Diagnostics in a Digital Age: Promises and Challenges

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www.idx-dx.org
Diagnostics in a Digital Age

• Context:
  – Diagnostics for infectious diseases
  – Developing world settings

• Disruptive innovation in the developing world

• Recent diagnostics innovation driven by:
  – HIV
  – Global health emergencies
  – Antimicrobial resistance

• Promises and challenges

• The way forward
Disruptive Innovation in the Developing World: The Mobile Phone
Cost: ~ $10,000
Payload: 5 lbs
Flight time: 30-60 min
Range: 20-60 miles

Operation: manual or pre-programmed for specific routes; need almost no room to land, and can even drop packages from a low hover; can deliver 100 HIV POC tests
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UNAIDS/WHO 2020 Targets for HIV

- 90% tested
- 90% on treatment
- 90% virally suppressed
Global Health Emergencies: Call for Open Technology Platforms

Source: J. Whitehorn
POC Test or test systems are needed to:

- improve the specificity of syndromic management leading to more targeted use of antibiotics
- detect and map AMR for surveillance and guiding treatment
- lower the cost of clinical trials for new drugs

**Incentivising Test Development:**

- The UK Longitude Prize £ 10 million
- The EC Horizon 2020 Prize: 1 million euros
- The US NIH AMR Prize of up to $ 20 million
The Ideal Diagnostic Test

A = Affordable
S = Sensitive
S = Specific
U = User-friendly
R = Rapid and robust
E = Equipment-free
D = Deliverable

- Accurate
- Fast/Simple
- Cheap

Pick 2 of 3!
## Tests: Wish List

<table>
<thead>
<tr>
<th>Site</th>
<th>Diagnostic test</th>
<th>Wish Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP</td>
<td>POCT for:</td>
<td>Bacterial vs viral infections</td>
</tr>
<tr>
<td></td>
<td>- Respiratory viruses (influenza, parainfluenza, adenovirus)</td>
<td></td>
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<tr>
<td></td>
<td>- Diarrhoea (crypto, salmonella)</td>
<td></td>
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<tr>
<td>Pediatrics</td>
<td>POCT</td>
<td>Bacterial vs viral infections</td>
</tr>
<tr>
<td>Obstetrics</td>
<td>POCT for Group B strep, HSV</td>
<td></td>
</tr>
<tr>
<td>A &amp; E</td>
<td>Nasal swab for influenza; Blood for malaria RDT</td>
<td>Sepsis biomarkers</td>
</tr>
<tr>
<td>Travellers</td>
<td>VHF, malaria, dengue, rickettsia etc, depending on travel history</td>
<td></td>
</tr>
</tbody>
</table>
Diagnostics Methods:
Ease of Detection vs Confidence in Diagnosis

DIRECT METHODS:
Pathogen Detection

- Microscopy
- Culture
- Genome detection
- Antigen detection

INDIRECT METHODS:
Host Biomarkers

- Serology IgM
- Serology IgG

Ease of detection

Time to Result:
- Days/Hours
- Minutes

Confidence

Adapted with permission from J. Cardosa
HIV Early Infant Diagnosis and Viral Load Product Pipeline

Sample in-answer out

- Alere Q
- LYNX Viral Load Platform
- Truelab PCR
- RT CPA HIV-1 Viral Load Assay with BART

- Alere
- EOSCAPE HIV™ Rapid RNA Assay System
- Cavidi AMP
- Gene-RADAR

- Wave 80 Biosciences
- IQuum
- Molbio/bigTec
- Nanobiosym

- SAMBA VL
- Roche Liat™ Analyser
- Gene Xpert Cepheid
- Viral Load Assay with BART Lumora

- DDU/Cambridge
- IQuum
- Cepheid
- Lumora

Alere i: Point-of-care Molecular Platform

- **Principle:** nucleic acid amplification system (iNAAT) that uses a fluorescence-based molecular signal for detection

- **Applications:**
  - Approved: Influenza virus A and B (Europe)
  - In clinical trials: Ct/Ng
  - In development: Strep A, C. difficile, RSV

- **Operation:**
  - adapted for use by non-laboratory staff
  - time to result: 15min (only 2 min of “hands on” time)

- **Connectivity:**
  - cloud based data storage
Cepheid: A Multi-disease Random Access Real-time PCR Platform

MTB/RIF, Flu A, B/RSV
MRSA, *C. difficile*, Norovirus
CT/Ng, HPV, Group B Strep
HIV Viral Load, early infant diagnosis
HCV

Omni:
- 9 in. tall
- 1 kg
- AC or battery operated
- controlled via dedicated mobile device
- wireless, web enabled
- USD 2,895

Samples per shift
5 20 80 500-1000
Roche: Cobas Liat RT-PCR System

• **Principle:** RT-PCR with an internal optical analyser that provides 6 independent optical detection channels for real-time detection and quantification of multiple targets

• **Applications:**
  • FDA and CE approved: Influenza virus A and B and Strep A
  • In development: HIV viral load, HCV

• **Operation:**
  • time to result: 15-20 min
  • AC or battery powered
  • Self checks and calibrations with Internal and volume controls

• **Connectivity:** to be confirmed
**Molbio: Truelab Real Time micro PCR System**

- **Principle:** nucleic acid amplification system that uses a fluorescence-based molecular signal for detection

- **Applications:**
  - Available: MTB, HBV, dengue, Chikungunya, Flu (H1N1), malaria
  - In development: Ct/Ng, HIV viral load

- **Operation:**
  - Sample prep: Trueprep MAG Prep Device and kits 20-25 min.
  - Take 6 ul of extract into reaction well of micro PCR chip
  - Insert chip into micro PCR analyser
  - Amplification with internal controls
  - Quantitative detection using fluorophores in 30 min.
  - time to result: 60 min

- **Connectivity:** not known
BioFire Film Array

• **Principle:** 2-stage nested multiplex PCR with reagents dried in a plastic pouch; tests 16 pathogens in a run

• **Applications:**
  - Respiratory panel*
  - Biothreat Panel

• **Operation:**
  - time to result: 60 min (only 2 min of “hands on” time)

• **Connectivity:**
  - Interoperable with global information grid

*Respiratory panel: Flu A and B, Parainfluenza 1-3, RSV, adenovirus, human metapneumovirus, corona virus, rhinovirus, enterovirus, *Mycoplasma pneumoniae*, *Bordetella pertussis*, and *Chlamydophila pneumoniae*
STI Multiplex Molecular BioChip Array

- Chlamydia trachomatis
- Neisseria gonorrhoea
- Herpes simplex I
- Herpes simplex II
- Treponema pallidum
- Trichomonas vaginalis
- Mycoplasma hominis
- Mycoplasma genitalium
- Ureaplasma urealyticum
- Haemophilus ducreyi

25 ul sample, 22 assays per biochip, 45 samples and 4 calibrators per run
Plasmonic Nanosensors

Molly Stevens (Imperial College)

Nanowire technology: From a finger-pricked sample of blood, it is possible to detect in 20 min:
- malaria parasites
- distinguish malaria species
- malaria drug resistance

Nanodot technology: can create molecular barcodes with nanodots. These barcodes can represent molecular signatures and allow the system to detect pathogens and their resistance genes or host responses such as cytokines.
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Promises:
- people-centred health care
- improved access to diagnostics for more evidence-based care
- open technology platforms requiring less capital investment and re-training
- automated surveillance through connectivity
Aspirin? Check. Shampoo? Check. Free HIV Test — Check?

Source: time.com
Wearable Biosensors

Algorithms would be used to monitor the data that the devices beam to the cloud and respond to users with specific health recommendations.

Medical tracking that both looks good and does good: jewelry-like varied sensors monitor specific vitals for different diseases.

Users could add tiles based on their specific health concerns. Do you want to measure your blood sugar? The air quality where you live? The food you eat?

BRING THE DOCTOR WITH YOU

THE LOGICAL NEXT STEP IN MANAGING CHRONIC DISEASE IS TECHNOLOGY THAT TRACKS OUR VITALS AND GUIDES US TO BETTER HEALTH

BY YVES BÉHAR
Reimagining the Future of the Diagnosis of Viral Infections

- 1,234 paired serum samples from laboratory confirmed dengue patients, archived between 2005-2011
- Accurately identified >90% of dengue cases from a single serum specimen collected during the first 10 days of illness by using either:
  - DENV-RT-PCR + IgM ELISA
  - NS1 antigen ELISA + IgM ELISA

Hunsperger et al JID Mar 2016
Early-Warning Sensing Systems for Infectious Diseases

Mobile POC Diagnostics

Patients & Public
- Better treatment, care & prevention

Social Media

Real Time Public Health Surveillance Systems
- Rapid interventions, prevention

- Patients & Public
- Mobile POC Diagnostics
- Social Media
- Real Time Public Health Surveillance Systems
Early-Warning Sensing Systems for Infectious Diseases in the UK

Clinical Care
Helping patients gain faster access to care

Public Health
Protecting the public
Monitor interventions

Accurate Information
Electronic prescriptions

Prevention Programmes
Local information

Early Detection

Rapid Response
Connectivity Solutions for Rapid Point-of-care Tests

Smartphone dongles performed a point-of-care HIV and syphilis test in Rwanda from finger prick whole blood in 15 minutes, operated by health care workers trained on a software app.

—Image courtesy of Samiksha Nayak for Columbia Engineering
Traditional centralized testing model in Zimbabwe
Connectivity Pilot in Zimbabwe

MOH, QA Managers, Reference Labs, NPHL, SCM, Provincial Medical Directors, District and Provincial Hospitals
The Challenges:

- technological innovations not accompanied by innovation in service delivery
- need to modify patient pathways – more difficult to make changes to health care systems
- data governance
Medical Device Connectivity Ecosystem

• strive to capture all the data feeds which either directly or indirectly impact patient care
  – electronic patient management systems
  – treatment decisions
  – Early warning or public health alerts

• couple these data feeds with:
  – supply chain management systems
  – resources allocation

• Enable government health planners, private and public funding organizations to seamlessly access either patient identified or de-identified data depending upon need but rules needs to be established for data access
The Way Forward

- New sample in-answer out nucleic acid amplification technologies offer improved performance over antigen detection POCTs and the potential to test for multiple pathogens using a single specimen
- Connectivity solutions linking data from diagnostic laboratories and POC test readers/devices provide opportunities for automated surveillance systems
- Promises of diagnostics in a digital age include more patient-centred care, improved access to diagnostics for more evidence-based care, and automated surveillance through data connectivity
- The challenges include modifying care pathways and data governance
Acknowledgement
LSHTM/IDC: Maurine Murtagh, Ben Cheng, Debra Boeras, Catherine Wedderburn, Olivia Varsaneux, Freddy Bates

Funding: UNITAID, WHO, UK EPSRC