AMRDETECTOOL
Detection in 30 min

# Current Pipeline and Benefits of Using Rapid Diagnostic Tests (RDTs)

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DPC-Saint Laszlo Hospital
Budapest

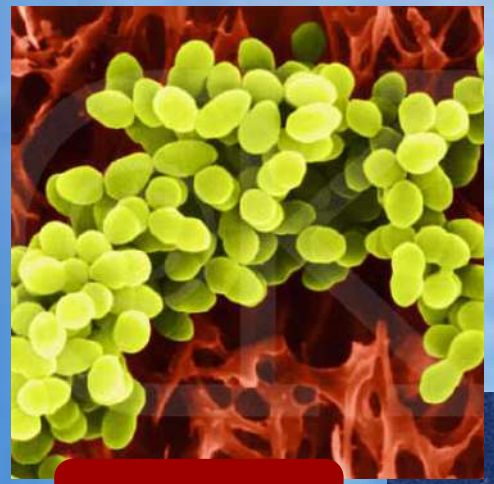
29-30 November 2021


eit Health

Funded by the European Union

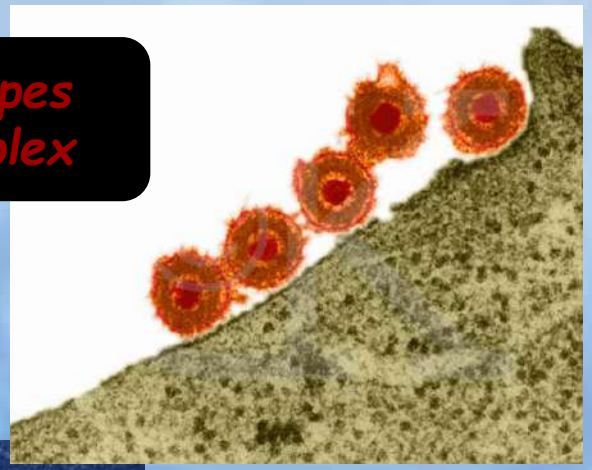
# Searching for pathogens…

„Which group of pathogens are the possible ones….”

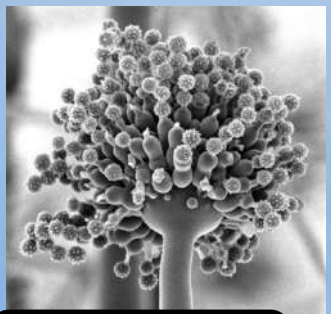


S.aureus

Herpes simplex



A.duodenale



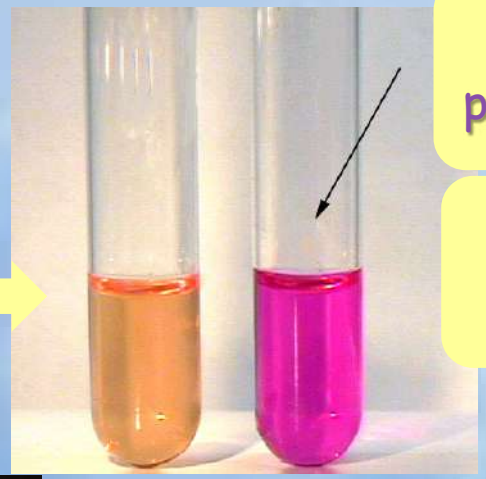
Aspergillus

N. meningitidis

K. pneumoniae

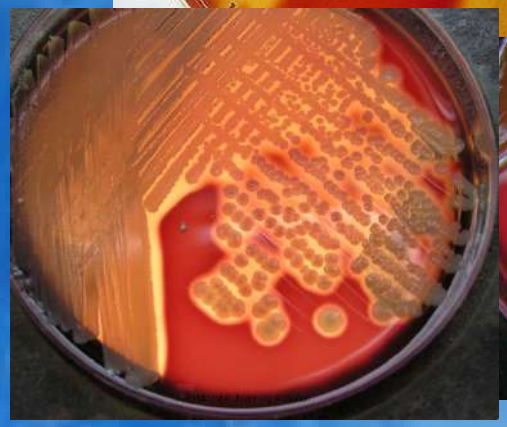
# The beauty and the base of our profession is **culturing**….colours..smells…

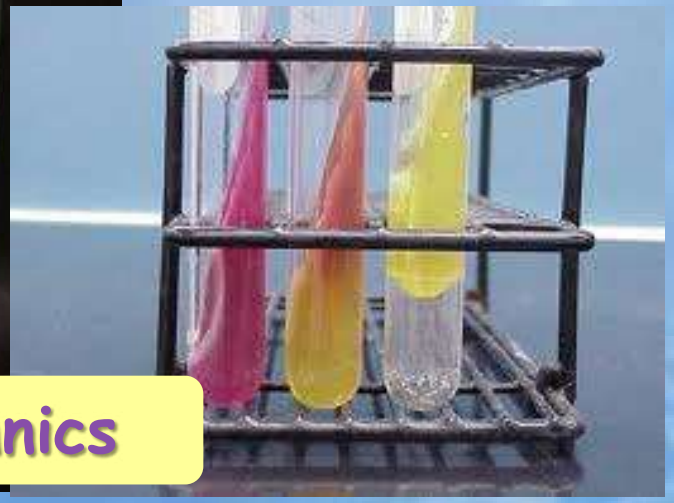
…Depending on the clinical picture, the nature of the most likely pathogen…



Require pure culture

..takes time..

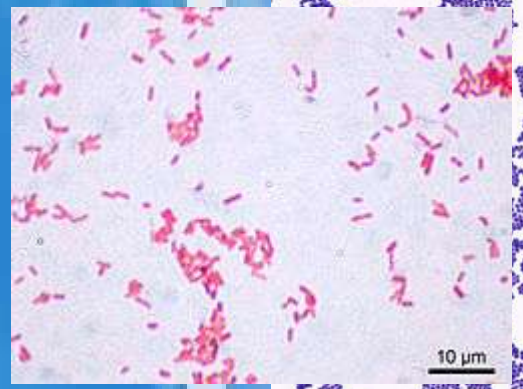


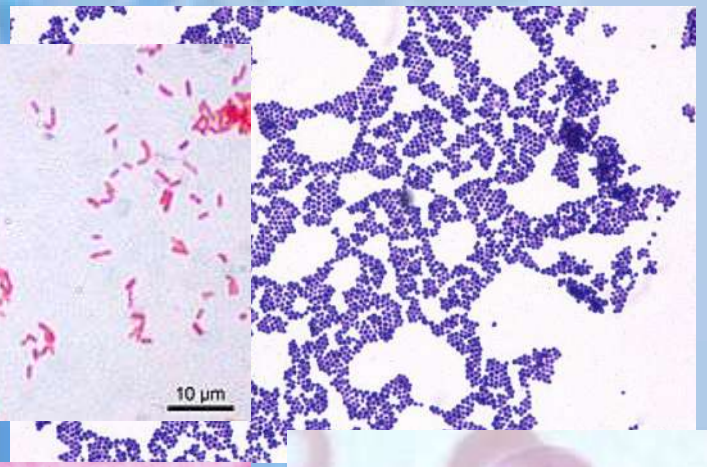


Traditional technics

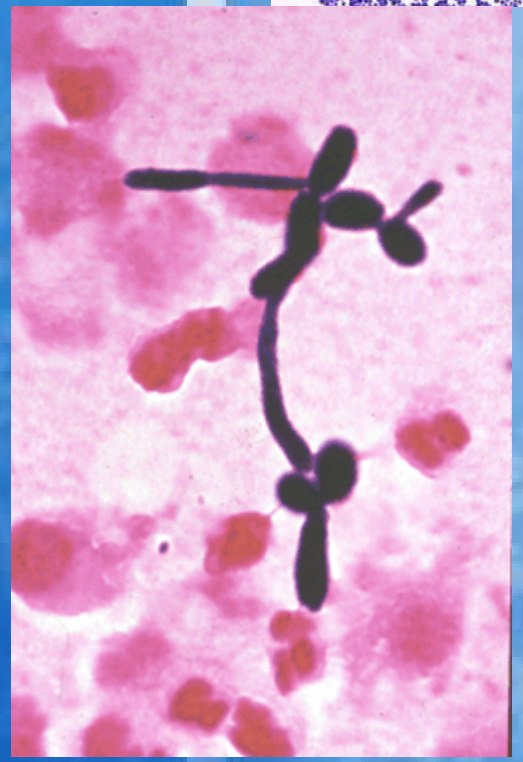
At least 24-48 hours…

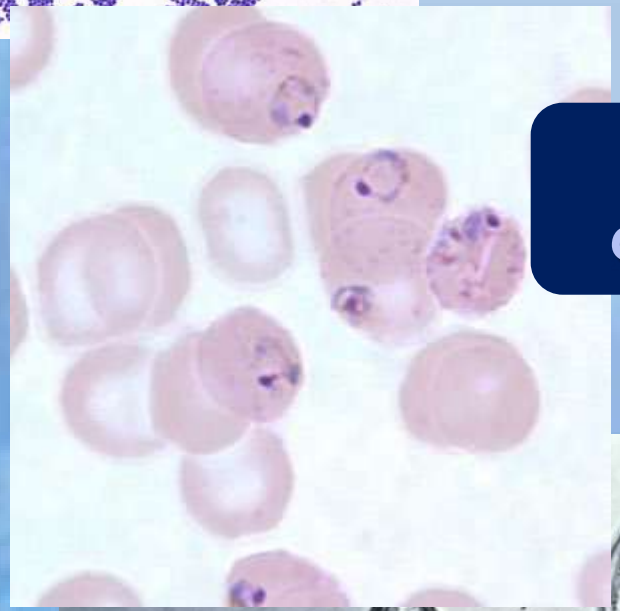
# Microscopy

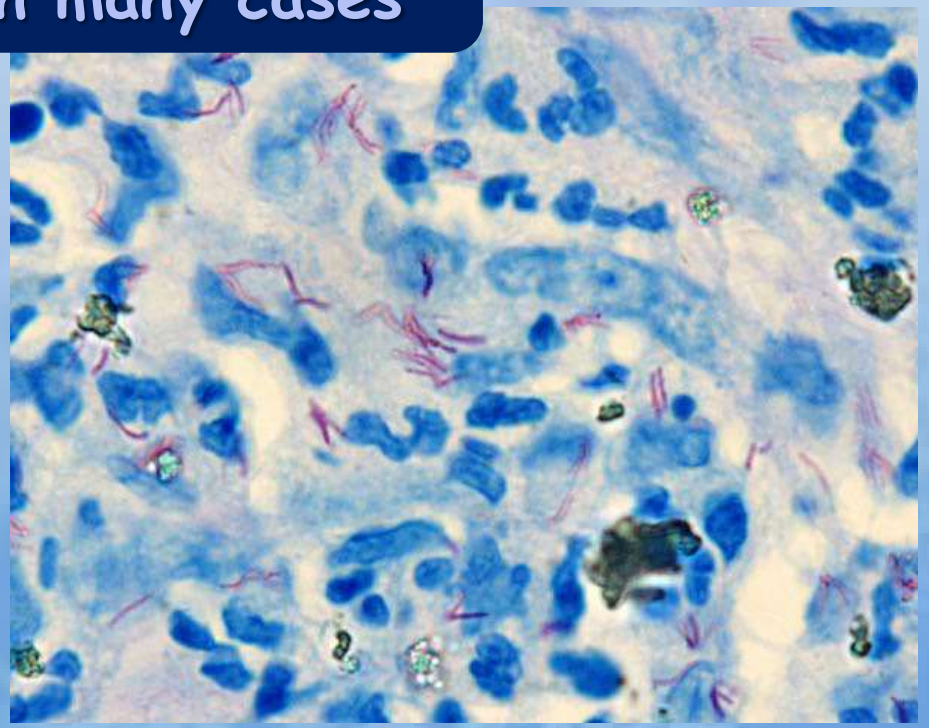


Rapid but accuracy is doubtful in many cases







- Roughly 50% of antibiotic treatments are started with wrong antibiotics…
- …and without a proper diagnosis of the pathogen …
- …every hour of delay in implementing an effective treatment in sepsis patients leads to a 7.6% increase in mortality..

The purpose is

**Personalised medicine:**

Using the right drug
for the indicated person
at the right time

# ESK/CAPE -bacteria

- *Enterococcus faecium*
- *Staphylococcus aureus*
- *Stenotrophomonas maltophilia*
- *Klebsiella pneumoniae*
- *Clostridioides difficile*
- *Acinetobacter baumannii*
- *Pseudomonas aeruginosa*
- *Enterobacter spp.*
- *Eserichia coli*

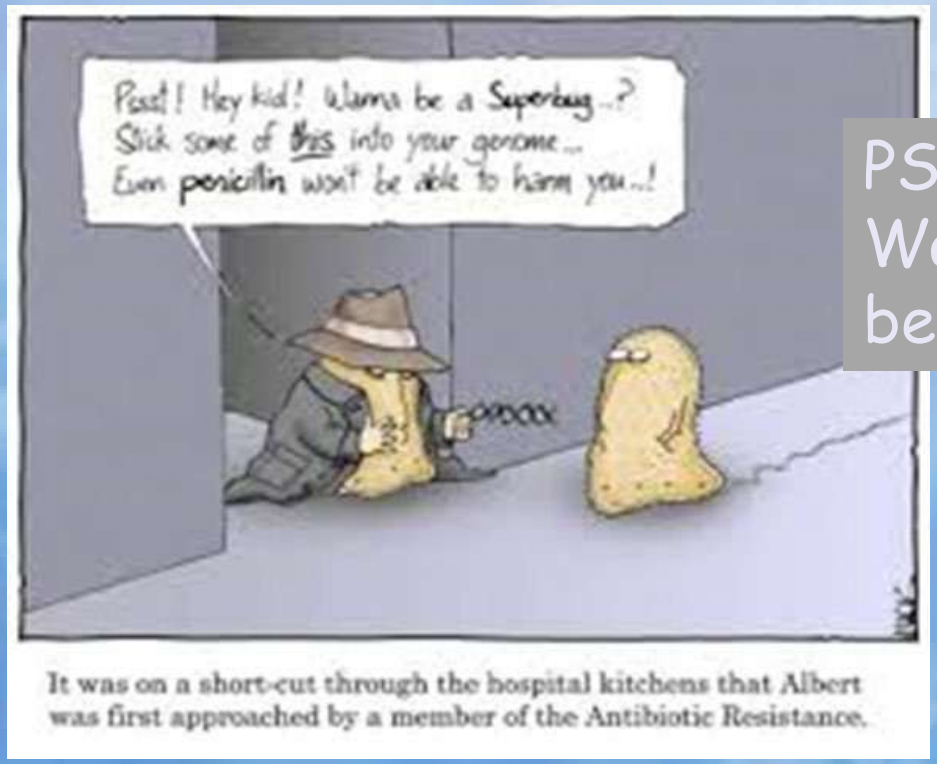
## Centers for Disease Control and Prevention:

- Carbapenem resistant Enterobacterales and carbepenem resistant *Acinetobacter* – urgent threats to public health…
- Extended spectrum β-lactamase producing Enterobacterales and multidrug resistant *Pseudomonas aeruginosa* – serious threats to public health…

- 59% mortality rate in blood stream infections (BSI) caused by ESBL-carrying Enterobacterales not correctly treated in 72 hours (18% - adequately treated)
- Mortality rates in BSIs caused by CRE organisms are 38% with appropriate therapy within 5 days vs 61% if delayed beyond 5 days
- MRSA BSIs have been associated with an excess length of stay of 9.2 days when compared to patients with MSSA infections
- A significant increase in mortality is associated with VRE comparing it to vancomycin sensitive Enterococcus

1. Tumbarello M, et al. Antimicrob Agents Chemother. 2007; 51(6):1987-94.
2. Gutierrez-Gutierrez B, et al. Lancet Infect Dis. 2017;17(7):726-734.
3. de Kraker ME, et al. PLoS Med. 2011; 8(10):e1001104.
4. DiazGrandos CA, et al. Clin Infect Dis. 2005; 41(3):327-33.

….we are hoping for a new test which is quick, sensitive and specific enough to enable us to choose the adequate antibiotics and make it possible to isolate the carriers to hinder the spread of the multiresistant strains…..




PSST! Hey kid!
Wanna
be a Superbag?..

…and they should be simple and affordable..

## ..at present significant changes occur in clinical microbiology laboratories led by automation …both in the field of identification of pathogens and resistance testing…

- Technological advances in molecular diagnostics (multiplex PCRs, Next Generation Sequencing…)
- MALDI-ToF – ID and detection of resistance markers
- Accelerate Pheno system (ID and phenotypic AST)
- mariAST®- Rapid phenotypic AST without pure culture (ID and phenotypic AST directly from sample)
- T2 magnetic resonance technology (ID and detection of resistance markers directly from sample….. )

# Rapid Diagnostic Tests

## ADVANTAGES

- Quick identification of the pathogen
- Quick detection of resistance markers
- Quick result of phenotypic antimicrobial susceptibility (directly from the sample or from the culture)
- Detection of nonculturable pathogenes
- Reduced overall hospital stay
- Improved patient outcomes in observational studies

## DISADVANTAGES

- Limited panel sizes
- Expensive to implement
- Require special training for the laboratory personnels
- Interpretation is sometimes complicated (viability, colonisation..)
- All systems require concurent conventional identification and antimicrobial susceptibility testing
- Co-implementation of ASP (Antimicrobial Stewardship Programs) may be required to appreciate full benefit

# Before implementation of a new test -

Assessement of the **clinical** utility should be conducted

- Local epidemiological data
- Antimicrobial stewardship programs (ASP)
- Rapid communication of results
- **Appropriate adjustment of antimicrobial therapy**


**RDT has an 80% chance of cost- effectiveness with ASP but only 41% in its absence (Blood culture)**

Pliakos EE, Andreatos N, Shehadeh F, et al. *Clin Microbiol Rev*. 2018;31(3):e00095-17.

# Sepsis

› The cornerstone of diagnosis is still blood culture,

Since the **positive culture is the prerequisite of AST**

(time to positivity depends not only on the CFU of the possible pathogen but on the nature of the bacterial strain)

**80% of sepsis death could be prevented with rapid diagnosis and treatment**

# Identification and antimicrobial sensitivity

- Traditional way – 24-48 hours or more….
- **Identification and resistance markers** directly from the positive bottle

MALDI-TOF (Peptide mass fingerprint)

multiplex PCR – based technology (BioFire-FilmArray…)

nanoparticle probe technology (Verigene Blood Culture Test)

**Providing actionable information much earlier**

**High positive predictive value** for on-panel targets

# But… limited targets…false negative results…

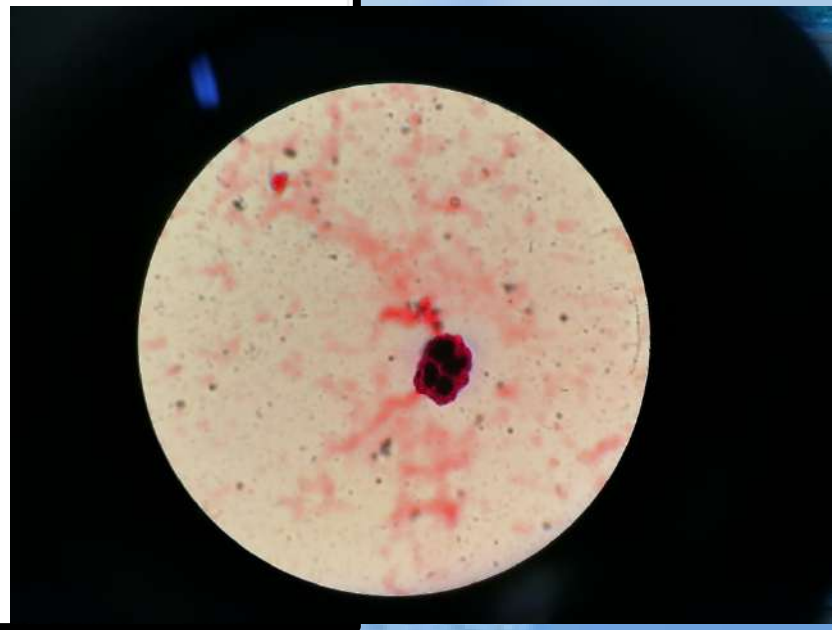
**BioFire-FilmArray Blood culture Panel2**

| Gram+ Bacteria | Gram– Bacteria |
|---|---|
| *Enterococcus faecalis* | *Acinetobacter calcoaceticus- baumannii complex* |
| *Enterococcus faecium* | *Bacteroides fragilis* |
| *Listeria monocytogenes* | *Enterobacterales* |
| *Staphylococcus* | *Enterobacter cloacae complex* |
| *Staphylococcus aureus* | *Escherichia coli* |
| *Staphylococcus epidermidis* | *Klebsiella aerogenes* |
| *Staphylococcus lugdunensis* | *Klebsiella oxytoca* |
| *Streptococcus* | *Klebsiella pneumoniae group* |
| *Streptococcus agalactiae* | *Proteus* |
| *Streptococcus pyogenes* | *Salmonella* |
| *Streptococcus pneumoniae* | *Serratia marcescens* |
| | *Haemophilus influenzae* |
| | *Neisseria meningitidis* |
| | *Pseudomonas aeruginosa* |
| | *Stenotrophomonas maltophilia* |

| Yeast | Antibiotic Resistance |
|---|---|
| *Candida albicans* | **Carbapenemases** |
| *Candida auris* | IMP |
| *Candida glabrata* | KPC |
| *Candida krusei* | OXA-48-like |
| *Candida parapsilosis* | NDM |
| *Candida tropicalis* | VIM |
| *Cryptococcus neoformans/gattii* | **Colistin Resistance** |
| | *mcr-1* |
| | **ESBL** |
| | CTX-M |
| | **Methicillin Resistance** |
| | *mecA/C* |
| | *mecA/C* and MREJ (MRSA) |
| | **Vancomycin Resistance** |
| | *vanA/B* |

***Cryptococcus neoformans***

**…missing from Panel1…**



- **Accelerate Pheno system** -Accelerate Diagnostics – automated rapid **identification** and **phenotypic AST directly** from **positive blood culture** bottle -

  utilizes for **ID FISH** technology & **MIC for AST**
- Turnaround time ≈ **7 hours**
- Compared with routine methods –

  sensitivity for ID : 95,6%

  specificity for ID : 99,5%

  agreement for AST : 95%  **BUT**

⇩

**… no ID and AST for Gram- positive rods, no AST for yeast…**

Charnot-Katsikas A, Tesic V, Love N, et al. *J Clin Microbiol*. 2017;56(1):e01166-17.

## Accelerate Pheno™ System

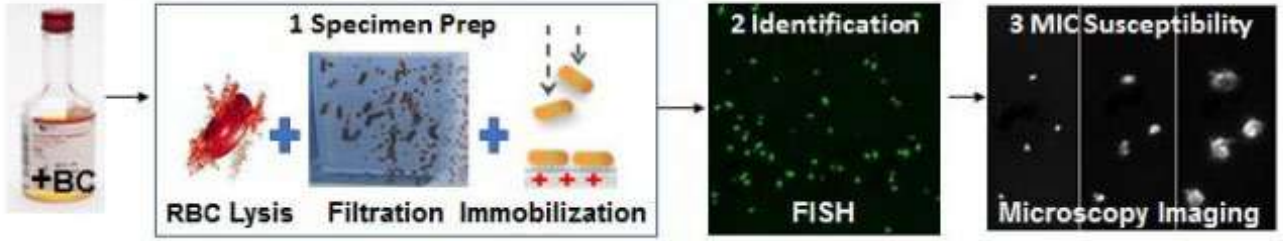
### System

- Automated Pipetting Robot
- Custom Microscope & Camera
- Multi Channel Fluidic Cassette

### Method

- Time-lapse imaging of bacterial growth
- Propriety Image Analysis Algorithm
- Translation of Bacterial Morphokinetics into Rapid MIC Results

### Process




**Fluorescence In Situ Hybridization**

**MIC**

This system lacks resistance gene testing

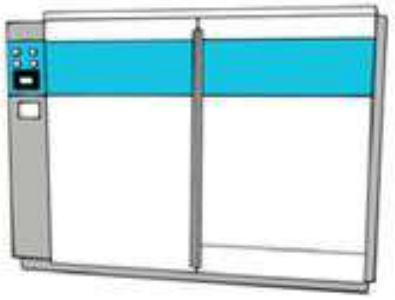
40 *E.coli*, *K.pneumoniae*, *P.mirabilis* strains were examined,
the CLSI ESBL confirmatory test was also evaluated.
ESBL production was well correlated with ceftriaxon nonsusceptibility.
These data support that ESBL production has a high likelihood of ceftriaxone non-susceptibility.

*Bhalodi AA, Magnano P 3rd, Humphries RM. Diagn Microbiol Infect Dis. 2020;98(4):115171.*

# Accelerate Pheno™ BC System = FAST Workflow

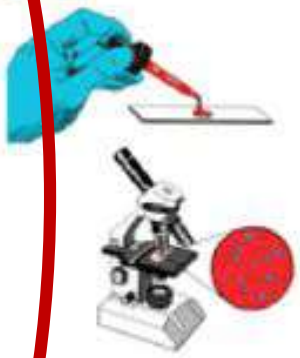
1 patient blood draw

2 blood bottle incubation & screen



Incubation depends on the organism's growth – typically from 6-18 hours

3 perform gram stain



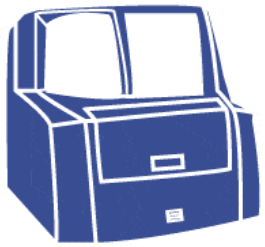
4 ID & susceptibility with MICs in < 7hrs

5 optimized therapy: de-escalate or escalate

**De-escalate or Escalate empiric antibiotic therapy**

**Place patients with MDROs on isolation precautions at 7hours**

# mariAST



mariAST

**Effective sample feed**
Continuous & Flexible
High capacity

**Short hands-on time**

**Easy to use**

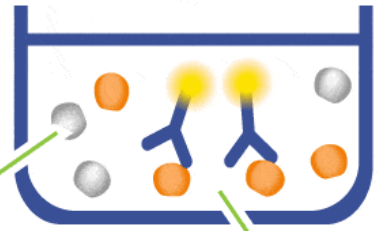
**POC**

**Real-time detection**

**Automated analysis and result read-out**

**Accurate and fast results**

Connection to laboratory information system



**Directly from polymicrobial samples**
containing commensal flora

**Bacterial in-well culture**
in the presence of antibiotic

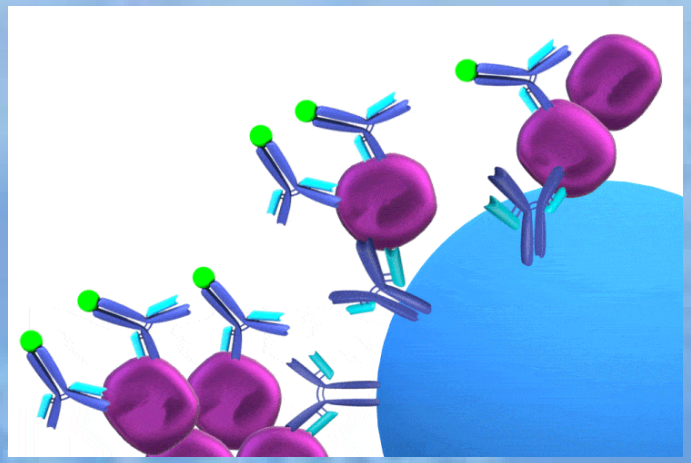
**Specific direct pathogen detection**

**Wash-free fluoroimmunoassay**

Research Use Only

combines in-well culture
(broth dilution - MIC)
and
specific bacterial detection
( fluoroimmunoassay)
ID in 20 minutes

**Directly from samples**
(polymicrobial..)

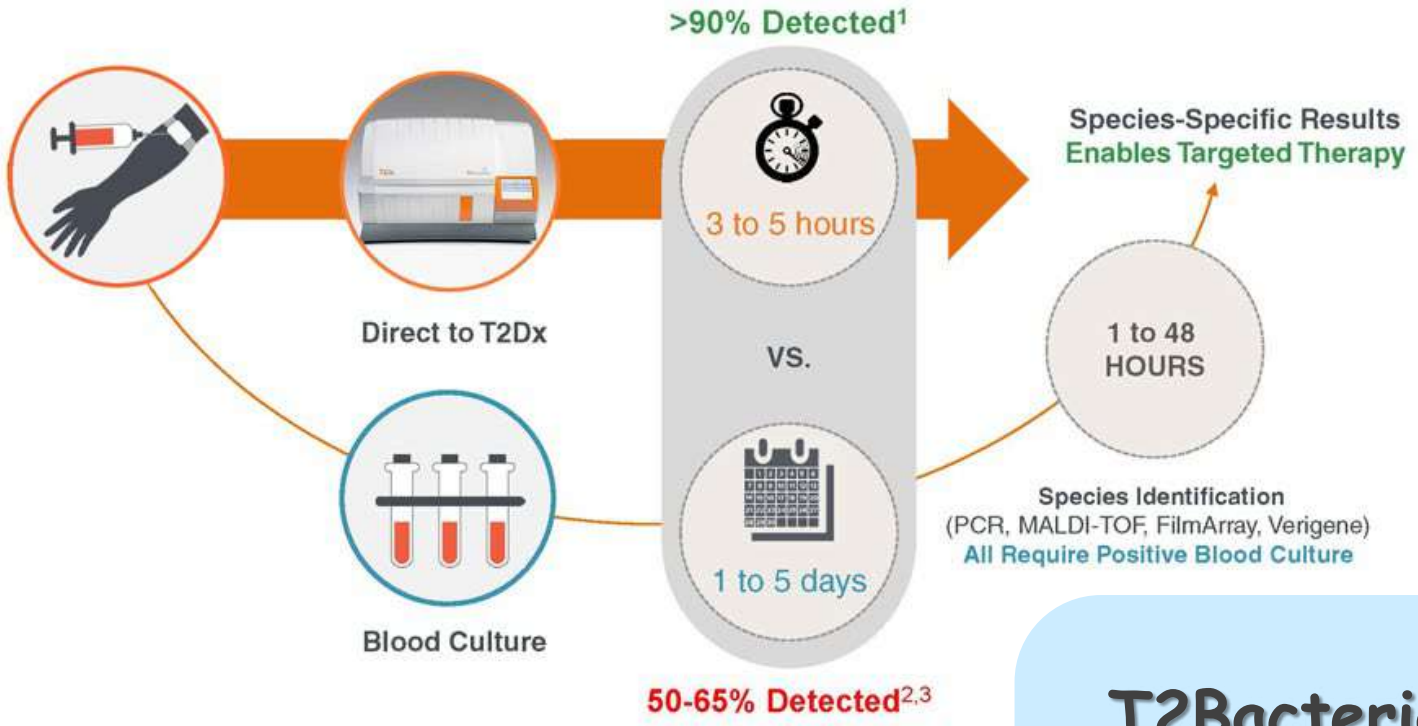


**Phenotypic antimicrobial sensitivity**

# T2MR: Establishing a New Standard in Sepsis Pathogen Detection

T2Biosystems

T2Sepsis diagnostics provide a faster and more accurate solution for sepsis pathogen detection




**T2MR**

**ID in ≈ 4 hours**

**Culture independent molecular Diagnostic method**

**T2Bacteria was positive in 3.2-fold more subjects with proven, probable or possible BSIs than were BCs**

1) Boucher et al. 2009; (2) Karlowsky, JA, et al. 2004; (3) T2Bacteria pivotal clinical study, 2018; (4) Combination of contrived (97% PPA) and prospective data (90% PPA).

## T2 magnetic resonance

Detecting amplified DNA from microbial cells **directly in whole blood**

### CANDIDA PANEL

- C. albicans
- C. tropicalis
- C. glabrata
- C. kruzei
- C. parapsilosis
- Sensitivity: 90%
- Specificity: 98%

### BACTERIAL PANEL

- E. coli
- K. pneumoniae
- P. aeruginosa
- A. baumannii
- S. aureus
- E. faecium
- Sensitivity: 89%
- Specificity: 98%

**13 resistance genes can be detected**

Sensitivity:91%

Specificity:98%

# T2Bacteria panel

- Limited only to 5 bacteria…(common ESKAPE pathogens)
- Negative predictive value:99,7% (for the 5 pathogens…)
- 10% false-positive (60% of it with probable/possible BSIs…)
- Nguyen MH, Clancy CJ, Pasculle AW, et al. *Ann Intern Med*. 2019;170(12):845-852.
- **25% more positives** were detected than blood culture (true positives??)
- ..covered 70.5% of all species detected by blood culture…
- Voigt C, Silbert S, Widen RH, et al. *J Emerg Med*. 2020;58(5):785-796.
- Among the probable and possible BSIs discrepancies appeared to be associated with closed space and localised infections (abscess, pyelonephritis, infected hematoma, osteomyelitis, pneumonia…) and recent use of antibiotics.
- Kalligeros M, Zacharioudakis IM, Tansarli GS, et al. *BMC Infect Dis*. 2020;20(1):326

# Candidemia -T2Candida PPV – 25-60%, NPV – 89-100%

Giannella M, Paolucci M, Roncarati G, et al. Potential role of T2Candida in the management of empirical antifungal treatment in patients at high risk of candidaemia: a pilot single-centre study. *J Antimicrob Chemother*. 2018;73(10):2856-2859. Clancy CJ, Pappas PG, Vazquez J, et al. Detecting infections rapidly and easily for candidemia trial, part 2 (DIRECT2): a prospective, multicenter study of the T2Candida Panel. *Clin Infect Dis*. 2018;66(11):1678-1686.

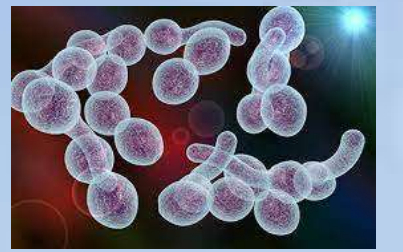
## Use of T2Candida was reported to **reduce times to appropriate antifungal therapy**, shorten courses of empirical therapy, and **save** an average of **US$**280 in antifungal costs per patient tested

Patch ME, Weisz E, Cubillos A et al. Impact of rapid, culture independent diagnosis of candidemia and invasive candidiasis in a community health system. JAntimicrobChemother 2018; 73 Suppl4:iv27–30

## Significant hospital cost savings have been seen due to **length of stay reductions** of 4-8 days

Kenney, R., Dwivedi, S., Kendall, R. et al. Implementation of T2 Magnetic Resonance into the Antimicrobial Stewardship Program Improves Management of Candidemia at HFHS. Poster Presentation IDWeek 2016.

T2MR - greater than **7-fold reduction in time to appropriate therapy** (5 hours vs. 39 hours prior to implementation of T2MR)



Mylonakis, E., Clancy, C.J., Ostrosky-Zeichner, L., et al. (2015). Clinical Infectious Diseases

*Candida* was definitively **identified in 93% of patients after implementation of T2MR** and in only 57% of patients prior to implementation of T2MR

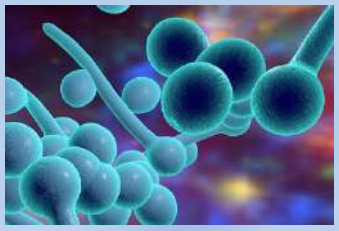
Nicole M. Wilson, George Alangaden, Robert J. Tibbetts, Linoj P. Samuel, Susan L. Davis, Rachel M. Kenney (2017); T2 Magnetic Resonance Assay Improves Timely Management of Candidemia. JAMS 2017; 1:12-18.

Negative T2 tests resulted in discontinuation of antifungal therapy in 23% and avoid antifungal therapy initiation in 41% of patients but **36% of patient's antifungal regimens were not discontinued despite a negative T2 result.**

Kateon H et al. Utilization of T2Candida Panel for the rapid detection of Candida species in a large community hospital. Poster Presentation IDWeek 2016.

- **Deep-seated invasive candidiasis** without candidemia: 27-33% positivity rate (culture positive, BC negative)


- Zurl C, Prattes J, Zollner-Schwetz I, et al. T2Candida magnetic resonance in patients with invasive candidiasis: strengths and limitations. *Med Mycol*. 2020;58(5):632-638 Lamoth F, Clancy CJ, Tissot F, et al. Performance of the T2Candida panel for the diagnosis of intra-abdominal candidiasis. *Open Forum Infect Dis*. 2020;7(3):ofaa075.

- **Antifungal deescalation** based solely on a negative result especially in patients with a high clinical suspicion of invasive candidiasis is **controversial….**

- In two publications only 27-47% of patients had their empiric antifungal therapy discontinued due to the negative TRCandida result ….

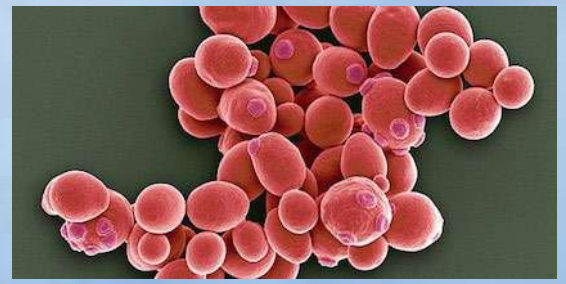

- Patch ME, Weisz E, Cubillos A, Estrada SJ, Pfaller MA. Impact of rapid, culture-independent diagnosis of candidaemia and invasive candidiasis in a community health system. *J Antimicrob Chemother*. 2018;73(suppl 4):iv27-iv30 Steuber TD, Tucker-Heard G, Edwards J, Sawyer A, Thottacherry E, Hassoun A. Utilization and impact of a rapid candida panel on antifungal stewardship program within a large community hospital. *Diagn Microbiol Infect Dis*. 2020;97(4):115086.

# Invasive candidiasis has a high mortality rate – ≈ 60% in cases of septic shock

Kollef M., Micek S., Hampton N., Doherty J.A., Kumar A. Septic shock attributed to *Candida* infection: Importance of empiric therapy and source control. *Clin. Infect. Dis.* 2012;54:1739–1746

- As much as 50% reduction in mortality can be achieved with prompt initiation of appropriate antifungal therapy and source control

Clancy CJ, Nguyen MH. *Curr Opin Infect Dis.* 2019;32(6):546-552.



- Blood culture – far from beeing ideal

2-3 days (ranging from 1-7 days)

possibility of negative growth in deep-seated candidiasis

(≈ 80% intra abdominal candidiasis…)

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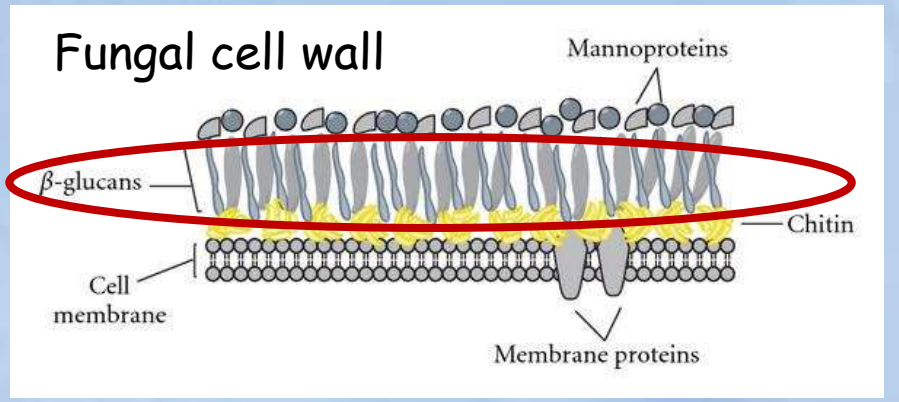
result is – overuse of empiric antifungal therapy for suspected invasive candidiasis

# Serological tests for fungal infections




› **Beta –D-glucan (BDG) test**

(clotting pathway is involved)

BDG - component of the cell wall

in *Candida spp.,Aspergillus spp.,*

***Pneumocystis jirovecii***, *Fusarium spp.*

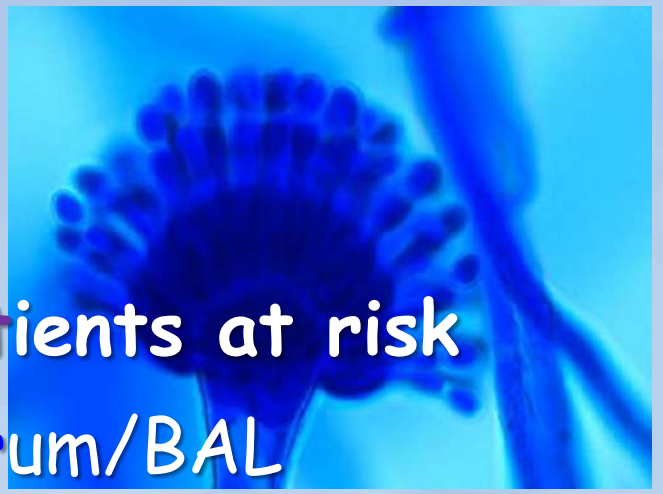
But *Mucorales, C. neoformans, B. dermatitidis* – missing

94.8 % sensitivity & ≈95% negative predictive value

**Cross reactivity** – false-**positive results:** hemodialysis, Immunglobulin therapy, albumin therapy selected antimicrobials, gauze (surgical procedures)

False-negative: due to lower systemic fungal burden…

# Aspergillus antigen detection



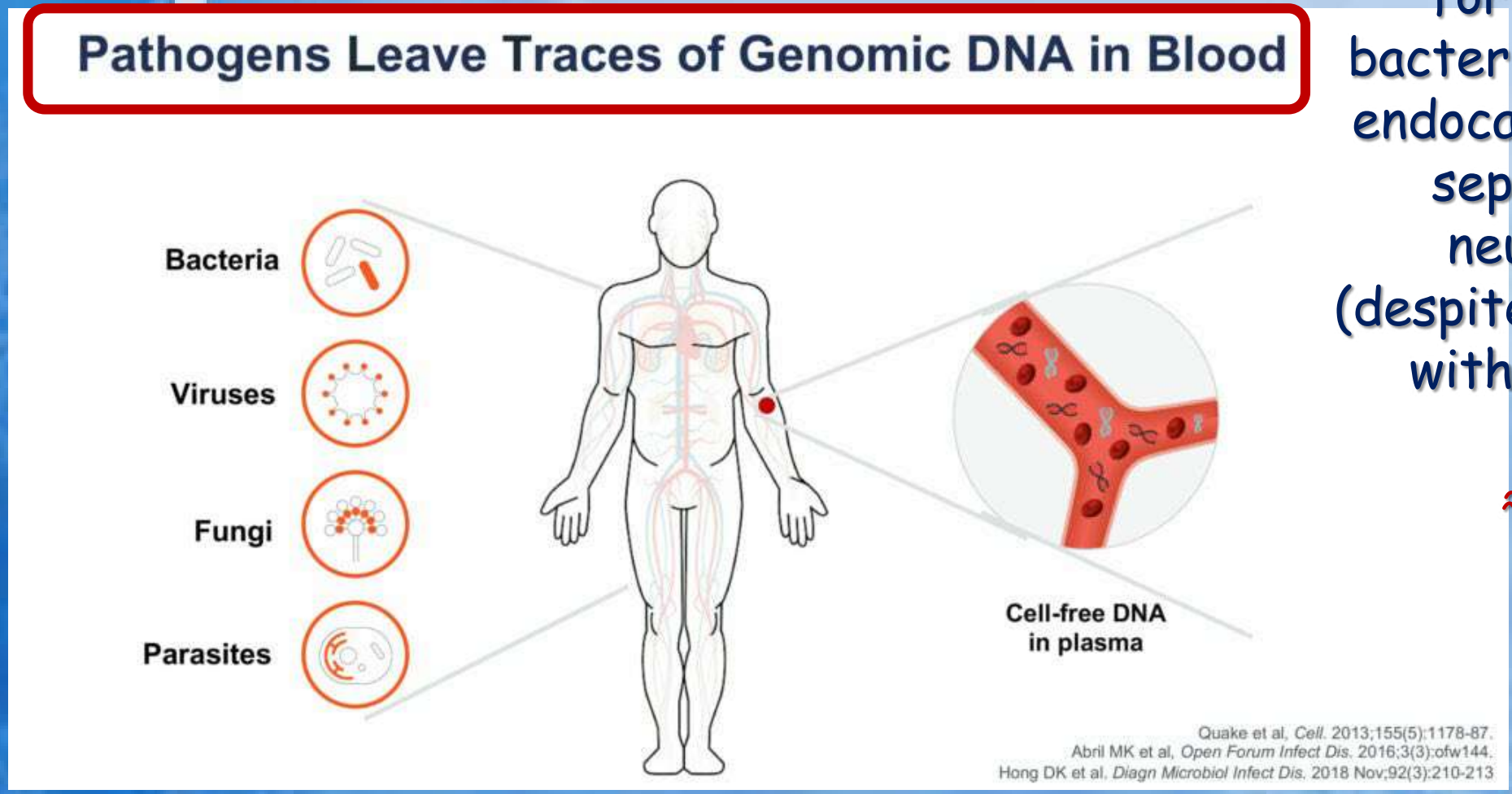
- Low sensitivity ➡ serial testing for patients at risk
- Positive predictive value: 77,8/86,2% serum/BAL
- **Negative predictive value: 92,9/95,2% serum/BAL**

| | EUROIMMUN Aspergillus Antigen ELISA (cut-off: ratio 0.4**) | Bio-Rad Platelia Aspergillus Ag ELISA (cut-off: ratio 0.5) |
|---|---|---|
| Sensitivity | 56% | 47% |
| Specificity | 97% | 99% |

*Dichtl et al., J. Clin Microbiol, Apr 2019

**Varies from the cut-off recommended by the manufacturer

# Karius Test - non invasive blood test - uses next-generation sequencing (NGS) of microbial cell-free DNA




Identifying etiologies for pneumonia, bacteremia, infective endocarditis, general sepsis…febrile neutropenia… (despite pretreatment with antibiotics)

Detection of
≈750 types of bacteria
≈100types of DNA viruses
≈350 types of fungi (mold/yeast)
parasites

| | KARIUS TEST | Specialized Culture | Urinary Antigen Test | PCR Test |
|---|---|---|---|---|
| **Specimen Type** | Plasma | Lower respiratory secretion, lung tissue, pleural fluid | Urine | Lower respiratory secretion, lung tissue, pleural fluid |
| **Turnaround Time** (after specimen receipt) | 1 day* | 7-16 days | 1-3 days | 1-3 days |
| **Detectable *Legionella* species** | 33 *Legionella* species | *Legionella* species | *L. pneumophila* serotype 1 | Varies depending on assay at laboratory |
| **Availability** | Sendout test | Generally a sendout test, but dependent on in-house capabilities | Generally a sendout test, but dependent on in-house capabilities | Generally a sendout test, but dependent on in-house capabilities |

„A 5 year-old child with leukemia with fever and neutropenia was admitted to the hospital
Blood cultures were positive – *K. pneumoniae* – Cefepime therapy cleared the fever…
Fever came back, blood cultures and PCR test were negative this time.
Karius test detected *Rhizopus oryzae* – the patient received targeted therapy and recovered." (Tim Blawkamp Chief Scientific Officer of Karius)

**Deep infections** require invasive organ biopsies to identify the pathogen.

By sequencing the genomic DNA fragments left in the blood by deep-seated infections, **diagnostic biopsies can often be avoided.**

**„Liquid biopsy"**

In invasive mold infections (IMI), among patients with haematological disorders NGS was able to detect both biopsy-proven/probable Aspergillus IMI with a sensitivity of 51%.

Specificity and PPV was estimated 100% (no findings of false positive in controls)…NPV 81-99%...

**NGS combined with serum galactomannan:sensitivity 84%**

**in proven/probable IMI**

Hill JA, Dalai SC, Hong DK, et al. *Clin Infect Dis.* 2020;ciaa1639.

- 53 adults with hip or knee periprosthetic joint infections
- Both peripheral blood NGS and standard-of-care intraoperative tissue and synovial fluid cultures were done
- Positives cultures – 46/53 (87%)
- NGS identified the joint pathogen in 35/53 cases (66%)
- NGS was positive in 4 cases which were culture negative

- **NGS increased the detection rate from 87% to 94%**

  **as an adjunct to cultures**

- **14 additional organisms were detected by NGS, not grown in cultures**

Cheverria AP, Cohn IS, Danko DC, et al. *J Bone Joint Surg Am*. 2021 Jul 22.

# Respiratory infections

- Difficulties in **distinguishing** between **bacterial** and **viral** etiologies in LRTIs (lower respiratory tract infections)

⇩

Overuse of antibiotics

- First step – **Procalcitonin** guided antibiotic stewardship

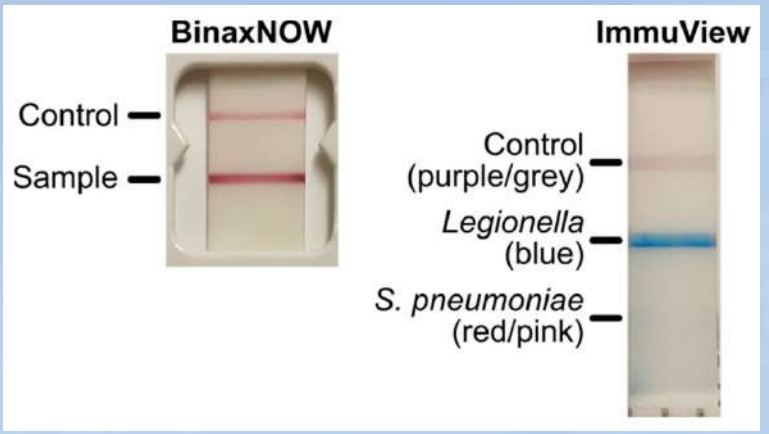
⇩

2,4-day reduction in antibiotic exposure

Schuetz P, Muller B, Christ-Crain M, et al. *Cochrane Database Syst Rev.* 2012(9):CD007498.

- ..but specificity and sensitivity are **too low**... to provide reliable evidence.....

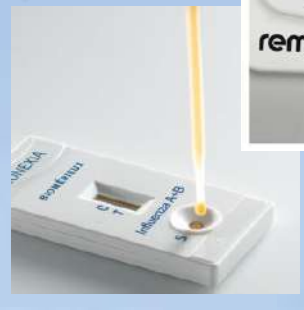
# Immunchromatography




- ***S. pyogenes*** – pharyngeal swab – 15 minutes, sensitivity/specificity 85%/95%
- ***L. pneumophila*** (O1),– **urine** sample (Legionella – 55 spp., 70 serogroups…) sensitivity/specificity 70-90%/90-100% - (NAAT > 95% in both)
- ***S.pneumoniae*** – **urine** sample – sensitivity: 60-75% (higher in bacteraemic pneumococcal pneumonia) specificity: 95-99%

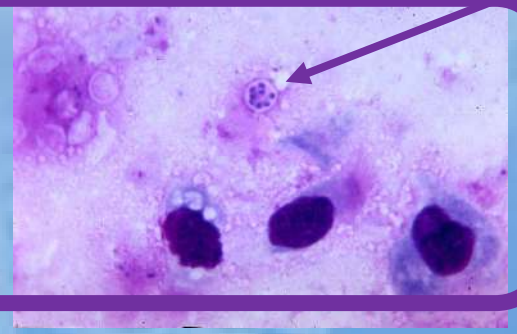
**(real-time PCR – high sensitivity but even if the measurement of „pneumococcal burden" in the respiratory sample is possible – the clinical implementation of the result is challenging)**

# Viral respiratory infections – Immunchromatograpy & NAAT

- **Children** – respiratory virus –
- 50% *CAPs*, 90% bronchiolitis, 85% asthma attacks
- **Adults** – respiratory virus –
  20-40% *CAPs*, 30-50% *COPD* attacks, 50-70% asthma attacks
- Mainly 20 types of viruses are involved – *Influenza A/B, RSV, Rhino, Adeno, parainfluenza 1-4, Corona….*
- Owing to their **high sensitivity**, NAATs are capable of detecting asymptomatic excretion or very low viral loads of dubious clinical significance.
- **Multiplex PCR**-respiratory panels with viral, bacterial pathogens and

***Pneumocystis jirovecii*** **- 100 times more sensitive than microscopy…. High sensitivity surves to rule out involvement of. *P. jirovecii***

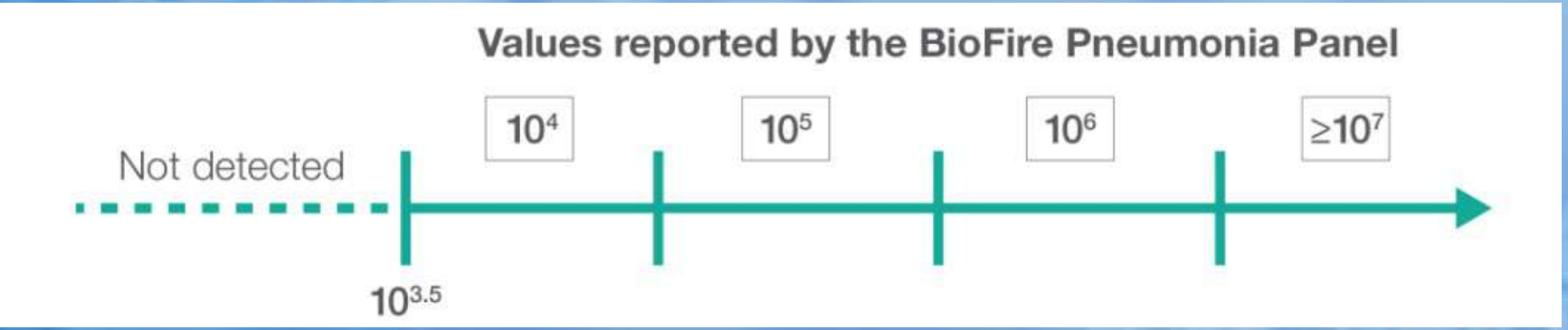


# Multiplex respiratory PCR panels … different numbers of targets, resistance markers are also detected…

- **BioFire-FilmArray pneumonia panel** – 8 viruses, 15 bacteria, 3 atypical bacteria, 8 resistance genes…

396 endotracheal and BAL samples – sensitivity 97,8% specificity 80,4%
PPV 80%, NPV 97,8 – for bacterial pathogens compared with culture – semiquantitative copy numbers were strongly correlated with the report of WBC count on initial Gram stain and conventional bacterial semiquantitation

Rand KH, Beal SG, Cherabuddi K, et al. *Open Forum Infect Dis*. 2021;8(1):ofaa560.



› The BioFire-FilmArray Pneumonia Panel may be useful

⇩

to rule out bacterial coinfection & avoid inappropriate prescribing of antibiotics …

BUT

Deescalation 63/159 (40%),
escalation 35/159 (22%)
Monard C, Pehlivan J, Auger G, et al. *Crit Care*. 2020;24(1):434.
(Retrospective multicenter study)

**positive results should be accepted with caution…**

eg.: Positive results of detected CTX-M and carbapenemase resistance genes could not be definitely linked to the microorganism detected…

⇩

**Panel results should be used with culture results to confirm susceptibility and resistance.**

# Surveillance and RDT – **MRSA nasal PCR** (Cepheid GeneXpert)

MRSA nasal PCR – to rule out MRSA pneumonia – **NPV 95%**

Parente DM, Cunha CB, Mylonakis E, et al. *Clin Infect Dis*. 2018;67(1):1-7.

Combined with ASP intervention – 2,1 days decrease of Vancomycin use

Willis C, Allen B, Tucker C, et al. *Am J Health Syst Pharm*. 2017;74(21):1765-1773.

Vancomycin avoidance in suspected/confirmed pneumonia in the ICU with MRSA nasal screening - $108 cost avoidance per patient (surveillance testing, vancomycin therapy and drug monitoring)

Smith MN, Erdman MJ, Ferreira JA, et al. *J Crit Care*. 2017;38:168-171.

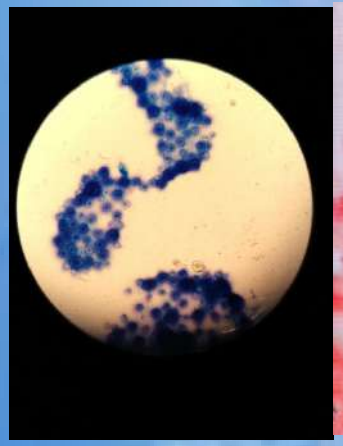
MRSA nasal PCR holds its **NPV for 7 days** after results

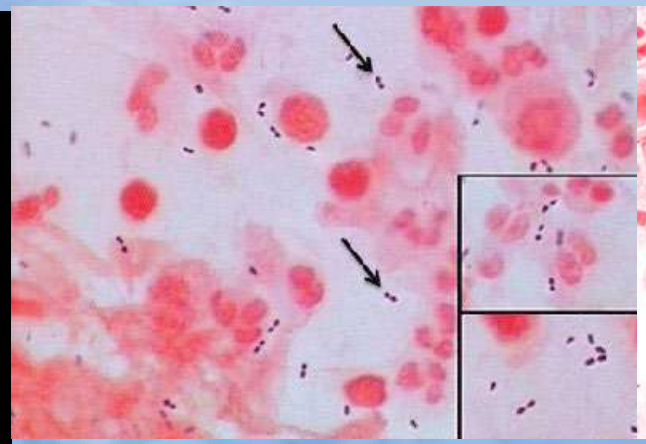
Smith MN, Brotherton AL, Lusardi K, et al. *Ann Pharmacother*. 2019;53(6):627-638.

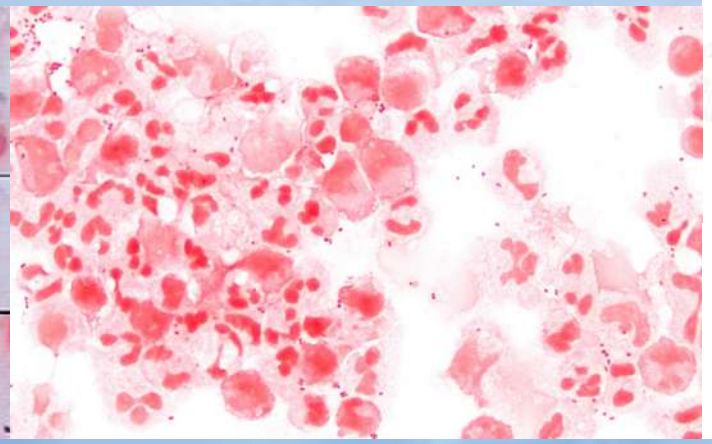
Carr AL, Daley MJ, Givens Merkel K, et al. *Pharmacotherapy*. 2018;38(12):1216-122

# Central nervous system

- In bacterial meningitis CSF cultures are positive:70-85% (without prior antibiotic treatment)
- In viral encephalitis > 10% CSF normal





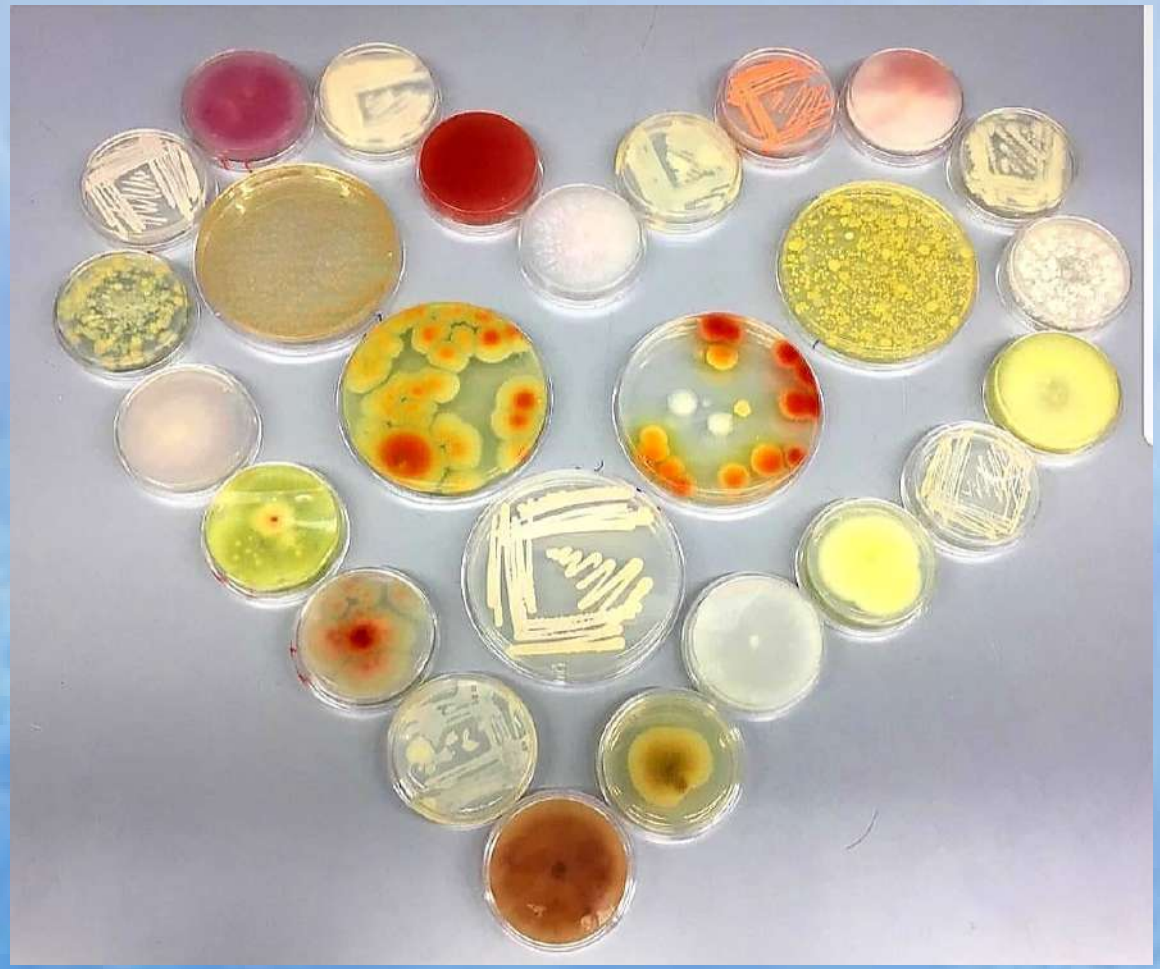


Latex agglutination test

- BioFire-FilmArray - and other **multiplex PCR** meningitis panels…**Quick and accurate result**
- But culturing is still the gold standard…..

# Gold standard is still culturing….

## for several reasons..



- **RDTs** are useful for the diagnosis of many infections facilitating a **better approach to infection** in all its aspects…
- RDTs for detecting **antigens** can be used **as POCTs…**
- **Nucleic acid amplification tests and other products of new technological advances** show higher percentages of specificity and sensitivity – even too sensitive…**before accepting the result as a solution of the given infectious case it should be taken into a sober consideration…**
- Use of different technics at the same time adds a special value to the final diagnosis…
- **Without ASP the value of RDT is much less…**

Future is like blooming flowers – continuous development - promising more accurate results and better timing

..but we should never forget the value of the traditions …..

Traditional and new technology –

## Let's keep in touch!

AMRDETECTOOL
Detection in 30 min

# Thank you for your attention!