Eighth Eurosurveillance Scientific Seminar

Infectious Disease POC Testing: Ready or Not, Here It Comes

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November 27, 2019
Industry Disclosures 2014-2019

- **Advisory Board/Consultant**
  - Merck
  - Verity
  - Cipher
  - Paladin Labs

- **Research Support**
  - Accelerate Diagnostics
  - bioMérieux
  - Bio-Rad

- **Honorarium**
  - Merck

- **Travel Reimbursement**
  - Merck
  - Copan

None of these industry disclosures relate to point-of-care devices.
Objectives

By the end of this session, you should be able to:

1. Describe the **role of infectious disease POC testing** along with predicted benefits

2. Illustrate **quality and ethical challenges** regarding the use of infectious disease POC tests

3. List **guidance documents** regarding the use of infectious disease POC to assure quality results
NEW TECHNOLOGIES

1. Automation and Smart Incubation
2. Rapid Microbial Identification
3. Rapid Antimicrobial Susceptibility Testing
4. Automated Random Access Syndromic Assays
5. Point-of-Care Testing
Paradigm Shift

BEFORE: 8-4pm LAB

NOW: 24/7 LAB

NOW/FUTURE: 24/7 LAB & POC
POC Testing Definition

1. Medical diagnostic testing at or near the **point of care**—that is, **at the time and place of patient care**.

2. **POC laboratories** set up in remote regions to facilitate access to testing.
POC Testing – Current State

- Previously lateral flow immunoassay based
- Now nucleic acid amplification based assays
- Many available but primarily target:
  1. GAS   2. Influenza   3. HIV   4. Hepatitis C
- Performed in clinics, emergency departments, ICUs, some pharmacies
- Primarily performed by physicians as well as pharmacists, nurses
<table>
<thead>
<tr>
<th>Disease or pathogen</th>
<th>Principle</th>
<th>Measurand</th>
<th>No. of tests</th>
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<tbody>
<tr>
<td><strong>Group A Streptococcus (GAS)</strong></td>
<td>LFIA</td>
<td>GAS antigen</td>
<td>79</td>
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<tr>
<td></td>
<td>Molecular</td>
<td>Bacterial DNA</td>
<td>2</td>
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<td><strong>Infectious mononucleosis</strong></td>
<td>LFIA</td>
<td>Heterophile antibodies</td>
<td>44</td>
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<td><strong>Helicobacter pylori</strong></td>
<td>LFIA</td>
<td>IgG antibodies to <em>H. pylori</em></td>
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<td></td>
<td>Biochemical</td>
<td>Urease enzyme activity</td>
<td>7</td>
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<tr>
<td></td>
<td>LFIA</td>
<td><em>H. pylori</em> antigen</td>
<td>1</td>
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<tr>
<td><strong>Influenza types A and B</strong></td>
<td>LFIA</td>
<td>Influenza type A and B antigens</td>
<td>12</td>
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<tr>
<td></td>
<td>Molecular</td>
<td>Viral RNA</td>
<td>2</td>
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<tr>
<td></td>
<td>Biochemical</td>
<td>Neuraminidase enzyme activity</td>
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<td><strong>Respiratory syncytial virus</strong></td>
<td>LFIA</td>
<td>Respiratory syncytial virus antigen</td>
<td>9</td>
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<td><strong>HIV-1 and HIV-2</strong></td>
<td>LFIA</td>
<td>Antibodies to HIV-1/2</td>
<td>4</td>
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<tr>
<td></td>
<td>LFIA</td>
<td>HIV-1 antigen, antibodies to HIV-1/2</td>
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<tr>
<td><strong>HIV-1</strong></td>
<td>LFIA</td>
<td>Antibodies to HIV-1</td>
<td>4</td>
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<tr>
<td><strong>Influenza type A</strong></td>
<td>LFIA</td>
<td>Influenza type A antigen</td>
<td>4</td>
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<tr>
<td><strong>Influenza type B</strong></td>
<td>LFIA</td>
<td>Influenza type B antigen</td>
<td>4</td>
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<tr>
<td><strong>Urinary tract infections</strong></td>
<td>LFIA</td>
<td>Catalase enzyme activity</td>
<td>2</td>
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<tr>
<td><strong>Influenza A/B and RSV</strong></td>
<td>LFIA</td>
<td>Viral RNA</td>
<td>2</td>
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<tr>
<td><strong>Trichomonas vaginalis</strong></td>
<td>LFIA</td>
<td><em>T. vaginalis</em> antigen</td>
<td>2</td>
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<tr>
<td><strong>Adenovirus</strong></td>
<td>LFIA</td>
<td>Adenoviral antigen</td>
<td>2</td>
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<tr>
<td><strong>Borrelia burgdorferi</strong> (Lyme disease)</td>
<td>LFIA</td>
<td>IgG and IgM antibodies to <em>B. burgdorferi</em></td>
<td>1</td>
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<tr>
<td><strong>Treponema pallidum</strong> (syphilis)</td>
<td>LFIA</td>
<td>Antibodies to <em>T. pallidum</em></td>
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<td><strong>Hepatitis C virus</strong></td>
<td>LFIA</td>
<td>Antibodies to hepatitis C virus</td>
<td>1</td>
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<tr>
<td><strong>Gardnerella vaginalis, Bacteroides spp., Prevotella spp., and Mobiluncus spp.</strong></td>
<td>Biochemical</td>
<td>Sialidase enzyme activity</td>
<td>1</td>
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</table>
POC Testing Regulations

• **US FDA:**
  - Categorizes in vitro diagnostics (IVD) tests by their complexity
    - CLIA-Waived*
    - Moderate complexity
    - High complexity

* insignificant risk of an erroneous result:
  - Methods so simple & accurate that chance of erroneous result negligible
  - No unreasonable risk of harm to the patient if performed incorrectly
Lateral Flow Immunoassay with optical reader (results in 5 min)
Lateral Flow Immunoassay (results in 20 min)
NEAR* based
(results in <15 min)

(*Nicking Enzyme Amplification Reaction)
PCR based
(results in ~20 min)

cobas Liat System, Roche
1. Increased menu to include more targets
   - NAAT based technologies
   - Novel methodologies

2. Focus on syndromic testing
   - Performed in increasing numbers of clinics, emergency departments, ICUs, pharmacies
   - Performed by physicians, pharmacists, nurses, other health care providers, patients
POC Testing – Future State

- Increasing use of POC

Drancourt et al. CMR 2016;29(3):429-47
POC Testing – Future State

- Increasing use of POC
- Reducing role of laboratory “proper”

Drancourt et al. CMR 2016;29(3):429-47
POC Testing – Future State

- Increasing use of wearable POC with real-time data analysis & artificial intelligence

Motivators – Predicted Benefits

- Reduced turn-around-times
- Accessibility
- Presumed improved outcomes
Motivators – Predicted Benefits

- POC flu A/B 20min POC (Liat) was associated with:
  - ↑ antiviral use for those with influenza (92 vs 70%) (P<0.05)
  - ↓ antiviral use in those without influenza (2 vs 25%) (P<0.005)
Challenges – Quality Management

- Device Selection
- Facilities
- Purchasing/Inventory
- Test Verification
- Operators
- Training
- Competency
- Documentation
- Quality Assurance
- Biosafety
- Critical Result Reporting
- Public Health Reporting
  - Enforcement
  - Oversight
Challenges – Ethics

- Ethics – potential for for-profit motivation (pharmacists, physicians)
On-the-spot strep throat tests offered at some Shoppers Drug Mart pharmacies

Some experts worry about accuracy of swabs, available in Alberta, B.C. and Nova Scotia
Pharmacies want to give $15 strep throat tests — but pediatricians say they're not accurate enough for kids

Medical guidelines say rapid point-of-care tests shouldn't be used to rule out strep in children
• BD Veritor System (lateral flow immunoassay): 
  Sn = 76.2%; Sp = 93.6%
• BD Veritor System (lateral flow immunoassay): 
  \[ Sn = 76.2\%; \quad Sp = 93.6\% \]

• Alere i Strep A Test (NEAR): 
  \[ Sn = 100\%; \quad Sp = 91.3\% \]
Convenience, at a cost? Pharmacies offering tests and treatment for strep, flu
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Chapter 3
Section 3.07
Laboratory Services in the Health Sector

Ministry of Health and Long-Term Care

Auditor General Report, Ontario, Dec 2017
Multiple Concerns Noted Based on 2015/2016 Data:

1. **Limited Investigation of Large In-Office Lab Test Volumes and Billings by MDs**
   - POC tests make up 4% of all laboratory testing
   - 50% of POC tests are ordered by <1% physicians
   - 15 highest billers billed $600,000 to $1.4 million CDN on 75,000 to 182,000 tests
     (average physician billed $4,700 CDN for 600 tests)
Multiple Concerns Noted Based on 2015/2016 Data:

2. No Licensing and Quality Management of Physicians’ In-Office Lab Testing
   • Noted in previous audits in 1995 and 2005 but the government has not taken action
POC Guidance

MINISTRY OF HEALTH AND LONG-TERM CARE

Point-of-Care Testing Policy

The policy applies to:

1. hospitals with a licensed laboratory,
2. hospitals without a licensed laboratory,
3. long-term care homes.

The policy is supplemented by a POCT Guidance Document specific to each type of facility.

Oversight must be completed by laboratory personnel.

MOHLTC POC Testing Policy, 2007
Point-of-care testing: A position statement from the Canadian Society of Clinical Chemists

P.M. Yip\textsuperscript{a}, A.A. Venner\textsuperscript{b}, J. Shea\textsuperscript{c}, A. Fuezery\textsuperscript{d}, Y. Huang\textsuperscript{e}, L. Massicotte\textsuperscript{f}, N. Tetreault\textsuperscript{g}, C. Tomalty\textsuperscript{h}, J.L.V. Shaw\textsuperscript{i,*}

POC Guidance

Changing Diagnostic Paradigms for Microbiology

American Academy of Microbiology Report on POC Microbiology, 2017
<table>
<thead>
<tr>
<th>Time</th>
<th>Session Title</th>
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<tbody>
<tr>
<td>11:30 – 12:30</td>
<td>Workflow optimization: methodologies and applications</td>
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</tbody>
</table>

**Chairs**

Harald Seifert (Cologne, Germany),
François Vandenesch (Lyon, France)

**National guidelines for implementation of point of care testing for infectious diseases in Denmark**

G. Lisby* (Hvidovre, Denmark)
Challenges with Enforcement

- Guidelines must be enforced in order to assure quality POC testing
  - Must reach all healthcare personnel who may be interested in using POC
  - Cannot be done through the laboratory
Expert Consensus Statement for Microbiology Point of Care Testing

1. ENFORCEMENT & REGULATION
2. LABORATORY OVERSIGHT
3. DEVICE SELECTION
4. FACILITIES
5. PURCHASING/INVENTORY AND EQUIPMENT
6. TEST VERIFICATION
7. TEST OPERATORS
8. TRAINING
9. INFORMATION MANAGEMENT AND DOCUMENTATION
10. QUALITY ASSURANCE
11. INFECTION PREVENTION AND CONTROL/BIOSAFETY AND BIOSECURITY
12. CRITICAL RESULTS REPORTING AND NOTIFIABLE DISEASES
13. ETHICS AND PROFESSIONAL CONDUCTS
Possible Solution

• **Consensus document** provided to local professional licensing bodies and hospitals

• Healthcare professional recertification and reappointments require:
  1. Documentation of use of POC tests
  2. Documentation of laboratory or expert oversight or relevant updated certified training
“The best way to predict the future is to create it”

Peter Drucker, Austrian-born Professor of Management, New York University Graduate School of Business
Infectious Disease POC Testing