Point of Care Testing: Taking Us Into the Future

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Ohio POC Webinar
Point-of-Care Testing (POCT): Definition

“Laboratory testing performed outside of the clinical laboratory”

OR

“Clinical laboratory testing conducted close to the site of patient care”

OR.....
“It is not the strongest of the species that survives, nor the most intelligent, but the one most responsive to change”

Charles Darwin
Point-of-Care Testing:
Is it all about change???
Drivers for Change

- Internal
  - Staffing shortages
  - Budget cuts
  - Automation
  - Healthcare networks/systems
  - Demand for “esoteric” tests
  - Revenue generation
  - Error reduction
Drivers for Change

- External
  - Reimbursement
  - Technology
  - Patient “self-empowerment”
  - Personalized Medicine
  - Practice guidelines
  - Accrediting agencies/regulations
  - Competition
  - Quality improvement
“Well, let’s stop arguing—we’re both here now.”

Victoria Roberts
Clinical Examples

- Pulmonary Embolism/Deep Vein Thrombosis (PE/DVT) - d-dimer
- Trauma – hemoglobin (hgb)
- Differential Dx vaginal bldg – hCG, hgb
- Diabetic Ketoacidosis (DKA) – glucose, pH, potassium
- Acute renal failure – BUN, creatinine
- AMI vs CHD – troponin, BNP
Clinical Use of POCT

- Risk screening:
  - Hs-C-Reactive Protein (HsCRP), Homocysteine, MRSA

- Diagnosis:
  - CRP, HbA1c, Ferritin/Hb, TSH, BNP, Troponin, Myoglobin, CK-MB, D-dimer, Flu, Hospital/Healthcare acquired/associated infections (HAI), glucose, blood gases, creatinine

- Treatment/Monitoring:
  - PT INR, HbA1c, CRP, Ferritin/Hgb, TSH/TT4, urine albumin, glucose
What’s “New” in POCT Literature?

- Review of literature 2008-2009
- Top 5 topics published most extensively:
  - Diabetes (Glucose)
  - Acute Coronary Syndrome (Troponin)
  - Coagulation (INR)
  - Acquired Immunodeficiency Syndrome (HIV)
  - Hemostasis (Platelet Function)

Melanson SEF, Point of Care 2008,8,4;166-170
NEW POC Tests with Anticipated High Growth Rates

- Influenza virus types A and B
- HIV, 1 and 2
- Brain Natriuretic Peptide (BNP)
- Estimated glomerular filtration rate (eGFR)
- Ketones and B-hydroxybutyrate
- High-sensitivity troponin
- Methicillin-resistant *Staphylococcus aureus* (MRSA)

Dooley JF, Point of Care, 2009, 8, 4; 154-156
Future Molecular-Based Rapid POC Tests

- Biodefense for biological threat agents
- Infectious diseases (e.g. Clostridium difficile, pandemic influenza, severe acute respiratory syndrome)
- VanA- and VanB-resistant genes of vancomycin-resistant enterococci
- Genetic polymorphisms in clotting factors II and V
- Mycobacterium tuberculosis and associated rifampin resistance from sputum

Dooley JF, Point of Care, 2009, 8, 4; 154-156
POC Pathogen Detection and Molecular assays

- Nucleic acid detection provides faster TAT and higher sensitivity vs blood culture
- Higher FP rates in blood cultures with antibiotics
- Nucleic acid tests detect pathogens irrespective of antimicrobial therapy
- POC nucleic acid tests could “revolutionize” pathogen detection in critically ill patients (e.g. septicemia) by initiating early targeted antimicrobial therapy

Tran NK et al. 2008 Vol 7, 3; 107-109
Factors that affect Laboratory Testing and POC - Current and Future

- Numbers - current state
- Market Profile
- Staffing
- Consumer “self empowerment”
- Quality
- Connectivity
- Economy
- Technology
Lab Medicine: The Numbers

- Approximately 6.8 billion lab tests performed annually in U.S.
- Lab services account for 2.3% health care costs and 2% of Medicare costs
- Revenues in 2007 projected at $52B
- Hospital-based labs generate 54% total testing revenue, projected $28.4B in 2007
- >4,000 lab tests available for clinical use
- 1,162 reimbursed by Medicare; approx 500 performed regularly
- 1,430 diseases detectable by genetic testing; 287 research only
- No. CLIA-certified labs >200,000 in 2007; POLs 54% with 80% only performing waived and PPM

CLN, August 2008, National Report (CDC)
Laboratory Testing—Where is it Performed Now?

- Centralized
  - Hospital laboratory, commercial laboratory (national, regional, independent), “core” laboratory within healthcare system, POL for group of physicians, referral labs for esoteric tests

- Decentralized
  - Point-of-Care testing (POCT), physician’s office, patient (self-testing)
Laboratory Testing – Where Will it be Performed – Future?

- Emphasis on POC?
- High volume, “non-POCT” (incl. STATs) only to central lab?
- Self-testing (patient-performed)?
- Emphasis on Physician’s office testing?
- Pharmacy (incl. pharmacies in grocery stores)?
- Other sites?
Market Profile

- Laboratory testing revenues were a projected $52B in revenue
- Clinical pathology is 66% of all lab tests and $32B in revenue
- Anatomic pathology and cytology are 23% of laboratory tests and $11B in revenue
- Molecular and esoteric testing are 8% of lab tests and $4B in revenue
- Drugs of abuse testing is 3% of lab tests and $1.5B in revenue

National Report (CDC)
## 2007 IVD Market, By Segment

<table>
<thead>
<tr>
<th>Segment</th>
<th>Market Size ($ million)</th>
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<tbody>
<tr>
<td>Central Laboratory</td>
<td>24,188</td>
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<tr>
<td>Blood Glucose</td>
<td>8,274</td>
</tr>
<tr>
<td>POC/POL</td>
<td>2,648</td>
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<tr>
<td>Molecular Diagnostics</td>
<td>2,559</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>37,669</strong></td>
</tr>
</tbody>
</table>

- Central Laboratory: 64%
- Blood Glucose: 22%
- POC/POL: 7%
- Molecular Diagnostics: 7%
Market Profile

- Consumer directed testing key area for market growth
- 2004 10-15% hospital and commercial labs offered DAT
- *No. of Over-the-Counter Tests (OTC) growing; >800 OTCs approved by FDA*
- Laboratories should assume greater role and promote informed self care by consumers
- Publicly available information about economic status and quality of lab medicine is limited, leaving gaps in reliable market revenues, spending, test volume and testing trends

National Report (CDC)
POCT IVD Market

2008:

• IVD Market $42.1B (US)

• POCT $13.1B with whole blood glucose (WBG) $8.7B (31%) of total

• Removing WBG, total IVD market drops to $33.4B with POCT $4.4B (13%)

Stephans EJ et al, Point of Care 2009, Vol 8, 4; 141-144
POCT IVD Market

2009:

- Mixed picture
- Impact worse for POC market than central lab
- POC showed 8-10% growth, but slower than previous years
- Exception-growth in decentralized coagulation testing (20%) especially in Europe

Stephans EJ et al, Point of Care 2009, Vol 8, 4; 141-144
POC Diagnostic Testing Markets

- Distinct from home testing, is composed of 2 segments: hospital testing and decentralized testing
- Strong growth in rapid tests in Europe compared with flat growth of central lab tests
- Opposite true for Japan; behind US and Europe in Professional POC market

Dooley JF, Point of Care 2009 8,4; 154-156
Laboratories - Come in Many “shapes and sizes”

- Hospital-based
- Outreach
- Physician Office Labs
- Independent
- Public Health
- Skilled Nursing Facility
- Home Health Agency
- Community Clinic
- ESRD Dialysis
- Ambulatory Surgical Centers
- Pharmacy
- Ambulance

- Ancillary Test Site in Health Facility
- School/Student Health
- Hospice
- Industrial mobile Laboratory
- HMO
- Health Fair
- Blood Banks
- Insurance
- Tissue Bank/Repositories
- Rural Health Clinics

CMS Data, 2006
POCT Manufacturers

- 4medica
- Accumetrics
- Aerscher Diagnostics
- Alfa Scientific
- Avox Systems
- Beckman Coulter
- Biosite
- Cholestech
- Dade Behring
- First Medical
- Helena Laboratories
- Hemocue
- Hemosense
- International Technidyne Corp
- Instrument Laboratories
- Litmus Concepts
- LXD Corporation
- Medical Analysis Systems
- Nanogen
- Nova Biomedical
- Ortho Clinical Diagnostics
- Polymedco
- Quidel
- Radiometer
- Roche
- ThermoBioStar

From Jarnot J, Presentation Boston, MA May 2007
Number of Certified Medical Technologist Graduates: 1980-2006

Source: American Society for Clinical Pathology
Medical Technologist Programs

Source: National Accrediting Agency for Clinical Laboratory Sciences
Direct Access Testing (DAT)
“How's the self-diagnosis coming?”
DAT – What is it?

- Also known as “direct-to-consumer” or “patient-authorized” testing
- Defined as consumer (as opposed to physician) initiated testing
- Consumer self-orders, pays for out-of-pocket, and is responsible for interpreting and follow up of results
DAT – Where is it done?

- Not all states permit DAT
  - 32 states allow DAT
  - 18 states prohibit DAT

- Some commercial labs offer DAT
  - Use independent physicians to review requests, authorize release of results, contact consumers/clients with critical values encouraging them to seek physician’s care
CLIA and DAT

- CLIA regulations and standards do not differentiate between facilities performing DAT and facilities performing provider ordered tests.
- CLIA authorizes regulation of laboratories that conduct testing, not the individuals who order tests or receive test results.
- Therefore, CLIA does not regulate DAT.

Website: www.cdc/cliac.gov
DAT

- DAT growing with trends in direct marketing of lab tests to consumers (web), consumer privacy concerns, convenience, cost savings, and consumer self-empowerment.

- Physician concerns include: consumers want “free” telephone consults, consumers not capable of interpreting results, physicians bypassed, consequences of false positive and false negative results.

- Important to recognize potential impact of DAT when strategic planning and growth is undertaken.
Quality
Equivalent QC or “EQC” developed in IG as a voluntary alternative QC-2004

- Option employed depends on the extent of the total testing process monitored by internal QC.
- Minimizes amount of external QC required.
- Helps save costs for laboratories.
- Technology is more robust.
- Director responsible for choice of QC plan.
- Remaining quality systems must be acceptable.

Liquid vs. Electronic QC

**LIQUID QC**
- Evaluates the instrument
- Evaluates the reagents
- Evaluates the operator
- Evaluates the testing process

**ELECTRONIC QC**
- Evaluates the instrument only
Equivalent Quality Control Follow Up

- Concerns expressed by industry, laboratories, experts, etc.
- Many laboratories adopted EQC successfully and have no quality issues.
- CMS reached out to CLSI to facilitate development of an objective consensus QC guideline.

QC for the Future

- CLSI convened the well-attended “QC for the Future” meeting in 2005.
- Sponsored by accrediting organizations, industry, professional organizations, and government agencies

Outcome:
- Stakeholder concern that manufacturers do not provide laboratories sufficient information
- “One-size-fits-all” QC does not work with new technology
CLSI meeting directed the development of a new evaluation protocol entitled *EP23—Laboratory Quality Control Based on Risk Management*.

- Chaired by James Nichols PhD, DABCC, FACB—Baystate Medical Center
- Assembled expert group
- Published October 2011
The “Right QC”

- CMS will incorporate key EP23 concepts into CLIA IG as an alternative QC policy.
- Once effective, the current EQC policy will no longer be available as a choice.
- Basic existing CLIA QC, quality system concepts, and requirements will not change.
The “Right QC”

- Permits laboratories to develop a custom alternative QC Plan (QCP) using many of their existing quality practices/information
- Applies to CMS-certified, nonwaived laboratories and is voluntary
- Default: 2 levels of external QC/day of testing
Potential Errors in POCT

- Scope and diversity of testing sites makes the potential for error in POCT high
- Errors in laboratory testing usually classified into the following:
  - Pre-analytic
  - Analytic
  - Post-analytic
Medical/Laboratory Errors

- Attributed to:
  - Pre-Post-analytic errors
  - Ineffective communication
  - Action taken by others
  - Poorly designed processes outside of laboratory
  - Misidentification of patients
  - Mistakes in written and oral communication
  - Disjointed policies and procedures
  - Insufficient knowledge of testing process
  - Limited testing oversight
  - Lack of metrics and analysis to identify problems and make improvements

Ehrmeyer S, Hausman P, Lebo R, Point of Care, vol 4, 2005
Know the limitations of the instrument/method
Blood Glucose Meters

POCT can differ from lab because:

- Glycolysis during transport
- Difference between whole blood and plasma (11%)
- Calibration difference between methods
- Sample matrix effects
- POCT less precise
- Preanalytical issues
- Staff compliance/competency
Differences in POCT Glucose CAP Survey Results

- There can be significant differences between POCT glucose meters for the same CAP survey specimens.

- Evaluation criteria used for acceptability is:
  - ± 20%
  - ± 12 mg/dL, or
  - ± 3 SD
  Whichever is greater.
# CAP Survey Results, WB2-A 2012, Specimen WB-02

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<tr>
<th>Method</th>
<th>No. Labs</th>
<th>Mean mg/dL</th>
<th>Low mg/dL</th>
<th>High mg/dL</th>
<th>%CV</th>
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<tbody>
<tr>
<td>Abbott Prcsn PCx/Xceed</td>
<td>5069</td>
<td>75.10</td>
<td>66.99</td>
<td>83.12</td>
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<td>Nova Statstrip</td>
<td>1731</td>
<td>85.67</td>
<td>76.21</td>
<td>95.13</td>
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<td>Roche Comf Curve</td>
<td>15343</td>
<td>53.71</td>
<td>47.59</td>
<td>59.83</td>
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<tr>
<td>Method</td>
<td>No. Labs</td>
<td>Mean</td>
<td>Low</td>
<td>High</td>
<td>%CV</td>
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<td>Abbott Prcsn PCX/Xceed</td>
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<td>451.36</td>
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<td>Nova Statstrip</td>
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<td>353.90</td>
<td>314.99</td>
<td>392.82</td>
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<tr>
<td>Roche Comf Curve</td>
<td>15255</td>
<td>375.49</td>
<td>347.49</td>
<td>403.49</td>
<td>3.7</td>
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Challenges

● For manufacturers:
  ■ improve quality
  ■ consistency of test strip/cartridge manufacturing
  ■ redesign strips/cartridges to minimize interferences and extend shelf life
Challenges

- For Laboratorians:
  - Educate clinicians who use POCT about
    - Limitations of devices/methods
    - Interpretation
    - Reliability of POCT results
Clinical Practice Guidelines
The National Academy of Clinical Biochemistry (NACB) has published Laboratory Medicine Practice Guidelines (LMPG) that are used as practice guidelines in clinical and laboratory medicine.

- “Evidence-Based Practice for Point-of-Care Testing”
- Divided into disease- and test-specific focus areas
Published NACB LMPGs

- Nutritional Status 1994
- Thyroid Disease (1st edition) 1996
- Newborn Infant 1998
- Therapeutic Drug Monitoring 1999
- Cardiac Markers 1999
- Hepatic Injury 2000
- Diabetes Mellitus 2002
- Thyroid Disease (2nd edition) 2002
- Tumor Markers in the Clinic 2003
- Emergency Toxicology 2005
- Maternal-fetal Risk Assessment 2006
- Biomarkers of ACS 2007
- Point of Care Testing 2007
- Tumor Marker Quality Requirements 2008
- Expanded Newborn Screening 2008
EXAMPLES of POCT
Recommendations

- Diabetes self-management
- Infectious Disease
- Colorectal Cancer (CRC) Screening: Fecal Occult Blood Tests (FOBT)
- pH Testing for Chemical Burns and Nasogastric Tube Placement
- Renal Function
- Reproductive Testing
Examples of CLSI Point-of-Care Testing Guidelines

- POCT04-A2: Point-of-Care *In Vitro* Diagnostic Testing; 2nd Edition
- POCT02-A: Implementation Guide of POCT01 for Health Care Providers
- AST04-A2: Glucose Monitoring in Settings Without Laboratory Support; 2nd Edition
- C30-A2: Point-of-Care Blood Glucose Testing in Acute and Chronic Care Facilities; 2nd Edition
- H49-A: Point-of-Care Monitoring of Anticoagulation Therapy
- HS02-A2: Provider-Performed Microscopy Testing
Examples of CLSI Point-of-Care Testing Guidelines (Con’t)

- POCT09-P: Selection Criteria for Point-of-Care Testing Devices
- POCT06-P: Guidelines for Comparison of Glucose Results Measured by Methodologies That Use Different Sample Types
- POCT07-P: Quality Management: Approaches to Reducing Errors at the Point of Care
Technology
NIBIB Recommendations 2005

• Support development of integrated sensor and lab-on-a-chip devices for point-of-care testing

  ■ Direction: Address issues assoc. with component integration and push use of complex biological. Samples for device testing/practical applications

NIBIB-Nat’l Inst of Biomedical Imaging and Bioengineering; part of NIH
NIBIB Recommendations 2005

- Strengthen the enabling technology development program area, with an emphasis on high-risk/high impact research areas such as nanotechnology
  - Direction: Need for improvement in sensitivity, specificity, multiplexing, and throughput in sensor and lab-on-a-chip devices. Encourage development of novel technologies that overcome current limitations and enable new applications.
## NIBIB Lab-on-a-Chip Study 2005

<table>
<thead>
<tr>
<th>Scientific Subcategory</th>
<th># Active Grants</th>
<th>Total Costs (million $)</th>
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<tbody>
<tr>
<td>Enabling Technologies</td>
<td>39</td>
<td>9.5</td>
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<tr>
<td>Clin Lab Dx</td>
<td>18</td>
<td>7</td>
</tr>
<tr>
<td>Noninvasive Monitoring</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Biodefense</td>
<td>8</td>
<td>1.5</td>
</tr>
<tr>
<td>Drug Discovery</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Basic Biology</td>
<td>4</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>79</strong></td>
<td><strong>$22 M</strong></td>
</tr>
</tbody>
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Technologies in Development

- Multiplex/lab on a chip assays (Claros Diagnostics) Examples: HIV, Syphilis, Hep C
- Lateral flow with fluorescence detection (Forecast Technology)
- Multiplex Enzyme Assay/Digital Microfluidics Examples: Newborn Screening for Pompe’s, Fabry, Hurler’s diseases
- Multiplex/Magnetic Biosensors/panel testing (Magnotech) Example: Cardiac disease

Oak Ridge Conference, April 2009
Future Directions for POCT

- POCT growing at a rapid pace
- Test menu expanding
- New technologies include:
  - In vivo and ex vivo monitoring
  - Minimally invasive techniques (transcutaneous measurements)
  - Nanotechnology
  - Noninvasive methods (reverse iontophoresis, magnetic resonance spectroscopy, near-infrared spectroscopy, optical imaging)
Summary

- Growth in POCT and applications of POCT
- Includes inpatient and outpatient settings
- Testing performed by wide range of health professionals and patients
- Understanding limits of tests and appropriate patient population setting important for testing process and interpretation of results
- EBM-based guidelines valuable source of information and should be implemented
- New applications and technologies pose both challenges and opportunities
AACC Presents

POINT-OF-CARE SPECIALIST CERTIFICATE PROGRAM

Program Overview

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