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Point-of-Care Testing for Disasters: Needs Assessment, Strategic Planning, and Future Design

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KEYWORDS

- Biohazard containment • Hurricane Katrina
- Modular test design • Newdemics • Sampling method
- Small-world network (SWN) • Tsunami

GOALS AND OBJECTIVES

The goals of point-of-care testing (POCT) are to facilitate rapid evidence-based decisions, to improve patient outcomes, and, ultimately, to be robust and reliable enough for on-site applications in emergency and disaster settings worldwide.

The objectives of this article are (1) to review current POC technologies used in disaster and emergency care, (2) to understand first responder needs, (3) to outline device design criteria based on gap analysis, and (4) to present strategies for improving future POCT for efficiency, effectiveness, and targeted treatment during on-site field operations.

This article is evidence-based in that it presents preliminary results of a needs assessment survey in the United States. Readers are encouraged to participate in the needs assessment survey. Please see the instructions provided in **Table 1**.

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Table 1
SurveyMonkey Instructions

Step	Instruction and Access
One	Visit UC Davis-LLNL POCT. Web site: http://www.ucdmc.ucdavis.edu/pathology/poctcenter
Two	The Clinical Needs Assessment survey link appears in the top right corner of the navigation bar. It is the first item under POC Technologies Center. Please click on "Needs Assessment Survey"
Three	Please contact Keith Brock, Research Specialist, at 530 752 8471, email: tkbrock@ucdavis.edu, to receive an accession number
Four	Follow the instructions on the screen to complete the survey. *Note:* Your progress will be saved after pressing the "next" button at the end of each page. Please note, your progress online is managed through your web browser cookies. Please complete the survey on the same computer and do not delete the cookies on your web browser before completion of the online survey
Five	Thank you for your time and input on the survey!

The 2004 tsunami in Southeast Asia and Hurricane Katrina in the United States exposed the lack of disaster preparedness worldwide.[1] Although the feasibility of POCT was proven, and the disaster responses were extensive, follow-up studies showed rescue was slow and inadequate.[1] In Hurricane Katrina, flooded hospitals, roads, and communications hindered rescue efforts by first responders who carried limited POCT devices such as oxygen saturation monitors (pulse oximeters), blood glucose meters, and other small handhelds.[1] Furthermore, POCT instruments failed to operate effectively under adverse environmental conditions at respective disaster locations, where temperatures reached 110°F (43°C) or higher in hospitals.[2,3]

Broadly regional catastrophes, such as these recent "newdemics,"[4,5] lead to sequentially magnified setbacks. Others, such as the current novel H1N1 pandemic, threaten entire nations. Typically, communities lack the POCT resources necessary to effectively handle the disaster situations they face.[1] Conversely, newdemics highlight the significant potential for POCT to positively impact preparedness, disaster response, and patient outcomes. Current experiences, including the surprise appearance of the novel H1N1 pandemic in Mexico (unpublished observation), emphasize the need for new sturdy, handheld, and robust POC technologies capable of effectively operating in a variety of field locations.

In the future, better prepared first responders will carry reliable POCT diagnostics wherever disaster and emergency situations arise. Thus, POC user needs are being established through objective evidence-based national surveys (see **Table 1**) as a first step in identifying suitable device designs, effective test clusters, and environmental operating conditions.[6] The preliminary survey results are reported.

NEEDS ASSESSMENT SURVEY: PRELIMINARY RESULTS

Participants

Forty disaster care experts were randomly selected from the editorial boards of the *American Journal of Disaster Medicine* (AJDM) and *Disaster Medicine Public Health and Preparedness* (DMPHP) using a random number generator (Minitab, State College, PA). This sample included physicians, public health officials, researchers, pathologists, first responders, and military personnel.

Development

A survey was developed based on literature review and multidisciplinary consultations that included professors of bioengineering, emergency medicine, infectious diseases, and critical care medicine. "Visual logistics," defined as graphics and pictorial media for common sense portrayal of questions, concepts, and designs, are introduced to build survey questions with the objective of generating easy to comprehend concepts without laborious text or lengthy explanation. Set theory (eg, Venn diagrams) was used whenever possible to compare 2 or more visual concepts, questions, and the results.

To encourage participation and simplify distribution and return, a visual logistics web-based survey was developed (SurveyMonkey, Portland, Oregon). Paper-based and web-based surveys used identical graphics and questions. The survey was divided into 4 parts: (1) demographic questions, (2) device design questions in 10 sections, (3) pathogen test cluster design questions in 4 sections, and (4) trade-off blocks that led to heuristic ranking of POC design features. At the time of this preliminary report, parts 1 to 3 were implemented.

Procedures

If possible, personal contact was initiated by phone followed by shipment of a FedEx package containing an invitation letter, the paper-based survey, and a prepaid return envelope. The invitation letter explained the goal of the survey, provided instructions for participation, and included a hyperlink to the web-based survey (see **Table 1**). Email also was used to distribute the survey request and hyperlink. This preliminary report reflects survey results obtained between March 1 and June 14, 2009. The survey was conducted in compliance with the UC Davis Institutional Review Board.

Statistics

Data obtained from the survey were analyzed using nonparametric Pearson chi-square exact tests (SAS, Gary, North Carolina). Statistical significance was defined as: *, $P<.05$; **, $P<.01$; and ***, $P<.001$.

Pathogen test cluster rank results were analyzed by assigning each pathogen a weighted score. The score for each rank was calculated using the following equation: $S_i = (11 - R_i)$. R_i is defined as the rank of each pathogen assigned by a survey participant, such that $i = [1, n]$, where *n* is the number of ranks. When the respondent designated the same rank for 2 or more organisms, the average rank was calculated and assigned to each organism.

The weighted score was calculated by summing the product of each score and corresponding frequency using the following equation: $WS_j = \sum_{i=1} S_i \times F_{ij}$. The frequency, F_{ij} is defined as the number of times survey participants ranked a pathogen a specific value, such that $j = [1, N]$, where *N* is the number of pathogens.

PRELIMINARY RESULTS

Demography

Of the 40 disaster medicine experts surveyed, 25 responses were received, giving a response rate of 62%. The respondents included 8 physicians (32%), 9 public health officials/hospital managers (36%), 3 pathologists (12%), and 5 emergency room doctors (20%).

Device Design

Fig. 1 illustrates visual logistics, specifically pictorial media that introduced the survey question on what the respondent preferred with regard to instrument formats for

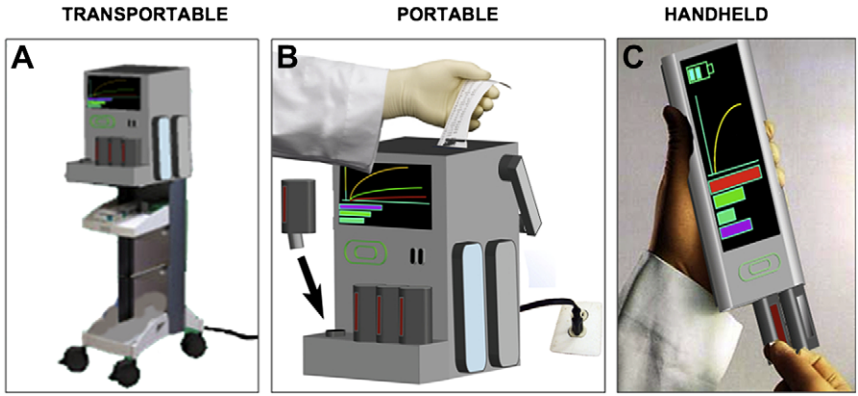

Fig. 1. Device design format. Visual logistics were used to illustrate 3 device format selections for POCT instruments. (*A*) Transportable device on a cart. (*B*) Portable, bench-top device with a handle for carrying. (*C*) Small battery-operated handheld device.

given clinical settings. The results showed that in disaster settings, respondents showed a significant preference for handheld diagnostics (**Fig. 2**) and cited increased portability and versatility as the rationale.

When respondents were asked to choose between a device that tests multiple patient samples in parallel for a single pathogen versus a device that performs multiplex testing of several pathogens for a single patient sample (**Fig. 3**), respondents preferred a multiplex test in the urgent care and emergency room settings (**Fig. 4**). Participants cited the need to quickly screen a large volume of patients in a disaster setting, whereas a full workup is necessary in urgent care and emergency room settings. Several of the respondents who chose the device that parallel processes

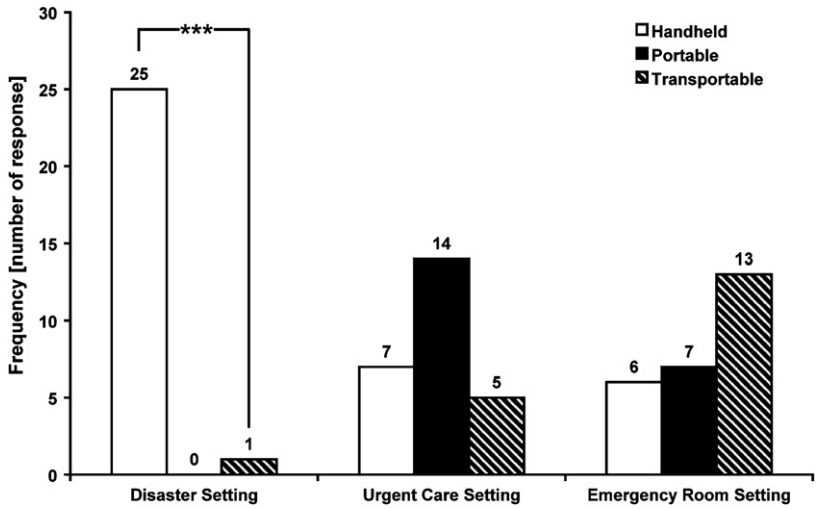

Fig. 2. Selection of format by survey respondents. In disaster settings, participants preferred handheld devices (***P<.001). For urgent care and emergency-room settings, there were no statistically significant differences in preferences.

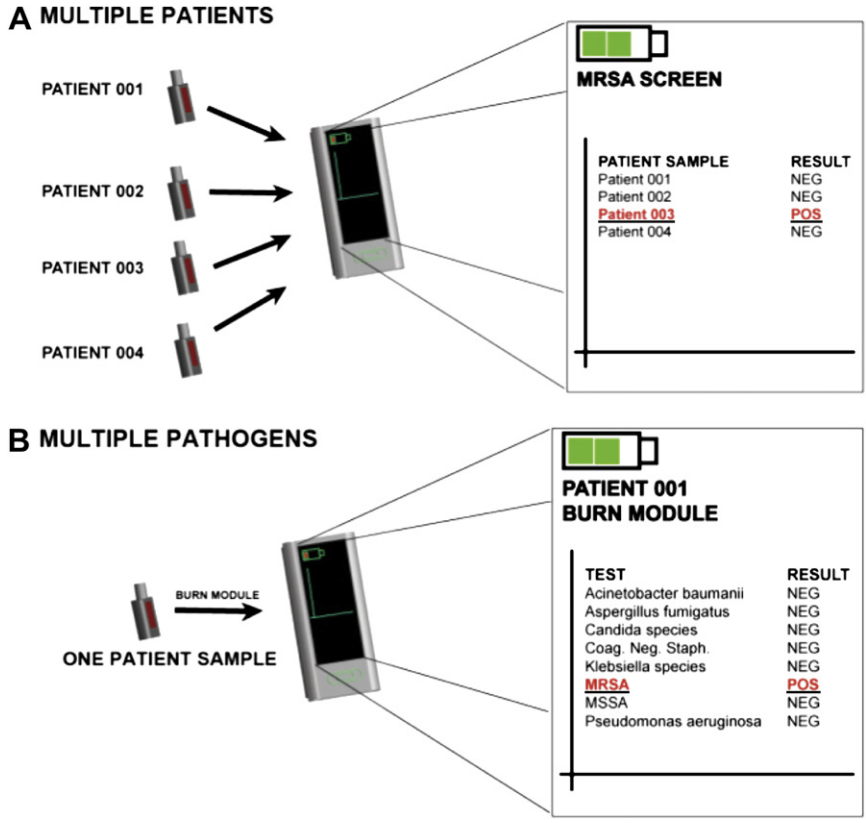

Fig. 3. Multiple patients versus multiplex pathogens. Visual logistics were used to illustrate 2 testing methods for POCT devices. (*A*) Testing multiple patients for 1 pathogen. (*B*) Multiplex pathogen testing, in which 1 patient sample is simultaneously tested for the presence of multiple pathogens (*underline*).

multiple patient samples for a single pathogen given a disaster setting, referenced biothreat or pandemic scenarios.

Fig. 5 shows 2 different sample collection methods, a test cassette and vacutainer. A test cassette provides a housing platform in which one can automate preanalytical processing steps that are critical to subsequent analytical steps that follow on the POC device. **Fig. 6** reflects general acceptance of test cassettes in disaster, urgent care, and emergency settings.

Respondents were also asked to state their preference between 2 potential waste disposal methods (**Fig. 7**). The first scheme suggests an instrument that stores biohazard waste in a reusable waste storage reservoir to be emptied periodically. A test cassette, used to transport the sample to the instrument, would also need to be properly discarded after a single use. The second scheme shows an instrument that stores all biohazard waste in the disposable test cassette, which then is discarded after a single use. **Fig. 8** shows a statistically significant preference of respondents for the disposable test cassette in the second scheme across all 3 clinical settings, with a higher level of statistical significance ($P<.01$) of the preference in disaster and emergency room settings.

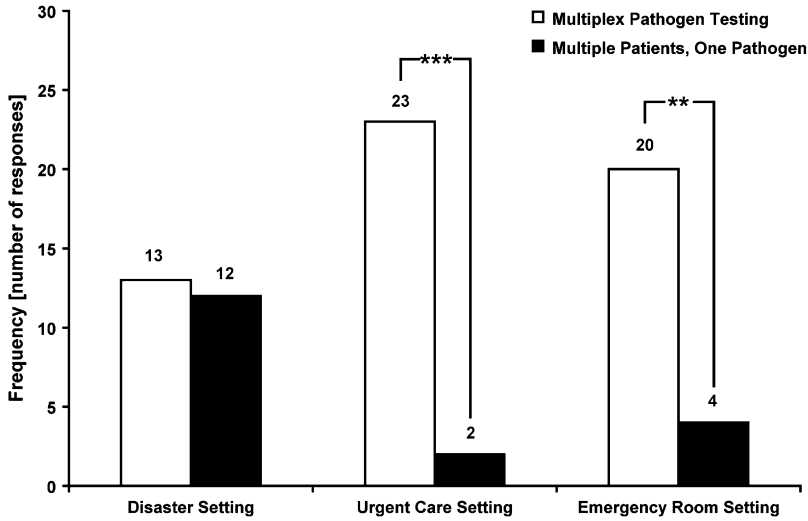

Fig. 4. Selection of testing method by survey respondents. In disaster settings, both approaches to pathogen detection may be useful. However, respondents preferred multiplex testing to testing multiple patients for 1 pathogen in urgent care (***P<.001) and emergency room (**P<.01) settings.

Pathogen Test Cluster Design

Table 2 shows the weighted scores of the top 10 pathogens for each of 4 scenario sections. For a general disaster test cluster, *Vibrio cholerae* had the highest weighted score (117); whereas for a blood donor screening test cluster, HIV 1 and 2 had the highest weighted score (224). Depending on the clinical scenario, the specific

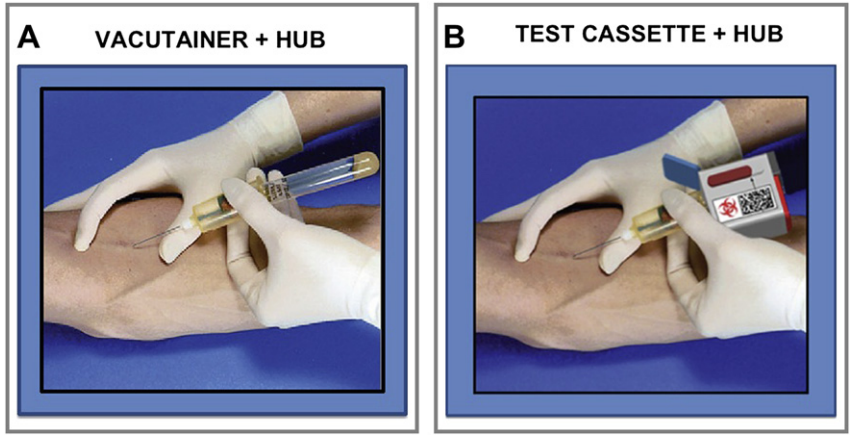

Fig. 5. Test cassettes versus vacutainers. Visual logistics were used to illustrate 2 sample collection methods for POCT instruments. (*A*) A vacutainer is used to collect the blood sample, allowing for multiple blood collection tubes to be drawn at one time. (*B*) Test cassette blood sample collection; blood is drawn directly into a disposable test cassette, processed, and a result given. Graphics updated for the survey currently in use.

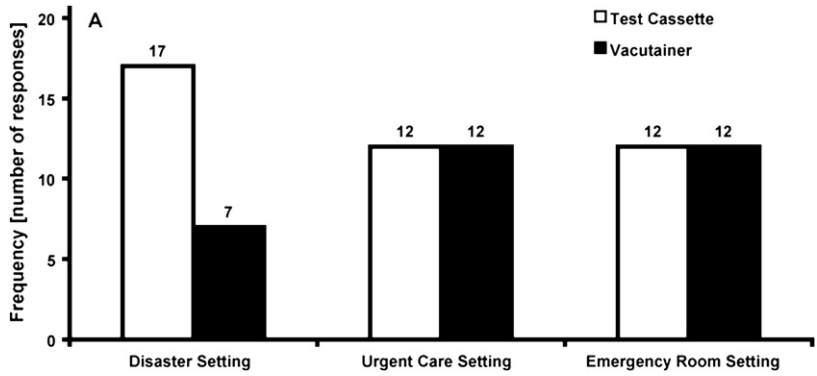

Fig. 6. Selection of sample collection method by survey respondents. Test cassettes and vacutainers were equivalent in all but the disaster setting, but this result was not statistically significant in this preliminary survey report.

Fig. 7. Biohazard disposal methods. Visual logistics were used to illustrate 2 biohazard disposal methods for POCT devices. (*A*) Biohazard waste in a reusable waste storage reservoir that must be emptied periodically, and a disposable test cassette for single use. (*B*) A device that stores all biohazard waste in a disposable test cassette that is discarded after a single use. Graphics updated for the survey currently in use.

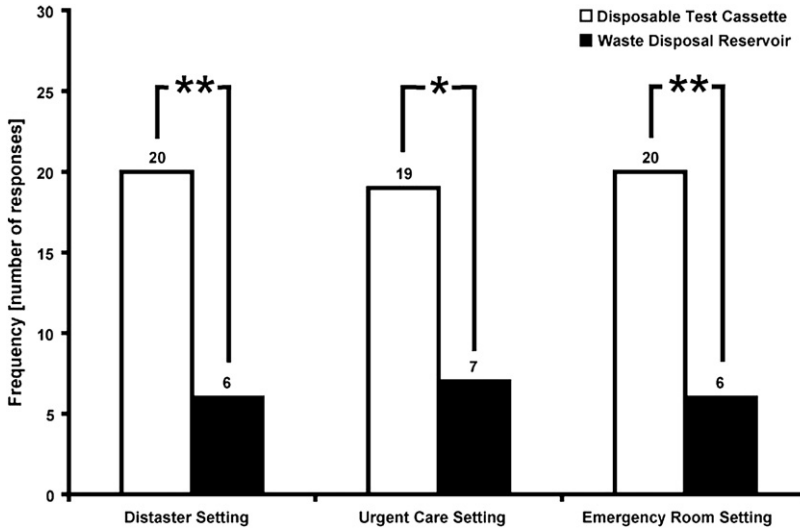

Fig. 8. Uniform selection of waste disposal by disposable test cassette by survey respondents. There is a statistically significant preference for disposable test cassettes across all 3 clinical settings ($P<.01$, 0.05, and 0.01). See **Fig. 6**. Disposable test cassettes have merit for sample collection and waste disposal in disaster settings. *$P<.05$; **$P<.01$.

pathogens a POC device would detect varies. For instance, methicillin-resistant *Staphylococcus aureus* (MRSA) had the highest weighted score at 147 for the bloodstream pathogen test cluster (see **Table 2**). However, in the pandemic test cluster, influenza A/B had the highest weighted score at 189, whereas MRSA was fifth with a weighted score of 112.5 (see **Table 2**).

PRELIMINARY RESULTS VERSUS CURRENT DISASTER PATHOGENS

Various POCT devices that test for a variety of analytes and pathogens are used during disaster and emergency situations, such as Hurricane Katrina. Emergency medical responders, disaster medical assistance teams (DMATs), international medical-surgical response teams (IMSuRTs), and other first responders deploy to disaster sites carrying POCT devices.[6] They use POCT devices to test, rapidly diagnose, and, as indicated, treat victims.[6] Depending on where responders are deployed, the pathogens they encounter will vary, possibly unpredictably and unexpectedly. **Table 3**[7–32] documents the variety of pathogens present in several modern disasters, such as flooding, hurricanes, and earthquakes. When comparing the top 10 pathogens identified by preliminary needs assessment survey results in various disaster scenarios (see **Table 2**) with pathogens found in major disasters, there was substantial overlap.

During Hurricane Katrina, for example, various pathogens were identified that also were selected and ranked by experts and surveyed as high priority for general disaster, blood donor screening, bloodstream pathogen, and pandemic test clusters. Specifically, in **Table 2** for the general disaster scenario and in **Table 3** for Hurricane Katrina, there is overlap for *Vibrio cholerae*, MRSA, and *Escherichia coli*. Thus, preliminary survey results demonstrate that survey experts identified pathogens encountered at disaster sites (see **Table 3**) as important for having POCT devices capable of detecting these organisms (see **Table 2**).

Table 2
Pathogen test clusters

	Weighted Score	Pathogen
A. General disaster test cluster (n = 18)	117	*Vibrio cholerae*
	108	*Escherichia coli*
	100	*Staphylococcus aureus*
	77	Yellow fever
	73	*Salmonella enterica*
	66	*Pseudomonas aeruginosa*
	62	*Plasmodium falciparum*
	54	*Enterobacter* species
	49	Dengue fever virus
	38	*Klebsiella* species
B. Blood donor screening test cluster (n = 23)	224	HIV 1 and 2
	190	Hepatitis B
	190	Hepatitis C
	125.5	Human T cell lymphotropic virus 1 and 2 (HTLV 1 and 2)
	109.5	West Nile virus
	109	*Cytomegalovirus*
	93	Dengue fever
	77	Parvovirus B19
	74	Epstein-Barr virus
	46	Chikungunya
C. Bloodstream pathogen test cluster (n = 20)	147	Methicillin-resistant *Staphylococcus aureus*
	118	*Escherichia coli*
	91	*Pseudomonas aeruginosa*
	90.5	*Streptococcus pneumoniae*
	90	*Enterobacter* species
	87.5	Methicillin-sensitive *Staphylococcus aureus*
	79	*Klebsiella* species
	61	*Enterococcus faecalis*
	50	*Streptococcus pyogenes*
	48	Coagulase-negative *Staphylococcus*
D. Pandemic test cluster (n = 22)	189	*Influenza* A/B
	121.5	*Parainfluenza* 1, 2, 3
	115.5	*Streptococcus pneumoniae*
	112.5	Respiratory syncytial virus
	112.5	Methicillin-resistant *Staphylococcus aureus*
	100	*Haemophilus influenza*
	90.5	*Mycobacterium tuberculosis*
	87	Adenovirus
	57	*Mycoplasm pneumoniae*
	51.5	Metapneumovirus

A similar finding was observed when comparing pathogens detected at the tsunami disaster site in Southeast Asia (see **Table 3**) versus the general disaster and bloodstream pathogen test clusters ranked highly in **Table 2**. Survey results identified several pathogens in the general disaster and bloodstream pathogen test clusters, such as *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, MRSA, and *Salmonella* species. These pathogens also were detected at tsunami disaster

sites in Southeast Asia. Having POCT devices capable of testing for these pathogens found at particular disaster sites can facilitate rapid diagnosis. Targeted therapy, in turn, can conserve drugs (eg, antimicrobials) that become depleted quickly during the initial crisis stages. These survey results should be used as a guide for development of new POCT devices capable of timely pathogen detection at disaster sites.

CURRENT USE OF POCT IN DISASTERS IN THE UNITED STATES

New POC devices must be capable of testing for a variety of pathogens present at a particular disaster site, and also properly integrated and used to decrease response

Table 3
Pathogens in disasters

Scenario	Location, Year	Pathogens Detected (Isolation Site)	Path of Infection
Drought	Florida, 5 epidemics since 1952[7,8]	Saint Louis encephalitis (blood)	Vector borne
		West Nile (blood)	Vector borne
	Indonesia, 1997[9]	Malaria (blood)	Vector borne
Earthquake	California, 1994[10]	*Coccidioides immitis* (skin)	Dust cloud
	China, 2008[11]	*Staphylococcus aureus* (pus and wound)	Wound
		Escherichia coli (pus and wound)	Wound
		Acinetobacter baumannii (pus and wound)	Wound
		Enterobacter cloacae (pus and wound)	Wound
		Pseudomonas aeruginosa (pus and wound)	Wound
	Turkey, 1999[12]	*Pseudomonas aeruginosa* (wound)	Wound
		Acinetobacter baumannii (wound)	Wound
		Methicillin-resistant *Staphylococcus aureus* (wound)	Wound
		Candida species (wound)	Wound
	Turkey, 1999[13]	*Acinetobacter* species (wound)	Wound
		Pseudomonas aeruginosa (wound, blood, urine)	Wound
		Methicillin-resistant *Staphylococcus aureus* (wound, blood, urine)	Wound
		Serratia marcescens (wound)	Wound
		Klebsiella pneumoniae (wound)	Wound
		Enterobacter species (wound)	Wound
		Candida albicans (wound)	Wound
Flooding	Bangladesh, 2004[14]	*Escherichia coli* (blood)	Water, food borne
		Vibrio cholerae (stool)	
	Global, 1980–2008[15]	Malaria (blood)	Vector borne
		Yellow fever (blood)	Vector borne
		West Nile (blood)	Vector borne
		Dengue (blood)	Vector borne
	Indonesia, 2004[16]	*Salmonella paratyphi* (blood)	Water, food borne
	Nonspecific[17,18]	*Streptococcus pneumoniae* (blood)	Inhalation

(*continued on next page*)

Table 3
(*continued*)

Scenario	Location, Year	Pathogens Detected (Isolation Site)	Path of Infection
Hurricanes/ tornadoes	Katrina, 2005[19–23]	Nontoxigenic *Vibrio cholerae* O1 (blood)	Food borne
		Vibrio cholerae non-O1 (blood)	Water borne
		Vibrio vulnificus (blood)	Wound, food borne
		Vibrio parahaemolyticus (blood)	Wound, food borne
		Methicillin-resistant *Staphylococcus aureus* (wound)	Wound
		Norovirus (stool)	Water borne
		Vibrio species (lake surface water)	Water borne
		Legionella species (lake surface water)	Water borne
		Cryptosporidium (interior canal water)	Water borne
		Giardia (interior canal water)	Water borne
		Escherichia coli (shoreline canal water)	Water borne
		Bifidobacterium (shoreline canal water)	Water borne
	Georgia, 2000[24]	*Serratia marcescens* (wound)	Wound
		Pseudomonas aeruginosa (wound)	Wound
		Enterococcus (wound)	Wound
Low-resource settings/ rural areas	Indonesia, 2001–2003[16]	*Salmonella enterica* (blood)	Food, water borne
		Salmonella paratyphi (blood)	Food, water borne
		Salmonella typhi (blood)	Food, water borne
	Philippines, 1994–1996[25]	*Streptococcus pneumoniae* (blood)	Inhalation
		Haemophilus influenzae (blood)	Inhalation
Tsunamis	Thailand, 2004[26–29]	*Aeromonas* (pus and wound)	Wound
		Escherichia coli (stool)	Water, food borne
		Klebsiella pneumoniae (pus and wound)	Wound
		Pseudomonas aeruginosa (pus and wound)	Wound
		Burkolderia pseudomallei (blood)	Soil, water borne
		Acinetobacter baumannii (blood)	Soil, water borne
		Stenotrophomonas (blood)	Soil, water borne
		Methicillin-resistant *Staphylococcus aureus* (wound)	Wound
		Staphylococcus aureus (wound)	Wound
		Candida species (blood)	Inhalation, wound
		Aspergillus species (blood)	Inhalation, wound
		Scedosporium species (blood)	Inhalation, wound
		Salmonella species (well water)	Water borne
		Clostridium species (wound)	Soil
		Aeromonas species (wound)	Water borne
World Trade Center disaster	New York, 2001[30–32]	Asthma and WTC cough (pathogens not named)	

US Army 14th Combat Support Hospital

Ortho-Diagnostics Blood Typing: ABO Blood Group

US Navy

Cardiac STATus: cTnI, CK-MB, Myoglobin

US Army 14th Combat Support Hospital

Rapidpoint Coag: PT, aPTT, Heparin Management Test

US Military, Local Surveyed Hospital

i-STAT: ACT, PT/INR, glucose, creatinine, cTnI, Na^{+}, K^{+}, Cl^{-}, Ca^{++}, pH, pCO_2, pO_2, SO_2, Hct, Hb, BUN, CK-MB, BNP

Hospitals, Evacuation Sites

Capillary Blood Glucose Meters

US Army, Navy, Marine Corps

Piccolo: Albumin, ALP, ALT, amylase, AST, BUN, creatinine, Ca, Cl , K , Na , Mg, LD, HDL, cholesterol, triglycerides, CK, glucose, TP, phosphorous, total bilirubin, direct bilirubin, TCO_2, GGT, uric acid

Donation to Local Red Cross

45,000 Blood Glucose Meters

US Air Force

Triage

Cardiac Panel: cTnI, CK-MB, myoglobin

Drugs of Abuse: Amphetamines, Methamphetamines

times and improve patient outcomes. During Hurricane Katrina, a variety of different locations and types of POCT were used featuring an array of POC tests covering chemistry, hematology, and other analyte categories.

Fig. 9 highlights POC instruments, including the various locations and POCT operators in Hurricane Katrina. Hospitals, evacuation sites, and local agencies were not prepared for the disaster and offered few POCT devices and tests. Hurricane Katrina is an example of a newdemic.[5] Supplies depleted quickly. Needs for chronic monitoring, such as outpatient glucose monitoring, were not met.

Fig. 10 displays Hurricane Katrina disaster sites, arrival, and responses of mostly military assets, and a suggested optimal POCT plan (upper right in figure) for timely disaster response. **Fig. 10** also documents that the disaster response time was slow. Current POCT disaster preparation does not meet adequate standards and must be improved for future preparedness. Proper strategic placement of POCT, possibly in alternate medical care facilities, is needed to facilitate rapid diagnosis and treatment.[33]

Pandemic influenza strains, such as novel H1N1, have the potential to significantly increase mortality and morbidity, as well as quickly deplete resources of current health care infrastructures. Thus, for example, rapidly diagnosing a particular influenza strain using POCT devices is advantageous. Furthermore, the World Health Organization (WHO) strongly recommends the use of POCT devices for quick influenza diagnosis. Commercially available POC tests for influenza A and B are listed in **Table 4**.[34–38] Several of the tests currently available are immunoassays that target nucleoprotein or matrix protein to identify influenza A or B types, but rarely offer further subtyping.

However, nucleic acid recognition (NAR) for detection of influenza A or B has shown promising benefits (see **Table 4**). These NAR devices exhibit greater sensitivity and can provide subtyping data. Once a subtype of influenza is positively identified, health care personnel and public health workers have the ability to start surveillance of new strains in a particular area. In addition, subtyping of influenza has the ability to guide antiviral treatment by identifying particular influenza strains that may be resistant or sensitive to antiviral treatment.

Fig. 9. Locations and types of POCT in Hurricane Katrina. Hospitals, evacuation sites, and local agencies were not prepared fully to assist quickly with POCT. They carried few POCT instruments. In contrast, US military ships and combat support units were equipped with POCT devices, including a variety of tests to facilitate rapid diagnosis and treatment. Donations of glucose meters proved valuable, but not fast enough or adequate for the large numbers of diabetic victims involved in the disaster. POC tests used during the disaster include: ALP, alkaline phosphatase; ALT, alanine aminotransferase; aPTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BNP, B-type natriuretic peptide; BUN, blood (serum) urea nitrogen; CK, creatine kinase; cTn, cardiac troponin; GGT, γ-glutamyltransferase; Hb, hemoglobin; Hct, hematocrit; HDL, high-density lipoprotein; INR, international normalized ratio; LD, lactate dehydrogenase; MB, MB fraction of CK; PT, prothrombin time; SO_2, oxygen saturation measured by pulse oximetry; TCO_2, total carbon dioxide content; TP, total protein. Instrument identifications: Bayer Acsensia, http://www.bayercarediabetes.com; Cardiac STATus, http://www.spectraldx.com; Cell-Dyn, http://www.abbottdiagnostics.com; i-STAT, http://www.i-stat.com; Ortho Diagnostics blood typing, http://www.orthoclinical.com; Piccolo, http://www.abaxis.com; Rapidpoint coag, http://www.bayer-poct.co.uk; and Triage, http://www.biosite.com. (*From* Kost GJ, Tran NK, Tuntideelert M, et al. Hurricane Katrina, the tsunami and point-of-care testing: optimizing rapid response diagnosis in disasters. Am J Clin Pathol 2006;126:513–20. © 2006 American Society for Clinical Pathology; *Courtesy of* Knowledge Optimization, Davis, CA; with permission.)

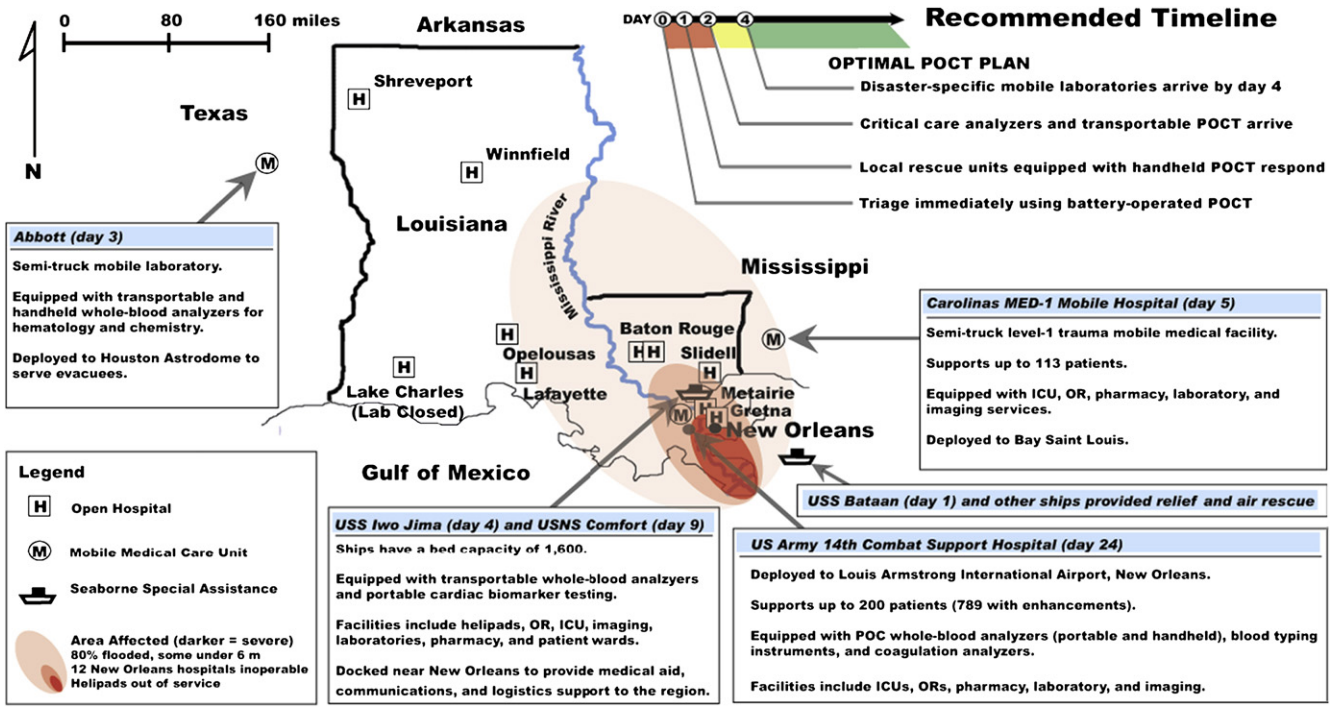

Fig. 10. Hurricane Katrina disaster areas, arrival times of military and civilian assets, sequential responses, and optimal POCT plan for disaster response. Mobile and military resources, including POCT, arrived on days 1, 3 to 5, 9, and 24. At the community and regional hospitals surveyed, beds averaged 154 (SD, 66; median, 173; range, 60–211) and 397 (SD, 249; median, 326; range, 174–763), respectively. Physicians ranged from 50 to 900. Displacement of 5944 physicians from the disaster area (223,000 km^2) hampered an already devastated health care infrastructure. The authors recommend (*upper right*) optimizing disaster response by prepositioning POCT for emergency use during the first 2 critical days. ICU, intensive care unit; OR, operating room. (*From* Kost GJ, Tran NK, Tuntideelert M, et al. Hurricane Katrina, the tsunami and point-of-care testing: optimizing rapid response diagnosis in disasters. Am J Clin Pathol 2006;126:513–20. © 2006 American Society for Clinical Pathology; *Courtesy of* Knowledge Optimization, Davis, CA; with permission.)

For instance, several H1N1 strains of influenza were resistant to oseltamivir in fall 2008; however, in spring 2009, the novel H1N1 influenza strain (''swine flu'') was sensitive to oseltamivir. Furthermore, in a recent study conducted by Dr Nishiura and colleagues,[39] the use of quarantine and rapid diagnostic testing to prevent or delay the spread of pandemic influenza across island nations was evaluated. In order for quarantine strategy to be effective in preventing or delaying the spread of pandemic influenza, rapid and reliable diagnostic testing must be used to positively identify index cases (first victims) with influenza.[39] Thus, the use of POCT to rapidly diagnose and subtype influenza has significant potential to refine pandemic disaster response and prevent newdemics from spreading outside the bounds of initial disaster or emergency locations.

This concept is important for disasters on the horizon, such as extensively drug-resistant malaria and tuberculosis. Globally, tuberculosis represents a major problem, especially in low-resource settings, such as impoverished African nations. Current tests available often fail to correctly identify tuberculosis, are not rapid, and cannot identify drug resistance.[40] Rapid-liquid culture shows promising results for tuberculosis detection by improving the sensitivity, speed, reliability, and multidrug-resistant tuberculosis detection.[40] Future thinking is required for developing POCT devices that are proven to simultaneously be rapid, simple, reliable, and cost-effective for diagnosing extensively drug-resistant tuberculosis.[40]

PREPAREDNESS: GAP ANALYSIS

POCT devices typically encounter harsh environmental conditions, temperature extremes, and high humidity in emergency and disaster care. Despite substantial improvements, gaps still exist between current POCT technologies and real-world needs. Inability of POCT instruments and reagents to withstand harsh conditions present at disaster and emergency sites compromises performance.[6] For example, glucose test strips and blood gas cartridges may not provide accurate measurements at disaster sites because thermal stresses adversely and inconsistently affect performance.[6] Because of these types of limitations and the obvious technical gaps in POC devices as we know them today, the United States and other countries are not prepared for disasters.

Box 1 highlights gaps between current POC devices and various problems with technologies currently available. Without durable and robust POCT equipment, diagnosis and treatment of victims at disaster sites becomes increasingly complicated and hindered. To effectively and efficiently diagnose, monitor, and treat patients, the current gaps in POCT technologies and devices must be closed. The POC Technologies Center (http://www.ucdmc.ucdavis.edu/pathology/poctcenter) is currently conducting static and dynamic environmental stress tests to understand the environmental limitations of POC devices and reagents in more detail.

Dynamic tests simulate realistic meteorologic conditions found in world regions with high risk for newdemics. US Food and Drug Administration (FDA)-approved product labelings typically state temperature limits, but current limits are inadequate for most disaster conditions. Also, a POCT method that may be proven to work in environmental extremes must also be validated for critically ill patient populations, which few currently do.

Problems with preanalytical processing present an additional major challenge for reliable POCT device performance. For example, in a recent study conducted by Dighe and colleagues,[41] unusually high false-positive potassium critical values led the laboratory to investigate the preanalytical processing after concluding that the

Table 4
POC influenza diagnostic tests

Instrument/Manufacturer				Performance Characteristics (%)			
Immunoassay Tests	**Type**	**Target**	**Time**	**Sensitivity**	**Specificity**	**PPV**	**NPV**
3M Rapid Detection Flu A+B[34,a] http://www.3M.com, St. Paul, MN	Chromatographic immunoassay	Influenza A Influenza B (nucleoprotein)	15 min	70 87	100 99	99 88	93 98
BD Directigen EZ Flu A+B,[a,b] http://www.bd.com, Franklin Lakes, NJ	Chromatographic immunoassay	Influenza A Influenza B	15 min	77–91 69–100	86–99 99–100	60–98 93–98	93–95 93–100
BD Directigen Flu A Kit[a,b] http://www.bd.com, Franklin Lakes, NJ	Immunoassay	Influenza A (nucleoprotein)	15 min	67–96	88–97	NA	NA
BD Directigen Flu A + BKit[35,b] http://www.bd.com, Franklin Lakes, NJ	Immunoassay	Influenza A Influenza B (nucleoprotein)	15 min	77–96 71–88	90–91 98–100	63–71 82–100	94–99 98–100
BinaxNOW Influenza A&B[36,a,b,c] http://www.binax.com, Scarborough, ME	Chromatographic immunoassay	Influenza A Influenza B (nucleoprotein)	15 min	77–83 50–69	96–99 100	88–97 82–100	95–96 99
ESPLINE Influenza A&B,[36] http://www.fujirebio.co.jp, Tokyo, Japan	Chromatographic immunoassay	Influenza A Influenza B (nucleoprotein)	15 min	67 30	100 100	100 100	89 96
fluID Rapid Influenza Test,[d] http://www.hxdiagnostics.com, Emeryville, CA	Lateral flow immunoassay	Influenza A Influenza B Subtype A/H1 Subtype A/H3	NA NA NA NA	NA NA NA NA	NA NA NA NA	NA NA NA NA	NA NA NA NA
Influ-A&B Respi-Strip, http://www.corisbio.com, Gembloux, Belgium	Chromatographic immunoassay	Influenza A Influenza B (nucleoprotein)	15 min	97 97	100 100	100 100	98 98

OSOM Influenza A & B Test,[a,c] http://www.genzymediagnostics.com, Framingham, MA	Chromatographic immunoassay	Influenza A Influenza B (nucleoprotein)	10 min	74 60	96 96	90 73	90 94
panfluID Rapid Influenza Test,[d] http://www.hxdiagnostics.com, Emeryville, CA	Lateral flow immunoassay	Avian Influenza	NA	NA	NA	NA	NA
QuickVue Influenza A+B Test,[c] http://www.quidel.com, San Diego, CA	Lateral flow immunoassay	Influenza A Influenza B (nucleoprotein)	10 min	77–94 62–82	89–99 97–99	62–91 80–90	95–99 94–97
QuickVue Influenza Test,[b,c] http://www.quidel.com, San Diego, CA	Lateral flow immunoassay	Influenza A+B No differentiation (nucleoprotein)	10 min	73–81	96–99	92–96	85–93
Rockeby Influenza A Test,[36,b] http://www.rockeby.com, Singapore	Immunoassay	Influenza A (nucleoprotein)	10 min	10	100	100	74
SAS FluAlert, http://www.sascientific.com, San Antonio, TX	Chromatographic immunoassay	Influenza A Influenza B (nucleoprotein)	15 min 15 min	76 91	98 99–100	93 100	91 99
Xpect Flu A&B Test Kit,[37] http://www.remelinc.com, Lenexa, KS	Chromatographic immunoassay	Influenza A Influenza B (nucleoprotein)	15 min	90–100 83–100	100 100	100 100	97–100 99–100
Nucleic Acid Tests							
Primer design, http://www.primerdesign.co.uk, Southampton, UK	Real time qPCR	H1N1 (swine flu)	<2 h	NA	NA	NA	NA
proFLU plus,[b] http://www.prodesse.com, Waukesha, WI	Real time RT-PCR	Influenza A (matrix) Influenza B (nonstructural NS1 & NS2)	3 h	100 98	93 99	71 80	100 100

(*continued on next page*)

Table 4
(*continued*)

Instrument/Manufacturer				Performance Characteristics (%)			
Nucleic Acid Tests	**Type**	**Target**	**Time**	**Sensitivity**	**Specificity**	**PPV**	**NPV**
xTAG Respiratory viral panel,[38,a] Luminex, http://www.luminexcorp.com, Austin, TX	Flow through microsphere array	Influenza A H1 H3 H5[b]	<4 h	98	100	99	100
		Influenza B SARS[b] Corona virus NL63[b] Corona virus 229E[b] Corona virus OC43[b] Corona virus HKU1[b] RSV, subtype A RSV, subtype B Parainfluenza 1 Parainfluenza 2 Parainfluenza 3 Parainfluenza 4[b] Metapneumovirus Rhinovirus/ Enterovirus Adenovirus		94	100	100	100

Data shown in the table are from product inserts unless otherwise noted.

Abbreviations: BD, Becton-Dickinson; NA, not available; NPV, negative predictive value; PPV, positive predictive value; qPCR, quantitative polymerase chain reaction; RSV, respiratory syncytial virus; RT, reverse transcriptase; SARS, severe acute respiratory syndrome.

[a] FDA-approved.
[b] CE-approved.
[c] CLIA-waived.
[d] In development.

Box 1
Strategic planning for POCT in disaster settings: gap analysis

Discovery

Novel new POC technologies for complex POCT in different global settings

Operational characteristics

Native sample testing from complex matrices with minimal prenalytical processing

Cassette-contained sample processing to avoid (pathogen) contamination

Back-end biohazard disposal in the same cassette, which can be disposed of intact

Internal, automated, and electronic quality control; external proficiency testing

Battery operation with flexible multiple power supplies

Format, licensing, and standardization

Durable handheld and portable formats for different emergency settings

Simple, fast, smart, and easy use codified to achieve CLIA-waived status

Competency demonstrated beforehand as part of preparedness in disaster plan

Standardized test results verified with "new math" (eg, LS MAD curves)

Environmental robustness

Sensors on board to document location and environmental conditions

Durable reagents and equipment not susceptible to environmental stresses

Environmental certification based on dynamic stress testing

Suitability for meteorologic profiles of disaster sites worldwide

Diagnostic performance

Quantitative POC tests capable of satisfactory accuracy, sensitivity, and specificity

Multiplex or multiple patient testing with needs-based test clusters

Index case (eg, H1N1) and risk (eg, HIV 1/2 in emergency blood donors) identification

Broad-spectrum pathogen surveillance for hazards (eg, World Trade Center [WTC] cough)

Mutations and detection of multiresistant strains (eg, tuberculosis) in challenging environments

Knowledge optimization

Full user awareness of performance characteristics based on field evaluations

Informatics compatibility, connectivity, and archival in small-world networks

Risk indexing of diagnostic targets, wireless results reporting, and outcomes monitoring

Cost-effectiveness for implementation in low-resource settings

instrument was not the source of the errors. Laboratory personnel noted that when false-positive potassium critical values were seen, a hemoglobin A1C test was also ordered.

On investigation of the sample processing, Dighe and colleagues[41] found that both tubes were being packaged with ice and transported to the testing facility. Icing blood tubes has been shown to lyse red blood cells and falsely elevate potassium levels.[41] Laboratory technologists subsequently altered the transport requirement for hemoglobin A1C and observed a substantial decrease in potassium false-positive values in ensuing months.[41] When POCT devices are reliable, these types of preanalytical

problems can be minimized or eliminated. To ensure best patient care, preanalytical processing methods used on field-worthy POCT devices should be self-contained and disposable, but free from confounding preanalytical errors.

Box 1 lists several other gaps that need to be addressed. For example, the introduction of locally smooth median absolute difference (LS MAD) curves as a mathematical statistical method to visually analyze the accuracy of POCT blood glucose meters shows that performance in hypoglycemic and hyperglycemic ranges of most blood glucose meters in current use exceeds error tolerance limits for adult critically ill patient populations.[42,43] POCT technologies intended for emergency and disaster settings and critically ill patient populations can be improved, standardized, and verified with this new math (see **Box 1**) to enable better performance and patient outcomes.

The search and discovery of novel new POC technologies should be actively pursued by researchers. Devices are needed in various global environments across the world. In these different conditions, POCT will encounter new challenges to be overcome. As noted above, POCT instruments must be environmentally robust and capable of withstanding dynamic stresses (see **Box 1**). In addition, POCT devices should be capable of diagnosing multiple pathogens with adequate clinical sensitivity and specificity (see **Box 1**), ideally including extensively drug-resistant tuberculosis, malaria, and influenza. New and novel POCT devices will be created in the future featuring improved operational characteristics, environmental robustness, diagnostic performance, and knowledge optimization that enable disaster responders to rapidly diagnose and treat victims and fill current technology gaps.

INTEGRATION STRATEGY: POCT AND SMALL-WORLD NETWORKS

Strategic placement of POCT devices within small-world networks (SWN) will effectively facilitate rapid evidence-based medical decisions.[5] SWNs enable information to be transmitted quickly from site to site and facilitate quick triage of patients to appropriate points of evaluation.[5] SWNs can help manage POCT operations to improve overall efficiency and cost-effectiveness by integrating health care delivery components, including home monitoring, primary care unit testing, mobile medical unit, alternate medical care site, triage, emergency room, and local hospital resources.[5]

Thus, when a disaster situation arises, such as Hurricane Katrina, the tsunami in Southeast Asia, or the novel H1N1 (swine flu) pandemic, SWNs can effectively allocate POCT resources to allow for rapid and cost-effective patient care or isolation of index cases, as needed, that is also efficient within the context of regional resources. This strategic integration of POCT into regional aspects of disaster and emergency response will ensure that patient care will be rapid and effective.

SUMMARY

Use of POCT in disaster and emergency situations will efficiently facilitate rapid evidence-based diagnosis at the site of patient care. A variety of tests are currently available for POCT in hospitals, but the spectrum of POC tests for emergency and disaster care must be broadened.

The development of pathogen test clusters, based on needs assessment survey results, must be incorporated into new POCT device designs. Besides developing innovative POCT devices, current gaps in POCT technology and availability must be filled to ensure optimal patient care wherever the patient might be.

Integration and global use of POCT in emergencies will help prevent newdemics from accelerating as seen during Hurricane Katrina and the current influenza pandemic (novel H1N1), while simultaneously improving immediate patient care.

When a disaster or emergency strikes and as POCT use becomes standard for SWN preparedness, emergency medical responders, alternate medical facilities, and hospitals will be ready to deal effectively with the crises and avoid the pitfalls of the past, when adequate POCT was not available or not used efficiently.

However, given current state-of-the-art POCT, the United States and other countries are not prepared. Having environmentally robust and rapid POCT devices that are deployable to disaster and emergency sites, and also validated for the care of the critically ill, will bring care to the point of need where physicians and nurses can make fast, evidence-based decisions for triage and treatment.

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REFERENCES

1. Kost GJ, Tran NK, Tuntideelert M, et al. Katrina, the tsunami and point-of-care testing: optimizing rapid response diagnosis in disasters. Am J Clin Pathol 2006;126:513–20.
2. Diiulio R. A New Orleans hospital weathers the storm. MLO Med Lab Obs 2007; 39:18–20.
3. Katrina's death: who's to blame? The Economist 2007;13:35.
4. Kost GJ, Minear M, Siegel PM, et al. Knowledge, education, mind connectivity: using telemedicine to achieve a global vision for point-of-care testing. Point Care 2008;7:69–71.
5. Kost GJ. Newdemics, public health, small-world networks, and point-of-care testing. Point Care 2006;5:138–44.
6. Louie RF, Sumner SL, Belcher S, et al. Thermal stress and point-of-care testing performance: suitability of glucose test strips and blood gas cartridges for disaster response. Disaster Med Public Health Prep 2009;3:13–7.
7. Shaman J, Day JF, Stieglitz M. Drought-induced amplification of Saint Louis encephalitis virus, Florida. Emerg Infect Dis 2002;8:575–80.
8. Shaman J, Day JK, Stieglitz M. Drought-induced amplification and epidemic transmission of West Nile virus in southern Florida. J Med Entomol 2005;42: 134–41.
9. Bangs MJ, Subianto DB. El Nino and associated outbreaks of severe malaria in highland populations in Irian Jaya, Indonesia: a review and epidemiological perspective. Southeast Asian J Trop Med Public Health 1999;30:608–19.
10. Schneider E, Hajjeh RA, Spiegel RA, et al. A coccidioidomycosis outbreak following the Northridge, Calif, Earthquake. JAMA 1997;277:904–8.
11. Tao C, Kang M, Chen Z, et al. Microbiologic study of the pathogens isolated from wound culture among Wengchuan earthquake survivors. Diagn Microbiol Infect Dis 2009;63:268–70.
12. Bulut M, Fedakar R, Akkose S, et al. Medical experience of university hospital in Turkey after the 1999 Marmara earthquake. Emerg Med J 2005;22:494–8.
13. Kazancioglu R, Cagatay A, Colangu S, et al. The characteristics of infections in crush syndrome. Clin Microbiol Infect 2002;8:202–6.

14. Qadri F, Khan A, Faruque A, et al. Enterotoxigenic *Escherichia coli* and *Vibrio cholerae* diarrhea, Bangladesh, 2004. Emerg Infect Dis 2005;11:1104–7.
15. World Health Organization. Flooding and communicable diseases fact sheet: risk assessment and preventative measures. Available at: http://www.who.int/hac/techguidance/ems/flood_cds/en/print.html. Accessed June 24, 2009.
16. Vollaard A, Ali S, Asten H, et al. Risk factors for typhoid and paratyphoid fever in Jakarta, Indonesia. JAMA 2004;209:2607–15.
17. Vernon D, Banner W, Cantwell P, et al. *Streptococcus pneumoniae* bacteremia associated with near-drowning. Crit Care Med 1990;18:1175–6.
18. Ender P, Dolan M. Pneumonia associated with near-drowning. Clin Infect Dis 1997;25:896–907.
19. Center for Disease Control and Prevention. Update on CDC's response to Hurricane Katrina – September 19th, 2005. Available at: http://www.cdc.gov/od/Katrina/09-19-05.htm. Accessed June 24, 2009.
20. Centers for Disease Control and Prevention (CDC). *Vibrio* illnesses after Hurricane Katrina – multiple states, August – September 2005. Morb Mortal Wkly Rep 2005;54:928–31.
21. Centers for Disease Control and Prevention (CDC). Infectious disease and dermatologic conditions in evacuees and rescue workers after Hurricane Katrina—multiple states, August-September, 2005. Morb Mortal Wkly Rep 2005;54:961–4.
22. MMWR. Norovirus outbreak among evacuees from Hurricane Katrina – Houston, TX, September 2005. Morb Mortal Wkly Rep 2005;54:1016–8.
23. Sinigalliano C, Gidley M, Shibata T, et al. Impacts of Hurricanes Katrina and Rita on the microbial landscape of the New Orleans area. Proc Natl Acad Sci U S A 2007;104:9029–34.
24. Millie M, Senkowski C, Stuart L, et al. Tornado disaster in rural Georgia: triage response, injury patterns, lessons learned. Am Surg 2000;66:223–8.
25. Lupisan S, Herva E, Sombrero L, et al. Invasive bacterial infections of children in a rural province in the central Philippines. Am J Trop Med Hyg 2000;62:341–6.
26. Hiransuthikul N, Tantisiriwat W, Lertutsahakul K, et al. Skin and soft tissue infections among tsunami survivors in Southern Thailand. Clin Infect Dis 2005;41:e93–6.
27. Uckay I, Sax H, Harbarth S, et al. Multi-resistant infections in repatriated patients after natural disasters: lessons learned from the 2004 tsunami for hospital infection control. J Hosp Infect 2008;68:1–8.
28. Rajendran P, Murugan S, Raju S, et al. Bacteriological analysis of water samples from tsunami hit coastal areas of Kanyakumari district, Tamil Nadu. Indian J Med Microbiol 2006;24:114–6.
29. Ivers LC, Ryan ET. Infectious diseases of severe weather-related and flood-related natural disasters. Curr Opin Infect Dis 2006;19:408–14.
30. Thomas PA, Brackbill R, Thalji L, et al. Respiratory and other health effects reported in children exposed to the World Trade Center disaster of 11 September 2001. Environ Health Perspect 2008;116:1383–90.
31. de la Hoz RE, Christie J, Teamer JA, et al. Reflux symptoms and disorders and pulmonary disease in former World Trade Center rescue and recovery workers and volunteers. J Occup Environ Med 2008;50:1351–4.
32. Farfel M, DiGrande L, Brackbill R, et al. An overview of 9/11 experiences and respiratory and mental health conditions among World Trade Center health registry enrollees. J Urban Health 2008;85:880–909.

33. Lam C, Waldhorn R, Toner E, et al. The prospect of using alternative medical care facilities in an influenza pandemic. Biosecur Bioterror 2006;4:384–90.
34. Ginocchio CC, Lotlikar M, Falk L, et al. Clinical performance of the 3M Rapid Detection Flu A+B Test compared to R-mix culture, DFA, and BinaxNow Influenza A+B Test. J Clin Virol 2009;45:146–9.
35. Grondhal B, Puppe W, Weigl J, et al. Comparison of the BD Directigin Flu A+B kit and the Abbott TestPack RSV with a multiplex RT-PCR ELISA for rapid detection of influenza viruses and respiratory synctial virus. Clin Microbiol Infect 2005;11: 848–50.
36. Hurt AC, Alexander R, Hibbert J, et al. Performance of six influenza rapid tests in detecting human influenza in clinical specimens. J Clin Virol 2007;39:132–5.
37. Cazacu AC, Demmler GJ, Neuman MA, et al. Comparison of a new lateral-flow chromatographic membrane immunoassay to viral culture for rapid detection and differentiation of influenza A and B viruses in respiratory specimens. J Clin Microbiol 2004;42:3661–4.
38. Pabbaraju K, Tokaryk KL, Wong S, et al. Comparison of the Luminex xTAG respiratory viral panel with in-house nucleic acid amplification tests for diagnosis of respiratory virus infections. J Clin Microbiol 2008;46:3056–62.
39. Nishiura H, Wilson N, Baker MG. Quarantine for pandemic influenza control at the borders of small island nations. BMC Infect Dis 2009;9:27 [Published online March 11, 2009]. Doi:10.1186/1471-2334-9-27.
40. Grandjean L, Moore DA. Tuberculosis in the developing world: recent advances in diagnosis with special consideration of extensively drug-resistant tuberculosis. Curr Opin Infect Dis 2008;21:454–61.
41. Dighe AS, Jones JB, Parham S, et al. Survey of critical value reporting and reduction of false-positive critical value results. Arch Pathol Lab Med 2008;132: 1666–71.
42. Kost GJ, Tran NK, Sifontes JR, et al. Locally smoothed median absolute difference curves and the first global performance cooperative. Point Care 2009;8: 45–52.
43. Kost GJ, Tran NK, Louie RF, et al. Assessing the performance of handheld glucose testing for critical care. Diabetes Technol Ther 2008;10:445–51.