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Research review paper

Point-of-care diagnostics for niche applications

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ABSTRACT

Point-of-care or point-of-use diagnostics are analytical devices that provide clinically relevant information without the need for a core clinical laboratory. In this review we define point-of-care diagnostics as portable versions of assays performed in a traditional clinical chemistry laboratory. This review discusses five areas relevant to human and animal health where increased attention could produce significant impact: veterinary medicine, space travel, sports medicine, emergency medicine, and operating room efficiency. For each of these areas, clinical need, available commercial products, and ongoing research into new devices are highlighted.

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1. Introduction

Point-of-care (POC) diagnostic tests provide clinically relevant information at the point-of-use, without the need for sample processing or analysis from a remote clinical chemistry laboratory. The blood glucose meter, used for the management of diabetes, and the home pregnancy test (dipstick) are the most popular examples. However, recent advances in microfluidics combined with the decreasing cost and size of advanced electrochemical and optical sensors (Vashist et al., 2015) have broadened the range of applications for POC diagnostics. For example, these advances have made possible the burgeoning field of POC diagnostics for resource-limited settings, such as developing nations. Excellent reviews of POC diagnostic tests for global health have been published recently and thus are not included here (Chin et al., 2011; Yager et al., 2008). In addition to global health, other areas where portability and low cost are key drivers have benefitted from improvements in POC diagnostic technology. In this review, we focus on some of these niche areas that have not been covered extensively in the literature and which have a small market size compared to health diagnostics in developed nations, or where the clinical benefit is still being actively investigated.

First, we briefly review the regulations governing POC diagnostics for human health, as they dictate how the diagnostics are used. Then we review POC diagnostics for veterinary medicine, space travel, sports medicine, emergency care, and operating room applications. A couple of these areas (e.g., veterinary medicine or emergency care) contain a vast number of potentially useful biomarkers that could be tested — enough to warrant a dedicated review article for each. Our goal here is not to exhaustively cover all possible applications within each area, but rather to increase the general awareness of the opportunities available and to focus on selected examples that have the greatest impact.

1.1. CLIA regulation

Healthcare-related diagnostic tests are an integral component of healthcare delivery in the US as they currently have a direct impact on up to 70% of healthcare-related decisions (www.lewin.com, 2005). This impact has been driven by the advances in science and technology of the 20th century. Prior to these advances, decision making was primarily based on patient history and physical examination (Burke, 2000). When these tests were first being used in diagnosis, most of these tests were performed at the side of the patient, and the individual practitioner had a significant amount of autonomy (Moore, 2005). However, the variability in quality of these tests ultimately led to regulation that mandated how these tests were to be performed (Berger, 1999a, 1999b).

This regulation was primarily enforced by the Clinical Laboratory Improvement Amendment (CLIA) of 1988, which established regulatory standards for all human-related laboratories testing for diagnostic purposes (1988). This was, specifically, in response to an alarmingly high number of false negative results from in-house laboratories. Since its enactment, CLIA has required that all labs performing diagnostic tests of human samples must register with the Centers for Medicare and Medicaid Services (CMS). The process of registration is based on the type of testing that is to be performed, and a set of compliance standards are required for the given lab classification. This lab classification is determined by the complexity and clinical significance of the testing to be performed. The resulting CLIA requirements are more stringent for more complicated tests. As outlined in Table 1, diagnostic tests are scored by the FDA using seven independent criteria. These scores are then summed to determine the risk associated with the test. Diagnostic tests with scores of 12 or less are in the moderate-complexity category. Scores higher than that are deemed high-complexity (www.fda.gov, 2015a). CLIA defines waived-tests to be "simple laboratory examinations and procedures that have an insignificant risk of an erroneous result." Sites that only perform waived tests must still have a CLIA certificate and follow the instructions from the manufacturer (Collopy et al., 2014; www.fda.gov, 2015b).

These CLIA regulations led clinical practices to outsource many of their diagnostic tests to core laboratories — either regional centers like those operated by LabCorp or local centers within the hospital. This workflow is well-suited for tests where the results are not needed immediately, as the delivery of care would not be changed even if the information was immediate. However, there is a fairly recent push to perform certain tests at the POC (Gubala et al., 2012; John and Price, 2013; McPartlin and O'Kennedy, 2014). Because POC tests are portable, they allow for an expedited workflow (Fig. 1) and potentially shorter turnaround times. As a result, they carry the promise of providing the care giver with information at time

Table 1
Criteria for the categorization of CLIA lab test (after Collopy et al., 2014).

Criteria	Score of 1	Score of 3
Knowledge	Minimal scientific and technical knowledge required; may be taught on the job	Specialized scientific knowledge required to perform preanalytic, analytic or postanalytic testing
Training and experience	Minimal training or limited experience required to perform test	Specialized training is essential or substantial experience necessary for test performance
Reagents and materials	Reagents and materials are stable and reliable; they are prepackaged or premeasured with no special handling required	Reagents and materials may be labile and require special handling. Preparation may include manual steps such as volumetric measurements
Characteristics of operational steps	Operational steps are either automatically executed or easily controlled	Steps require close monitoring or control; may require special preparation, precise temperature control or procedural steps
Calibration, quality control and proficiency testing	Calibration and QC materials are stable and readily available	Calibration, QC and proficiency materials may be labile
Test system troubleshooting and equipment maintenance	Troubleshooting is automatic or self-correcting or requires minimal judgment. Maintenance is seldom required and can be easily performed	Troubleshooting requires decision making and direct intervention to solve most problems. Maintenance requires special knowledge and skills
Interpretation and judgment	Test processes require minimal judgment or interpretation	Testing processes require extensive judgment, resolution of problems requires extensive interpretation