New microbiological identification techniques And Point of Care Labs

Brief survey from a clinical point of view

CASE REPORT 1

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL
Farrin A, N Engl J Med 2015; 372:1454-146

A 28 Y.O. Woman with Headache, fever and rash

Culture of 2 blood samples from ED
Growth detected after 24 H in aerobic bottles
Gram staining: Gram – diplococci with coffee bean shape
after sub culture on solid medium

Identification by MALDI TOF MS: N. meningitidis

Case report 2

International Journal of Infectious Diseases 33 (2015) 196–198

Contents lists available at ScienceDirect

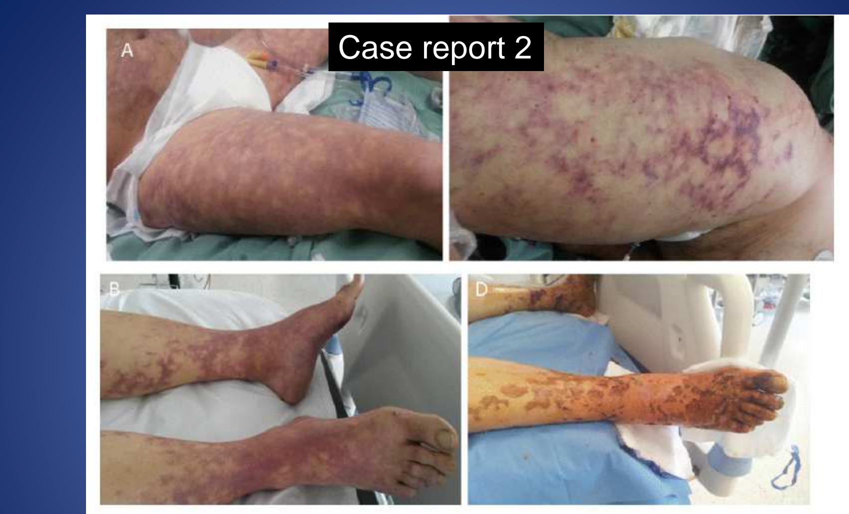
International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Case Report

Acute generalized livedo racemosa caused by *Capnocytophaga canimorsus* identified by MALDI-TOF MS

Adamantia Sotiriou[a], Stefania Sventzouri[b], Martha Nepka[c], Eleni E. Magira[a,*]



Blood culture on day 1 revealed a slow-growing unidentifiable Gram –

MALDI-TOF MS was applied to the colony specimen.

Unique molecular fingerprint of the organism identified it as C. canimorsus.

Classical steps in clinical microbiology
(bacterial infectious disease) since > 50 years

1 To grow an isolate from a biological specimen (ideally before first antibitherapy) :
blood, urine, CSF, BAL, sputum, stool, tissue sample from operating room …(rich or selective media)

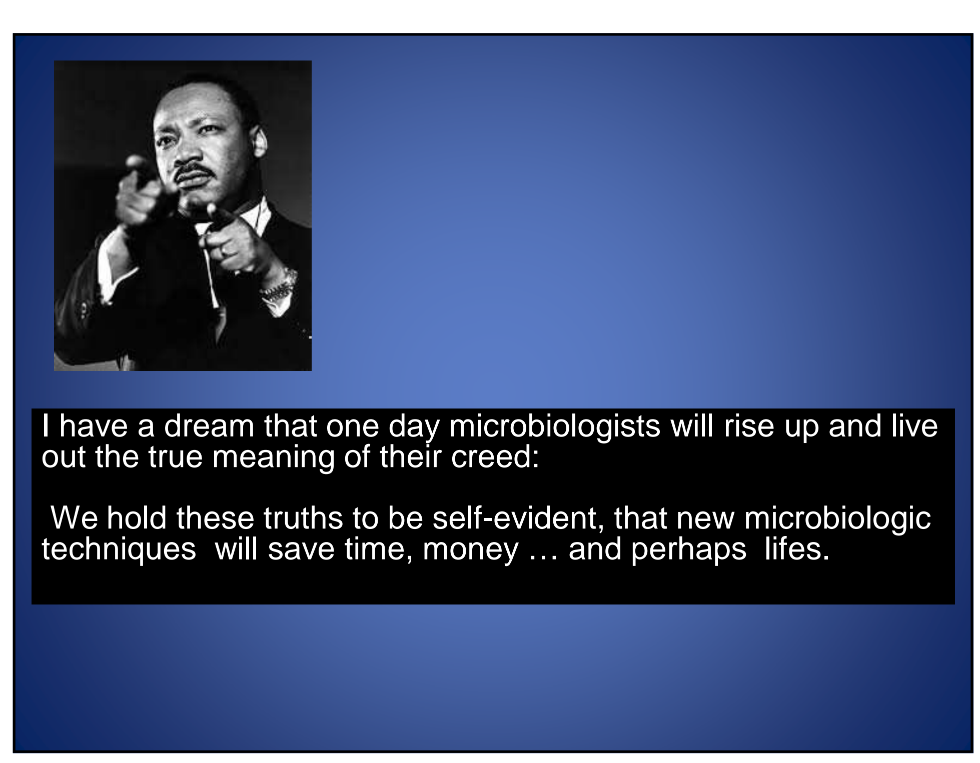
2 To identify genius, species (+/- strain): Gram staining + biochemical properties

3 To determine its pathogenic character

4 To test its susceptibility to antibiotics.

From two days (E. Coli) to 3 months (M. tuberculosis)

In E.D. we already have some fast, overnight, POC tests in case of sepsis :
- PCT
- Arterial lactate
- --
Antigenuria :Legion and pneumoc
Influenza A and B rapid test
Plasmodium Blood smear
Fast and precious
2014


I have a dream that one day microbiologists will rise up and live out the true meaning of their creed:
We hold these truths to be self-evident, that new microbiologic techniques will save time, money … and perhaps lifes.

New microbiological identification techniques
And Point of Care Labs

1 MALDI TOF MS
2 Multiplex PCR
3 (Fast) Whole Genome Sequencing
4 Fluorescent in situ hybridization FISH
5 Flow cytometry

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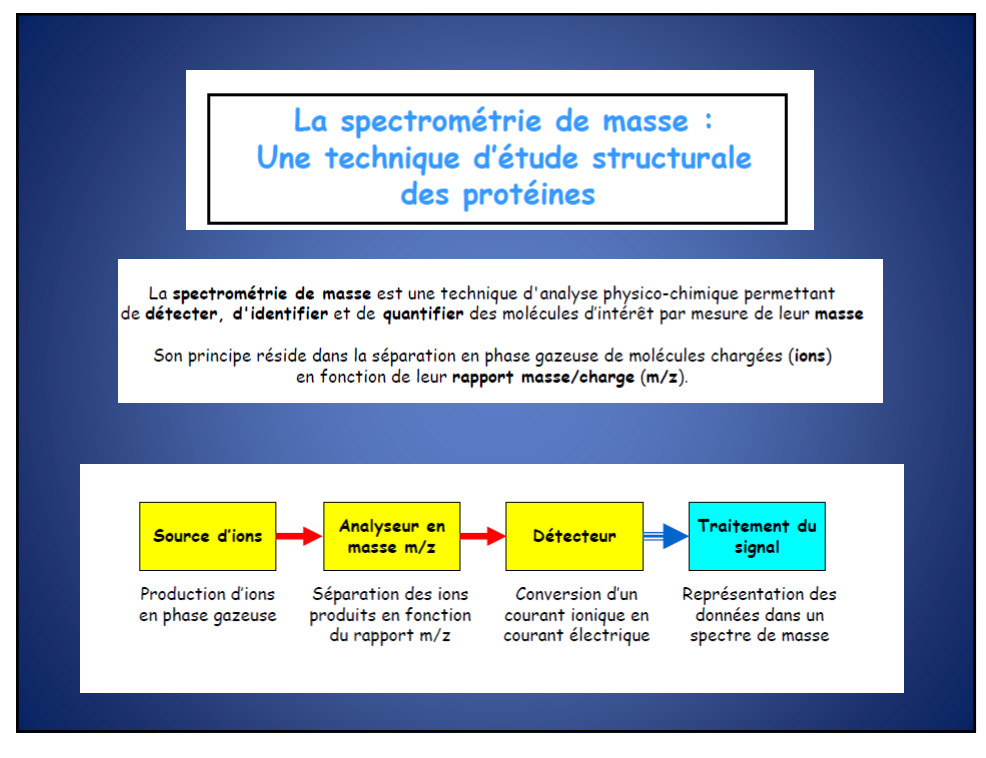
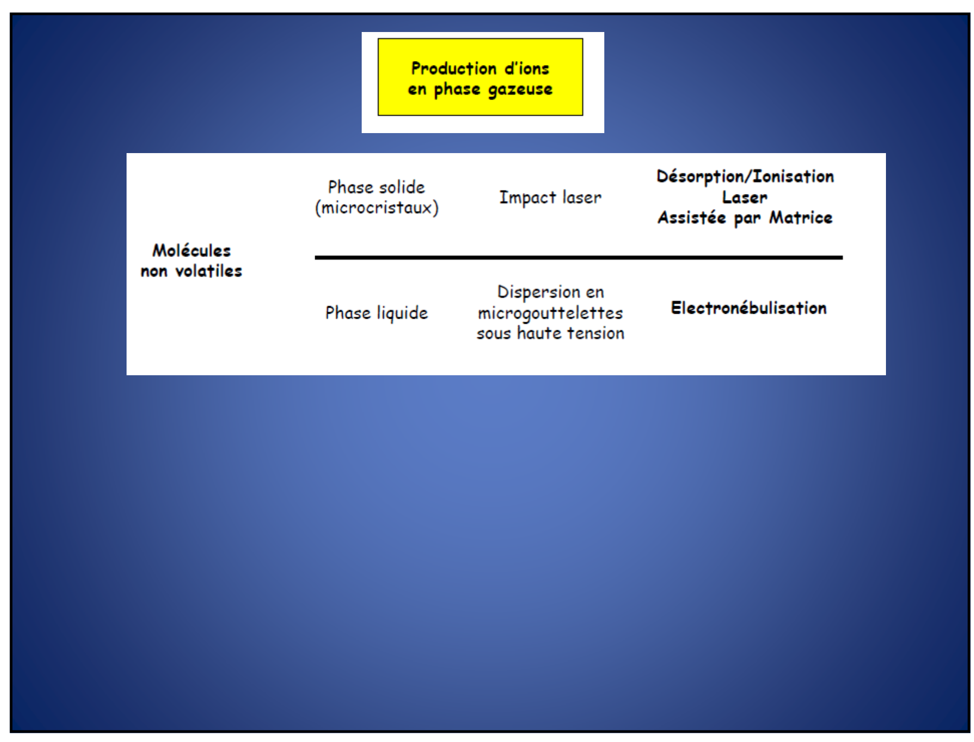
MALDI TOF MS

Matrix assisted laser desorption ionization

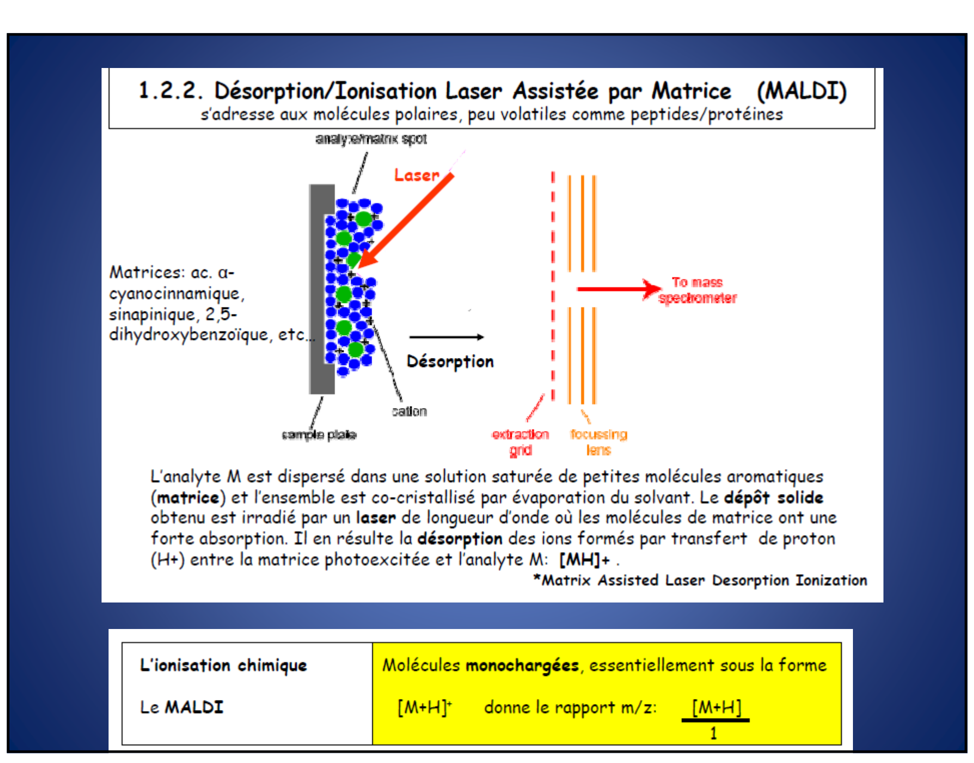
Time Of Flight

Mass Spectrometry

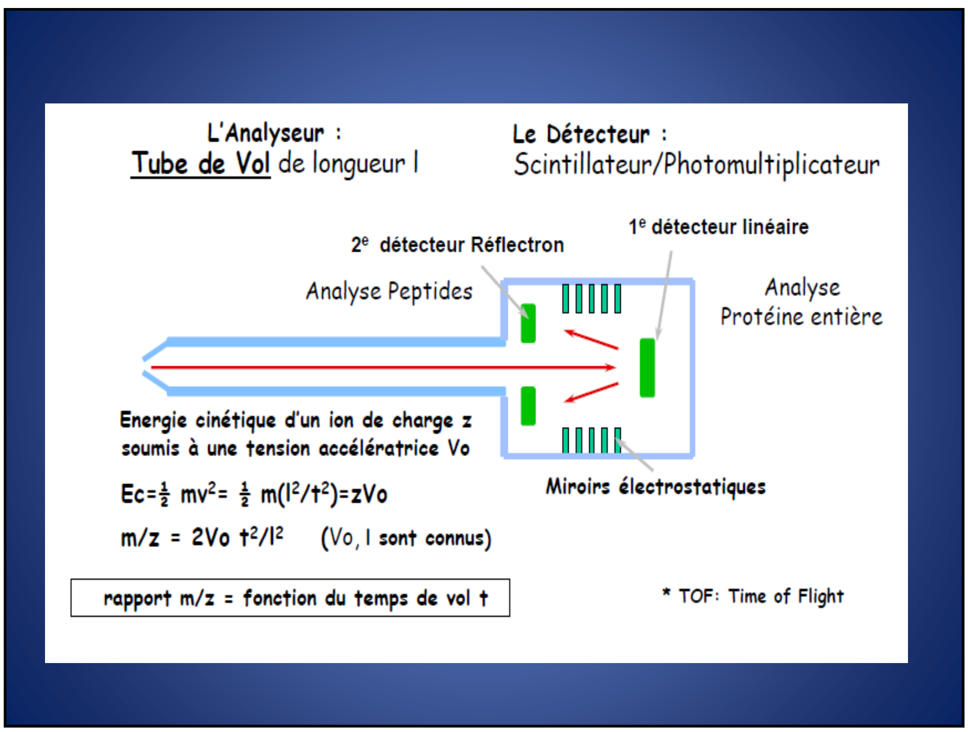




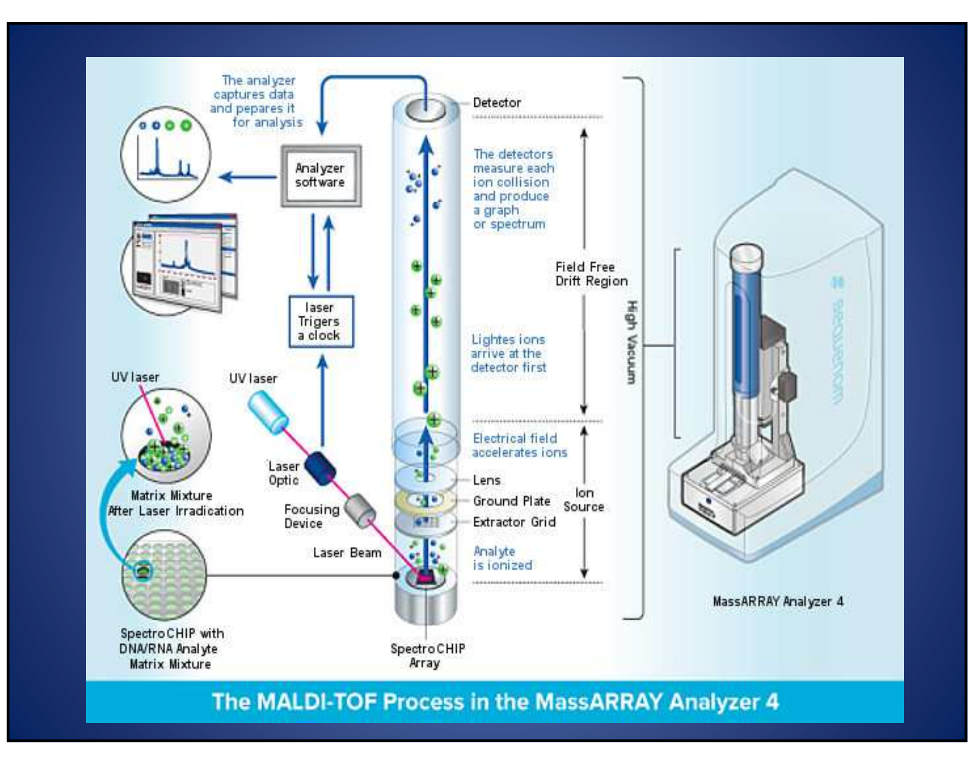
Production d'ions
en phase gazeuse
Molécules
non volatiles
Phase solide
(microcristaux)
Impact laser
Désorption/Ionisation
Laser
Assistée par Matrice
Phase liquide
Dispersion en
microgouttelettes
sous haute tension
Electronébulisation



1.2.2. Désorption/Ionisation Laser Assistée par Matrice (MALDI)
s'adresse aux molécules polaires, peu volatiles comme peptides/protéines
analyte/matrix spot
Laser
Matrices: ac. α-cyanocinnamique, sinapinique, 2,5-dihydroxybenzoïque, etc..
To mass spectrometer
Désorption
cation
sample plate
extraction grid
focussing lens
L'analyte M est dispersé dans une solution saturée de petites molécules aromatiques (matrice) et l'ensemble est co-cristallisé par évaporation du solvant. Le dépôt solide obtenu est irradié par un laser de longueur d'onde où les molécules de matrice ont une forte absorption. Il en résulte la désorption des ions formés par transfert de proton (H+) entre la matrice photoexcitée et l'analyte M: [MH]+ .
*Matrix Assisted Laser Desorption Ionization
L'ionisation chimique
Le MALDI
Molécules monochargées, essentiellement sous la forme
[M+H]+ donne le rapport m/z: [M+H] / 1



L'Analyseur :
Tube de Vol de longueur l
Le Détecteur :
Scintillateur/Photomultiplicateur
1e détecteur linéaire
2e détecteur Réflectron
Analyse Peptides
Analyse
Protéine entière
Energie cinétique d'un ion de charge z
soumis à une tension accélératrice Vo
Miroirs électrostatiques
$Ec = \frac{1}{2} mv^2 = \frac{1}{2} m(l^2/t^2) = zVo$
$m/z = 2Vo\ t^2/l^2$ (Vo, l sont connus)
rapport m/z = fonction du temps de vol t
* TOF: Time of Flight

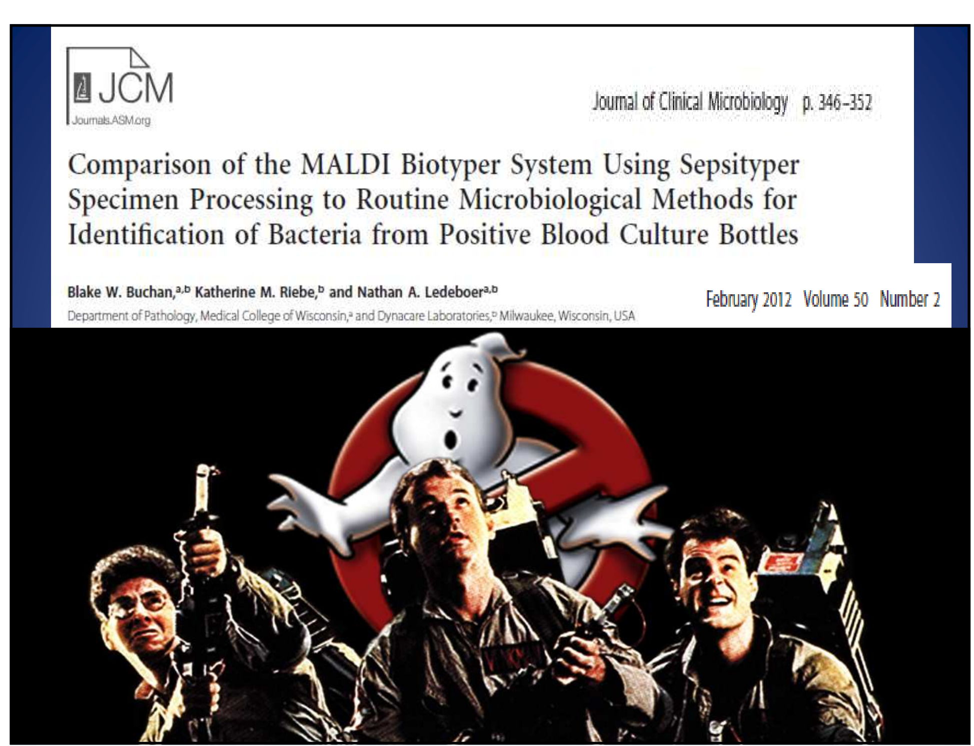


The analyzer captures data and pepares it for analysis
Detector
Analyzer software
The detectors measure each ion collision and produce a graph or spectrum
Field Free Drift Region
High Vacuum
laser Trigers a clock
Lightes ions arrive at the detector first
UV laser
UV laser
Electrical field accelerates ions
Laser Optic
Lens
Ground Plate
Extractor Grid
Ion Source
Matrix Mixture After Laser Irradication
Focusing Device
Laser Beam
Analyte is ionized
MassARRAY Analyzer 4
SpectroCHIP with DNA/RNA Analyte Matrix Mixture
SpectroCHIP Array
The MALDI-TOF Process in the MassARRAY Analyzer 4

Sensibilité de la spectrométrie de masse

De l'ordre de l'attomole

1 mole		$\mathcal{N} = 6{,}03 \cdot 10^{23}$
milli mole	10^{-3}	
micro	10^{-6}	
nano	10^{-9}	
pico	10^{-12}	
femto	10^{-15}	
atto	10^{-18}	$6{,}03 \cdot 10^{5}$
		soit 600 000 molécules !!!



JCM
Journals.ASM.org

Comparison of the MALDI Biotyper System Using Sepsityper Specimen Processing to Routine Microbiological Methods for Identification of Bacteria from Positive Blood Culture Bottles

Blake W. Buchan,[a,b] Katherine M. Riebe,[b] and Nathan A. Ledeboer[a,b]
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Bloodstream infections are leading cause of admissions to ICU and have high mortality rate.

Rapid identification of the infecting organism is mandatory.

We compared:
MALDI Biotyper syst (Sepsityper spec processing)
from Bruker Daltonics to routine methods
for identification of microorganisms from 164 + blood cultures.

The MALDI Biotyp/Sepsityp identified 85.5% of bacterial isolates directly from monomicrobial blood cultures with 97.6% concordance to genus and 94.1% concordance to species with routine identification methods.

Gram - isolates were more likely to produce acceptable confidence scores (97.8%) than Gram + isolates(80.0%).

Modified blood culture-specific parameters resulted in an improved overall identification rate for Gram + (89.0%)

Median times to identification using the MALDI Biotyper/Sepsityper were 23 to 83 h faster than routine methods for Gram + and 34 to 51 h faster for Gram - .

TABLE 2 Performance of MALDI-TOF/Sepsityper for identification of Gram-negative bacteria from positive blood culture bottles

Organism (identified by routine methods)	No. of isolates	MALDI score[c]			Organism identified by MALDI (if discrepant)
		<1.7	1.7–1.99	>2.0	
Bacteroides fragilis	1		1		
Enterobacter cloacae	3			3 (1)	*Enterobacter asburiae*[a]
Escherichia coli	22			22	
Haemophilus influenzae	1		1		
Haemophilus parainfluenzae	1			1	
Klebsiella oxytoca	3			3 (1)	*Enterobacter cloacae*[b]
Klebsiella pneumoniae	6			6	
Neisseria gonorrhoeae	1	1 (1)			MALDI failed to generate ID
Proteus mirabilis	1			1	
Pseudomonas aeruginosa	4			4	
Serratia marcescens	1			1	
Stenotrophomonas maltophilia	1		1		
Total no. of isolates	45	3	41		
% genus agreement		0	100	97.6	
% species agreement		0	100	95.1	

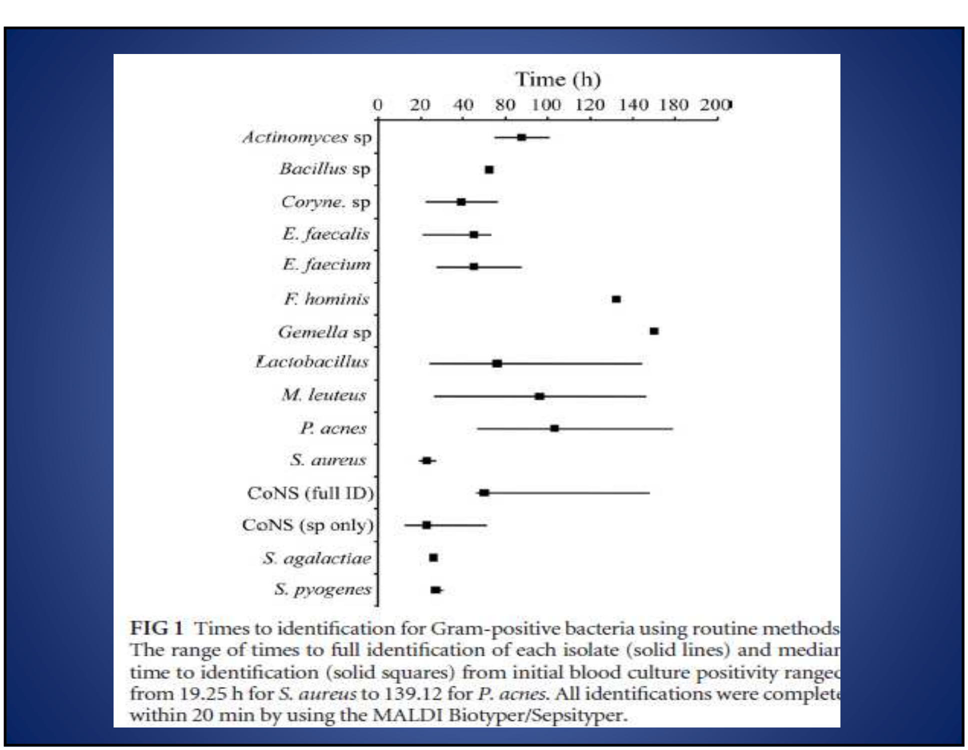


FIG 1 Times to identification for Gram-positive bacteria using routine methods. The range of times to full identification of each isolate (solid lines) and median time to identification (solid squares) from initial blood culture positivity ranged from 19.25 h for *S. aureus* to 139.12 for *P. acnes*. All identifications were complete within 20 min by using the MALDI Biotyper/Sepsityper.

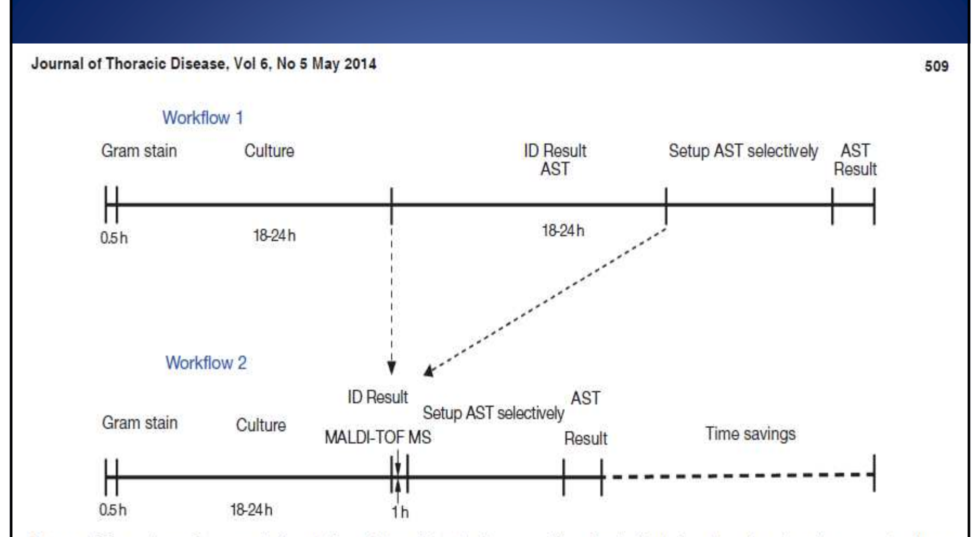
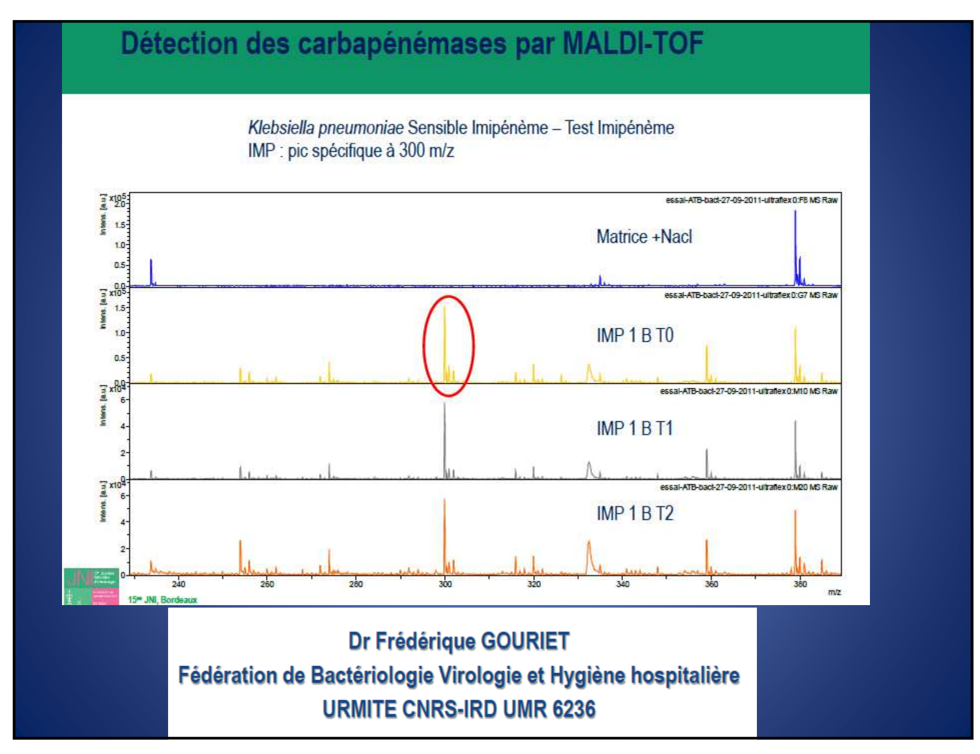
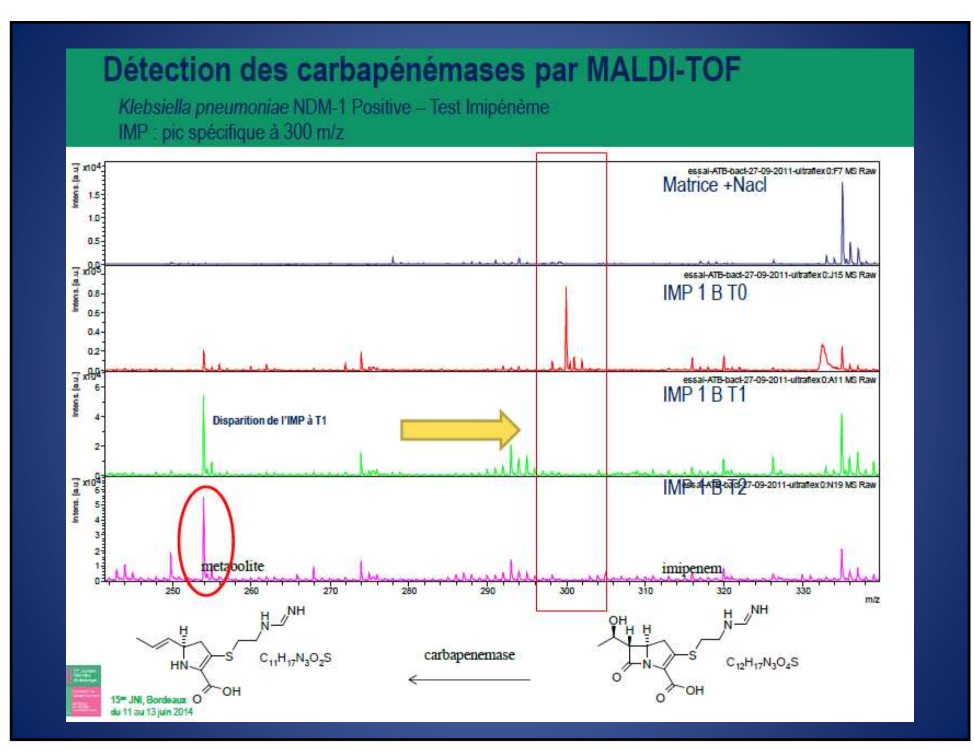
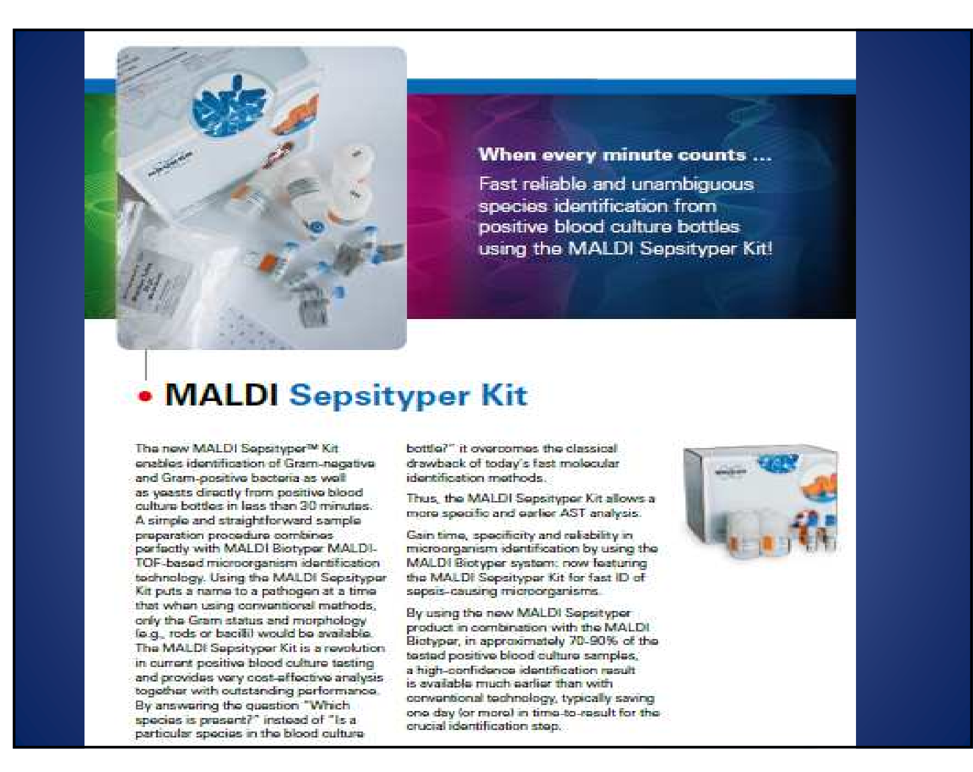


Figure 1 Comparison of new method workflow with traditional culture workflow. In the ideal situation when there is one predominant colony grow from the culture. If there are mixed cultures with different colonies, the time of saving could be two days as the subcultures are needed for pure colony and for identification by conventional method. Workflow 1, conventional culture; workflow 2, new method with MALDI-TOF MS; ID, identification; AST, antimicrobial susceptibility testing.

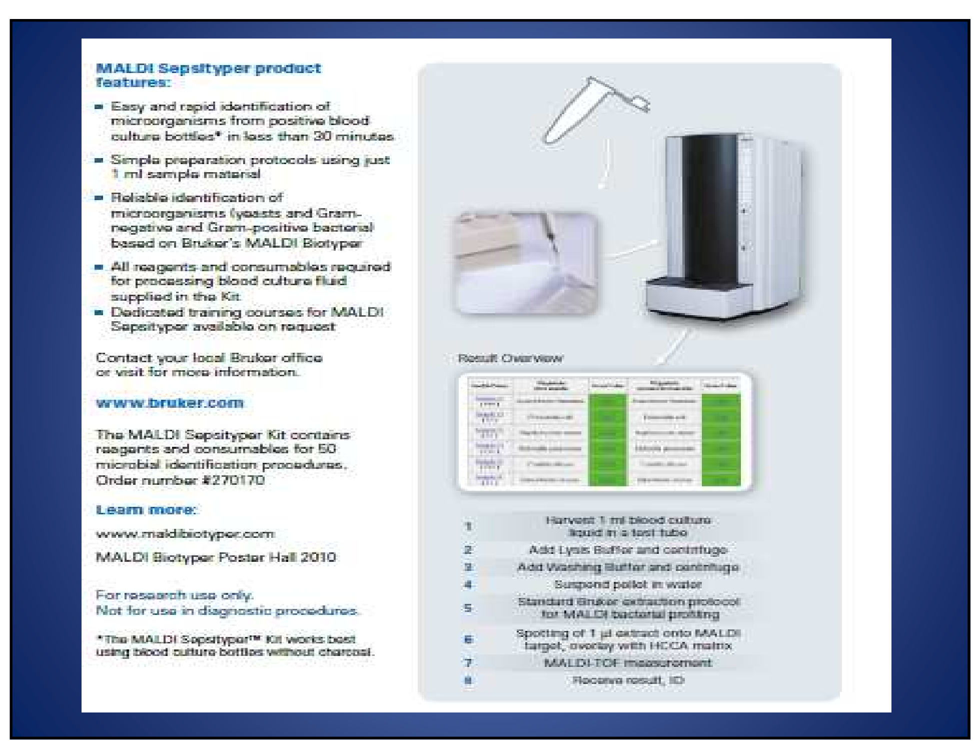




Détection des carbapénémases par MALDI-TOF
Klebsiella pneumoniae NDM-1 Positive – Test Imipénème
IMP : pic spécifique à 300 m/z
Matrice +Nacl
IMP 1 B T0
IMP 1 B T1
IMP 1 B T2
Disparition de l'IMP à T1
metabolite
imipenem
carbapenemase
15ème JNI, Bordeaux du 11 au 13 juin 2014



When every minute counts ...
Fast reliable and unambiguous species identification from positive blood culture bottles using the MALDI Sepsityper Kit!
MALDI Sepsityper Kit
The new MALDI Sepsityper™ Kit enables identification of Gram-negative and Gram-positive bacteria as well as yeasts directly from positive blood culture bottles in less than 30 minutes. A simple and straightforward sample preparation procedure combines perfectly with MALDI Biotyper MALDI-TOF-based microorganism identification technology. Using the MALDI Sepsityper Kit puts a name to a pathogen at a time that when using conventional methods, only the Gram status and morphology (e.g., rods or bacilli) would be available. The MALDI Sepsityper Kit is a revolution in current positive blood culture testing and provides very cost-effective analysis together with outstanding performance. By answering the question "Which species is present?" instead of "Is a particular species in the blood culture bottle?" it overcomes the classical drawback of today's fast molecular identification methods.
Thus, the MALDI Sepsityper Kit allows a more specific and earlier AST analysis.
Gain time, specificity and reliability in microorganism identification by using the MALDI Biotyper system: now featuring the MALDI Sepsityper Kit for fast ID of sepsis-causing microorganisms.
By using the new MALDI Sepsityper product in combination with the MALDI Biotyper, in approximately 70-90% of the tested positive blood culture samples, a high-confidence identification result is available much earlier than with conventional technology, typically saving one day (or more) in time-to-result for the crucial identification step.


MALDI Sepsityper product features:
Easy and rapid identification of microorganisms from positive blood culture bottles* in less than 30 minutes
Simple preparation protocols using just 1 ml sample material
Reliable identification of microorganisms (yeasts and Gram-negative and Gram-positive bacteria) based on Bruker's MALDI Biotyper
All reagents and consumables required for processing blood culture fluid supplied in the Kit
Dedicated training courses for MALDI Sepsityper available on request
Contact your local Bruker office or visit for more information.
www.bruker.com
The MALDI Sepsityper Kit contains reagents and consumables for 50 microbial identification procedures. Order number #270170
Learn more:
www.maldibiotyper.com
MALDI Biotyper Poster Hall 2010
For research use only.
Not for use in diagnostic procedures.
*The MALDI Sepsityper™ Kit works best using blood culture bottles without charcoal.
Result Overview
1 Harvest 1 ml blood culture liquid in a test tube
2 Add Lysis Buffer and centrifuge
3 Add Washing Buffer and centrifuge
4 Suspend pellet in water
5 Standard Bruker extraction protocol for MALDI bacterial profiling
6 Spotting of 1 µl extract onto MALDI target, overlay with HCCA matrix
7 MALDI-TOF measurement
8 Receive result, ID

IDENTIFICATION & SUSCEPTIBILITY TESTING
VITEK MS
Fast
Flexible
Innovative
VITEK 2
BIOMÉRIEUX
Api Strip
1) Phenol red: pH indicator
2) A carbapenem: imipenem (carbapenemase substrate) + Zinc, required for the detection of metallodependent carbapenemase-producing strains
Rapidec Carba NP
E test

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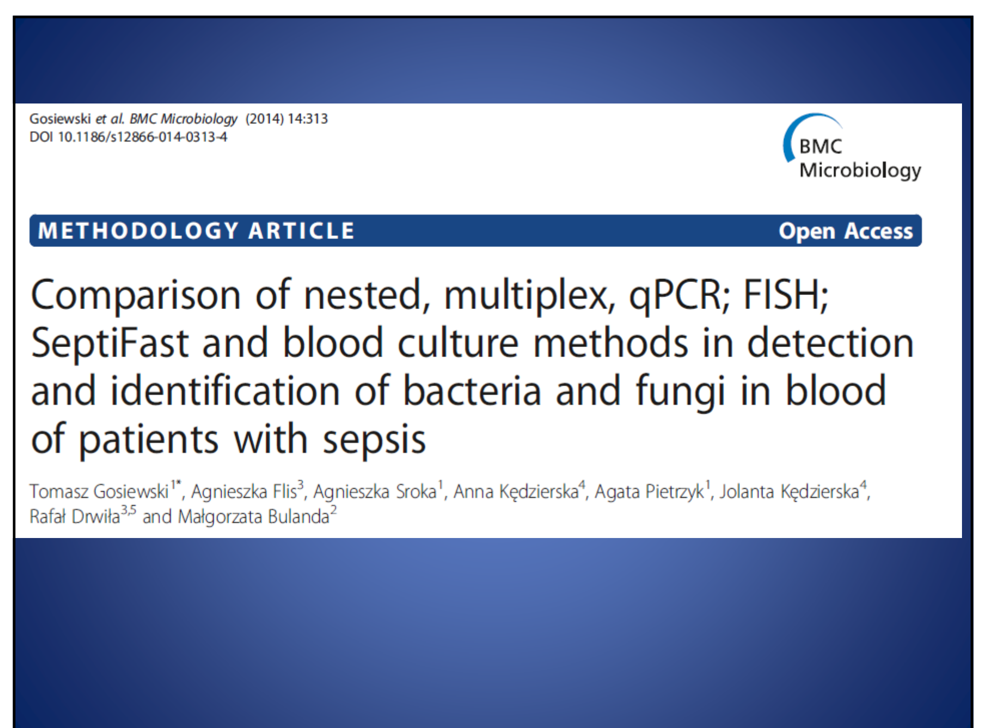
5 Flow cytometry



Gosiewski *et al. BMC Microbiology* (2014) 14:313
DOI 10.1186/s12866-014-0313-4

BMC Microbiology

METHODOLOGY ARTICLE Open Access

Comparison of nested, multiplex, qPCR; FISH; SeptiFast and blood culture methods in detection and identification of bacteria and fungi in blood of patients with sepsis

Tomasz Gosiewski[1*], Agnieszka Flis[3], Agnieszka Sroka[1], Anna Kędzierska[4], Agata Pietrzyk[1], Jolanta Kędzierska[4], Rafał Drwiła[3,5] and Małgorzata Bulanda[2]

LightCycler® SeptiFast Test MGRADE

Rapid detection and identification of bloodstream infections by real-time PCR – directly from blood

Provides rapid species identification of pathogens causing blood stream infections.

SeptiFast is designed to detect and identify the most important bacteria and fungi causing nosocomial bloodstream infections – within just a few hours! SeptiFast detects the pathogenic bacteria and fungi directly from whole blood, no preculture is required.

Rapid pathogen detection by molecular diagnostic tools may facilitate the rapid diagnosis of bacteremia/fungemia and earlier administration of appropriate antibiotic therapy, while also reducing inappropriate overuse of broad-spectrum antibiotics.

Designed for the LightCycler® 2.0 Instrument – Combines rapid amplification with highly specific melting point analysis for rapid species results
SeptiFast Identification Software consolidates all data points into one patient report

Optional mecA gene detection – when samples test positive for Staphylococcus aureus, test for the presence of the mecA gene in a subsequent run using the LightCycler® SeptiFast MecA Test MGRADE

Gram (-)
Escherichia coli
Klebsiella (pneumoniae/oxytoca)
Serratia marcescensEnterobacter (cloacae/aerogenes)
Proteus mirabilis
Pseudomonas aeruginosa
Acinetobacter baumanniiStenotrophomonas maltophilia

Gram (+)
Staphylococcus aureus
CoNS (Coagulase negative Staphylococci)
Streptococcus pneumoniae
Streptococcus spp.
Enterococcus faecium
Enterococcus faecalis

Fungi
Candida albicans
Candida tropicalis
Candida parapsilosis
Candida krusei
Candida glabrata
Aspergillus fumigatu

Abstract

Background: Microbiological diagnosis of sepsis relies primarily on blood culture data. This study compares four diagnostic methods, i.e. those developed by us: nested, multiplex, qPCR (qPCR) and FISH with commercial methods: SeptiFast (Roche) (SF) and BacT/ALERT® 3D blood culture system (bioMérieux). Blood samples were derived from adult patients with clinical symptoms of sepsis, according to SIRS criteria, hospitalized in the Intensive Care Unit.

Results: Using qPCR, FISH, SF, and culture, microbial presence was found in 71.8%, 29.6%, 25.3%, and 36.6% of samples, respectively. It was demonstrated that qPCR was significantly more likely to detect microorganisms than the remaining methods; qPCR confirmed the results obtained with the SF kit in all cases wherein bacteria were detected with simultaneous confirmation of Gram-typing. All data collected through the FISH method were corroborated by qPCR.

Conclusions: The qPCR and FISH methods described in this study may constitute alternatives to blood culture and to the few existing commercial molecular assays since they enable the detection of the majority of microbial species, and the qPCR method allows their identification in a higher number of samples than the SF test. FISH made it possible to show the presence of microbes in a blood sample even before its culture.

Keywords: Nested, Multiplex qPCR, FISH, SeptiFast, Blood culture, Sepsis

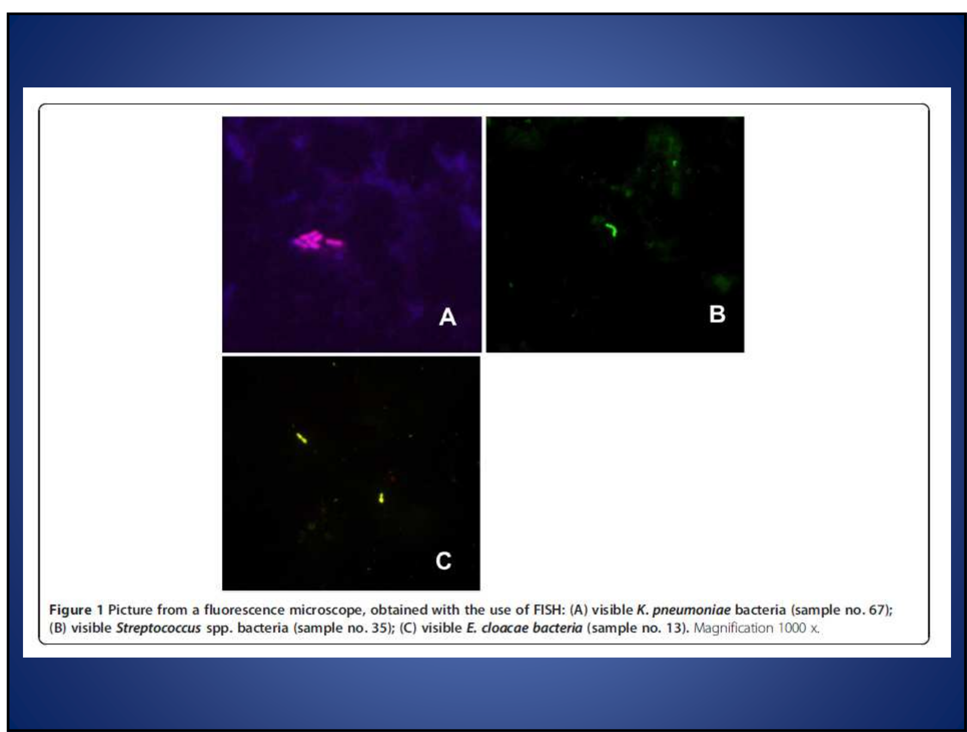
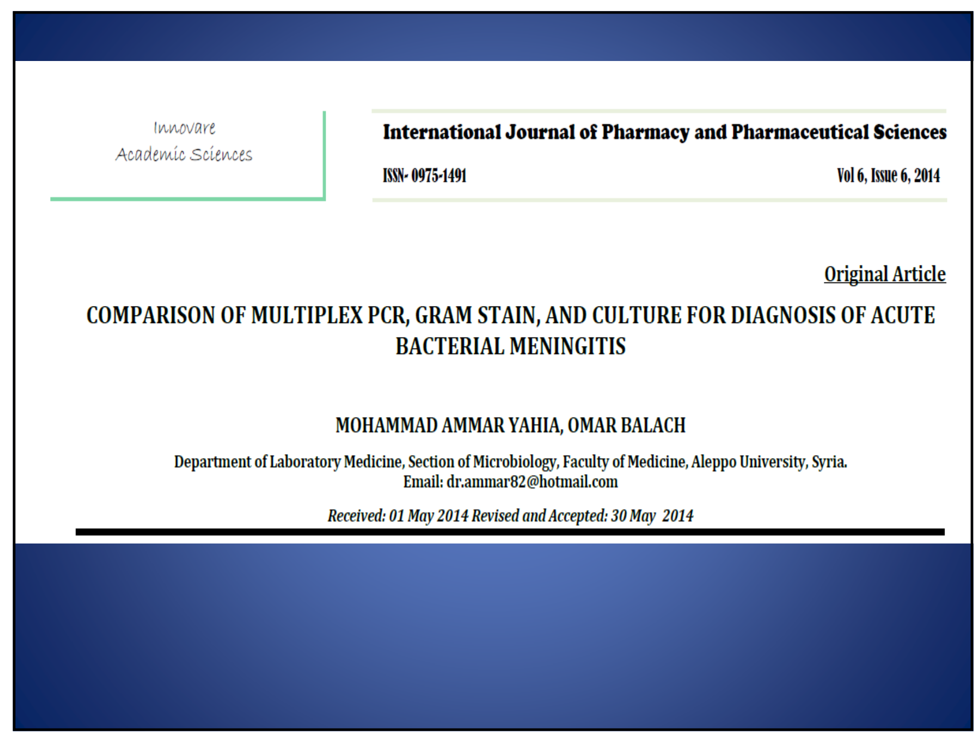


Figure 1 Picture from a fluorescence microscope, obtained with the use of FISH: (A) visible *K. pneumoniae* bacteria (sample no. 67); (B) visible *Streptococcus* spp. bacteria (sample no. 35); (C) visible *E. cloacae bacteria* (sample no. 13). Magnification 1000 x.



Comparison of, Gram stain and bacterial culture, multiplex PCR (5 Bacteria) in CSF :

Streptococcus pneumoniae
Haemophilus influenzae type b
Neisseria meningitides
Group B streptococcus
Listeria monocytogenes

110 CSF samples from 110 patients suspected of acute bacterial meningitis .

Results:

Gram stain for any bacteria was positive in 32 cases (29.1%), including the five pathogens in 11 cases (10%).

Bacterial culture was positive in 38 cases (34.5%), including the five pathogens in 8 cases (7.2%).

Multiplex PCR was positive in 60 cases (54.5%)

Streptococcus pneumoniae in 39/60 cases (65%)
Neisseria meningitides in 8/60 cases (13.3%).

50 cases of acute bacterial meningitis were diagnosed by multiplex PCR, while both gram stain and bacterial culture were negative .

Conclusions: The PCR method is rapid, sensitive, and specific diagnostic test for acute bacterial meningitis. **PCR is particularly useful for analyzing CSF of patients who have been treated with antibiotics before lumbar puncture.**

1 MALDI TOF MS

2 Multiplex PCR

3 (Fast) Whole Genome Sequencing

4 Fluorescent in situ hybridization FISH

5 Flow cytometry

Transforming clinical microbiology with bacterial genome sequencing

Nature Reviews, genetics volume 13, Sept 2012, 601-612

Xavier Didelot, Rory Bowden, Daniel J. Wilson, Tim E. A. Peto, Derrick W. Crook

Genome sequence of an isolate contains all of the information required to treat.

It 's becoming clear that rapid, inexpensive genome sequencing holds potential to replace old complex multifaceted procedures used to characterize a pathogen after culture.

But there are still substantial challenges to be overcome

Success will depend on development of genomic knowledge and analytical methods required to extract and interpret informations.

Application of new sequencing technologies will be highly disruptive, and it will take many years to fully transform clinical microbiology laboratories .
Deployment will require validation of genotypic prediction of the phenotype, particularly for antimicrobial resistance; **this work is yet to be done.**

Pathology (April 2015) 47(3), pp. 199–210

OPEN

MOLECULAR DIAGNOSTICS IN MICROBIOLOGY

Whole genome sequencing in clinical and public health microbiology

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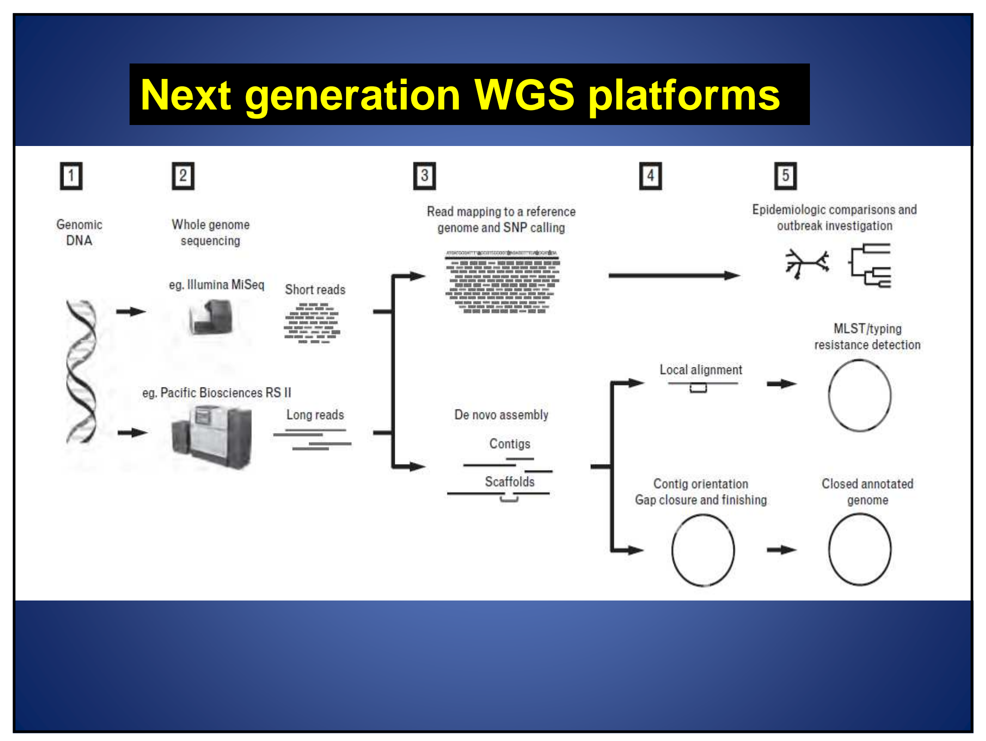
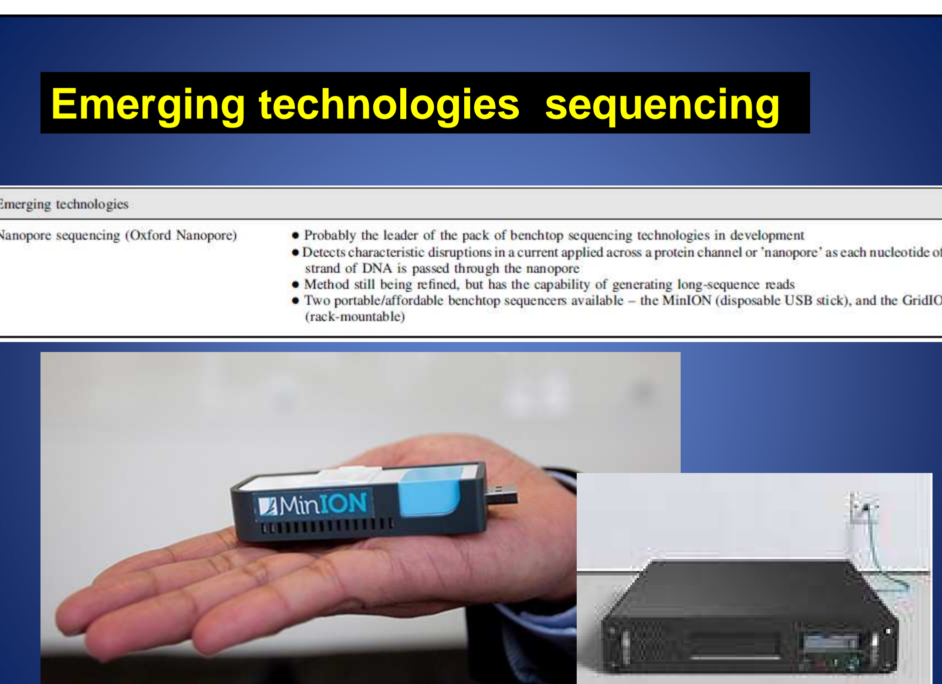
[1]Microbiological Diagnostic Unit Public Health Laboratory, Department of Microbiology and Immunology, the University of Melbourne, at the Doherty Institute for Infection and Immunity, Melbourne, Vic, [2]Department of Infectious Diseases, Austin Health, Heidelberg, Vic, [3]Marie Bashir Institute for Infectious Diseases and Biosecurity and Sydney Medical School, The University of Sydney, Sydney, NSW, [4]Centre for Infectious Diseases and Microbiology-Public Health, Institute of Clinical Pathology and Medical Research, Westmead Hospital, Sydney, NSW, and [5]Department of Microbiology, Monash University, Clayton, Vic, Australia

Principles of next generation sequencing

Next-generation sequencing technologies	
Pyrosequencing (Roche 454)	• Detects pyrophosphate release on addition of a complementary nucleotide to determine the template sequenc • Lower throughput and subsequently higher sequencing cost per base • One of the earlier next-generation technologies, but now being phased out with Roche intending to cease production in 2016
SOLiD sequencing (Life Technologies)	• Sequencing by Oligonucleotide Ligation and Detection (SOLiD) uses a ligation-based approach • Less popular than Life Technologies' other platform, the Ion Torrent, and likely to be superseded by newer technologies
Ion semiconductor sequencing (Life Technologies Ion Torrent)	• Uses a sequencing-by-synthesis method, detecting changes in pH due to hydrogen ion release with synthesis complementary DNA • Popular due to lower sequencer cost and speed of sequencing • Requires separate emulsion PCR library amplification prior to sequencing (slow and complicated), though automation can be performed using the separate Ion Chef system • Higher error rates, particularly homopolymers, than other platforms and poor coverage of extremely AT-rich GC-rich regions • Ion Torrent Personal Genome Machine (PGM) and newer, higher throughput Ion Proton available
Illumina sequencing	• Uses a sequencing-by-synthesis method, detecting release of fluorescent labels from incorporated nucleotides determine sequence • Current market leader with high sequence throughput, with low error rate and low sequencing cost per base • Limitations of short read sequences and a longer sequencing run time • Several platforms with moderate (MiSeq), moderate-high (NextSeq) and high (HiSeq) throughput • TruSeq long read technology recently introduced to produce synthetic reads of 10 kb in length (currently onl HiSeq 2000/2500)
Single molecule real-time sequencing (Pacific Biosciences)	• Novel method – observes natural synthesis of unmodified DNA by DNA polymerase, with reads up to 40 kb length, using nucleotides with fluorescent labels attached to the terminal phosphate (rather than the base) • Higher raw error rates, but errors are randomly distributed (vs. ends of reads or homopolymers), and overlappin reads can produce a consensus sequence with high accuracy • Has significantly improved *de novo* assembly and bacterial genome completion without needing traditional PCR-based gap closure • High setup cost and low throughput have limited implementation, though outsourcing options are available

Next generation WGS platforms





Emerging technologies	
Nanopore sequencing (Oxford Nanopore)	• Probably the leader of the pack of benchtop sequencing technologies in development • Detects characteristic disruptions in a current applied across a protein channel or 'nanopore' as each nucleotide of strand of DNA is passed through the nanopore • Method still being refined, but has the capability of generating long-sequence reads • Two portable/affordable benchtop sequencers available – the MinION (disposable USB stick), and the GridION (rack-mountable)

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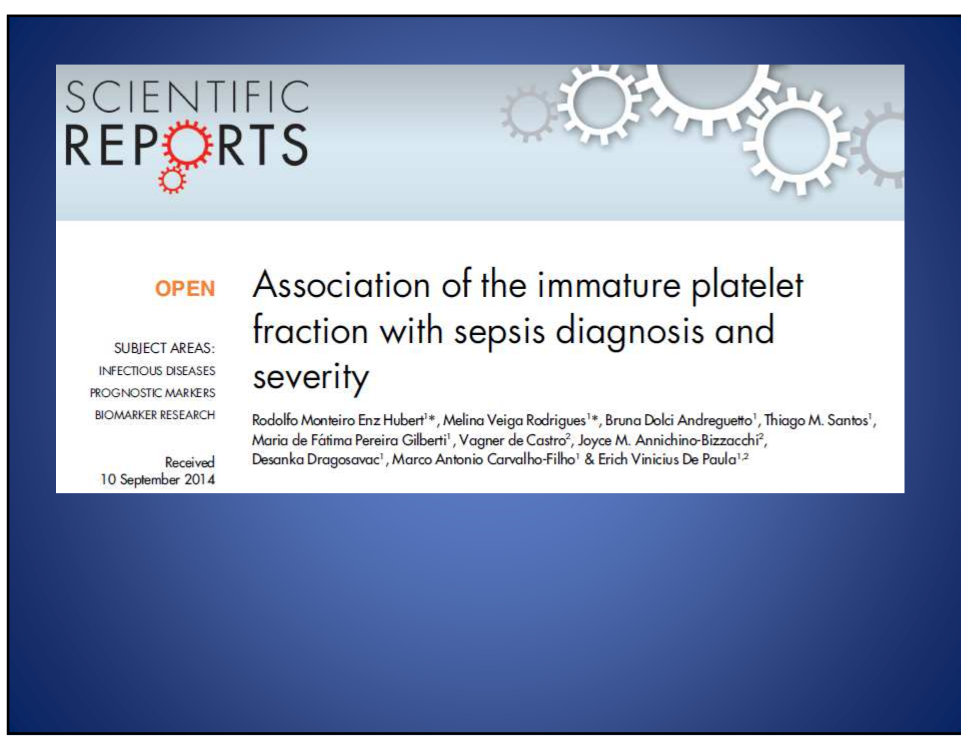
SCIENTIFIC REPORTS

OPEN

SUBJECT AREAS:
INFECTIOUS DISEASES
PROGNOSTIC MARKERS
BIOMARKER RESEARCH

Received
10 September 2014

Association of the immature platelet fraction with sepsis diagnosis and severity

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Measurement of IPF.

IPF were obtained in an automated hematology analyzer (Sysmex XE5000, Kobe, Japan) at admission.

IPF were measured in a dedicated reticulocyte/platelet channel of the hematology analyzer by flow cytometry, using a proprietary fluorescent dye containing polymethine and oxazine.

This dye penetrates the cell membrane, staining RNA in immature (or reticulated) platelets.

By analyzing cell volume and fluorescent intensity from these cells, a computer algorithm discriminates platelets with higher RNA content, referred to as immature platelets.

The IPF correspond to the fraction (%) of immature platelets from the total platelet population.

An accessible sepsis biomarker should segregate infected from non-infected pts, provide prognosis information.

Recently, a study performed in critically-ill patients suggested that IPF could be more accurate than CRP and PCT.

We evaluated retrospectively the performance of IPF as biomarkers of sepsis diagnosis and severity in 41 pts admitted to two ICU:
12 of which with severe sepsis or septic shock
11 with non-complicated sepsis.

Significantly higher IPF levels were observed in patients with severe sepsis/ septic shock.
IPF correlated with sepsis severity scores and presented the highest diagnostic accuracy for the presence of sepsis of all studied clinical and laboratory parameters.

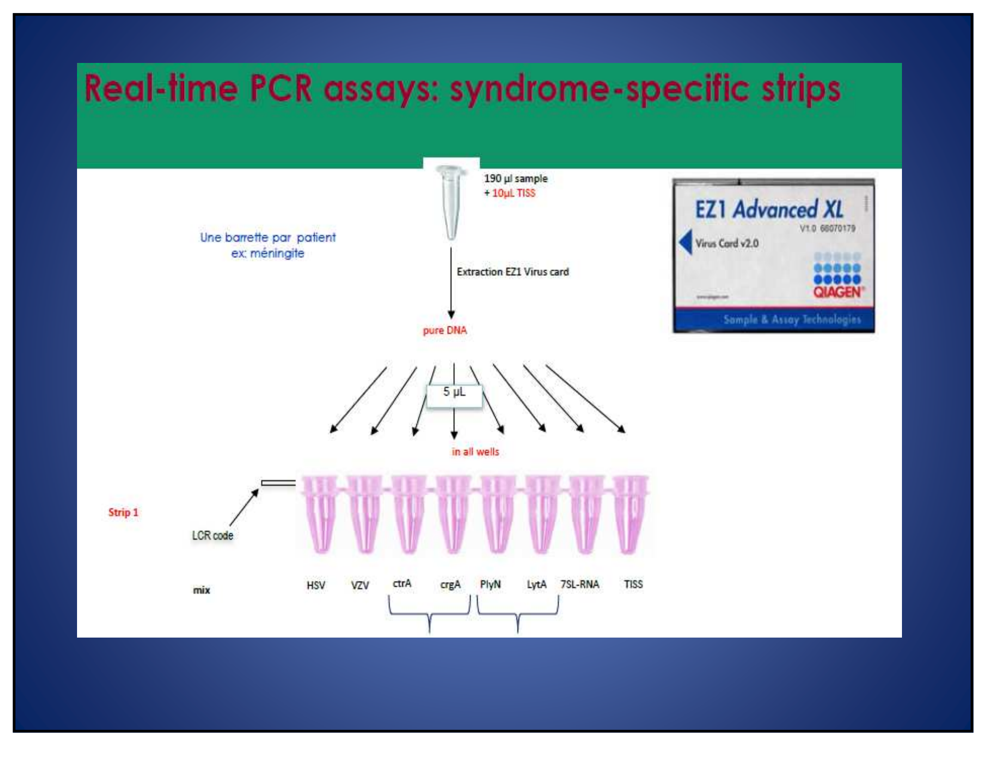
Our results suggest that IPF levels could be used as a biomarker of sepsis diagnosis and severity.

Table 1 | Patient characteristics

	Sepsis (n = 11)	Severe sepsis/ septic shock (n = 12)	P*
Sex (male:female ratio)	7:4	5:7	ns
Age (years) (median, range)	56 (22–85)	59 (38–52)	ns
SOFA – admission (median,range)	**3 (2–9)**	**10 (2–17)**	**0.01**
APACHE-II – admission (median, range)	**12 (6–27)**	**20 (12–37)**	**<0.001**
SIRS criteria (mean ± SD)			
Temperature (°C)	37.0 ± 0.8	37.1 ± 0.9	ns
Heart rate (beats per minute)	107.5 ± 18.8	113.5 ± 15.9	ns
Breath rate (per minute)	27.8 ± 14.9	22.7 ± 9.6	ns
White blood cell count (*10³/µl)	16.1 ± 10.5	15.9 ± 7.4	ns
Immature forms (%)	10.5 ± 12.6	6.0 ± 9.8	ns
Additional clinical and laboratory variables (mean ± SD)			
PaO_2/FIO_2 (mmHg)	296.0 ± 115.8	235.6 ± 132.3	ns
Platelet count (*10⁹/l)	271 ± 138	206 ± 102	ns
Mean arterial pressure (mmHg)	97.1 ± 29.7	102.1 ± 11.1	ns
Urine output (l/day)	1.6 ± 5.9	2.1 ± 2.1	ns
Creatinine (mg/dl)	1.7 ± 1.5	1.3 ± 0.8	ns
Bilirrubin (mg/dl)	0.9 ± 0.9	1.8 ± 2.9	ns
C-reactive protein (mg/l)	11.6 ± 8.0	11.6 ± 7.5	ns
Lactate (mmol/l)	**1.1 ± 0.5**	**4.0 ± 2.7**	**<0.001**
D-dimer(µg/ml)	3.1 ± 1.8	3.0 ± 1.5	ns
Prothrombin time (INR)	1.6 ± 1.3	1.5 ± 0.4	ns
aPTT ratio	1.1 ± 0.3	1.2 ± 0.3	ns
Advanced hematological parameters (mean ± SD)			
Immature platelet fraction (%)	**3.6 ± 2.6**	**6.2 ± 3.0**	**0.03**
Immature reticulocyte fraction (%)	12.6 ± 6.0	20.6 ± 15.4	ns

*D-dimer levels available for 17 patients. aPTT: activated partial thromboplastin time.

Critères de sélection des analyses au POC
Résultats en moins de 4 heures, transmission SMS
bonne valeur prédictive
dépistage par syndrome
Résultats modifient la prise en charge
Immunochromatographie
PCR en temps réel


Real-time PCR assays: syndrome-specific strips
190 µl sample
+ 10µL TISS
Une barrette par patient
ex: méningite
Extraction EZ1 Virus card
pure DNA
5 µL
in all wells
Strip 1
LCR code
mix
HSV
VZV
ctrA
crgA
PlyN
LytA
7SL-RNA
TISS
EZ1 Advanced XL
Virus Card v2.0
QIAGEN
Sample & Assay Technologies

Avenir proche ?
« Trousses » associant plusieurs tecniques:
- Classiques et BM, POC
- Adaptés au contexte clinique: et au site :
Méningite, pneumonies, bactériémies …