GLOBAL POINT OF CARE
DISASTER MANAGEMENT AND
EBOLA PREPAREDNESS

Gerald J. Kost, MD, PhD, MS, FACB,
in collaboration with POCT•CTR Researchers

Point-of-Care Testing Center for Teaching and Research (POCT•CTR)
University of California, Davis, USA

[Disclaimer: Research results may be preliminary. Final conclusions may differ. Please consult published papers. Device use must comply with regulatory & legal requirements.]

Copyright © 2015-16 by Knowledge Optimization®, Davis CA, USA
Please email questions to Dr. Kost at gjkost@ucdavis.edu. Thank you.
DISASTER MANAGEMENT: PRACTICAL NEEDS

- Disaster protocol for the hospital & laboratory
- Personnel training, certification, & registry
- Understanding of environmental impact (IQCP)
- POC technologies to detect, triage, & monitor
- Disaster cache and deployment plan
- POC Coordinator for preparation & oversight
- Ancillary care facility—where people will go
- Isolation capability with appropriate laboratory
- Mobility and telecommunications
- Resilience for both acute and chronic care
LEARNING OBJECTIVES

• To demonstrate how to determine needs: Needs assessment helps define the role of POCT in pandemics, complex emergencies, and disasters. “FAST POC” will help stop outbreaks.

• To understand environmental stresses: Environmental stresses affect test results and must be avoided, so that POCT can be effective for decision-making in crises.

• To illustrate the design of POCT caches: Disaster caches should be designed, expanded, and harmonized for worldwide collaborative use, in part, to address new threats, such as Ebola & MERS CoV.

• To describe Spatial Care Paths™ (SCP) and point of care culture: The spatial care path™ starts with the patient, positions POCT optimally, and accelerates care—one “tunes” testing for cultural acceptance. National POCT policy and guidelines in limited-resource and other settings then enhance community resilience effectively.
NEEDS ASSESSMENT FOR RAPID DECISION MAKING IN
PANDEMICS, COMPLEX EMERGENCIES, AND DISASTERS:
A GLOBAL PERSPECTIVE

GERALD J. KOST, RICHARD F. LOUIE, ANH-THU TRUONG, AND CORBIN M. CURTIS

OVERVIEW

Clinical needs assessment defines unmet healthcare needs and determines how to fill them. The goal of this chapter is to describe the process of performing needs assessment in the context of translating needs into innovative point-of-care (POC) technologies. We performed need assessment surveys to identify diagnostic testing gaps in complex emergencies, disasters, and public health and used SurveyMonkey® to administer them. Literature searches also were conducted using the PubMed database and keywords, such as point of care, needs assessment, and POC disaster needs assessment. An emerging technologic model summed up our approach. Original research by the University of California, Davis POC Technologies Center and publications by other investigators revealed insights about POC testing (POCT) needs for emergency and disaster response. Laboratory, POC coordinators, medical doctors, researchers, and POC experts and others indicated the importance of (a) having specific POC tests in emergencies and disasters, (b) desired sampling methods that preserve integrity of the sample while minimizing biohazard risks, and (c) defined essential test clusters for bloodstream and respiratory infections. Evidence also revealed strong need for influenza testing and resistance markers useful in public health. Developers can reduce product development risks by conducting formal needs assessment that helps identify end-user product features and requirements early on. Needs assessment guides the product development pipeline of new technologies by helping (a) to identify and prioritize diagnostic testing needs, (b) to determine technological gaps and deficiencies that impact patient care, and (c) to design specifications for new POC technologies. Needs assessment has been successfully applied to identify POC diagnostic testing in complex emergencies, disasters, and public health as illustrated in this review and therefore can be used broadly in the point of care field to accelerate progress.

Based on a 2012 World Health Organization Health Statistics report, a median of 61% of the world health expenditure was paid by the government in 2009 (1). Needs assessment can reduce global health care expenditures, improve healthcare resource, and enhance standards of care. Needs assessment, per se, represents a systematic process for determining and addressing what emergency users want, as well as for discovering gaps and deficiencies in the current delivery and practice of diagnostic testing at the sites of decision making (2).

Fundamentally, POC grew out of satisfying clinical needs for bedside glucose testing, coagulation monitoring, and intensive care, where the advent of ionized calcium (Ca²⁺), free calcium: Figure 1-1) (3, 4) proved that whole-blood analysis (5) was necessary for the diagnosis and treatment of critically ill patients with rapid therapeutic turnaround time (4) that could not be accomplished with centrifuged samples processed distantly in the conventional clinical laboratory. Once speed was achieved within a comprehensive value proposition of convenience, impactful bedside information, and improved outcomes, the paradigm of testing shifted to the point-of-care where it is likely to remain.

Enhanced healthcare delivery in complex emergencies and disasters can improve crisis standards of care (6). The Southeast Asia Tsunami in 2004, Hurricane Katrina in 2006, Haiti Earthquake in 2010, and Sandy Superstorm in 2012 disrupted, flooded, and destroyed infrastructure, including hospital laboratories and microbiology testing services thereby prolonging patient treatment (7–9). Public health officials should understand the methods of needs assessment, its importance, and current healthcare delivery models in order to push developers to deliver appropriate POC technologies that will enhance standards of care (6).

Strategically integrated POC can provide rapid diagnostic data, facilitate triage, and improve management of victims during disasters (10). POC is testing performed at or near the site of the patient care (11). Recent disasters have demonstrated the feasibility of POC, but POC devices lack crucial test clusters and are vulnerable to harsh disaster environments (12–22). The goal of this chapter is to describe the process of performing needs assessment in the context of translating needs into innovative POC technologies.
Needs Assessment Results from AACC members

First Responders are the preferred group to perform POC testing in disasters

Respondents preferred patient-side testing in the field over testing inside a vehicle or tent.
Respondents chose CBC, Lytes/Chemistry, Blood Bank, & O₂ Saturation as the highest priority diagnostic tests for a disaster.

* P < 0.05, ** P < 0.01, *** P < 0.001

How To: Monitor $O_2$ Saturation & Hemoglobin

Respondents chose 3 physical challenges as the most important environmental factors to overcome in future POC device designs for extreme conditions.

THE IMPACT OF ENVIRONMENTAL STRESS ON DIAGNOSTIC TESTING AND IMPLICATIONS FOR PATIENT CARE DURING CRISIS RESPONSE

RICHARD F. LOUIE, WILLIAM J. FERGUSON, CORBIN M. CURTIS, ANH-THU TRUONG, MANDY H. LAM, AND GERALD J. KOST

OVERVIEW

Strategic integration of point-of-care (POC) diagnostic tools during crisis response can accelerate triage and improve management of victims. Timely differential diagnosis is essential whenever care is provided to rule out or rule in disease, expedite life-saving treatment, and improve utilization of limited resources.

POC testing (POCT) needs to be accurate in any environment in which it is used. Devices are exposed to potentially adverse storage and operating conditions, such as high and low temperature and humidity during emergencies and field rescues. Therefore, characterizing environmental conditions allows technology developers, operators, and responders to understand the broad operational requirements of test reagents, instruments, and equipment in order to improve the quality and delivery of care in complex emergencies, disasters, and austere environmental settings.

This chapter aims (a) to describe the effects of environmental stress on POCT performance and its impact on decision making; (b) to describe how to study the effects; and (c) to summarize approaches to minimize or nullify the effects of environmental stresses through good laboratory practice, development of robust reagents, and producing novel thermal packaging solutions.

ENVIRONMENTAL STRESSORS AND POC TESTING

In crisis response, strategic integration of POC diagnostic tools, such as portable multiplex cardiac biomarker testing, at alternate care facilities can accelerate triage and improve management of victims (1). Timely differential diagnosis is essential whenever care is provided to rule out or rule in disease, expedite appropriate life-saving treatment, and improve utilization of limited resources (1).

Between 1980 and 2013, the United States experienced 640 disaster events. Of those events 64.5% (413/640) were weather related (2). Deaths associated with weather-related events account for 87.8% of all disaster deaths (2). Table 23-1 (3–5) summarizes the environmental conditions observed in recent disasters. With careful implementation and integration of POC tests for onsite triaging and diagnosis, lives potentially could have been saved.

To ensure accurate and safe use, POCT needs to deliver excellent performance in any environment in which it is used (6). Erroneous results can cause serious harm and alter clinical decision making, such as improper insulin dosage (7). Emergency and disaster responders equipped with POCT technologies for rapid triage, diagnosis, and monitoring must function effectively in adverse conditions. These conditions may exceed the storage and operating specifications of both POC test reagents and the instruments.

Tables 23-2, and 23-3 (8) summarize the storage and operating specifications of select POC devices. Test reagents typically are refrigerated or stored in ambient conditions between 15–30°C (59–86°F). Reagents requiring refrigeration can be stored at ambient conditions (e.g., room temperature), but are then stable for a shorter duration. The US Pharmacopoeia defines room temperature as 20–25°C (68–77°F) with allowable short-term excursions spanning 15–30°C (59–86°F), and a mean kinetic temperature (MKT) not more than 25°C (77°F).

Mean Kinetic Temperature.

MKT, a simplified way of expressing the overall temperature impact on first-order chemical reactions, weighs the effects of temperature variations over an extended period of time according to the following equation (9):
Environmental Stress Testing Workflow

POC Reagent Testing Chamber & Profile

Test Stressed Strips & Cartridges

- Facilitate Device Design
- Enhance Guidelines Development for POCT in Emergency and Disaster Settings

Short-Term Thermal-Humidity Shock Affects Point-of-Care Glucose Testing: Implications for Health Professionals and Patients

Mandy Lam¹, Richard F. Louie, PhD, FACB¹, Corbin M. Curtis, BS¹, William J. Ferguson, BS¹, John H. Vy, BS¹, Anh-Thu Truong¹, Stephanie L. Sumner, BS¹, and Gerald J. Kost, MD, PhD, MS, FACB¹

Abstract
The objective was to assess the effects of short-term (≤1 hour) static high temperature and humidity stresses on the performance of point-of-care (POC) glucose test strips and meters. Glucose meters are used by medical responders and patients in a variety of settings including hospitals, clinics, homes, and the field. Reagent test strips and instruments are potentially exposed to austere environmental conditions. Glucose test strips and meters were exposed to a mean relative humidity of 83.0% (SD = 8.0%) and temperature of 42°C (107.6°F, SD = 3.2°C) in a Tenney BTRC environmental chamber. Stressed and unstressed glucose reagent strips and meters were tested with spiked blood samples (n = 40 measurements per time point for each of 4 trials) after 15, 30, 45, and 60 minutes of exposure. Wilcoxon’s signed rank test was applied to compare measurements test strip and meter measurements to isolate and characterize the magnitude of meter versus test strip effects individually. Stressed POC meters and test strips produced elevated glucose results, with stressed meter bias as high as 20 mg/dL (17.7% error), and stressed test strip bias as high as 13 mg/dL (12.2% error). The aggregate stress effect on meter and test strips yielded a positive bias as high as 33 mg/dL (30.1% error) after 15 minutes of exposure. Short-term exposure (15 minutes) to high temperature and humidity can significantly affect the performance of POC glucose test strips and meters, with measurement biases that potentially affect clinical decision making and patient safety.

Keywords
clinical decision making, environmental stress, glucose test strip and meter performance, measurement error, patient safety, quality assurance

Glucose meter systems aid responders in triaging, screening, monitoring, and the diagnosis of victims and patients at the site of crisis care. Temperature and humidity conditions at the site of patient care, whether inside or outside the victims’ home or hospital, may exceed manufacturer specifications for storage and operation. Operation of devices outside of product specifications could produce inaccurate results.

Point-of-care (POC) devices deployed with disaster response teams are recommended to be housed in climate controlled settings.¹ However, these devices may be exposed to austere conditions when mobilized for field testing. Temperature extremes can be found in a variety of settings including the patient’s home, distinct geographic locations, and with the settings.

This study aims to simulate realistic operation of POC glucose devices in austere environments, to compare measurements obtained from unstressed devices and test reagents, and to characterize how short-term stress affects meter and test strip performance. We discuss the potential implications of these effects on clinical decision making.

¹UC Davis POC Technologies Center, Point-of-Care Testing Center for Teaching and Research, Pathology and Laboratory Medicine, University of California, Davis, CA, USA

Corresponding Author:
Richard F. Louie, PhD, FACB, Point-of-Care Testing Center for Teaching and Research, Pathology and Laboratory Medicine, University of California, Davis, CA, USA.
Effects of environmental conditions on point-of-care cardiac biomarker test performance during a simulated rescue: Implications for emergency and disaster response

Richard F. Louie, PhD, FACC; William J. Ferguson, BS; Corbin M. Curtis, BS; John H. Vy, BS; Chloé S. Tang, BS; Gerald J. Kost, MD, PhD, MS, FACC

Abstract

Objective: To characterize the effects of environmental stress on point-of-care (POC) cardiac biomarker testing during a simulated rescue.

Design: Multiplex test cassettes for cardiac troponin I (cTnI), brain natriuretic peptide (BNP), CK-MB, myoglobin, and D-dimer were exposed to environmental stresses simulating a 24-hour rescue from Hawaii to the Marshall Islands and back. We used Tencoy environmental chambers (T2RC and BTRC) to simulate flight conditions (20°C, 10 percent relative humidity) and ground conditions (22.3-33.9°C, 73-77 percent). We obtained paired measurements using stressed versus control (room temperature) cassettes at seven time points ($T_1$, with $T_{1.2.6.7}$ during flight and $T_{3.5}$ on ground). We analyzed paired differences (stressed minus control) with Wilcoxon signed rank test. We assessed the impact on decision-making at clinical thresholds.

Results: cTnI results from stressed test cassettes ($n = 10$) at $T_4$ ($p < 0.05$), $T_5$ ($p < 0.01$), and $T_7$ ($p < 0.05$) differed significantly from control, when testing samples with median cTnI concentration of 80 ng/L. During the ground rescue, 36.7 percent (11/30) of cTnI measurements from stressed cassettes generated significantly lowered results. At $T_9$, 20 percent (2/10) of cTnI results were highly discrepant—stressed cassettes reported normal results, while control results were $> 100$ ng/mL. With sample median concentration of 108 pg/mL, BNP results from stressed test cassettes differed significantly from controls ($p < 0.05$).

Conclusion: Despite modest, short-term temperature elevation, environmental stresses led to erroneous results. False negative cTnI and BNP results potentially could miss acute myocardial infarction and congestive heart failure, confounded treatment, and increased mortality and morbidity. Therefore, rescuers should protect POC reagents from temperature extremes.

Key words: austere environments, disaster preparedness, medical errors, Pacific Islands, and quality assurance

Introduction

Emergency medical responders are deployed with limited point-of-care (POC) tests during crises, which restricts triaging in the field. Quantitative measurement of cardiac troponin I (cTnI), brain natriuretic peptide (BNP), CK-MB, myoglobin, and D-dimer in whole blood and plasma specimens can aid in the diagnosis of myocardial infarction, heart failure, pulmonary embolism, and deep vein thrombosis. Environmental conditions present during rescue operations may exceed storage and operating specifications of POC devices and test reagents.\(^1\)\(^3\)

The objective of this study was to characterize the performance of POC cardiac biomarker tests in a simulated rescue between the Hawaiian Islands and Marshall Islands.
WBC & 5-PART DIFFERENTIAL—ENVIRONMENTAL STRESS VALIDATION IN PROGRESS

1. Fill microcuvette.

2. Place microcuvette into analyzer.

3. View results.

The microcuvette cavity is analyzed in separate layers to enable detection of cells at different depths. The camera lens moves in small steps taking several images through the cavity of the microcuvette. All cells in all images will be cut out. Identification when each cell is in focus. Mount the focused cells into one image. Total WBC and differential counting as final step.

Neutrophils
Lymphocytes
Monocytes
Eosinophils
Basophils

Transferring characteristics into mathematical algorithms. WBC DIFF uses over 30 features and state-of-the-art image analysis technology.
THE CURRENT AND FUTURE DESIGN OF POINT OF CARE IN NATIONAL DISASTER CACHES

CORBIN M. CURTIS, RICHARD F. LOUIE, AND GERALD J. KOST

OVERVIEW

The objective of this chapter is to describe, innovate, recommend, and foster the implementation of point-of-care testing (POCT) in disaster caches in order to enhance crisis standards of care and improve triage, diagnosis, monitoring, treatment, and management of victims and volunteers in complex emergencies and disasters. The authors compared point-of-care (POC) technologies in US disaster caches to commercially available POC technologies to enhance the cache and reflect current state-of-the-art diagnostic capabilities. We also provided recommendations based on literature review and knowledge from newly developed POC Technologies from the University of California, Davis Point-of-Care Technologies Center on designing POC caches applicable to meet global needs.

US POC testing includes a variety of methods. Most POC testing is performed at the point of care; however, some analyses may be performed centrally. Deficiencies in existing POCs for cardiac biomarkers, hematological, and infectious diseases should be eliminated. POC resources can be customized for pandemics, complex emergencies, or disasters based on geographic location and the potential for pandemics. Additionally, new therapeutically stabilized containers can help alleviate environmental stresses that reduce test quality. Innovations in POC technologies can improve response preparedness with enhanced diagnostic capabilities. Several innovations, such as the i-STAT Wireless (Abbott Point of Care, Princeton, NJ, USA), OraQuick ADVANCE® HIV-1/2 (OraSure Technologies, Bethlehem, PA, USA), VeriFog™ Lab-on-a-Chip (Veredus Laboratories, Singapore), and new compact hematology analyzers will improve test clusters that facilitate evidence-based decision making and crisis standards of care during national disaster responses. Additionally, strategic resources and operator training should be globally harmonized to improve the efficiency of international responses.

Our goal is to describe, innovate, recommend, and accelerate the implementation of POC in disaster caches in order to (a) enhance crisis standards of care; (b) improve diagnosis, triage, and monitoring in complex emergencies and disasters; and (c) harmonize evidence-based decision making during responses globally. The Office of the Assistant Secretary for Preparedness and Response (ASPR) under the US Department of Health and Human Services (DHHS) maintains three Mission Support Centers (MSCs) located in the western, central, and eastern United States. The eastern region and largest cache warehouse (200,000 ft²) serves as a training facility, home base for cache management, and national headquarters. Disaster response supplies deploy by trucks from any of the three locations to reach a disaster site in the contiguous United States or by airplane to sites outside the landlocked states such as Hawaii, Alaska, and the Republic of the Marshall Islands, within 12 h.

The caches within each facility hold supplies that Disaster Medical Assistance Teams (DMATs) use to triage, diagnose, and monitor victims following catastrophic events. Each facility has an inventory of pharmaceuticals, DMAT response packages, Basic Load Resupply packages to replenish 3 days of supplies for 175 patients per day, temporary portable housing, electricity generators, communication supplies, and vehicles to deliver resources to disaster sites where they converge with DMATs. The packages load straight onto trucks or airplanes without needing further organization. POC devices

This study was supported by the Point-of-Care Testing Center for Teaching and Research (POCT-CTR) and by a National Institute for Biomedical Imaging and Bioengineering (NIBIB) Point-of-Care Technologies Center grant (Dr. Kost, PI, NIH U54 EB007959). The content is solely the responsibility of the author and does not necessarily represent the official views of the NIBIB or the National Institutes of Health.

* 1 ft² = xxx m².
Lab Basic Kit
Disaster Point of Care

POC Hematology Analyzer
- WBC, Differential, RBC, Plt, Hb, and Indices

Sure-Vue® Urine hCG Cartridge
- Rapid tests for Strep Throat, Mono and D-dimer

Coming:
Orasure Ebola POC Test

Onyx® II 9560 Fingertip Pulse Oximeter

Oraquick ADVANCE® HIV 1/2

QuickVue® Influenza Test

CoaguChek® XS Plus System for PT/INR

ABORhCard® Blood Typing Test Card

Multistix® 10 SG Urinalysis Strips
- Bilirubin, Blood, Glucose, Ketone, Leukocyte Esterase, Nitrite, pH, Protein, Specific Gravity, Urobilinogen

Min-Max Temp

Patient Health Security Card

StatStrip Glucose, Lactate, β-hydroxybutyrate and Creatinine

Masimo Rad-57™ Oxygen Saturation and Hemoglobin plus pediatric probes
Kalasin: above to her right

Maha Sarakham: below to her left
THE SPATIAL CARE PATH™

- **Definition**: The most effective route taken by the patient when receiving definitive care in a small-world network.

- **Hypothesis**: Integrates prevention and intervention to shift the focus upstream to the patient site early on, in order to save resources, time, and lives, and to stop outbreaks.

- **Features**: Starts with the patient rather than the institution, empowers primary care, establishes critical access using geographic information systems, positions POCT, and optimizes decision-making with “FAST POC.”

- **Status**: Exploratory research.

Reference: Kost GJ, Ferguson WJ, Kost LE. Principles of point of care culture, the spatial care path™, and enabling community and global resilience. e-JIFCC. 2014;25(2):4-23.
Principles of point of care culture, the spatial care path™, and enabling community and global resilience

Gerald J. Kost, MD, PhD, MS, FACB\textsuperscript{a,b,c}; William J. Ferguson, BS\textsuperscript{a}; Laurie E. Kost, BS, MS\textsuperscript{d}

\textsuperscript{a}Point-of-Care Center for Teaching and Research (POCT•CTR), School of Medicine, UC Davis, CA
\textsuperscript{b}Knowledge Optimization\textsuperscript{®}, Davis, CA
\textsuperscript{c}Affiliate Faculty, College of Population Studies, Chulalongkorn University, Bangkok, Thailand
\textsuperscript{d}Harvard School of Public Health, Harvard University, Boston, MA

\textbf{ARTICLE INFO}

\textbf{Corresponding author}
Gerald J. Kost, MD, PhD, MS, FACB
Point-of-Care Testing Center for Teaching and Research (POCT•CTR)
School of Medicine, University of California
3455 Tupper Hall, Davis, CA 95616

\textbf{Running title}
Enabling Community and Global Resilience

\textbf{Abstract}

Goals: This article a) defines point of care (POC) culture; b) presents seven underlying fundamental principles; c) describes the importance of needs assessment; d) introduces a new innovation, the spatial care path™; and e) illustrates how POC testing that properly fulfills needs and spatial care paths™ enable community and global resilience.

Observations: Often, POC testing supplants the conventional clinical laboratory, which may be too distant, prohibitively expensive, or simply not available in limited-resource settings. New POC technologies “fit” future medical problem solving. Screening and testing directly in the home or primary care facilitate rapid diagnosis, monitoring, and treatment. In contrast to the past where attention has been placed on emergency departments, hospitals, and referral centers, the spatial care path™ starts with the patient and guides him or her through an efficient strategy of care in small-world networks (SWNs) defined by local geography and topology, long-standing customs, public health jurisdictions, and geographic information systems (GIS).

Conclusions: POC testing needs in limited-resource settings are striking. Fulfillment is best guided by thorough understanding of POC culture. Quick feedback and fast decision-making enable effective response.
Transforming the Physical Domain to the Temporal Domain in Small-World Network Spatial Care Paths™

Shortcut to Heart Center if cTn is Elevated

The Ebola Spatial Care Path™: Accelerating point-of-care diagnosis, decision making, and community resilience in outbreaks.

Kost GJ, Ferguson WJ, Hoe J, Truong AT, Banpavichit A, Kongpila S.

Author information:

1. Point-of-Care Center for Teaching and Research (POCT-CTR), School of Medicine, University of California, Davis, Davis, California; President and CEO, Knowledge Optimization®, Davis, California; Affiliate Faculty, College of Population Studies, Chulalongkorn University, Bangkok.

2. POCT-CTR, School of Medicine, University of California, Davis, Davis, California.

3. Managing Director, Owner, Connect Diagnostics, Bangkok, Thailand.


Abstract

OBJECTIVES:

To present a vision where point-of-care testing (POCT) accelerates an Ebola Spatial Care Path™ (SCP) and future molecular diagnostics enable facilitated-access self-testing (FAST POC); to design an alternate care facility (ACF) for the SCP; to innovate an Ebola diagnostic center (DC); and to propel rapid POCT to the frontline to create resilience that stops future outbreaks.

DESIGN:


OUTCOMES:

The authors designed an ACF and DC to integrate SCP principles for urgent Ebola care. FDA emergency use authorizations for Ebola molecular diagnostics were discovered, but no portable, handheld, or self-contained molecular POC instruments are yet available, although feasible. The WHO initiated design criteria and an acceptance protocol for testing. Financial investment in POCT will downsize Ebola outbreaks.

CONCLUSIONS:

POCT is facilitating global health. Now, global health problems are elevating POCT to new levels of importance for accelerating diagnosis and evidence-based decision making during disease outbreaks. Authorities concur that rapid diagnosis has potential to stop disease spread. With embedded POCT, strategic SCPs planned by communities fulfill CDC recommendations. POC devices should consolidate multiplex test clusters supporting patients with Ebola in isolation. The ultimate future solution is FAST POC. New technologies offer minimally significant risks. Diagnostic centers in ACFs and transportable formats also will optimize Ebola SCPs.

PMID: 26312494 [PubMed - in process]
EBOLA
Signs and Symptoms
If You Have Fever, Diarrhea and Vomiting With or Without Bleeding
GO IMMEDIATELY TO THE NEAREST HEALTH FACILITY
For more information call 117 (Call free)
EBOLA PREPAREDNESS AND RESILIENCE

First, let’s recognize that we are not yet prepared!
…and what of others, MERS CoV or new highly infectious threats?

- POCT to detect threats early, isolate effectively, & stop outbreaks
- Portable molecular diagnostics with ultrahigh sensitivity and specificity
- “FAST-POC” (facilitated-access self-testing) to avoid exposure of the healthcare workforce
- Accelerated availability of “EUA” devices (emergency use authorization, US FDA approval)
- Harmonized strategies for communities at risk
- National POCT policy and guidelines for foundation and integrated “point of care culture”
Developing a Spatial Care Path™ for Ebola

Enzootic Cycle

New evidence strongly implicates bats as the reservoir hosts for ebolaviruses, though the means of local enzootic maintenance and transmission of the virus within bat populations remain unknown.

Ebolaviruses:
- Ebola virus (formerly Zaire virus)
- Sudan virus
- Taï Forest virus
- Bundibugyo virus
- Reston virus (non-human)

Epizootic Cycle

Epizootics caused by ebolaviruses appear sporadically, producing high mortality among non-human primates and duikers and may precede human outbreaks. Epidemics caused by ebolaviruses produce acute disease among humans, with the exception of Reston virus which does not produce detectable disease in humans. Little is known about how the virus first passes to humans, triggering waves of human-to-human transmission, and an epidemic.

Human-to-human transmission is a predominant feature of epidemics.

Following initial human infection through contact with an infected bat or other wild animal, human-to-human transmission often occurs.
Laboratory Diagnosis of Ebola—Too Slow!

**TIMELINE OF INFECTION**

- **Within a few days after symptoms begin**

- **Later in disease course or after recovery**

- **Retrospectively in deceased patients**

**DIAGNOSTIC TESTS AVAILABLE**

- Antigen-capture enzyme-linked immunosorbent assay (ELISA) test
- IgM ELISA
- Polymerase chain reaction (PCR)
- Virus isolation
- IgM and IgG antibodies
- Immunohistochemistry test
- PCR
- Virus isolation

Ebola Containment

Top (A)
High Risk Zone

Bottom (B)
A Complete Center

Move POC testing upstream in the spatial care path.™ Detect the disease before the patient spreads it!

World Health Organization

“Target Product Profile for Zaire Ebola virus rapid, simple test to be used in the control of the Ebola outbreak in West Africa”

Source: http://www.who.int/medicines/publications/target-product-profile.pdf?ua=1
Source: Preparing for Ebola: What U.S. Hospitals Can Learn From Emory Healthcare and Nebraska Medical Center. Planning to Treat Patients with Ebola Virus Infection by Dr. Ribner. Emory Serious Communicable Disease Unit. CDC Webinar. 2014.
### Point-of-Care Tests Established in Ebola Isolation Areas

#### A. Emory University Hospital Specialized Isolation Area

<table>
<thead>
<tr>
<th>Manufacturer Website</th>
<th>Instrument</th>
<th>Test(s)</th>
</tr>
</thead>
</table>
| Abaxis               | Piccolo Express             | Chemistry profiles, Magnesium, Phosphate, liver enzyme assays, others available
| www.abaxis.com       |                             |                                                                         |
| Instrumentation Laboratory | GEM Premier 4000 | pH, pCO₂, pO₂, Na⁺, K⁺, Ca²⁺, Cl⁻, Glu, Lac, Hct, THb, CO-Oximetry, TBil |
| www.instrumentationlaboratory.com |                   |                                                                         |
| Siemens              | CLINITEK Status automated urinalysis | Albumin, Bilirubin, Cr, Glu, Ketone, Leukocytes, Nitrite, pH, Protein, Specific Gravity, Urobilinogen, others available
| www.healthcare.siemens.com |                       |                                                                         |
| Hoffman-La Roche     | CoaguChek                  | PT/INR                                                                 |
| www.coaguchek.com    |                             |                                                                         |
| Sysmex               | pocH-100i                  | CBC: WBC (3-part differential), RBC, Hb, Hct, MCV, MCH, MCHC, Platelets |
| www.sysmex.com       |                             |                                                                         |
| Alere                | BinaxNOW                   | Malaria                                                                |
| www.alere.com        |                             |                                                                         |
| BioFire Diagnostics  | FilmArray                  | Infectious diseases including Ebola (see Table 1)                       |
| www.biofiredx.com    |                             |                                                                         |

Ebola proved the absolute need for POCT!
Alternate Care Facility for Ebola Triage and Care
Mini Review

Belen Fernandez-Puntero*, Ruben Gomez-Rioja, Maria Jose Alcaide, Paloma Oliver, Pilar Fernandez-Calle, Jose Manuel Iturzaeta and Antonio Buno

The Laboratory Medicine and the care of patients infected by the Ebola virus. Experience in a reference hospital of Madrid, Spain

Abstract

The ongoing Ebola virus outbreak in several countries in West Africa was considered by the World Health Organisation (WHO) as a public health emergency of international concern. Healthcare providers must be prepared by organising specific procedures in our hospitals based on recommendations from national and international healthcare organisations. Two aims should be considered: appropriate medical care for patients with suspected or confirmed disease must be ensured, as must measures to prevent transmission to healthcare workers. The clinical laboratory plays an important role and must define and establish its own procedures in accordance with clinicians and integrated into those of the institution, starting with the definition of the organisation model in the laboratory to achieve those goals. In this review we present our experience based on the care of three patients with confirmed cases. We hope it will help other colleagues to plan for Ebola.
<table>
<thead>
<tr>
<th>Container</th>
<th>Device</th>
<th>Tests</th>
<th>Container</th>
<th>Device</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Tube of dipotassium EDTA</td>
<td>Poch-100i (Sysmex-Roche, Madrid, Spain)</td>
<td>Differential blood count 3 diff</td>
<td>1 Tube dipotassium EDTA</td>
<td>Poch-100i (Sysmex-Roche, Madrid, Spain)</td>
<td>Differential blood count</td>
</tr>
<tr>
<td>SPOTCHEM-EZ (Arkray-Menalini, Madrid, Spain)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3 diff</td>
</tr>
<tr>
<td></td>
<td>Glucose</td>
<td>Cholesterol</td>
<td>Total proteins</td>
<td>Creatinine</td>
<td>BUN</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Syringe lithium heparin</td>
<td>SPOTCHEM-EL (Arkray-Menalini, Madrid, Spain) NPT-7 (Radiometer, Madrid, Spain)</td>
<td>Sodium, Potassium, Chlorine ions pH PaCO₂ PaO₂ Oxygen saturation Cooximetry Bicarbonate Excess of base Total CO₂ concentration</td>
<td>1 Syringe lithium heparin</td>
<td>EPOCAL (Alere, Madrid, Spain)</td>
<td>Sodium and Potassium ions Glucose Ionized calcium Lactate pH PaCO₂ PaO₂ Oxygen saturation Bicarbonate Excess of base Total CO₂ concentration</td>
</tr>
<tr>
<td>1 Drop whole blood</td>
<td>COAGUCHECK (Roche, Madrid, Spain)</td>
<td>INR</td>
<td>1 Syringe without anticoagulant with whole blood</td>
<td>COAGUCHECK (Roche, Madrid, Spain)</td>
<td>INR</td>
</tr>
</tbody>
</table>
SPATIAL CARE PATH™

SYMPTOMATIC PATIENT

RAPID MOLECULAR TESTING → TN, FN(t)

EXPOSED PATIENT

CLINICAL EVALUATION & DIAGNOSTIC TESTING
POC WBC, DIFFERENTIAL & PLATELET COUNT
INR, aPTT, Bleeding Time, ALT, & AST

LIMITED QUARANTINE VACCINATION

HIGHLY INFECTIOUS DISEASE BEDS WITH ANTEROOM

BLOOD SAMPLE PROCESSED IN ISOLATION UNIT &/OR TRANSPORTED TO REFERRAL LAB:
-CDC
-PUBLIC HEALTH

SLOWER RESPONSE GREATER EXPENSE

ALTERNATE CARE FACILITY
- Dynamic Segregation
- POC Coordinator
- Fully Equipped POCT
- Telehealth

HIGHER EFFICIENCY LOWER RISK

OPTIMIZED POC SOLUTION

COMMUNITY RESILIENCE

SYMBOLS:
- Nurse Station
- Bed
- Pediatrics
- Bluetooth/WiFi
- Washing Area
- Door
- Isolation Door

SWN

INTEGRATED PLANNING
CDC REQUIREMENTS FOR EBOLA CENTERS

- Accept patients within eight hours of being notified,
- Have the capacity to treat at least two Ebola patients at the same time,
- Have respiratory infectious disease isolation capacity or negative pressure rooms for at least 10 patients,
- Conduct quarterly trainings and exercises,
- Receive an annual readiness assessment from the soon-to-be-established National Ebola Training and Education Center, composed of experts from health care facilities that have safely and successfully cared for patients with Ebola in the U.S., and funded by ASPR and the Centers for Disease Control and Prevention, to ensure clinical staff is adequately prepared and trained to safely treat patients with Ebola and other infectious diseases,
- Be able to treat pediatric patients with Ebola or other infectious diseases or partner with a neighboring facility to do so, and,
- Be able to safely handle Ebola-contaminated or other highly contaminated infectious waste.

Does not require POC resources or strategies. No harmonized POC testing, molecular diagnostics, or early detection. Neglects integrated community resilience and optimized geospatial care (no SCP).

Source: ASPR Press Office. HHS selects nine regional Ebola and other special pathogen treatment centers. June 12, 2015. HSS.gov or http://www.hhs.gov/news
HOW MERS GOT TO SOUTH KOREA

Update late June, 2015
16+ Dead
172 Infected
4,035 being monitored
New case in Thailand

Rising numbers: 122 Confirmed cases 10 Dead 4 Recovered 3,439 Quarantined

Patient Zero
male, 68

Arrived in South Korea from Qatar on May 4
Developed symptoms on May 11
Confirmed May 20 that he had MERS

Samsung Medical Center, Seoul: May 17-20
Chonho 365 Open hospital, Seoul: May 17
St. Mary's, Pyeongtaek: May 15-17
Dunpo Seoul hospital, Asan: May 12-14

SOURCE: South Korean government, June 11, 2015
Molecular detection and point-of-care testing in Ebola virus disease and other threats: a new global public health framework to stop outbreaks


Gerald J Kost*, William Ferguson, Anh-Thu Truong, Jackie Hoe, Daisy Prom, Arirat Banpavichit and Surin Kongpila

University of California, Davis, USA
*Author for correspondence: gjkost@ucdavis.edu

Ultrahigh sensitivity and specificity assays that detect Ebola virus disease or other highly contagious and deadly diseases quickly and successfully upstream in Spatial Care Paths™ can stop outbreaks from escalating into devastating epidemics ravaging communities locally and countries globally. Even had the WHO and CDC responded more quickly and not misjudged the dissemination of Ebola in West Africa and other world regions, mobile rapid diagnostics were, and still are, not readily available for immediate and definitive diagnosis, a stunning strategic flaw that needs correcting worldwide. This article strategizes point-of-care testing for diagnosis, triage, monitoring, recovery and stopping outbreaks in the USA and other countries; reviews Ebola molecular diagnostics, summarizes USA. FDA emergency use authorizations and documents why they should not be stop-gaps; and reduces community risk from internal and external infectious disease threats by enabling public health at points of need.

FREE ACCESS FOR ONE WEEK! USE THIS LINK—

http://www.tandfonline.com/doi/full/10.1586/14737159.2015.1079776
<table>
<thead>
<tr>
<th>Instrument(s) &amp;/or Assay/Kit Manufacturer</th>
<th>Principle</th>
<th>Sample(s)</th>
<th>Time to Results</th>
<th>FDA Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xpert Ebola Assay Cepheid</td>
<td>rRT-PCR Cartridge-based</td>
<td>Blood</td>
<td>2 h</td>
<td>EUA 3/23/15</td>
</tr>
<tr>
<td>Corgenix ReEBOV &amp; Fio Corp†</td>
<td>Lateral flow Ag immunoassay, Deki reader, smartphone data capture, &amp; case tracking</td>
<td>Blood or plasma</td>
<td>15 min</td>
<td>EUA 3/16/15 [eligible for WHO procurement]</td>
</tr>
<tr>
<td>LightMix Roche cobas z480</td>
<td>rRT-PCR</td>
<td>Blood</td>
<td>Over 3 h</td>
<td>EUA 12/23/14</td>
</tr>
<tr>
<td>QIAamp Viral Kit RealStar Filovirus: ABI Prism 7500 SDS LightCycler 480 II CFX96/Dx RT Sys</td>
<td>rRT-PCR (Kit 1.0)</td>
<td>Blood, plasma</td>
<td>Varies with instrument</td>
<td>EUA 11/26/14 [eligible for WHO procurement]</td>
</tr>
<tr>
<td>BioFire Defense Biothreat-ENGDS bioMerieux® [in 300 hospitals]</td>
<td>Film Array EZV Auto’d. rRT-PCR</td>
<td>Blood, urine (if matched to blood)</td>
<td>1 h</td>
<td>EUA 10/25/14 3/2/15 (RI)</td>
</tr>
<tr>
<td>MagMax Pathogen Kit, Dynal Bead Re. ABI 7500 BioRad CFX96</td>
<td>CDC NP rRT-PCR VP40 rRT-PCR</td>
<td>Blood, plasma, serum, urine (if matched)</td>
<td>NS</td>
<td>EUA 10/10/14 3/2/15 (RI)</td>
</tr>
<tr>
<td>ABI 7500 LightCycler 480 JBAIDS</td>
<td>DOD EZ1 rRT-PCR TaqMan Assay</td>
<td>Inactivated whole blood &amp; plasma</td>
<td>Varies with instrument</td>
<td>EUA 10/10/14</td>
</tr>
<tr>
<td>Nanomix [Corgenix &amp; Tulane University]</td>
<td>Carbon nanotube biosensor† Handheld multiplex cartridge-based</td>
<td>Pinprick capillary blood</td>
<td>10 min</td>
<td>No EUA* (see above)</td>
</tr>
<tr>
<td>Lucigen AmpliFire [Douglas Sci., UTMB, CDC]</td>
<td>LAMP (isothermal) 1-step, battery-operated, portable††</td>
<td>RNA extract [plan 50 μL POC fingerstick capillary blood]</td>
<td>40 min</td>
<td>No EUA*</td>
</tr>
<tr>
<td>Biomarkers USAMRIID/ECBC/TFS</td>
<td>Mass spectrometry</td>
<td>In development</td>
<td>NS</td>
<td>No EUA*</td>
</tr>
<tr>
<td>OraQuick** Orasure</td>
<td>CLF Ag assay [EZV, SEV, &amp; BEV not differentiated]</td>
<td>In development: saliva sample</td>
<td>Est. 20 min</td>
<td>EUA* 7/31/15 [venous WB &amp; fingerstick WB; not for screening, e.g., in airports; not for contact tracing]</td>
</tr>
</tbody>
</table>
COMPACT PCR-BASED MOLECULAR DIAGNOSTICS

- Lid
- Test Base Holder
- Sample Receiver Holder
- LCD Color Display Screen
- Audio Speaker
- LED Status Indicator

Influenza A & B CLIA Waived

Sensitivity A 99.3%  B 98.1%
Specificity A 98.9%  B 99.6%
CONCEPT SOLUTION
USING “FAST POC™” TO STOP OUTBREAKS!

Definition: *Facilitated-access Self-testing Point of Care*

The patient obtains his or her own (capillary blood, saliva, urine, or other) sample with an automatic retractable lancet or suitably simple sampling device built into a self-aspirating and self-contained microcassette, microcuvette, or cartridge, which then seals for automatic testing and automated processing by a POC instrument, while another person, the “facilitator,” instructs and guides hands off, so there is extremely limited or no exposure to infectious agents.
Next Step
Insert the FAST strip with your sample into the reagent cassette.
Influenza A & B (CLIA Waived)
Sensitivity A 100%  B 100%
Specificity A 96.8% B 94.1%

Strep A
Sensitivity 98.3%
Specificity 94.2%
(CLIA Waived)

20 min PCR assay
Research in limited-resource and other settings. POC culture is medical empowerment of the individual and family nucleus integrated with norms, behaviors, beliefs, attitudes, expectations, POC technology, and outcomes—the final
WHAT WE HAVE LEARNED!

• **Needs assessment defines the role of POCT** in pandemics, complex emergencies, disasters, and outbreaks.

• **Environmental stresses affect test results and must be avoided**, so that POCT can be effective for decision-making in urgent care, emergencies, & crises (Ebola, MERS CoV).

• **Disaster caches should be designed and harmonized for collaborative use** throughout the world, and for pandemics.

• **Spatial Care Paths™** start with the patient, position POCT optimally, and accelerate care, while ones “tunes” cultural acceptance. Then, national POCT policy and guidelines and fiscal planning will enhance and sustain community resilience, keys to stopping outbreaks.
NATIONAL POLICY & GUIDELINES


- Uniquely combines policy and guidelines in one document

- Endorsed by the Ministry of Health

- One of the first nationally harmonized approaches to point-of-care testing

- Needs extension for disaster management and Ebola preparedness

PHILIPPINES CHALLENGE! To produce national POCT policy and guidelines that will increase funding, enhance quality, harmonize POC, & improve outcomes! A step toward “Sustaining Quality through Global Standards.”
Progress in Asia

China—

A new 2015 book (right) by Professor Liu et al., Editors, Wuhan (with Dr. Kost, Honorary Editor)

A new concept:

“Point of Careology”!

Other countries—

Developing policy and guidelines, e.g., in Thailand
ACKNOWLEDGEMENTS

Point-of-Care Testing Center for Teaching and Research (POCT•CTR), founded 1995 and continuing 20 years, and the UC Davis POC Technologies Center [U54, NIBIB, NIH], 2007-2014

FOUNDERS
Gerald J. Kost, MD, PhD, MS, FACB; Richard F. Louie, PhD, FACB; and Nam K. Tran, PhD, MS, FACB

CONTRIBUTING AUTHORS AND INTERNATIONAL RESEARCHERS
Ajarns Dew & Dee, Faculty of Sociology, SWU, Bangkok; Keith Brock; Wanvisa Boonlert, PhD (Naresuan University, Thailand); Simrin K. Cheema; Corbin M. Curtis; Anna M. Dillier; William J. Ferguson; Nicole L. Gentile, PhD; Kristin N. Hale; Pratheep Katip, MT (Chulalongkorn University, Bangkok); Tyler K. Kitano; Angela Kost, MS; Laurie Kost, MS (School of Public Health, Harvard University); Daniel M. Mecozzi; Jorge Sifontes; Harpreet Singh; Rebecca J. Sonu, MD (ARRA NIH Center Fellow); Chloe S. Tang; John H. Vy; Jimmy Yu; and Yimeng Zhou (Edmondson Fellow, Carleton College; POCT•CTR Global Health Fellow in China)

STUDENT AUTHORS AND RESEARCHERS
Anup Abraham; Shaunyé Belcher; Corinne A. Gamache (WNEU,MA); Jackie Hoe; Lilya Kraynov; Mandy Lam; Marine Lhote, MS (France); Ron Mathew; Mathieu Pirart, MS (France); Stephanie L. Sumner; and Anh-Thu Truong [v3, 10-29-14]
DISCLOSURES (…WITH APPRECIATION!)

- **Major long-term funding**—National Institute of Biomedical Imaging and Bioengineering (NIBIB), National Institutes of Health, U54 Point-of-Care Technologies Center and ARRA/PPP funds (substantial portions of the results in this presentation, completed)

- **Industry contributions of counsel, equipment, reagents, and in some cases travel support**—Abbott, Alere, HemoCue, Nova Biomedical, Roche Diagnostics (Malaysia, Switzerland, Thailand, & USA), Connect Diagnostics (Thailand), et al. (including in China)

- **The University of California**—UC Davis Outreach and International Programs and UC Systemwide grants and travel awards; Faculty research awards

- **Various Donors**—matching funds for global development, education, and research

- **Fulbright Scholar Award**—Point-of-Care Testing, Demography, and Economics research; teaching, mentoring, and lecturing in SE Asia (10 countries)

- **Ministries of Public Health**—currently sponsoring the development of national guidelines in Thailand, previously in Malaysia, and soon in development in the Philippines

- **Collegial and Professional**—Chulalongkorn and Srinakharinwirot (SWU) Univs., Bangkok, Thailand, and others; POCT Task Force, IFCC (travel funds); & CPOCT Division, AACC