Rapid Bacterial Diagnostics – Are We There Yet?
Prof. Stephen Brecher, Boston University School of Medicine
A Webber Training Teleclass

Rapid Bacterial Diagnostics Are We There Yet?

Stephen M. Brecher, Ph.D.
VA Boston HealthCare System
BU School of Medicine

Hosted by Nicole Kenny
Virox Technologies Inc.

Disclosures

- Bacterioscan – Advisory Board
- Cubist – Speakers Bureau, in-house training
- Merck – Speakers Bureau
- Theravance – Advisory Board
- Cepheid – Collaborative Studies

Objectives

- **Define "Rapid", "We" and "There"**
- **Old technology – Don't throw out the baby with the bath water**
- **New technology –Keeping me from retirement**
- **Are we there yet?**

Rapid

Minutes to 3 hours

Which includes results communicated to the health care provider

Who are "WE"

- **Clinical Microbiology Laboratory**
- **Physician**
  - **Admit/treat/do not treat**
- **Pharmacy/Antibiotic Stewardship**
- **Infection Control**
- **Team approach: all of the above**
  - **e.g., ID, pharmacy, lab, IC, etc.**

Team Approach

- **No result sitting in a lab by itself is useful**
- **In order for RBD to work, need a systems approach**
- **Who calls who with what?**
- **What is the desired intervention?**
- **How does it effect outcome?**

What is "There"

- A single pathogen
- Multiple pathogens
- Any potential pathogen
- Complex disease pathogens (e.g. CF)
- Anatomical specific pathogens
- Antibiotic specific result: S or R

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Desired Outcomes

- Reduce time to appropriate therapy
- Reduce length of stay
- Reduce transmission of pathogen
- Reduce cost

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Goals

Micro/ID/Pharmacy/IC
Reduce time to appropriate treatment Directed rather than empirical therapy
Improve patient care/reduce length of stay/decrease transmission via IC
Decrease emergence of antibiotic resistance/antibiotic stewardship

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Rapid Diagnosis Directly From Specimens

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Old Technology

Gram Stains

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Gram Stains Can Work

- To make a Gram stain work requires work
  - Appropriate specimens
    - Sputum not spit
    - Aspirate not swab
- Selection within specimen
  - Sputum is heterogeneous
  - Select mucous plugs

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"Working" Gram Stains The Chodosh Method

- Gram stains predicted community respiratory pathogens in AECBB study patients with high accuracy and PPV
- Mucous plugs selected, examined for neutrophils and if present, slide gram stained. If GS showed a predominant organism, the other half of the mucous plug was used for culture

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Predicting Pathogens in CA-AECBB[1]

- **480 patients at study entry**
  - GS predicted the cultured pathogen 321 times (67%)
  - Predicted 2 pathogens but grew only 1 73 times (15%)
  - Predicted 2 pathogens and grew 2 pathogens 35 times (7%)
  - Predicted 1 or 2 pathogens and grew 1 predicted and 1 not predicted 38 times (8%)
  - Predicted a pathogen and a pathogen not grown 13 times (3%)
  - Also predicted absence of pathogen

1. Brecher et al. Gram stains and cultures from sputum collected for 24 hours in selected patients with AECB.1996. ASM Annual Meeting. Abstract C226. New Orleans

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Expectorated Sputum

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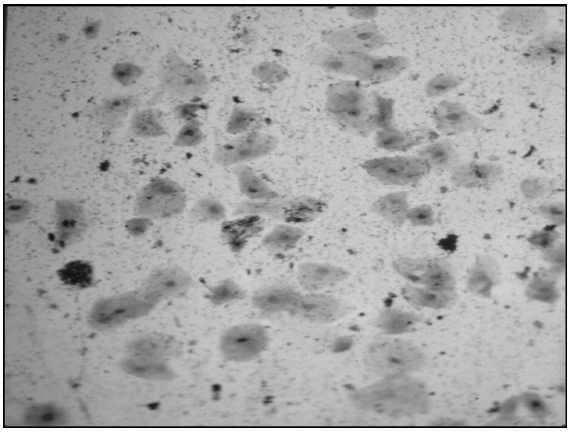

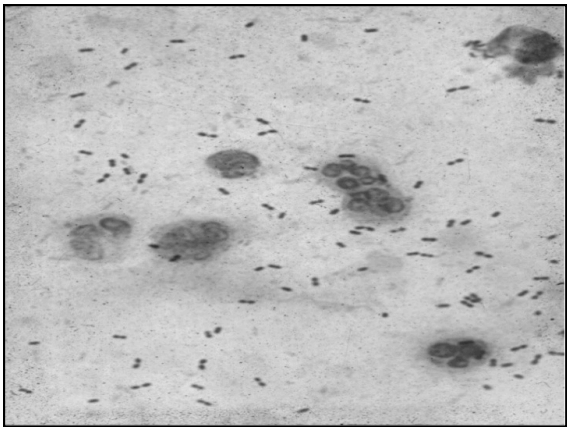

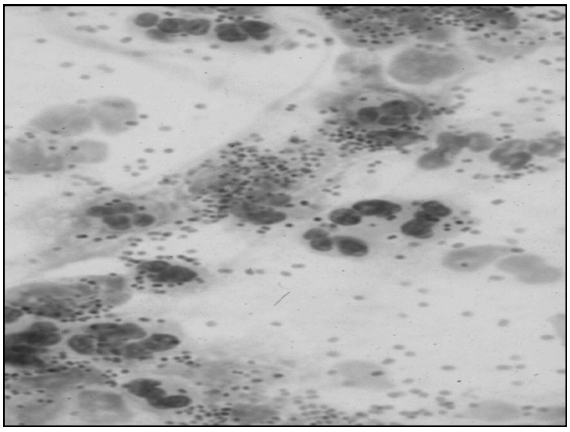

Predicting the Pathogen in Suctioned Respiratory Secretions

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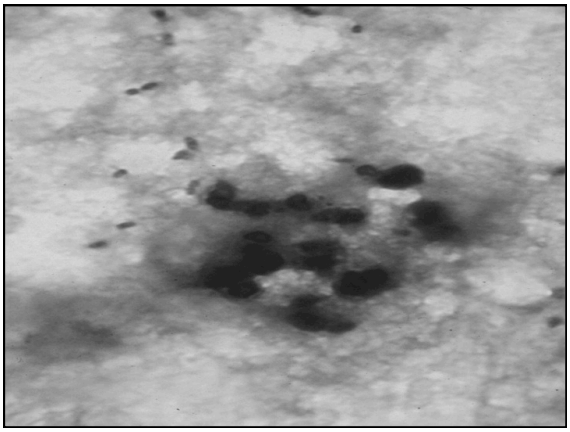

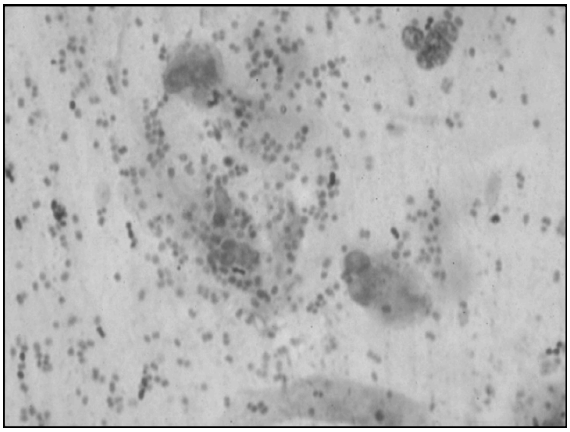

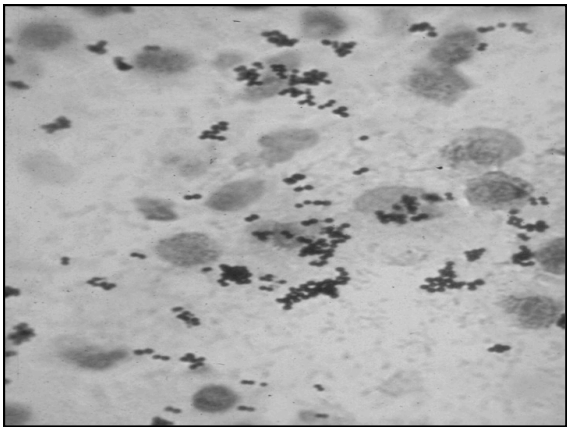

Mural Dyslexia

- "The inability to see the big picture"
- The value of an assay should be measured by its impact on patient outcome, not solely on its cost
  - Length of stay
  - Prescription drugs
  - Infection control
- The most expensive test is one that does not work

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The Holy Grail
Rapid Bacterial Diagnosis
Directly From Blood

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Limitations to the Rapid Detection of Bacteria in Blood

- **Very Few Targets**
  - **Most bacteremic patients have very few bacteria/ml of blood**
  - **To diagnose bacteremia we take 20 ml of blood x 2 and put 10 ml in each of 4 bottles**
  - **Positive patients often have only 1 or 2 positive bottles**
  - **Takes 1-5 days to get results**

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Procalcitonin as a Marker for Sepsis Meta–Analysis[1]

- **Protein produced by numerous cells/ organs in response to inflammation due to bacterial infections (+ other things)**
- **30 studies, 3244 patients with sepsis**
  - **Mean sensitivity = 77%**
  - **Mean specificity = 79%**
- **Useful in dx of severe sepsis but results have to be interpreted with caution**

1. Wacker, C. et al. 2013. Lancet Infect Dis.13:426-435

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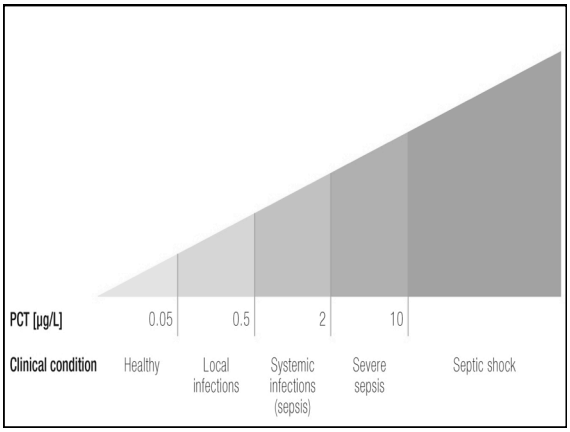


T2 MR-Based Rapid Detection of Candidemia

RESEARCH ARTICLE

DIAGNOSTICS

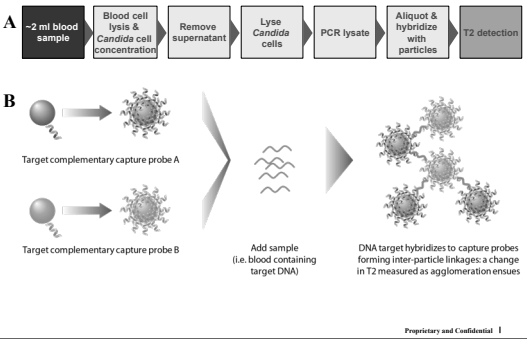
T2 Magnetic Resonance Enables Nanoparticle-Mediated Rapid Detection of Candidemia in Whole Blood

Lori A. Neely,[1] Mark Audeh,[1] Nu Ai Phung,[1] Michael Min,[1] Adam Suchocki,[1] Daniella Plourde,[1] Matthew Blanco,[1] Vasiliki Demas,[1] Lynell R. Skevis,[1] Theodora Anagnostou,[2] Jeffrey J. Coleman,[2,3] Parris Wellman,[1] Eleftherios Mylonakis,[2,3] Thomas J. Lowery[1]*

Candida spp. cause both local and disseminated infections in immunocompromised patients. Bloodstream infections of *Candida* spp., known as "candidemia," are associated with a high mortality rate (40%), which is mainly attributed to the long diagnostic time required by blood culture. We introduce a diagnostic platform based on T2 magnetic resonance (T2MR), which is capable of sensitive and rapid detection of fungal targets in whole blood. In our approach, blood-compatible polymerase chain reaction is followed by hybridization of the amplified pathogen DNA to capture probe–decorated nanoparticles. Hybridization yields nanoparticle microclusters that cause large changes in the sample's T2MR signal. With this T2MR-based method, *Candida* spp. can be detected directly in whole blood, thus eliminating the need for analyte purification. Using a small, portable T2MR detection device, we were able to rapidly, accurately, and reproducibly detect five *Candida* species within human whole blood with a limit of detection of 1 colony-forming unit/ml and a time to result of <3 hours. Spiked blood samples showed 98% positive agreement and 100% negative agreement between T2MR and blood culture. Additionally, performance of the assay was evaluated on 21 biobanked clinical specimens collected serially. This study shows that the nanoparticle- and T2MR-based detection method is rapid and amenable to automation and offers clinicians the opportunity to detect and identify multiple human pathogens within hours of sample collection.

www.ScienceTranslationalMedicine.org 24 April 2013 Vol 5 Issue 182 182ra54

Assay Design



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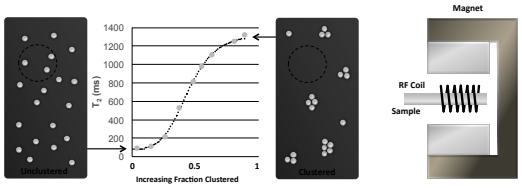
T2MR Direct Detection



- No background interference eliminates sample preparation and extraction of targets
- No manipulation or extraction of the target analyte enables superior specificity and sensitivity
- Measuring the magnetic properties of the entire water population and not just the target provides breakthrough sensitivity in dirty samples

1. Neely et al. *Science Translational Medicine* 2013 5(2) 182.

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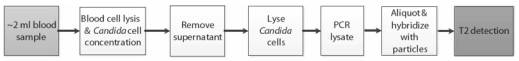
T2Candida – Critical Performance Metrics



Target Species	LoD
C. albicans	3 CFU/mL
C. tropicalis	3 CFU/mL
C. parapsilosis	1 CFU/mL
C. glabrata	2 CFU/mL
C. krusei	2 CFU/mL

- Limit of Detection (LoD) as low as 1 CFU/mL[1]
- Anti-fungals in a patient sample can prohibit cell growth in blood culture, leading to a false negative result[1]
- Equivalent or better sensitivity than blood culture with 25x faster turn-around time[2]

1. Neely et al. *Science Translational Medicine* 2013 5(2) 182.
2. Beyda, M. Jahangir Alam, Kevin W. Garey, *Diagnostic Microbiology & Infectious Disease* 2013 in press.

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Detection of Pathogens from Positive Blood Culture Bottles

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Understanding Positive Blood Cultures

- Often, very few organisms/ml of blood
- Bottles usually positive in 16-48 hours
- Gram stain + bottles, subculture and wait 24 hours to get colonies
- Set up ID and susceptibility
- Results available in another 24 hours

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FilmArray

- **Two minutes of hands-on time**
- **Results in about 1 hour**
- **From a positive blood culture bottle, 27 targets**
- **From a nasal swab, 20 viral and bacterial pathogens**
- **Closed System – Contamination is not an issue**
- **PCR based Molecular**

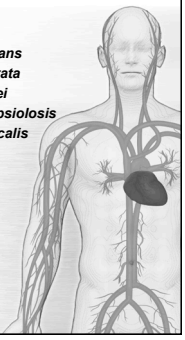
Blood Culture Identification Panel FDA Cleared

Gram + Bacteria:
Enterococcus
L. monocytogenes
Staphylococcus
S. aureus
Streptococcus
S. agalactiae
S. pyogenes
S. pneumoniae

Antibiotic Resistance:
mecA
Van A/B
KPC

Gram - Bacteria:
A. baumannii
H. influenzae
N. meningitidis
P. aeruginosa
Enterobacteriaceae
Enterobacter cloacae complex
E. coli
K. oxytoca
K. pneumoniae
Proteus
S. marcescens

Yeast:
C. albicans
C. glabrata
C. krusei
C. parapsiolosis
C. tropicalis



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The Verigene BC-GP

Intended Use

- Verigene BC-GP is a multiplexed *in vitro* diagnostic test for the detection and identification of pathogenic gram-positive bacteria
- Verigene BC-GP is indicated for use in conjunction with other clinical and laboratory findings such as culture and is not used to monitor bloodstream infections
  - Sub-culturing is necessary for susceptibility testing, identification of non-detected organisms, differentiation of mixed growth, association of resistance marker or epidemiological typing
- Our system detects and identifies the following bacterial genera/species and resistances

Gram-Positive Blood Culture (BC-GP) Test			
Genus	*Staphylococcus* spp.	Species	*Staphylococcus aureus* *Staphylococcus epidermidis* *Staphylococcus lugdunensis*
	Streptococcus spp.		
	Listeria spp.		*Streptococcus pneumoniae* *Streptococcus anginosus* Group *Streptococcus agalactiae* (GBS) *Streptococcus pyogenes* (GAS)
Resistance	*mecA*[1]		
	vanA[2]		
	vanB[2]		*Enterococcus faecalis* *Enterococcus faecium*

1. The *mecA* resistance marker is only tested for if *S. epidermidis* and/or *S. aureus* is "Detected"
2. The *vanA/vanB* resistance marker is only tested for if *E. faecalis* and/or *E. faecium* is "Detected"

Nanosphere 37 Approved for Customer Use

The Verigene BC-GN

Intended Use

- Verigene BC-GN is a multiplexed *in vitro* diagnostic test for the detection and identification of pathogenic gram-negative bacteria
- Verigene BC-GN is indicated for use in conjunction with other clinical and laboratory findings such as culture and is not used to monitor bloodstream infections
  - Sub-culturing of positive blood cultures is necessary to recover organisms for susceptibility testing, identification of organisms not detected by BC-GN, differentiation of mixed growth, association of antimicrobial resistance marker genes to a specific organism, or for epidemiological typing
- BC-GN independently detects and identifies the following:

Gram-Negative Blood Culture (BC-GN) Test			
Genus	*Acinetobacter spp.*	Species	*Escherichia coli*[1]
	Proteus spp.		*Klebsiella pneumoniae*
	Citrobacter spp.		*Klebsiella oxytoca*
	Enterobacter spp.		*Pseudomonas aeruginosa*
Resistance	KPC	1. BC-GN will not distinguish ***Escherichia coli*** from ***Shigella spp.*** including ***S. dysenteriae, S. flexneri, S. boydii,*** and ***S. sonnei***	
	NDM		
	CTX-M		
	VIM		
	IMP		
	OXA		

~~FDA Cleared. For *in vitro* Diagnostic Use.~~

Nanosphere 38 Approved for Customer Use

Matrix Assisted Laser Desorption Ionization – Time of Flight (MALDI-TOF)

- **Identify bacteria/yeast/fungi/ mycobacteria from colonies in minutes**
- **ID bacteria/yeast from positive blood culture bottles (not FDA approved)**
- **Replace gram stain of bacterial colonies**
  - **Not a reason to buy one but once you have one a potential good use**

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Impact of Rapid MALDI-TOF Results in Bacteremic Adults[1]

- **Intervention team: 2 ID physicians, 3 ID pharmacists, ID Pharmacy resident**
- **Team members received real time notification based on GS, ID, and susceptibility results from lab and communicated results to prescribers**
  - **MALDI results from colonies (not directly from BC broth)**
- **Made evidence-based antibiotic recommendations**
- **Compared 256 bacteremic results preintervention to 245 patients post intervention**

1. Huang, AM et al. 2013. CID. 57: 1237-1245

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Results of Intervention

	Preintervention	Postintervention
Time to organism ID	**84.0 hours**	**55.9 hours**
Time to effective therapy	**30.1 hours**	**20.4 hours**
Time to optimal therapy	**90.3 hours**	**47.3 hours**
ICU stay	**14.9 days**	**8.3 days**

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Matrix Assisted Laser Desorption Ionization – Time of Flight

- **Identify bacteria/yeast/fungi/ mycobacteria from colonies in minutes**
- **Replace gram stain of bacterial colonies[1]**
  - **Not a reason to buy one but once you have one a potential good use**

1. Mudie, K and SM Brecher. 2014. ASM submitted Abstract.

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*Quick*FISH/PNA FISH Positive Blood Cultures

- ***Quick*FISH: Gram-Negative Bacilli (20 minutes)**
  - ***E. coli. K. pneumoniae*, or *P. aeruginosa***
- ***Quick*FISH: Gram-Positive Cocci (20 minutes)**
  - ***S. aureus*/CNS**
  - ***E. faecalis/E. faecium***
- **PNA FISH for Candida (*Quick*FISH coming)**

***Quick*FISH is a trademark of AdvanDx**

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Rapid Bacterial and Viral Diagnosis Multi-Plex PCR

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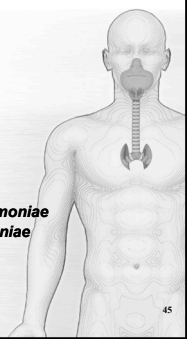
Respiratory Panel FDA Cleared

Viral
Adenovirus
Coronavirus 229E
Coronavirus HKU1
Coronavirus OC43
Coronavirus NL63
Human Metapneumovirus
Human Rhinovirus/ Enterovirus
Influenza A
Influenza A/H1
Influenza A/H1-2009
Influenza A/H3
Influenza B

Parainfluenza 1
Parainfluenza 2
Parainfluenza 3
Parainfluenza 4
RSV

Bacterial
Bordetella pertussis
Chlamydophila pneumoniae
Mycoplasma pneumoniae



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The Evidence

FilmArray®
The fastest way to better results.

- Overall, 95% sensitivity and 99% specificity

Clinical Sensitivity and Specificity of the FilmArray Respiratory Pouch

Pathogen	Sensitivity		Specificity
	Prospective	Retrospective	Prospective
Adenovirus	88.9%	100%	98.3%
Coronavirus HKU1	95.8%	n/a	99.8%
Coronavirus NL63	95.8%	n/a	100%
Coronavirus 229E	100%	100%	99.80%
Coronavirus OC43	100%	100%	99.60%
Human Metapneumovirus	94.6%	n/a	99.2%
Human Rhinovirus/Enterovirus	92.7%	95.7%	94.6%
Influenza A	90.0%	n/a	99.8%
Influenza A/H1	n/a	100%	100%
Influenza A/H3	n/a	100%	100%
Influenza A/H1-2009	88.9%	100%	99.6%
Influenza B	n/a	100%	100%
Parainfluenza Virus 1	100%*	97.1%	99.9%
Parainfluenza Virus 2	87.4%*	100%	99.8%
Parainfluenza Virus 3	95.8%	100%	98.8%
Parainfluenza Virus 4	100%*	100%	99.9%
Respiratory Syncytial Virus	100%	n/a	99.1%
Bordetella pertussis	100%*	94.6%	99.90%
Chlamydophila pneumoniae	100%*	100%†	100%
Mycoplasma pneumoniae	100%*	84.4%	100%

*Spiked Chlamydophila pneumoniae samples were used to test retrospective sensitivity.
†Due to low prevalence in the prospective study, clinical sensitivity for these pathogens was based on less than 10 positive samples.

Value and Use of Rapid Respiratory Multi-Plex Panels

- **If assay is run on ER patients and the TAT is less than 2 hours, save money by answering the following questions**
  - **Viral? Bacterial?**
  - **Admit or not?**
  - **Antibiotics? Oseltamavir?**
  - **If admit, ? Precautions, IC protocols**

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"Lab's Respiratory Panel Found to Curb Antibiotic Use"[1]

The following quote is from CAP today with respect to the use of a respiratory panel PCR for pediatric patients in an ED

"Fewer children with respiratory disease symptoms hospitalized from the ED without a diagnosis, less antibiotic use, and a favorable ratio of reimbursement to expense…"

1. CAP Today January, 2014

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Rapid Bacterial Diagnosis Directly From Urine

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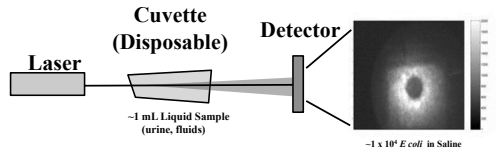
Narrow Angle Laser Forward Scatter Measurement



- Measurement of scattered light intensity and motion
- Particle size of interest: 0.2 to 10 microns
- Analogous to OD measurement - optimized for very low concentrations
- Samples held at 37° C to promote organism growth
- Automated for real-time observation of growth over minutes, hours, days

BacterioScan

Rapid AST Using Laser Microbial Growth Monitor

- Laser Scatter Measurement with onboard incubation of up to 24 samples at a time
- Five logs of linear dynamic range for quantitation of bacteria from ~ 10^4 to ~ 10^9 CFU/mL in clear fluids
- *Available early 2014*

BacterioScan 224r Instrument and 4-Sample Cuvettes

BacterioScan

UTI Detection Performance

•Fast Positive Detection (10 minutes)

Sensitivity	87.5%
Specificity	87.9%
PPV	51.9%
NPV	97.9%

•Elimination of Negatives (90 minutes)

Sensitivity	96.9%
Specificity	85.1%
PPV	49.2%
NPV	99.5%

Clinical Study conducted with St Louis University Hospital Jan-May 2013 in 248 patients with 14.6% UTI positive at >1 x 10^4 CFU/ml, in matched pairings of preserved and unpreserved/refrigerated specimens, tested 24 hours after collection.

Directly from Stool GI Pathogens

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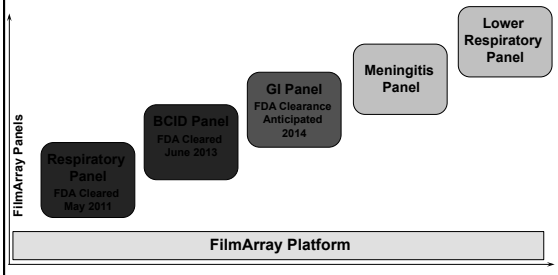
The Panels



After all panels are FDA-cleared, FilmArray will have assays covering 125 of the most common pathogens that cause death and disease.

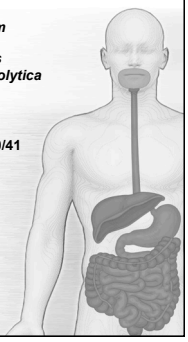
GI Panel (In development: Not FDA Approved)

Bacteria:
Aeromonas
Campylobacter
Clostridium difficile (Toxin A/B)
Plesiomonas shigelloides
Salmonella
Vibrio
Vibrio cholerae
Yersinia enterocolitica

Diarrheagenic *E. coli* / *Shigella*
E. coli O157
Enteroaggregative *E. coli* (EAEC)
Enteropathogenic *E. coli* (EPEC)
Enterotoxigenic *E. coli* (ETEC)
Shiga-like toxin-producing *E. coli* (STEC)
Shigella/Enteroinvasive *E. coli* (EIEC)

Protozoa:
Cryptosporidium
Cyclospora cayetanensis
Entamoeba histolytica
Giardia lamblia

Viruses:
Adenovirus F 40/41
Astrovirus
Norovirus GI/GII
Rotavirus A
Sapovirus



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Clostridium difficile

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Rapid Diagnosis of *C. difficile*

- PCR has replaced EIA in CDI diagnostics
  - EIA was quick but not accurate
- About 10 FDA approved PCR assays
  - Rapid, accurate, very sensitive (rare false negatives), maybe too specific (false positives)
  - Test only patients at risk
    - ↑WBC, antibiotics, >3 BM/24h
  - Test only loose stool (Brecher Guidelines[1])
    - "If it ain't loose, it's of no use"
    - "If the stick stands, the test is banned, if the stick falls, test them all"

1. Brecher, SM et al. 2013. Clin Infect Dis. 57: 1175-1181

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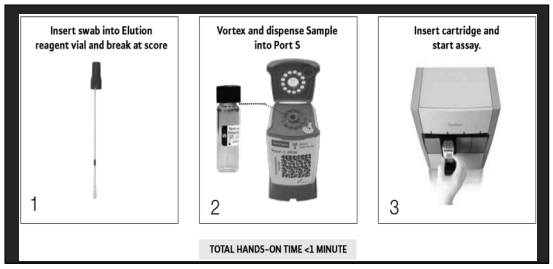
Xpert® *C. difficile* PCR Test for *Clostridium difficile*



Rapid Bacterial Diagnosis M. TB Complex

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Rapid Molecular Detection of MTB Complex and Rifampin Resistance Directly in Respiratory Specimens

- MTB/RIF automated molecular (PCR) Test
  - Detects genes for MTB Complex (7 different Mycobacteria) and rifampin resistance (marker for multi-drug resistance)

  Detected 551/561 culture positive, smear positive cases and 124/171 culture positive, smear negative cases
  - Correctly identified 200/205 rifampin resistant bacteria and 504/514 rifampin sensitive bacteria
  - May be used to replace AFB smears for respiratory specimens

http://www.nejm.org/doi/full/10.1056/NEJMoa907847

Rapid Molecular Testing for TB to Guide Respiratory Isolation in the U.S.: A Cost-Benefit Analysis[1]

- Compared isolation days and hospital costs in a retrospective analysis of a hypothetical cohort of 234 patients undergoing evaluation for possible TB
  - Compared results of 2 sputa AFB smears with 1 molecular PCR assay
  - PCR results available within hours; 2 smear results obtained at least 8 hours apart
  - PCR is significantly more expensive and more accurate than AFB smears
  - PCR reduced isolation bed utilization from 2.7 to 1.4 days per patient
  - System cost savings was over $500,000/year

1. Millman, AJ. Et al. 2013. PLOS one. Volume 8: Issue 11.79669

Can PCR Replace AFB Smears to Rule Out *M. tuberculosis*?

- Issues to consider
  - Cost
  - Prevalence
  - Severity of disease
  - How many specimens?
  - Quality of specimens

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Whole Genome Sequencing

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Clinical Insights from Metagenomic Analysis of Sputum Samples from Patients with Cystic Fibrosis[1]

- Selected 3 patients and cultured/sequenced "climax" and "attack" communities over "clinical event " time sequences
  - Onset, treatment, post treatment, stable
  - Bacteria, viruses, fungi
  - Potential metabolic markers of different communities
- "…this pilot study provides an example of how metagenomic data might be used ….. For the development of treatments tailored to individual patients"

1. Lim, YW et al. 2014. J Clin Microbiol. 52: 425-437

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Whole Genome Sequencing Infection Control and Molecular Epidemiology

- WGS demonstrated that patient-to-patient transmission rarely accounts for acquisition of *Staphylococcus aureus* in an intensive care unit[1]
- WGS used successfully to help unravel the CRE outbreak at NIH[2]
- In the near future, WGS will be the method of choice for ME/IC
- ? Screen stool for fecal transplant

1. Price, JR. et al. 2014. CID. 58: 609-618 2. Palmore, TN and DK Henderson. 2013. CID 57: 1593-1599

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Volatile Organic Compounds

65

Diagnosis of Invasive Aspergillosis

- " In patients with suspected IFD, detection of a combination of farnesene, β-vatirenene, and cis-geranylacetone in the breath accurately and noninvasively discriminates IA patients from patients without IA."[1]
  - 54 immunosuppressed patients
  - Accurately dx 27/29 IA and 24/25 w/o IA
  - Sensitivity of 93%, Specificity of 96%

1. Koo, S. et. al. 2013. ICAAC Abstract M-219. Denver

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Rapid Bacterial Diagnostics – Are We There Yet?

Prof. Stephen Brecher, Boston University School of Medicine

A Webber Training Teleclass

Point of Care Testing

- R/O MTB in Pulmonary Clinics
- Group B Streptococci in OBGYN
- GC/Chlamydia, HIV, Herpes in STD Clinics
- Influenza and other respiratory viruses in the ER

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Better Tests, Better Care: Improved Diagnostics for Infectious Diseases

Caliendo, A. M. et al. CID 2013. 57: S139-S170

In this IDSA policy paper, we review the current diagnostic landscape, including unmet needs and emerging technologies, and assess the challenges to the development and clinical integration of improved tests. To fulfill the promise of emerging diagnostics, IDSA presents recommendations that address a host of identified barriers. Achieving these goals will require the engagement and coordination of a number of stakeholders, including Congress, funding and regulatory bodies, public health agencies, the diagnostics industry, healthcare systems, professional societies, and individual clinicians.

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The Ultimate in Rapid The Selfie

Dr. Brecher,

I was a previously healthy 28 year old, very muscular male. I have traveled in Asia and Africa. I love the outdoors, have had numerous mosquito bites, and may have been exposed to *Wuchereria bancrofti.* I think I may have elephantiasis. Please see attached "selfie".

Thanks for your help.

Hans

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Are We There Yet?

We are off the back roads

Stay tuned for

"Fast Times on the Technology Highway"

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March 7 (Free WHO Teleclass ... Europe)
HOW TO PREVENT THE SPREAD OF MULTIRESISTANT BACTERIA
Dr. Stephan Harbarth, University of Geneva Hospitals, Switzerland

March 20 **FRIDAY OUTBREAKS – FACT OR FICTION?**
Chingiz Amirov, Baycrest Centre for Geriatric Care, Toronto

March 27 (Free Teleclass)
INTEGRATING HUMAN FACTORS WITH INFECTION PREVENTION AND CONTROL
Jules Storr, Claire Kilpatrick, Dr. Neil Wigglesworth, The Health Foundation

April 3 **HOW TO BRIDGE THE GAP BETWEEN KNOWLEDGE AND PRACTICE**
Gertie van Knippenberg-Gordebeke, APIC International Section, Netherlands

April 8 (Free British Teleclass ... Denver Russell Memorial Teleclass Lecture)
ANTIBACTERIAL EFFICACY OF ATMOSPHERIC PRESSURE NON-THERMAL PLASMA

www.webbertraining.com/schedulep1.php

Hosted by Nicole Kenny, Virox Technologies Inc.
www.webbertraining.com

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