.. The particular public health interest in the use of point-of-care testing for HIV is its ability to contribute to health goals which include preventing new HIV infections, reducing the number of HIV individuals who are unaware of their status, and promoting linkage of

HIV-positive individuals to care. The ethical framework surrounding informed consent for a rapid test is the same as for a standard blood test, but the dissemination of testing and potential lack of experience of staff administering tests and handling the results requires careful consideration.<sup>32</sup>

### **POCT tests for tropical infectious diseases**

In the tropical medicine literature, POCTs are more commonly referred to as rapid diagnostic tests (RDTs). The most extensive work has been put into developing RDTs for the diagnosis of malaria, due to the high morbidity and mortality which is a feature of this disease. The tests currently available exploit distinctive aspects of the *Plasmodium* parasite’s biochemistry. One of the first lateral-flow assays to be widely available was based on the discovery that, during its growth and division in red blood cells, *Plasmodium falciparum* produces a unique protein, histidine-rich protein 2 (HRP2). This can be detected in the peripheral blood of an infected patient and is particularly high when schizonts burst.<sup>33</sup> The test proved to perform acceptably in comparison with the ‘gold standard’ of microscopy and to be useful in a wide range of situations, showing that there was a market for kits based on this technology. The HRP-2 test does have the disadvantage that it cannot detect any of the other *Plasmodium* spp. that are human pathogens, although the recent refinement to include detection of an aldolase produced by all species (called pan-malarial antigen [PMA]) has solved this problem to some extent.<sup>34</sup> Another type of assay to be devised relied on the fact that *Plasmodium* spp. produce a specific isoform of the isoenzyme lactate dehydrogenase (LDH). There is a parasite LDH (pLDH) produced by *P. falciparum* alone, and another produced by all

*Plasmodium* spp., which means that the test is designed to detect all species of the parasite and explicitly identify *P. falciparum*. This test is reported to perform well generally, although some limitations have been noted with the detection of *P. ovale*.<sup>35,36</sup> Studies indicate that the HRP2 and pLDH tests have good sensitivity rates and they have been taken up by laboratories in non-endemic areas, where expertise in diagnosing malaria might be limited, to complement standard blood slide microscopy. However, the problems with specificity and a relatively high cost per test have not precluded their use in endemic areas. In remote rural settings, where good quality laboratory support is not always available, suitably trained personnel can use these RDTs to diagnose malaria accurately. This approach has been advocated to help to eliminate the misdiagnosis of 'presumptive malaria' for anyone with a fever, allowing other causes of infection to be investigated and to reduce the indiscriminate use of antimalarials, thus lessening the opportunities for drug resistance to develop among the parasites.<sup>37</sup> But the rapid test sometimes fails in spite of high parasite density. If this is borne in mind, malaria rapid tests may be used for emergency diagnosis, in accordance with the recommendations of the German Society for Tropical Medicine, if light microscopy of a thick drop or smear examination is not available.

In endemic areas it can be clinically extremely useful to distinguish between dengue and other possible causes of pyrexia and influenza-like symptoms. Accurate and quick diagnosis can be important to allow correct management of the patient and also to prevent unnecessary administration of antibiotics or antimalarials. There are a number of RDTs intended to aid the diagnosis of dengue fever currently on the

market, the majority being of lateral-flow format.<sup>38</sup> Most are designed to detect IgM to dengue virus in patients' blood and thus are intended to diagnose acute primary infection, although some can detect IgM and IgG and thus distinguish between acute and secondary infection. However, none are able to confirm which of the four serotypes of dengue is present, which can be important for epidemiological purposes during an outbreak. Evaluations of the RDT kits report that they all have generally high specificities but poor sensitivities. However, a recent refinement to include detection of the dengue NS1 antigen which is common to all serotypes, and thus viraemia, appears to have improved performance. In spite of the limitations of the test kits, work in dengue endemic areas has highlighted the value of achieving a fast result using an RDT on which the clinician can act. Using an RDT in combination with training for healthcare personnel increased the accuracy of the diagnosis of dengue and therefore reduced the likelihood of unnecessary drug prescription on the presumption of another possible cause of pyrexia, such as bacterial infection.<sup>39</sup>

### **POCT tests for respiratory infections**

Three established rapid tests of great practical importance are available for the diagnosis of respiratory infections. These are for the detection of the antigens of influenza, pneumococci, and *Legionellae*. The greatest benefits of these systems are the improvement in diagnostic yield (pneumococci, *Legionellae*) and in the time saved in diagnosis. For comparison, pneumococcal culture requires 24 to 48 h; influenza detection from short-term culture requires more than 3 days; legionella culture requires 3 to 7 days. For pneumococci, the pathogen can only be detected by sputum culture in 40% to 50% of patients with

pneumococcal pneumonia, even in patients with bacteremia<sup>40,41</sup>. The main reasons for the failure of culture detection are non optimal sample isolation, excessive transport times, and prior antimicrobial therapy. In comparison, the pneumococcus rapid test is much less sensitive to interference, and detects pneumococcus pathogen in some patients with negative culture (sensitivity: 50% to 80%; specificity: 90%). On the other hand, the sensitivity of the urine antigen test is directly dependent on the severity of the disease. The sensitivity drops to 60% in patients with less severe disease<sup>42</sup>. Together with the fact that pneumococci are almost always well covered by the most frequently selected antibiotics (betalactams), this leads to the conclusion that the pneumococci antigen test should currently only be regarded as a complement to routine tests. There are also problems in the diagnosis of infections in children and infants, for as many of 20% of these may carry pneumococci as commensals and this can lead to false positive test results<sup>43</sup>. *Legionellae* are important pathogens of both community-acquired and nosocomial pneumonia. They are particularly dangerous for patients with a weakened immune system, especially after an organ transplant. *Legionella pneumophila* of serotype 1 is responsible for about 60% to 70% of infections<sup>40,41,42</sup>. *Legionella* can only be detected by culture in a few patients—in some hospitals, less than 10%—and usually requires 3 to 7 days<sup>43</sup>. On the other hand, the infection may be peracute and rapidly fatal and requires special treatment (macrolide or fluoroquinolones). It follows that acute diagnosis by detecting the legionella antigen in urine is of great clinical value. The sensitivity of the tests is currently about 94% and the specificity 99% to 100%. This should be compared with the sensitivity of 10% to 80% in culture, with the specificity of 100%. Infections with serotypes other

than 1 can be detected by cross-reactions, although the sensitivity is clearly lower<sup>44</sup>. The development of the rapid test for influenza virus was greatly accelerated by the recognition that early therapy within 48 h with neuraminidase inhibitors is more likely to be successful. Currently available tests give a diagnosis with a sensitivity of 50% to 96% and specificity of 72% to 100%, depending on the selected "gold standard". Additional factors include the type of test material—nasal swabs are better than throat swabs—and the patient's age. If there is an outbreak, with relatively high prevalence, current publications suggest that the positive predictive value of this test can be exploited in patient management—even though clinical evaluation by an experienced physician gives a similarly good positive predictive value.<sup>45</sup> In settings with low prevalence (for example, at the start of an outbreak or in an inter-epidemic phase), there liability is greatly restricted by the low predictive value. In this phase, it is very probable that positive rapid test results are false positives. Therefore, they must be checked with a second independent test<sup>46,47</sup>.

### **POCT for patient monitoring**

Leprosy in the acute stages produces painless skin lesions that may go unnoticed. When the infection is not recognised early and is allowed to progress, it can lead to severely disfiguring skin lesions and damage to peripheral nerves causing loss of sensation and thus disability. The prognosis appears to depend on the levels of bacteria detectable in skin lesions. Patients with low concentrations are classified as paucibacillary (PB) and this is associated with a good prognosis, while patients with high bacterial loads are classed as multibacillary (MB), which is more likely to result in a poor outcome.<sup>46</sup> Thus it is important to characterise the nature of the

infection as soon as the patient presents so that the appropriate treatment, management and counseling can be provided. Initial laboratory diagnosis involves examination of skin biopsies for the presence of *M. leprae* bacteria using the Ziehl-Neelsen stain, and to identify the characteristic histological changes. Counting acid-fast bacilli in skin slit specimens can then be used to determine the bacterial load and thus the prognosis. However, there is a clear relationship between detection of serum IgM against a unique *M. leprae* antigen, phenolic glycolipid-I (PGL-I), and bacterial load. Patients who are classified as PB are usually seronegative, while antibodies are generally detectable in those with the more serious MB, so an enzyme-linked immunosorbent assay (ELISA) test is often used instead of microscopy<sup>46,47</sup>. Another application of this Immunological test is to determine the risk of contacts of confirmed leprosy patients developing the disease; again, those who are seropositive for PGL-I antibodies are more likely to become symptomatic. An immunochromatographic assay has recently become available to test for IgM to PGL-I in patient serum.<sup>47</sup> This RDT has been shown to perform well in comparison both to the laboratory-based ELISA for IgM to PGL-I14 and examination of skin slits by experienced microbiology staff.<sup>48</sup> Clearly, it is important to make an accurate classification of the leprosy to ensure the best outcome for the patient. In remote areas in endemic regions, even if a laboratory service is accessible locally, the expert staff and specialized equipment to perform histopathology or ELISA might not be available. This RDT could be used in such situations. The scope and applications for POCT in the diagnosis of infectious diseases are widening rapidly. In the UK and other countries in Europe, microbiology services are exploring how to use them to extend their remit outside the laboratory in order to

respond to patient wellbeing and the clinical requirement for rapid turnaround times. However, there are clear applications for this format of test in developing countries for similar and equally important reasons.<sup>49</sup> It is hoped that the more widespread uptake of POCTs and advances in technology will reduce the cost per test to levels that make them available in all parts of the world where they could enhance patient care.

Successful management of HIV requires patients receiving ART to be monitored routinely to assess treatment efficacy and detect treatment failure due to drug resistance. The standard of care to monitor ART is quantitative viral load testing based on plasma HIV RNA concentration<sup>50</sup>. Although CD4 count has also been used to monitor ART, recent studies suggest that it may not detect early treatment failure adequately<sup>51</sup>. POC test for CD4 count could help clinicians in resource limited settings to decide when to start antiretroviral treatment, and a POC test for viral load would be of great value in identifying treatment failure and the need for second-line treatment. POC devices for CD4 immunologic monitoring and viral load assay are currently being evaluated<sup>52,53,54</sup>. If validated, these devices could rapidly and accurately identify CD4 counts with minimal operator training, infrastructural setup, and with less cost than standard laboratory-based equipment such as flow cytometers for CD4 count or RT-PCR for viral load assay. PIMA analyzer is a WHO prequalified simple, effective point-of-care CD4 count test. It gives a CD4 count in 20 minutes from a finger stick or venous sample. Recent evaluations in Zimbabwe and Mozambique have shown good performance in comparison to flow cytometry<sup>53,54</sup>. VISITECT CD4 is a disposable, semiquantitative point-of-care rapid test for the determination of CD4 counts in whole blood. VISITECT CD4 can

guide treatment decisions at the point-of-care, without the need for extensive training or sophisticated equipment. The test is a convenient solution for use in laboratories and remote clinics worldwide and provides a visual “TREAT” or “NO TREAT” result within 40 minutes. Antiretroviral drugs, especially stavudine, are associated with severe side effects such as lactic acidosis, pancreatitis, and hepatitis<sup>55</sup>. POC tests for toxicity monitoring e.g., lactate, renal function tests, and liver function tests are also being evaluated<sup>56,57</sup> and will help in monitoring drug toxicity in patients.

### **POCTs in disease screening**

Another area of work in which RDTs have proved valuable is in screening of populations to evaluate a control programme. It is necessary to determine the prevalence of the disease before and after the intervention, but, in the case of diseases that affect people in remote regions spread across wide geographical areas, it is not always feasible to collect large numbers of samples and transport them to a distant laboratory. Currently, there is a concerted effort to reduce the burden of disease caused by filarial parasites, such as lymphatic filariasis caused by *Wuchereria bancrofti*.<sup>58</sup> The symptoms of infection by this nematode include inflammation and enlargement of the lymph glands and also elephantiasis, which in extreme cases renders the sufferer severely disabled. The parasite is transmitted to humans by mosquitoes, although the vector species depends on the location. In Africa, for example, *W. bancrofti* is carried by species of *Anopheles* which can also be vectors for *Plasmodium* spp. (creating the possibility of one mosquito passing on both filariasis and malaria to an unfortunate victim).<sup>59</sup> The standard laboratory test for this infection is detection of the filarial worm in biopsy samples. However, an RDT

to detect the filarial antigen in patients' peripheral blood is now available. The sensitivity of this test is reported to be very good and to compare favourably with traditional microscopy methods. It has been evaluated in endemic areas<sup>60</sup> and found to be useful. One of the logistical problems with accurate diagnosis of filariasis is that the peak concentration of parasites in the peripheral blood is around midnight. It is reported that the RDT method can detect microfilaria in blood at very low counts and thus blood specimens for testing can be taken at anytime of the day.<sup>61</sup> Therefore, this test is well suited to routine screening of populations to assess the effectiveness of interventions to reduce filariasis<sup>59</sup>.

### **Advantages of POCT**

#### **Decreased Turnaround Time**

When using a POC device in microbiology, the test is ordered, the specimen collected and analyzed and a clinician reacts depending on the result. In comparison, when testing in the laboratory, the test is ordered, the request processed, specimen collected, transported to the laboratory, processed, analyzed, results reviewed by the laboratory staff and then reported to the clinician. Obviously, POCT streamlines the process, resulting in decreased turnaround time, allowing the clinician to act on the results more quickly. Decreased turnaround time seems to stem from the fact that specimen processing and transport are eliminated. The logic would indicate that specimen transport is a major factor in turnaround time and the greater the length of transport time, the longer the overall test turnaround time. Decreased turnaround time also reduces the amount of unnecessary tests as well as medications administered to patients awaiting lab results. From a patient's point of view, benefits may include

reduced waiting time, more convenience and faster treatment. A good example of benefits of POCT is diagnosis of group A streptococcal pharyngitis. When 2,400 patients with suspected streptococcal pharyngitis were evaluated by a rapid latex test at the POC vs. laboratory culture, the rapid test results were available while the patient was still on site and usually in less than 20 minutes. Physicians were able to provide same-day treatment for 90 percent of the patients with streptococcal pharyngitis, reducing the length of symptoms and preventing other problems. Another study reported the effect of POCT in an emergency department setting where patient follow-up after throat culture was inadequate and patients may be treated inappropriately. According to the study, the rapid testing for the diagnosis of pharyngitis was significantly superior to clinical impression alone in determining the presence of disease.<sup>62</sup>

### **Cost Effectiveness**

"Hospital laboratories traditionally operate as cost centers in and of themselves without looking at the total health care cost of what they do and how they provide a service. "It may be simple to say, 'I'm not going to provide a specific test performed in the central laboratory on a stat basis because it's going to cost the lab more—it's better to batch these tests and perform them less frequently.' Similarly, lab personnel may be reluctant to accept the need to transition a test performed in the central lab to a POCT setting. Their concept is that the central lab can get the job done. And even if they accept the need for a POCT setting, they always bring up the issue of accuracy and demonstration of real cost and clinical benefit derived from POCT. In addition, POCT may lead to reduction in duplicate test orders, additional supplementary test

requests and the premature or unnecessary consumption of other expensive ancillary services and pharmaceuticals that may be averted or postponed to a more appropriate stage of care.<sup>63</sup> Additional cost benefits may also be derived from decreased length of stay associated with POCT. While cost savings would seem to be a driving advocate for POCT in the microbiology lab, this may take time because there has not been much in the way of validating these claims.

"Any progressive laboratory needs to continue to assess what types of POCT are available and whether it's appropriate for the clinicians and patients they serve. "The biggest obstacles relating to POCT are how good the tests are and who will reliably perform the testing."

**Key benefits of POCT:** patient identification, immediate diagnostic test results, Reduction and/or elimination of specimen/sample transport, elimination of blood collection tubes and centrifugation with fresh whole blood specimen, reduced blood specimen volume, room temperature storage of test devices, data management and connectivity.<sup>64,4</sup>

### **Operational benefits of POCT**

More rapid decision making and triage, reducing operating times, high-dependency., postoperative care time, emergency room time, number of outpatient clinic visits, number of hospital beds required and ensuring optimal use of professional time etc.

### **POCT issues and concerns**

The key issue of alignment and concordance of POCT with Central Lab Methods cannot be overlooked by laboratories, regulators, and industry. Lack of alignment with

definitive methods remains a potential barrier to further acceptance and growth of POCT. Manufacturers must demonstrate traceability of their methods to definitive methods.<sup>65</sup>

### **Validation of POCT**

Before implementing POCT analysis, of reduced turnaround time/cost differences compared with lab testing, of accuracy and precision for intended purposes, of an awareness of how the POCT will fit into the clinical setting, of partnership with all involved in POCT and of who performs testing, how competency is assessed and who is responsible for QC should be done.

"POCT in microbiology may be more expensive or add incremental cost to traditional methods performed in the central lab. What lab personnel have to realize is that it may cost more to perform the POCT, but the payback is in terms of decreasing the per episode cost of managing the patients. We need better outcome analysis studies validating these potential benefits.

When considering future POCT applications in microbiology, laboratorians should exercise caution and not to let technological development dictate clinical need for certain tests.

"POCT in microbiology can be beneficial, but it must be well-evaluated. Testing that offers rapid turnaround times but lacks accuracy and reliability due to operator or instrument limitations will not meet the needs of patients.

Of course, we are in an era of increasing fiscal constraints and rising health care costs, but laboratorians must carefully evaluate the benefits of POCT and have measures in place to act on results to justify its implementation."<sup>66</sup>

### **Quality assurance**

To obtain valid measurement results and also to protect the user, care should be taken that the test is used properly. This includes correct sampling and compliance with the manufacturer's instructions for performing the test. As the systems are so simple, extensive training is generally unnecessary. The responsible physician evaluates the results of the laboratory diagnostic tests and makes the diagnosis. The current guideline of the German Medical Association on quality assurance of laboratory medical investigations should also be considered when using the POCT devices. There are special simplified regulations for POCT when these are the so-called unit-use reagents and the corresponding measurement systems.

This means that reagents for single determinations should be split into portions and used up during a single investigation. QA involvement in POCT is of even greater significance, since laboratory testing is being performed by non-laboratory professionals whose training in quality issues may have been less rigorous than that given to laboratory professionals. This argument presents a strong case for mandatory competency.

Quality Assurance is an overview and examination of a complete system, from approaching the patient with the intention of obtaining a sample to looking at the subsequent result report from the laboratory or POCT analyser. Large parts of Quality Assurance involve Quality Control (QC), Proficiency Testing and External Quality Assessment (EQA). Without successful QC results, correct patient results cannot be assumed. Attention must be given to: analyser maintenance schedules, hardware and software replacements and upgrades,

service records, annual preventative maintenance reports, complete documentation records and quality control records.<sup>67</sup>

### **Why do we need POCT**

POCTs enhance surveillance of pathogens and infectious diseases: e.g. H1N1 flu pandemic, POCTs support rapid initiation and cessation of treatment. Sepsis is associated with 7% increased mortality for every hour delay in the administration of appropriate antibiotics. There has been under-investment in rapid diagnostics for improving the quality of care for patients with suspected infections, Diagnostics influence 60-70% of health care decision making but account for less than 5% of hospital costs. POCTs improve antibiotic targeting to only those who will benefit, thus reducing overuse.<sup>68</sup>

### **Current status of POCT**

The test systems available today are technically mature and offer good to very good performance. For HIV, malaria, group A streptococci, and *Legionellae*, POCT testing, when indicated, are as reliable as conventional procedures. POCT can be successful only if the tests are performed correctly by trained personnel, quality management procedures are followed, and the severity of illness and the epidemiological circumstances are taken into account when interpreting the results.<sup>69</sup> These test systems reduce the amount of unnecessary tests as well as medications administered to patients awaiting lab results. Reduction of patient's waiting time more convenience and faster treatment are the other benefits for the patients. POCT may lead to reduction in duplicate test orders, additional supplementary test requests and the premature or unnecessary consumption of other expensive ancillary services and

pharmaceuticals that may be averted or postponed to a more appropriate stage of care. In spite of all these advantages, POCTs should be properly validated before putting to use in order to meet the goal of the clinical microbiological laboratory.

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