

# T2Bacteria

- T2 Magnetic Resonance technology
- Whole blood (EDTA), fully automated, FDA-cleared
- PCR
- Hybridization to supramagnetic nanoparticles
- Amplicon-induced agglomeration of supramagnetic particle, Disruption of microscopic magnetic field → measure

Target	Limit of Detection (CFU/mL)
<i>E. faecium</i>	5
<i>E. coli</i>	11
<i>K. pneumoniae</i>	2
<i>P. aeruginosa</i>	5
<i>S. aureus</i>	1

*A. baumannii*: RUO



# Clinical performance of T2Bacteria among patients with BSIs

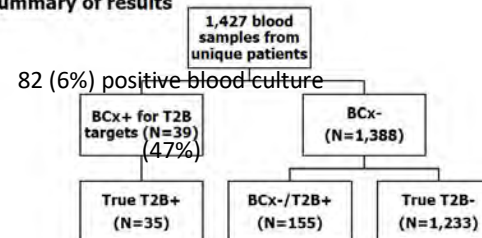
Clinical performance of T2Bacteria among patients with bloodstream infections due to five common bacterial species

MH Nguyen, W Pascual, PG Pappas, G Alangaden, G Pankey, B Schmitt, M Weinstein, R Widen, D Hernandez,

D Wolk, TJ Walsh, J Perfect, CJ Clancy, E Mylonakis

University of Pittsburgh, University of Alabama at Birmingham, Henry Ford Hospital, Ochsner Health System, Indiana University School of Medicine, Robert Wood Johnson University Hospital, Tampa General Hospital, Gesinger Health System, Weill Cornell Medicine of Cornell University, New York Presbyterian Hospital, Duke University, Alpert Medical School of Brown University

## Summary of results



T2B Target	Receipt of in vitro effective antibiotic on the day of paired BCx+/T2B+ draw
<i>E. coli</i>	20% (2/10)
<i>E. faecium</i>	0% (0/1)
<i>K. pneumoniae</i>	17% (1/6)
<i>P. aeruginosa</i>	20% (1/5)
<i>S. aureus</i>	46% (6/13)

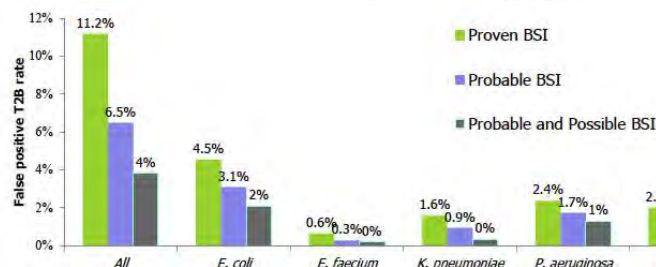
*In vitro* effective therapy was defined as receipt of ≥1 dose of an antibiotic that has *in vitro* activity against >70% of the BSI bacterium based on antibiogram from four medical centers

- Mean time of BC+: 51+/-43h (7.1-171h)
- Mean time to identification: 83.7 +/-47.6h (22.8-243.6h)
- Mean time to T2 results: 5.4+/-1.6h (3.6-10h)



# T2Bacteria

T2B Target	Sensitivity	95% CI
<b>Overall</b>	<b>90% (35/39)</b>	<b>75-97%</b>
<i>E. coli</i>	91% (10/11)	62-98%
<i>E. faecium</i>	100% (1/1)	21-100%
<i>K. pneumoniae</i>	100% (6/6)	61-100%
<i>P. aeruginosa</i>	100% (5/5)	57-100%
<i>S. aureus</i>	81% (13/16)	57-93%



- Discordant BCx-/T2B+ results were obtained in 11% (155/1,388) of samples

# Xpert MTB/RIF Ultra

- Recommended by WHO to replace the current Xpert MTB/RIF in March 2017
- Turn around time < 80 min
- Larger chamber for DNA amplification
  - 50 µL vs. 25 µL
- Two additional molecular targets
  - IS6110 and IS1081
- Fully nested nucleic acid amplification, more rapid thermal cycling, improved fluidics and enzymes
- High, medium, low, very low, **trace**
- Improved ability of detect low number of bacilli 16 bacilli/mL vs. 114-131 bacilli/mL
- RIF resistance: melting temperature-based analysis with 4 probes instead of PCR
  - Differentiate silent mutation from resistance conferring mutation





## Xpert MTB/RIF Ultra for detection of *Mycobacterium tuberculosis* and rifampicin resistance: a prospective multicentre diagnostic accuracy study

Susan E Dorman\*, Samuel G Schumacher\*, David Alland, Pamela Nabeta, Derek T Armstrong, Bonnie King, Sandra L Hall, Soumitesh Chakravorty, Daniela M Cirillo, Nestani Tukvadze, Nino Babilashvili, Wendy Stevens, Lesley Scott, Camilla Rodrigues, Mubini Kazi, Moses Joloba, Lydia Nakiyingi, Mark P Nicol, Yonas Ghebreyesus, Irene Anyango, Wilfred Murithi, Reynaldo Dietze, Renata Lyrio Peres, Alena Skrahina, Vera Auchynka, Kamal Kishore Chopra, Mahmud Hanif, Xin Liu, Xing Yuan, Catharina C Boehme, Jerrold J Ellner, Claudia M Denking, on behalf of the study team†

- 8 countries: South Africa, Uganda, Kenya, China, India, Georgia, Belarus, Brazil
- 1753 adults with symptoms of pulmonary TB

	Tuberculosis detection*			Detection of rifampicin resistance†		
	Sensitivity: all culture-positive (95% CI; n/N)	Sensitivity: smear-negative (95% CI; n/N)	Sensitivity: HIV-negative (95% CI; n/N)‡	Sensitivity: HIV-positive (95% CI; n/N)‡	Specificity (95% CI; n/N)	Specificity (95% CI; n/N)
Xpert	83% (79 to 86; 383/462)	46% (37 to 55; 63/137)§	90% (84 to 94; 143/159)	77% (68 to 84; 88/115)	98% (97 to 99; 960/977)	95% (91 to 98; 167/175)
Xpert Ultra	88% (85 to 91; 408/462)	63% (54 to 71; 86/137)§	91% (86 to 95; 145/159)	90% (83 to 95; 103/115)	96% (94 to 97; 934/977)	95% (91 to 98; 166/175)
Difference (Xpert Ultra minus Xpert)	5.4% (3.3 to 8.0; 25/162)	17% (10 to 24; 23/137)	1.3% (-1.8 to 4.9; 2/159)	13% (6.4 to 21; 15/115)	-2.7% (-3.9 to -1.7; 36/977)	0.3% (-0.7 to 1.5; 1/376)
Non-inferiority margin	Not predefined	-7%	Not predefined	Not predefined	-3%	-3%

Lancet Infect Dis 2018;18:76-84.

	Sensitivity		Specificity		
	All culture-positive (95% CI; n/N)	Smear-negative, culture-positive (95% CI; n/N)	All culture-negative (95% CI; n/N)	No history of tuberculosis (95% CI; n/N)	Any history of tuberculosis (95% CI; n/N)
Xpert	83% (79-86; 383/462)	46% (37-55; 63/137)	98% (97-99; 960/977)	98% (97-99; 715/727)	98% (95-99; 244/249)
Xpert Ultra	88% (85-91; 408/462)	63% (54-71; 86/137)	96% (94-97; 934/977)	96% (95-98; 701/727)	93% (89-96; 232/249)
Xpert Ultra, no trace*	86% (82-89; 395/462)	54% (45-63; 74/137)	98% (96-98; 953/977)	98% (96-99; 709/727)	98% (95-99; 243/249)
Xpert Ultra, conditional trace†	88% (85-91; 406/462)	61% (53-70; 84/137)	97% (95-98; 945/977)	96% (95-98; 701/727)	98% (95-99; 243/249)
Xpert Ultra, trace-repeat‡	87% (84-90; 404/462)	61% (52-69; 83/137)	97% (95-98; 944/977)	97% (96-98; 707/727)	95% (91-97; 236/249)

Sensitivity varied little by history of tuberculosis and did not vary systematically. Data on tuberculosis history were not available for one patient. \*Study participants testing tuberculosis-positive based on a trace-positive Xpert Ultra result (n=32) were reclassified as tuberculosis-negative. †Study participants testing tuberculosis-positive based on a trace-positive Xpert Ultra result had Xpert Ultra testing on a subsequent sputum specimen: if the subsequent sputum Xpert Ultra result was negative for *M. tuberculosis* then the participant was reclassified as tuberculosis-negative; if the subsequent Xpert Ultra result was positive for *M. tuberculosis* (any semiquantitative threshold), then the participant was not reclassified and remained tuberculosis-positive (14 out of 32 participants tested tuberculosis-negative on sample 2 and were reclassified; 14 tested tuberculosis-positive on sample 2 and were not reclassified; and four were non-determinate by Xpert Ultra on sample 2 and were not reclassified).



Dorman SE. Lancet Infect Dis 2018;18:76-84.

## Diagnostic accuracy of Xpert MTB/RIF Ultra for tuberculous meningitis in HIV-infected adults: a prospective cohort study

Nathan C Bahr, Edwin Nuwagira, Emily E Evans, Fiona V Cresswell, Philip V Bystrom, Adolph Byamukama, Sarah C Bridge, Ananta S Bangdiwala, David B Meya, Claudia M Denking, Conrad Muzaora, David R Boulware, on behalf of the ASTRO-CM Trial Team

- 129 HIV-infected patients with suspected TB meningitis, Uganda
- 0.5 mL centrifuged CSF; better if at least 6 mL

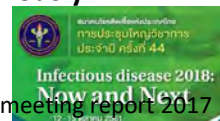
	Sensitivity vs composite endpoint (95% CI; n/N)	Sensitivity vs case definition (95% CI; n/N) Uniform Clinical Case Criteria	Assay error rate
Xpert Ultra	95% (77-99; 21/22)	70% (47-87; 16/23) NPV93%	2.3% (3/129)
Xpert	45% (24-68; 10/22)	43% (23-66; 10/23)	4.7% (6/129)
MGIT culture	45% (24-68; 10/22)	43% (23-66; 10/23)	1.6% (2/129)

All three tests were done in all 129 participants. Composite endpoint included any positive CSF Xpert Ultra, Xpert, or Bactec960 MGIT culture. Sensitivity vs uniform clinical case definition for definite (n=14) or probable (n=9) tuberculous meningitis excluded Xpert Ultra results in defining case status.<sup>10</sup> Error in culture reflects contamination with non-tuberculous mycobacterium growth. Xpert=Xpert MTB/RIF. MGIT=mycobacteria growth indicator tube. CSF=cerebrospinal fluid.

Lancet Infect Dis 2018;18:68-75.

## Xpert MTB/RIF Ultra

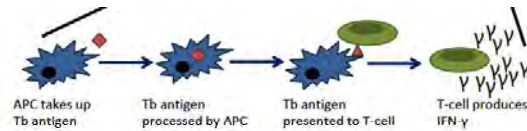
- Evaluation of 1520 persons with signs and symptoms of TB, 10 study sites
  - More sensitivity: +5% especially in
    - smear-negative-culture-positive (+17%)
    - HIV (+12%)
    - pediatrics (71% vs. 47%)**
    - extrapulmonary [CSF 95% vs. 43%]
    - At least good accuracy to detect rifampicin resistance (low sample size)
  - Decrease specificity (-3.2%, 94% vs. 96%)
    - Reference?
    - Non-viable, non-replicating? "trace call" in previously treated



WHO meeting report 2017

# Interferon-γ Releasing Assays

- IGRA
  - Indirect tests for infection with *M. tuberculosis*
  - Detect IFN-γ produced by MTb 'primed' T-cells following exposure to MTb antigen



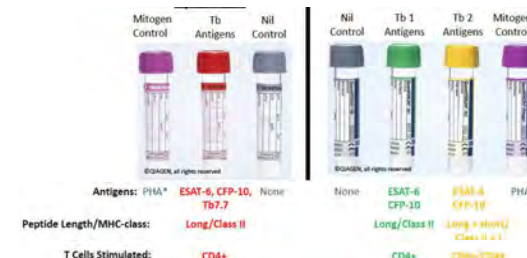
- 3 US FDA-cleared IGRA:
  - T.SPOT-TB (Oxford Immunotec)
  - QuantiFERON-TB Gold In-Tube (QFT-GIT; Qiagen- will be discontinued)
  - QuantiFERON-TB Gold Plus (QFT-Plus; Qiagen)**



# QuantiFERON Gold Plus

- US FDA-cleared in June 2017, use in Europe since 2015
- Developed with the goal to increase sensitivity for both LTBI and active disease-HIV-young children

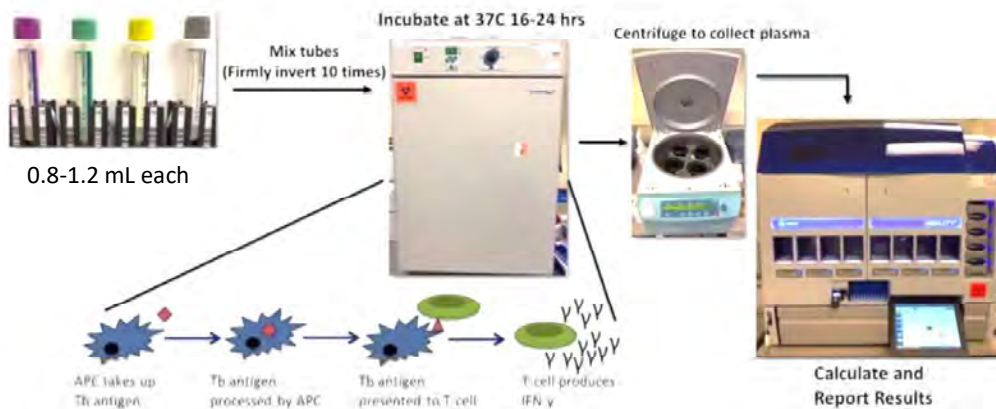
	QFT GIT	QFT Gold Plus
Tube	3	4
CD4	ESAT-6, CFP-10, TB7.7	ESAT-6, CFP-10
CD8	None	ESAT-6, CFP-10, Proprietary 6 MHC class I peptide



- Can collect in single Lithium-Heparin tube
  - RT 12h
  - 2-8°C 16-48h



# QuantiFERON Gold Plus



# QuantiFERON Gold Plus

## QuantiFERON-TB Gold Plus: Results and Interpretation

Nil	TB1 - Nil	TB2 - Nil	Mitogen - Nil	Qualitative Result	Interpretation
≤8.0 IU/mL	≥0.35 and ≥25% of Nil	Any	Any	Positive	<i>M. tuberculosis</i> infection likely
	Any	≥0.35 IU/mL and ≥25% of Nil			
	<0.35 IU/mL OR ≥0.35 IU/mL and <25% of Nil		≥0.5 IU/mL	Negative	<i>M. tuberculosis</i> infection NOT likely
			<0.5 IU/mL	Indeterminate	Likelihood of <i>M. tuberculosis</i> infection cannot be determined
>8.0 IU/mL	Any				

- Cutoff criteria identical to QFT
- QFT-Plus is considered positive if either one or both Tb Ag tubes are positive
- Data suggests non-inferior or similar performance between these two IGRAs [Sensitivity 89-96%, specificity 98-99%]
- Additional studies are ongoing: active or recent infections (cut off?), children or immunocompromised patients, Thai?**





# IGRA: Summary

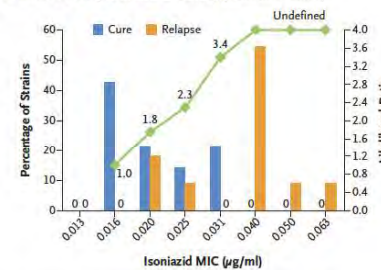
Characteristic	QFT-GIT	QFT-Plus	T.SPOT.TB
A single visit is required	✓	✓	✓
Does not cross-react with BCG	✓	✓	✓
Can be collected into a single tube	✗	✓	✓
Can be separated and tested >24h after collection	✗	✓	✓
Test all forms of cellular immunity (CD4 and CD8)	✗	✓	✗
High sensitivity	✓	✓	✓
High specificity	✓	✓	✓
Use a standard inoculum	✗	✗	✓

McCormick-Baw C. CMN 2018;40:139-143.

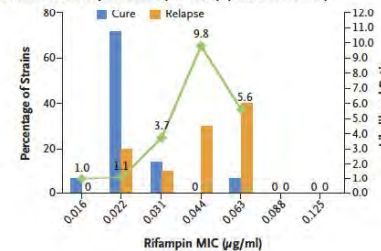


# TB MIC

A Likelihood of Relapse in Isoniazid Group (Validation Cohort)



B Likelihood of Relapse in Rifampin Group (Validation Cohort)



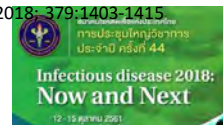
- TB MIC and relapse
  - Higher MIC of INH and RIF, albeit below break points (0.1 mg/L for I and 1 mg/L for R), increased risk of relapse
- Dosage of Intermediate-SDD purposed by Monte-Carlo simulation
  - INH 0.0312-0.5 mg/L: 900mg/d
  - RIF 0.0625-0.25 mg/L: 1800mg/d
  - PZA 37.5-50 mg/L: 4 g/d
- WGS to predict phenotypic susceptibility

Colangeli R. NEJM2018;379:823-33

Zur MA. CID2018.doi:10.1092/cid/ciy346.

CRyPTIC consortium and the 10000 genome project.

NEJM2018; 379:1403-1415



# Syphilis reverse algorithm: revisit

## Performance of Treponemal Tests for the Diagnosis of Syphilis

Ima U. Park,<sup>1,2</sup> Yetunde F. Fakile,<sup>2</sup> Joan M. Choe,<sup>3</sup> Kathleen J. Gustafson,<sup>1</sup> Heather Jost,<sup>2</sup> Jeffrey M. Schapiro,<sup>2</sup> Susan Novak-Weekley,<sup>2</sup> Anthony Tran,<sup>4</sup> Jim H. Nommura,<sup>5</sup> Victor Chen,<sup>6</sup> Munir Belsheshi,<sup>6</sup> Townsend Tsai,<sup>6</sup> Karen Hoover,<sup>6</sup> and Gail Bolan<sup>1</sup>

<sup>1</sup>Sexually Transmitted Disease Control Branch, Division of Communicable Diseases Control, California Department of Public Health, Richmond; <sup>2</sup>Division of Sexually Transmitted Disease Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia; and <sup>3</sup>Palmer Permanente Northern California Regional Laboratory, Berkeley; <sup>4</sup>Southern California Permanente Medical Group Regional Reference Laboratory, North Hollywood; <sup>5</sup>San Francisco Department of Public Health; and <sup>6</sup>Southern California Permanente Medical Group, California

- A few studies comparing head-to-head performance of treponemal tests in clinically characterized sera
- Will help inform selection of the most appropriate second treponemal test

CID 2018.doi:10.1093/cid/ciy558

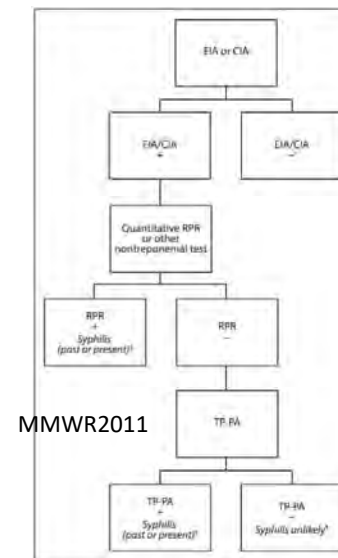
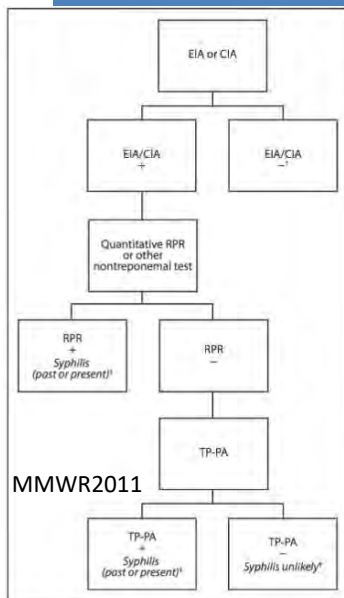


## Laboratory Evaluation of a Commercially Available Rapid Syphilis Test

Lara E. Pereira,<sup>a</sup> Joshua McCormick,<sup>b</sup> Tandin Dorji,<sup>a</sup> Joseph Kang,<sup>a</sup> Yongcheng Sun,<sup>a</sup> Mayur Shukla,<sup>c</sup> Andre Hopkins,<sup>a</sup> John Deutsch,<sup>b</sup> Ellen N. Kersh,<sup>a</sup> Kyle Bernstein,<sup>a</sup> Yetunde F. Fakile<sup>a</sup>

- Syphilis Health Check: rapid treponemal test
- 1406 archived samples
- Sens. 88.7% Spec 93.1% compared with treponemal test;
- Sens. 66.7% in HIV

JCM2018;56:e00832-18.



## Performance of Treponemal Tests for the Diagnosis of Syphilis

Ina U. Park,<sup>1,2</sup> Yetunde F. Fakile,<sup>2</sup> Joan M. Chow,<sup>1</sup> Kathleen J. Gustafson,<sup>1</sup> Heather Jost,<sup>2</sup> Jeffrey M. Schapiro,<sup>3</sup> Susan Novak-Weekley,<sup>4</sup> Anthony Tran,<sup>5</sup> Jim H. Nomura,<sup>6</sup> Victor Chen,<sup>6</sup> Manie Beheshti,<sup>6</sup> Townson Tsai,<sup>6</sup> Karen Hoover,<sup>7</sup> and Gail Bolan<sup>2</sup>

<sup>1</sup>Sexually Transmitted Disease Control Branch, Division of Communicable Disease Control, California Department of Public Health, Richmond; <sup>2</sup>Division of Sexually Transmitted Disease Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia; and <sup>3</sup>Kaiser Permanente Northern California Regional Laboratory, Berkeley; <sup>4</sup>Southern California Permanente Medical Group Regional Reference Laboratory, North Hollywood; <sup>5</sup>San Francisco Department of Public Health, and <sup>6</sup>Southern California Permanente Medical Group, California

Assay	Sensitivity by Stage				Overall Sensitivity (n = 262)	Overall Specificity (n = 403)
	Primary (n = 55)	Secondary (n = 98)	Early Latent (n = 41)	Late Latent (n = 68)		
FTA-ABS	78.2 <sup>a</sup> (65.0–88.2)	92.8 <sup>a</sup> (85.7–97.0)	100 (90.7–100)	92.6 (83.7–97.6)	90.8 <sup>a</sup> (86.7–94.0)	98.0 (96.1–99.1)
TPPA	94.5 (84.9–98.9)	100 (96.2–100)	100 (90.7–100)	86.8 <sup>b</sup> (76.4–93.8)	95.4 (92.1–97.6)	100 (99.0–100)
Centaur CIA	94.5 (84.9–98.9)	100 (96.2–100)	100 (90.7–100)	94.1 (85.6–98.4)	97.3 (94.6–98.9)	95.5 (93.0–97.3)
Trep-Sure EIA	94.5 (84.9–98.9)	100 (96.2–100)	100 (90.7–100)	98.5 (92.1–99.9)	98.5 (96.1–99.6)	82.6 <sup>c</sup> (78.4–86.1)
LIAISON CIA	96.4 (94.5–98.2)	100 (96.2–100)	97.6 (87.4–99.9)	92.6 (83.7–97.6)	96.9 (94.1–98.7)	94.5 (91.8–96.5)
Bioplex MBIA	96.4 (94.5–98.2)	100 (96.2–100)	95.1 (83.8–99.4)	94.1 (85.6–98.4)	96.9 (94.1–98.7)	96.7 (94.4–98.2)
INNO-LIA	96.4 (94.5–98.2)	100 (96.2–100)	100 (90.7–100)	91.1 (81.7–96.7)	96.9 (94.1–98.7)	98.5 (96.8–99.5)

- EIA, CIA, MBIA, TPPA would be preferred for confirming RPR using traditional algorithm
- TPPA is preferred to adjudicate cases of discordant reverse sequence algorithm
  - INNO-LIA would be an acceptable alternative
  - Centaur CIA and Bioplex MBIA: alternative in high prevalence

- ADVIA Centaur CIA-IgG, Bioplex-aMBIA IgG, INNO-LIA-manual line immunoassay IgG, FTA-ABS:manual IgA IgG, IGM, LIAISON-CIA IgG IgM, Trep-Sure-EIA IgG IgM

CID 2018.doi:10.1093/cid/ciy558

## Revised taxa: Communication is The Key

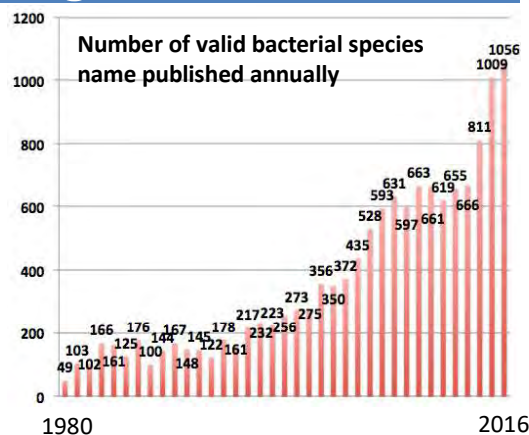
Previous taxa	Revised taxa
<i>Enterobacter aerogenes</i>	<i>Klebsiella aerogenes</i> !!!
<i>Enterobacteriaceae</i> and 7 new families	<i>Enterobacterales</i> ord. nov.
<i>Propionibacterium acnes</i> , <i>P. avidum</i> , <i>P. granulosum</i>	<i>Cutibacterium</i>
<i>Propionibacterium propionicum</i>	<i>Pseudopropionibacterium</i>
<i>Clostridium difficile</i>	<i>Clostridioides difficile</i>
<i>Borellia burgdorferi</i>	<i>Borrelia</i>
<i>Emmonsia pasteurianus</i>	<i>Emergomyces</i> (together with <i>E. africanus</i> , <i>E. canadensis</i> , <i>E. europaeus</i> , <i>E. orientalis</i> )
<i>Emmonsia parva</i>	<i>Blastomyces parvus</i>
<i>Balantidium coli</i>	<i>Neobalantidium coli</i>
<i>Dipyllobothrium latum</i>	<i>Dibothriocephalus latus</i>

Munson E, Carroll KC. JCM. Sept2018.doi:10.1128/JCM.01181-18.  
Warnock DW. JCM. Sept2018.doi:10.1128/JCM.01183-18.  
Mathison BA, Pritt BS. JCM. Oct2018.doi:10.1128/JCM.01067-18.

## Modern Taxonomy Clinical Significant?

### “Species proliferation”

- Total number of published bacterial species (as of May 2017) = 15,626



- <10% of newly proposed nomenclatures isolated from clinical specimens (mostly from environment, single strain)

<https://www.bacteriology.com>  
Janda JM. CMN. Apr2018.doi:10.1128/CMN.01181-18.

UK case of *Neisseria gonorrhoeae* with high-level resistance to azithromycin and resistance to ceftriaxone acquired abroad

- The first global report of HLAziR (MIC >256 mg/L, which also resistant to ceftriaxone (MIC 0.5 mg/L)
  - Followed by 2 cases in Australia in April
- A heterosexual male, one regular UK partner and sexual contact in SEA 1 month prior
- Positive culture after 1 g ceftriaxone and subsequently with spectinomycin
- Ertapenem MIC 0.032 mg/L



CRO MIC  
EUCAST R >0.125  
CLSI R >0.5  
AZT MIC  
EUCAST R >0.5  
ECV NWT ≥2

Infectious disease 2018: Now and Next  
12-15 พฤษภาคม 2561



*Clostridium innocuum* is a vancomycin-resistant pathogen that may cause antibiotic-associated diarrhoea

J.-H. Chia <sup>1,4,5,\*</sup>, T.-S. Wu <sup>2,\*</sup>, T.-L. Wu <sup>1,4,\*</sup>, C.-L. Chen <sup>3</sup>, C.-H. Chuang <sup>7,8</sup>, L.-H. Su <sup>1,4</sup>, H.-J. Chang <sup>2</sup>, C.-C. Lu <sup>9</sup>, A.-J. Kuo <sup>1,4</sup>, H.-C. Lai <sup>4,\*</sup>, C.-H. Chiu <sup>3,6,\*\*</sup>

- *C. innocuum*: intrinsic low-level vancomycin resistance
  - Colony may resemble *C. difficile*, negative for *C. difficile* toxin A/B
  - *racemase* gene and *ddl<sub>C.innocuum</sub>*: synthesis of a peptidoglycan precursor terminating in serine
  - Bacteremia, endocarditis in immunocompromised, empyema, IAI, pelvic abscess, recurrent diarrhea in patients with prior CDI
- 136 isolates (5.5%) from 2471 stool culture for *C. difficile*; 103 patients, Taiwan: MIC90: metronidazole 0.5 mg/L, vancomycin 16 mg/L
- Watery diarrhea (61.2%), mucous in stool (9.7%), bloody diarrhea (27.2%), pseudomembranous colitis (1.9%)

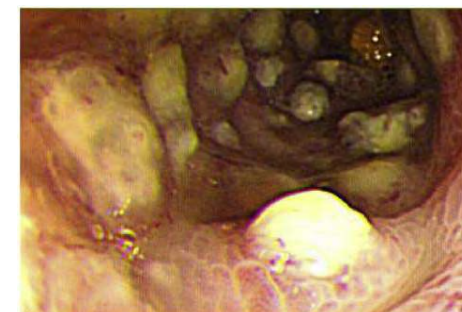


CMI 2018. doi:10.1016/j.cmi.2018.02.015

*Clostridium innocuum* is a vancomycin-resistant pathogen that may cause antibiotic-associated diarrhoea

J.-H. Chia <sup>1,4,5,\*</sup>, T.-S. Wu <sup>2,\*</sup>, T.-L. Wu <sup>1,4,\*</sup>, C.-L. Chen <sup>3</sup>, C.-H. Chuang <sup>7,8</sup>, L.-H. Su <sup>1,4</sup>, H.-J. Chang <sup>2</sup>, C.-C. Lu <sup>9</sup>, A.-J. Kuo <sup>1,4</sup>, H.-C. Lai <sup>4,\*</sup>, C.-H. Chiu <sup>3,6,\*\*</sup>

- 89% received antibiotics within 2 weeks
  - Cephalosporins (63)
  - penicillins (36)
  - aminoglycosides (33)
  - glycopeptides (30)
  - fluoroquinolones (29)
  - carbapenems (17)
  - clindamycin (14)
- Treatment failure with vancomycin 125 mg q 6 h
  - 40% in severe colitis and 11.8% in diarrhea group
- 13.6% mortality rate, 50% in severe colitis



- Cytotoxicity to Vero cells and HT-29, Apoptotic change and cell death
- Tissue damages, necrotic changes and edema in mouse ileal loop
- Virulence factor: unknown; bound to cell surface envelope



Chai JH. CMI 2018. doi:10.1016/j.cmi.2018.02.015

## FDA-cleared Panels: Positive blood culture

Assay	Company	Method	Instrument required?	# of targets	Organism	Resistance gene	TAT
Xpert® MRSA/SA	Cepheid	RT-PCR	Yes	2	<i>S. aureus</i>	<i>mecA</i>	1 h
BD Max™ StaphSR	BD	RT-PCR	Yes	2	<i>S. aureus</i>	<i>mecA</i>	~ 1.5 h
PNA FISH®, QuickFISH™, <i>mecA</i> XpressFISH™	AdvanDx	PNA-FISH	No (Fluorescent microscope)	2 - 5	<i>S. aureus</i> Other panels	<i>mecA</i>	20 min
Staph ID/R	Great Basin Scientific	HDA	Yes	4	<i>S. aureus</i> , <i>S. lugdunensis</i> , other CoNS	<i>mecA</i>	~ 2 h
Verigene® BC-GP, and BC-GN	Luminex	Microarray	Yes (2 parts)	15 per panel	Gram positives Gram negative	<i>mecA</i> , <i>vanA/B</i> , <i>CTX-M</i> , <i>IMI</i> , <i>VIM</i> , <i>KPC</i> , <i>NDM</i> , <i>OXA</i>	2.5 hrs
FilmArray® BCID	BioFire Diagnostics	Nested PCR	Yes	27	Gram positive, Gram negative, Yeast	<i>mecA</i> , <i>vanA/B</i> , <i>KPC</i>	1 h
Pheno System	Accelerate	FISH +	Yes	16	Gram positive, Gram negative, Yeast	NA Phenotypic AST	1 h; 7 h

## Multiplex assays from positive blood cultures



- Array-based method, no amplification
- 2.5h TAT; BC-GP 15 targets, BC-GN 14 targets



- Multiplex- Nested PCR with melting curve analysis
- 2 min hand-on time, 1 h TAT; 27 targets
- Limit sensitivity for polymicrobial infection
- Sensitivity for *vanA/B*, *KPC* 100%; *mecA* 98.4%

Verigene BC-GP/ BC-GN	Filmarray BCID *includes 5 Candida
<i>S. aureus</i>	<i>S. aureus</i>
<i>S. epidermidis</i>	
<i>S. lugdunensis</i>	
<i>S. anginosus</i> group	
<i>S. agalactiae</i>	<i>S. agalactiae</i>
<i>S. pneumoniae</i> *	<i>S. pneumoniae</i> *
<i>S. pyogenes</i>	<i>S. pyogenes</i>
<i>E. faecalis</i>	<i>Enterococcus</i> spp.
<i>E. faecium</i>	
<i>Staphylococcus</i> spp.	<i>Staphylococcus</i> spp.
<i>Streptococcus</i> spp.	<i>Streptococcus</i> spp.
<i>Listeria</i> spp.	<i>L. monocytogenes</i>
<i>mecA</i> , <i>vanA</i> , <i>vanB</i>	<i>mecA</i> , <i>vanA/B</i>
<i>E. coli</i> *	<i>E. coli</i> *
<i>K. pneumoniae</i>	<i>K. pneumoniae</i>
<i>K. oxytoca</i>	<i>K. oxytoca</i>
<i>P. aeruginosa</i>	<i>P. aeruginosa</i>
<i>Acinetobacter</i> spp.	<i>A. baumannii</i>
<i>Citrobacter</i> spp.	
<i>Enterobacter</i> spp.	<i>E. cloacae</i> complex
<i>Proteus</i> spp.	<i>Proteus</i> spp.
	<i>Enterobacteriaceae</i>
	<i>H. influenzae</i>
	<i>N. meningitidis</i>
CTX-M, IMP, KPC, OXA, VIM, NDM	KPC

## FDA-cleared multiplex gastrointestinal tests

	BD MAX Enteric Bacterial Panel	BioFire Filmarray GI Panel	Luminex xTAG GPP	Nanosphere Verigene Enteric Pathogen Panel	Prodesse/Hologic SSCS
Specimen types	Stool Cary-Blair Stool	Cary-Blair Stool	Stool	Stool	Cary-Blair or Para-Pak C&S Stool
<i>Campylobacter</i>	X	X	X	X	X
<i>C. difficile</i>		X	X		
<i>E. coli</i> O157	[X]	X	X	[X]	[X]
EAEC, EPEC		X			
ETEC		X	X		
<i>Plesiomonas shigelloides</i>		X			
STEC	X	X	X	X	X
<i>Salmonella</i>	X	X	X	X	X
<i>Shigella</i> [EIEC]	X	X	X	X	X
<i>Vibrio</i>		X		X	
<i>Yersinia enterocolitica</i>		X		X	
Adenovirus 40/41 Astrovirus, Sapovirus		X			
Norovirus GI/GII		X	X		
Rotavirus		X	X		
<i>Giardia</i>		X	X		
<i>Cryptosporidium</i>		X	X		
<i>Entamoeba histolytica</i> , <i>Cyclospora</i>		X			

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## FDA-cleared multiplex respiratory virus tests

	BioFire Filmarray RPP*	Luminex xTAG RVP	GenMark eSensor RVP	GenMark ePlex RPP
INF A	X H1, H3, H1/09	X H1, H3	X H1, H3, H1/09	X H1, H3, H1/09
INF B	X	X	X	X
RSV	X	X A and B	X A and B	X A and B
PIV 1	X	X	X	X
PIV 2	X	X	X	X
PIV 3	X	X	X	X
PIV 4	X			X
MPV	X	X	X	X
RHV	X	X	X	X
EV	[X]	[X]		[X]
CoV	X HKU1, NL63, 229E, OC43			X HKU1, NL63, 229E, OC43
ADENO	X	X	X B, C and E	X
Off board extraction	No	Yes	Yes	No
No. of steps	1	5	4	1
Hands-on time	3 min	70 min	55 min	minimal
Instrument time	1.1 h	6.6 h	6 h	
Total time to results	1.17 h	7.75 h	7.25 h	

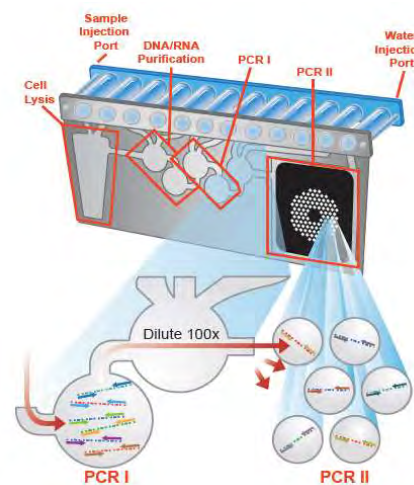
\*also includes *B. pertussis*, *C. pneumoniae*, *M. pneumoniae*

\*\* also includes *C. pneumoniae*, *M. pneumoniae*

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## FilmArray Meningitis/Encephalitis Panel

- Syndromic testing
- Approved March 2016
- 200 µL, TAT~1h, 2 min hands-on time
- 14 analytes
- Bacteria
  - E. coli* K1, GBS, *L. monocytogenes*, *N. meningitidis*, *H. influenzae*, *S. pneumoniae*
- Viruses
  - HSV-1, HSV-2, EVs, Human parechovirus, VZV, CMV, HHV-6
- Yeast
  - C. neoformans/gattii*



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Clinical Infectious Diseases

MAJOR ARTICLE

### Clinical Impact of a Multiplex Gastroenteritis Polymerase Chain Reaction Panel

Robert J. Cybulski Jr.,<sup>1,2</sup> Allen G. Bateman,<sup>1,2,3</sup> Lori Dourson,<sup>1</sup> Andrew Bryan,<sup>1</sup> Barb Beal,<sup>1</sup> Momen Kabir,<sup>1,4,5</sup> Emilez Ahmed,<sup>1,6</sup> Biplob Hossain,<sup>1</sup> Masud Alam,<sup>1</sup> Shahnoor Ahmed,<sup>1</sup> Mani Tamirchi,<sup>1</sup> Carol A. Glickert,<sup>1</sup> Eric R. Hoog,<sup>1</sup> A. S. G. Farooque,<sup>1</sup> William A. Petri Jr.,<sup>1</sup> and Rashidul Raqeeb<sup>1</sup>

<sup>1</sup>Department of Laboratory Medicine, University of Washington, <sup>2</sup>Harborview Medical Center Clinical Microbiology, <sup>3</sup>University of Washington School of Medicine, Seattle; <sup>4</sup>National Center for Clinical Microbiology Research, Dhaka, Bangladesh; and <sup>5</sup>Department of Medicine, Division of Infectious Diseases and International Health, University of Virginia, Charlottesville

**Background.** Molecular syndromic diagnostic panels can enhance episodes of acute gastroenteritis that occur annually worldwide. However, **Methods.** We conducted a prospective, multi-center study to investigate polymerase chain reaction panel on clinical diagnosis and decision-making results obtained exclusively with the FilmArray with those detected fecal specimens were tested in parallel by FilmArray and stool culture. La rates of detection, turnaround times, clinical features, and the nature and **Results.** FilmArray detected pathogens in 35.3% of specimens, compared to result was 18 hours for FilmArray and 47 hours for culture. Median time was 22 hours for FilmArray and 72 hours for culture. Patients diagnosed than empirical therapy, compared to those diagnosed by culture ( $P = .01$ ) reported 47 hours faster with FilmArray and facilitated discontinuation by FilmArray had clinical characteristics similar to those identified by culture. **Conclusions.** FilmArray markedly improved clinical sensitivity in acute gastroenteritis, compared to those identified by culture, and enabled clinicians to

- CIDT
- No susceptibility
- Cost effectiveness

Clinical Infectious Diseases

MAJOR ARTICLE

### *Giardia/Cryptosporidium* QUIK CHEK Assay Is More Specific Than Quantitative Polymerase Chain Reaction for Rapid Point-of-care Diagnosis of Cryptosporidiosis in Infants in Bangladesh

Momen Kabir,<sup>1,2</sup> Emilez Ahmed,<sup>1,3</sup> Biplob Hossain,<sup>1</sup> Masud Alam,<sup>1</sup> Shahnoor Ahmed,<sup>1</sup> Mani Tamirchi,<sup>1</sup> Carol A. Glickert,<sup>1</sup> Eric R. Hoog,<sup>1</sup> A. S. G. Farooque,<sup>1</sup> William A. Petri Jr.,<sup>1</sup> and Rashidul Raqeeb<sup>1</sup>

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Letter to the Editor  
Culture-confirmed cryptococcal meningitis not detected by *Cryptococcus* PCR on the BioFire meningitis/encephalitis panel<sup>®</sup>

BRIEF REPORT

### Misdiagnosis of *Bordetella bronchiseptica* Respiratory Infection as *Bordetella pertussis* by Multiplex Molecular Assay

Maura C. McNulty,<sup>1</sup> Dora R. Shih,<sup>1,2</sup> Jennifer L. Steinback,<sup>1</sup> Kathleen Mullins,<sup>1</sup> Jennifer Pissano,<sup>1</sup> Scott Matschke,<sup>1</sup> Kathleen G. Beavis,<sup>1</sup> Vera Teich,<sup>1</sup> and David Pines<sup>1</sup>

<sup>1</sup>Section of Infectious Diseases and Global Health, University of Chicago, Illinois; <sup>2</sup>Department of Pathology, University of Illinois Health Sciences Center, and <sup>3</sup>Illinois City Veterans Affairs Health Care System and Infectious Diseases, Northwest Community Hospital, Arlington Heights, Illinois; and <sup>4</sup>Department of Pathology, University of Chicago, Illinois

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Thank you

