New Diagnostic approaches and Antimicrobial Management of Infectious Diseases: An Overview from Kuwait

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Outline

- Introduction
- Antimicrobial usage in the 21st Century
- Need for new diagnostic approaches
- What infections are priorities for such approaches??
  - Sepsis
  - Pneumonia
- Impact on antimicrobial management of ID
- Overview from Kuwait

Introduction

- In 1969 Surgeon General William H. Stewart declared in a message to the US Congress:

- "It is time to close the book on infectious diseases …
- … The war against pestilence is over."

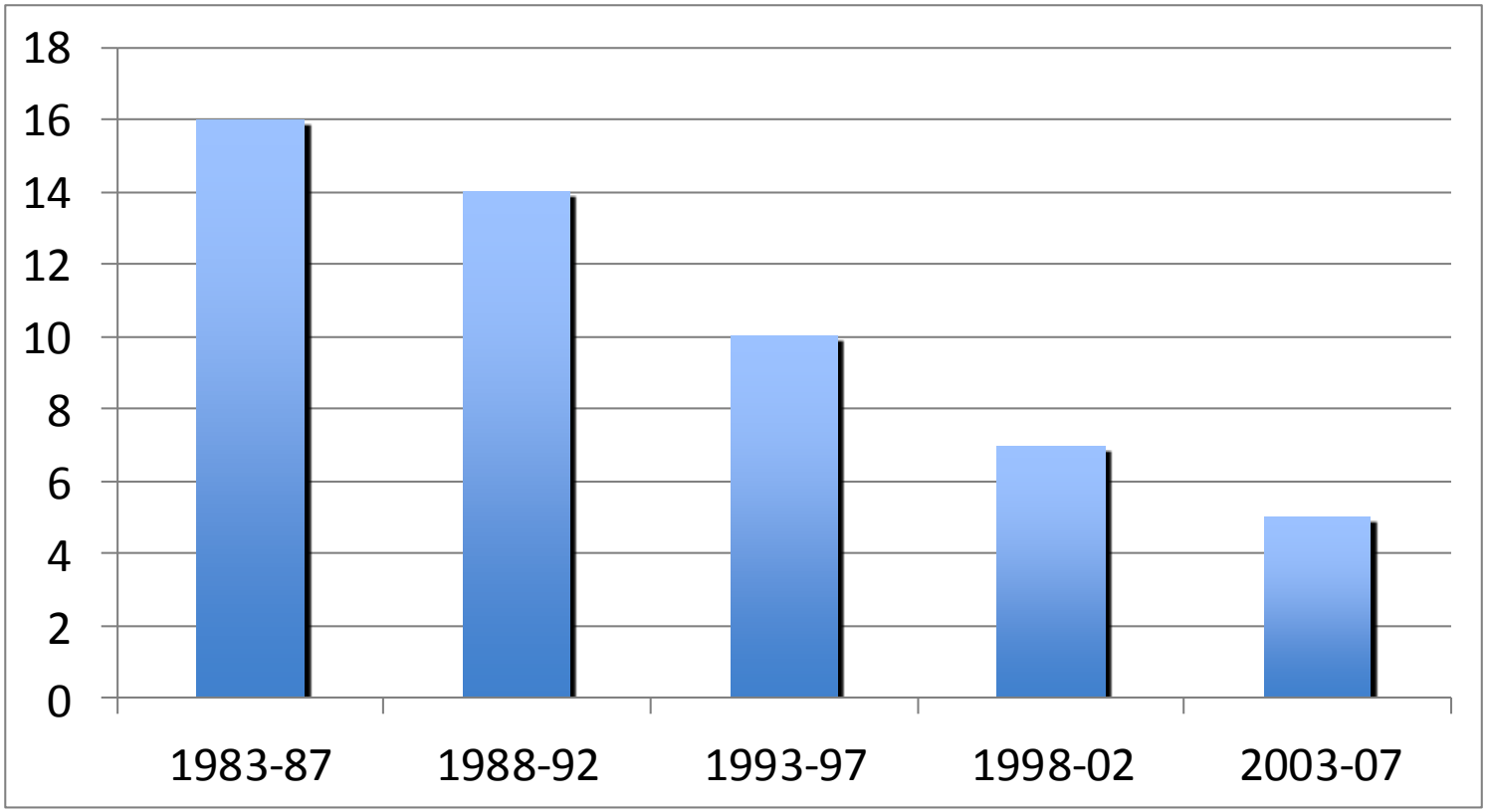
Definition of New Antibiotics

“ New Antibiotic: Anything that we introduce to bacteria and going to see resistance to!”

Antibiotic therapy if indiscriminately used may turn out to be medical flood that temporarily cleans and heals but ultimately destroys life itself

Felix Marti-Ibanez, 1955

…As Antibiotic Options Decline



The Situation in 2004

Infectious Diseases Society of America
http://www.idsociety.org/badbugsnodrugs.html

The Situation Worsens
nine Years Later

- Bad Bugs, No Drugs: No ESKAPE
  - *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter* spp
- Dry pipeline
  - Some important molecules for MRSA
  - Few novel molecules for other ESKAPE pathogens
  - No new drugs for infection due to MDR Gram (-) bacilli (e.g., *A baumannii* and *P aeruginosa*)
  - Few advantages over currently available therapies

Rice LB. *J Infect Dis*. 2008;197:1079
Boucher HW, et al. *Clin Infect Dis*. 2009;48:1

Defining ESKAPE?

Highlighting troublesome bacteria with the ability to "escape" the effects of current antimicrobial agents…

E	*Enterococcus faecium*
S	*Staphylococcus aureus*
C	***Clostridium difficile***
A	*Acinetobacter baumannii*
P	*Pseudomonas aeruginosa*
E	***Enterobacteriaceae***

Peterson LR. *Clin Infect Dis*. 2009;49:992

The 10 × '20 Initiative: Pursuing a Global Commitment to Develop 10 New Antibacterial Drugs by 2020

Infectious Diseases Society of America*

Infectious Diseases Society of America, Arlington, Virginia

IDSA. Clin Infect Dis 2010;50:1081

THE ANTIMICROBIAL RESISTANCE CHALLENGES

Hit hard
Hit fast

Paul Ehrlich

Get it right first time

If and when antibiotics are indicated, the philosophy is now based on attempting to

Does Inappropriate antimicroboial therapy result in antibiotics resistance???

OR

Antibiotic resistance leads to inappropriate therapy???

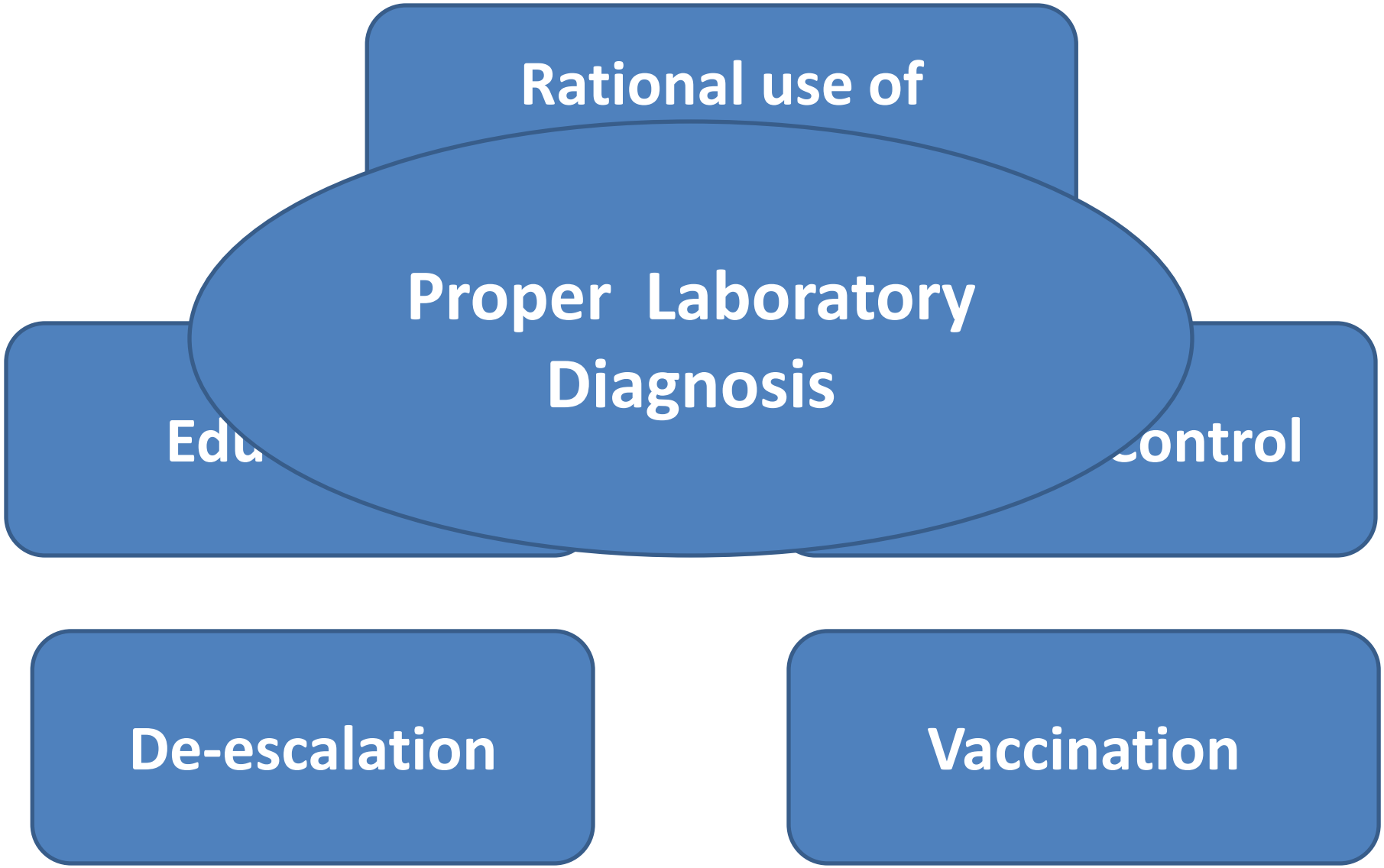
VICIOUS CYCLE ???


COMBAT
DRUG
RESISTANCE
DRUG RESISTANCE
No action today,
no cure tomorrow
7 APRIL 2011 WORLD HEALTH DAY
World Health Organization

What could be the actions today???

Antimicrobial Stewardship

The process of appropriate usage of antimicrobial agents aiming at prevention of antimicrobial resistance


Rational use of
Proper Laboratory Diagnosis
Edu
ontrol
De-escalation
Vaccination

1. Role of new and rapid diagnostic tools in the early diagnosis of sepsis

SEPSIS

=

Infection

+

Systemic inflammation

Sepsis

Worldwide:

30,000,000 cases / year

USA:
1.000.000 / year

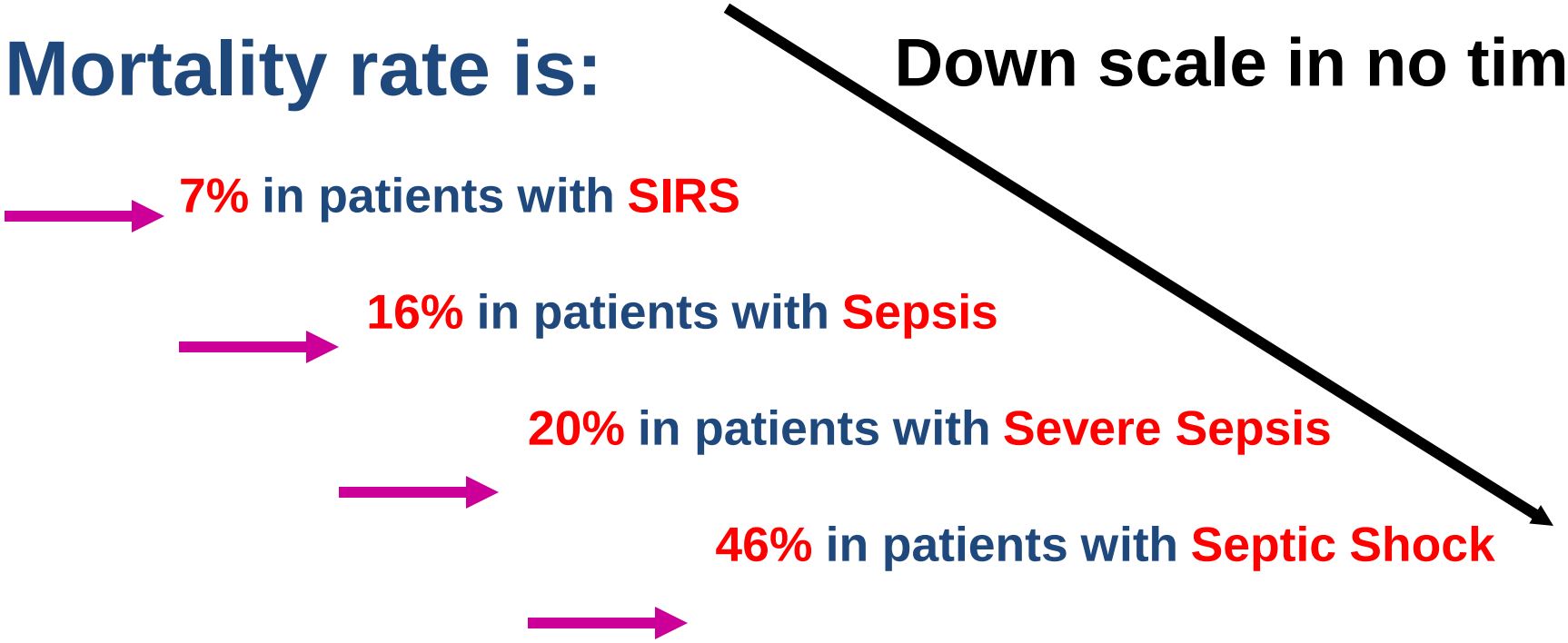
Martin GS et al. N Engl J Med 2003;348:1546-54
Angus DC et al. Crit Care Med 2001; 29: 1303-1310

Germany:
~125.000 - 300.000 / year

Rychlik R et al. Gesundh Ökon Qual Manag 2000; 5:67-72

Mortality rate increases with increasing severity

Mortality rate is:



Rangel-Frausto et al. (JAMA 1995)

And

We ought to spend more time to search for an accurate diagnosis rather than search for the Magic Bullet for the treatment of Sepsis"

Roger Bone, 1996

Prompt Diagnosis of Sepsis: ***Unachievable goal***

Experience from Kuwait

A. Molecular diagnosis of sepsis

Conventional culture system

1. < 50% positive
2. TAT 48-72 hrs

Evaluation of the comperative performance of Verigine Blood Culture Nucliec acid System to Conventional Techniques in a Tertiary-care Hospital in Kuwait

*Mokaddas EM[1, 2], Behbehani A [2], Abdullah A [2], Shatti S [2].

[1] Microbiology Department, Faculty of Medicine, Kuwait University, Kuwait.

[2] Laboratory Department, Ibn Sina Hospital, Kuwait

The diagnosis of bacteremia and sepsis is a priority in a Clinical Microbiology Department as they carry high mortality (20-50%).

Early correct antibiotic treatment is correlated with higher survival rates.

This is the main reason why broad spectrum antibiotics are usually administered until the microbiology results are known.

Once the bacterial pathogen is known, treatment can be adjusted to a more specific antibiotioc therapy.

A key predictor of mortality rates in patients with severe blood stream infection is the time to identification of the causative pathogen and initiation of targeted therapy.

Rapid Diagnosis
And
Antimicrobial stewardship

R
imp
as well as antimicrobial stewardship.

The Verigene Gram-positive and Gram negative Blood Culture (BC-GP, BC-GN)) system (Nanosphere, USA) is a

qualitative, multiplexed automated

nu t for

p eria

ar ers.

With a TAT of 2 hrs

Verigene BC-GP and BC-GN identifiable targets

Gram-Positive Blood Culture (BC – GP) Tests :

Genus	Staphylococcus Spp. Streptococcus Spp. Micrococcus Spp. Listeria Spp.	Species	S. aureus S. epidermidis S. lugdumesis
			S. pneumoniae S. anginosus. Group S. agalaticae
Resistance	Mec A. Van A. Van B.		S. pyogenes Enterococcus faecalis Enterococcus faecium

NB. Of the staphylococci only *S.aures, S. epidermidis* and *S. lugdumesis* can be identified as the other staphylococci are not present in the data base.

Targets	Organism/Gene	
Bacterial Targets	*Acinetobacter* spp.	
	Citrobacter spp.	
	Enterobacter spp.	
	Proteus spp.	
	E. coli	
	Klebsiella pneumoniae	
	Klebsiella oxytoca	
	Pseudomonas aerogenes	
	Serratia marcescens	
Resistance Marker	CTX-M	VIM
	KPC	IMP
	NDM	OXA (48/23/40/58)

N.B. *Stenotrophomonas maltophilia* cannot be identified as it is not present in the data base

Objectives

- **To evaluate the performance of Verigene (BC-GP and BC-GN) nucleic acid test for the direct identification of Gram-positive and Gram-negative bacteria from positive blood culture bottles in comparison with Gene–Xpert system (Cephide, USA) for Gram-positive bacteria and with the conventional culture technique for both Gram-positive and Gram-negative bacteria.**
- **To evaluate the performance of Verigene (BC-GP) and (BC-GN) for the detection of resistant markers directly from positive blood culture bottles in comparison with conventional culture technique.**
- **To evaluate the impact of rapid detection of the causative pathogens from blood on the management of patients**

Materials and Methods

- All the demographic data including the age, sex, patient location, underlying clinical condition, clinical and laboratory data suggesting sepsis, **initial empirical therapy, adjusted therapy and outcome of the patients were collected.**
- **For Gram-positive bacteria:**
  - All blood culture bottles (Bactec, Bekton Dickinson, USA) showing Gram-positive cocci by Gram stain were processed in:
    - Verigene for BC-GP according to the manufacturer's instructions
    - GeneXpert (Cepheid, USA) for BC-GP (only for Gram-positive cocci in clusters)
  - All the positive blood culture bottles were simultaneously cultured by conventional methods for both ID as well as susceptibility using Vitek II, and Vitek MS (Biomerioux, France)

Materials and Methods

- **For Gram-negative bacteria:**
  - All blood culture bottles showing Gram-negative bacilli by Gram stain were processed in:
    - Verigene for BC-GN according to the manufacturer's instructions
  - All the positive blood culture bottles were simultaneously cultured by conventional methods for both ID as well as susceptibility using Vitek II, and Vitek MS
- A total of 11 QC strains of different streptococci were included in the evaluation

Results

A. Gram-positive

A total of 63 patients with positive blood culture for Gram-positive cocci were included in the evaluation

Table 1: Comparison between results of Verigine and conventional culture for Gram-positive bacteria

Gram-positive	Virigine	Conventional culture
Staphylococcus aureus	16	16
S.epidermidis	19	17
S.homonis	0	1
S.hemolyticus	0	3
Other Staphylococci	9	6
Enterococcus fecalis	9	9
Enterococcus fecium	4	4
Streptococcus pneumoniae	2	2
Streptococcus mitis	1	2
Streptococcus spp.	2	1
Micrococcus spp.	1	0

Table 2: Comparison between results of Verigine and conventional culture for 11 QC strains

Gram-positive cocci (QC strains)	Verigine	Conventional	% Concordance
Streptococcus pneumoniae	3	3	100
Streptococcus agalactiae	4	4	100
Streptococcus pyogenes	3	3	100
Enterococcus fecium	1	1	100

Table 3: Comparison between Verigine, Cephid Gene Xpert and conventional culture for *Staphylococcus* spp.

Staphylococcus spp.	Verigine	Gene Xpert	Conventional culture	% Concordance
Methicillin sensitive *Staphylococcus aureus*	8	8	8	100
S.epidermidis	12	12	12	100
S.homonis	1	1	1	100
S.hemolyticus	2	2	2	100

Table 4: Comparison between Verigine and conventional culture for detection of reistance markers for *Staphylococcus* spp.

Conventional Culture	Verigine	
	Mec A negative	Mec A positive
Methicillin sensitive *staphylococcus aureus*	TN 11	FP 2
MRSA	FN 2	TP 1
Methicillin-resistant coagulase-negative Staphylococci	0	TP 15

Table 5: Comparison between Verigine and conventional culture for detection of reistance markers for *Enterococcus* spp.

	Verigine	
Conventional Culture	**VAN A and B negative**	**VAN A and B positive**
Vancomycin sensitive *Enterococcus fecalis*	**TN 9**	**0**
Vancomycin-sensitive *Enterococcus fecium*	**2**	**0**
Vancomycin-resistant *Enterococcus fecium*	**FN 2**	**0**

A total of 63 patients with positive blood culture for Gram-negative cocci were included in the evaluation

3 of them were *Stenotrophomonas maltophila*

Not detected

Table 6: Comparison between results of Verigine and conventional culture for Gram-negative bacteria

Gram negative	Verigine	Conventional culture	% Concordance
E.coli	24	24	100
Acinitobacter spp.	15	15	100
Klebsiella pneumoniae	8	8	100
Pseudomonas aeruginosa	7	7	100
Pseudomonas oryzihabitans	1	1	100
Enterobacter spp.	2	2	100
Proteus spp.	1	1	100
Serratia marcescens	1	1	100

Table 7: Comparison between Verigine and conventional culture for detection of reistance markers for Gram-negative bacteria

Bacteria (No.)	Verigine	Conventional culture	% Concordance
E.coli (24)			
ESBL	10	10	100
Non-ESBL	14	14	100
klebsiella pneumoniae (8)			
ESBL	4	4	100
Non-ESBL	4	4	100
Enterobacter spp (2)			
ESBL	2	2	100
Non-ESBL	2	2	100
Serratia marcescens (1)			
ESBL	1	1	100
Non-ESBL	1	1	100
Pseudomonas aeruginosa (7)			
Carbapenem resistant	0	3	0
Non-carbapenem resistant	7	4	57
Acinitobacter spp. (15)			
Carbapenem resistant	1	6	17
Non-carbapenem resistant	9	4	44

Table 8: Impact of rapid adentification of Gram-positive bacteria on the modification of the empirical antibiotic therapy

Gram positive bacteria	De-escalate	Escalate	Continue same antibiotic	Stop antibiotic
Staphylococcus spp.	11	2	16	14
Enterococcus spp.	0	0	13	0
Streptococcus pneumoniae	0	0	2	0
Streptococcus mitis	0	0	0	1

Table 9: Impact of rapid adentification of Gram-negative bacteria on the modification of the empirical antibiotic therapy

Gram- negative bacteria	De-escalate	Escalate	Continue same antibiotic
Enterobacteriacae	2	11	21
Pseudomonas aeruginosa	0	3	4
Acinitobacter spp.	0	6	9

Molecular diagnosis of sepsis

TAT 2 hrs

B. Procalcitonin as a septic marker

Biomarkers for stratification of septic patients

- **To** achieve early and accurate detection of sepsis
- **To** differentiate infection from noninfectious SIRS
- **To** prognosticate clinical outcome

Hospitals and particularly ICUs have a great need
for markers which are specific and reliable
indicators of Sepsis!

Expectations on an innovative Sepsis Marker

Clinical aspects

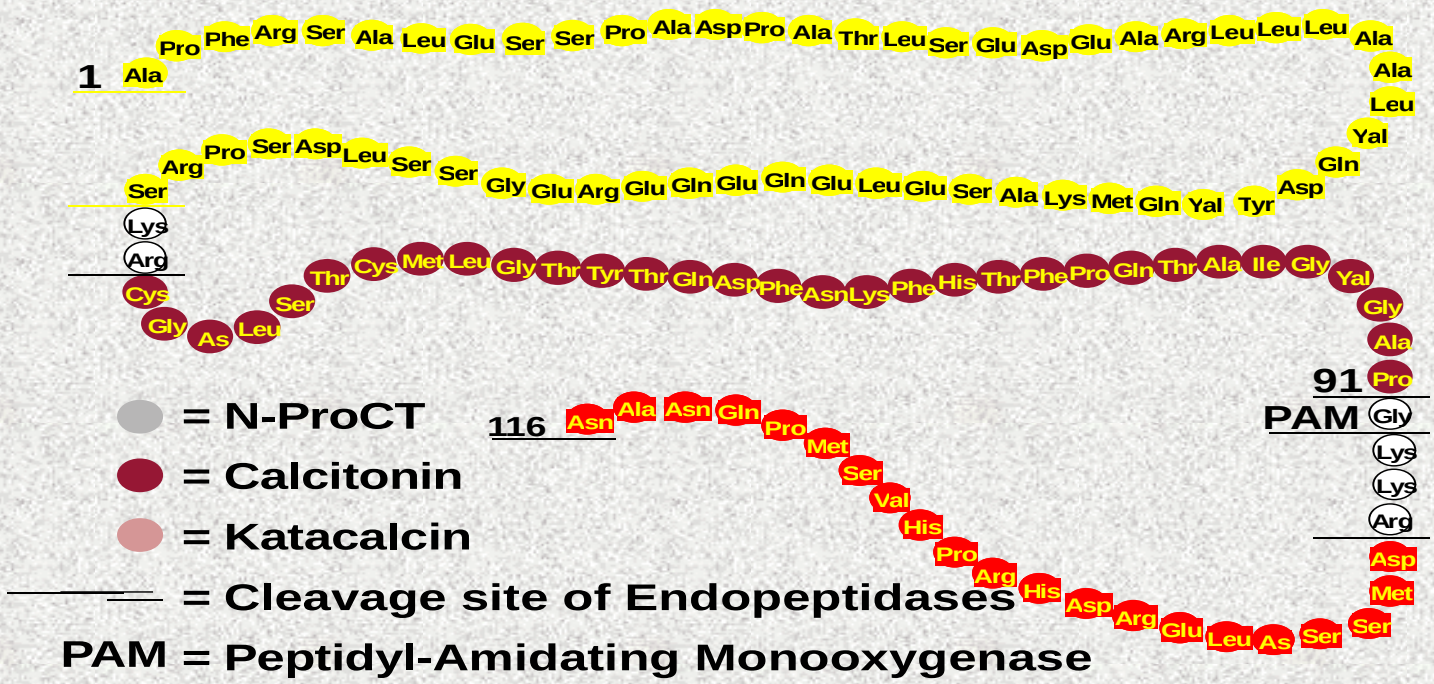
- **specific**
  - Recognises **only** septic conditions **(no false positives)**
- **Sensitive**
  - Recognises **all** septic conditions **(no false negatives)**

Technical aspects

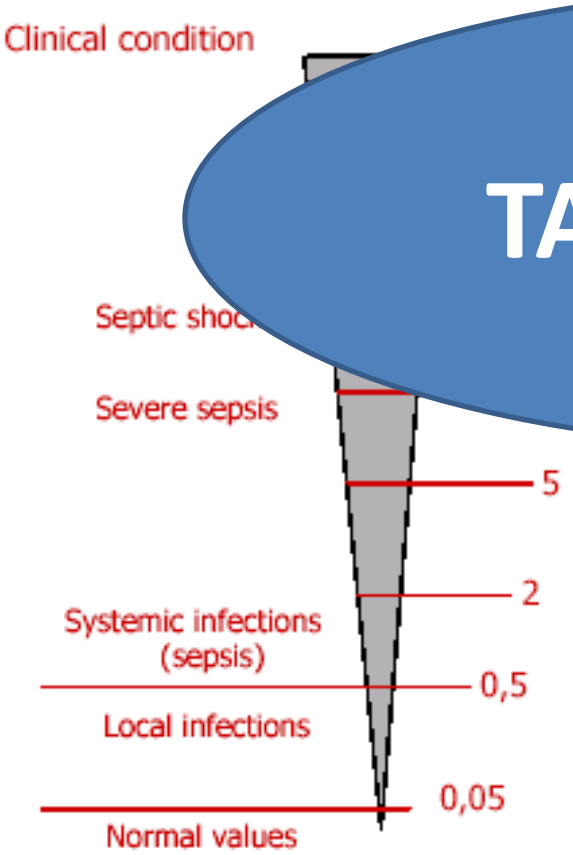
- **Applicable in lab routine**
- **Available 24/7**
- **Short time to result**

Procalcitonin
PCT

The Aminoacid-Sequence of Procalcitonin (PCT)



PCT Levels increase with Extension of Infection and Severity of Disease



TAT is 30 mints

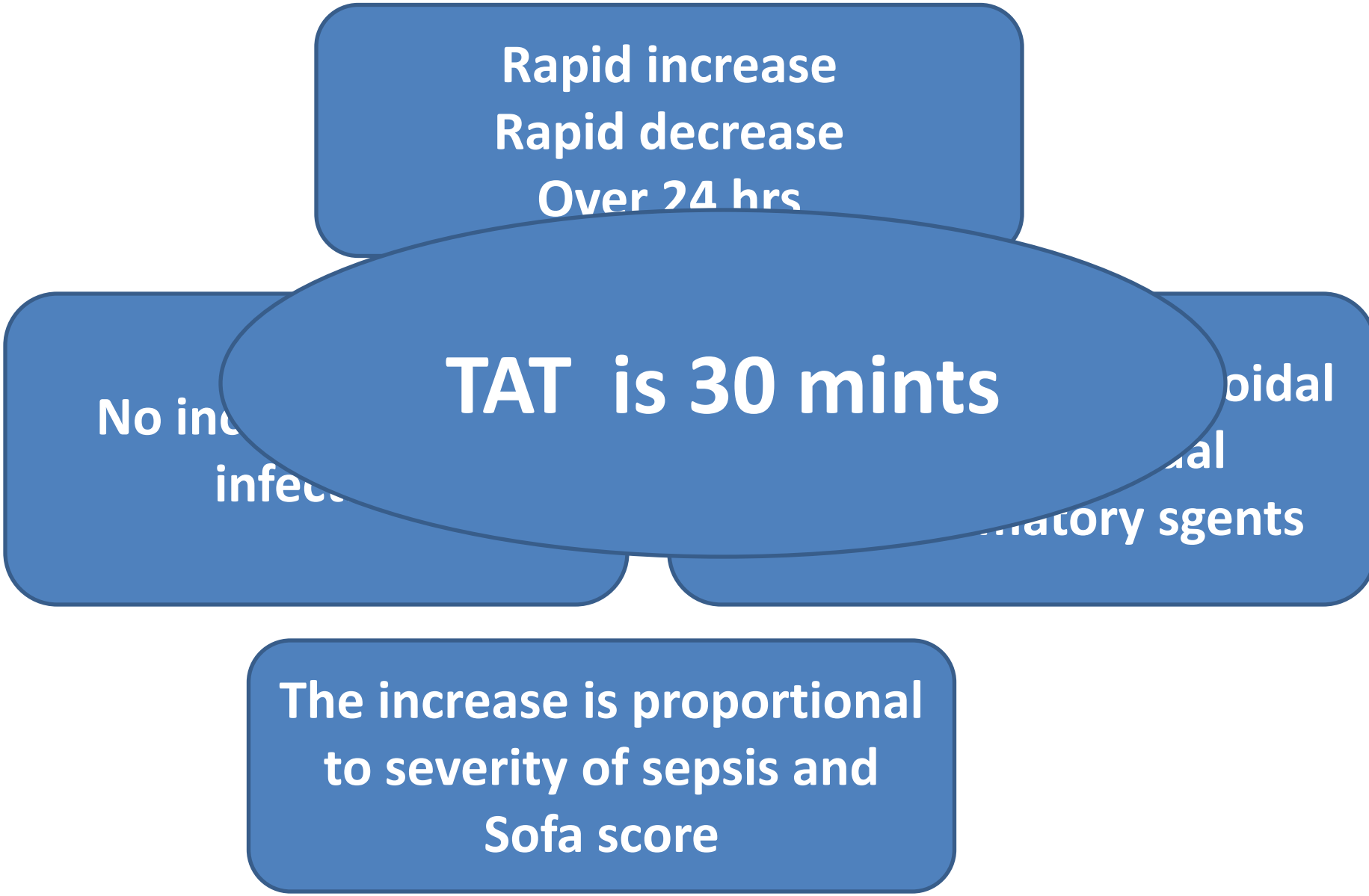
Sepsis/Sev.Sep/SS!

- *Stable in Blood Samples*
  - *Store at Room Temperature*
- *Half-Life in Plasma: 25-30hrs (1 Day)*
  - *Measure 1x per Day*

IDSA
October 2013
San Fransisco

PCT Controversies!!!

Pro-PCT



Intensive care Medicine,2011, 37: 796-800

Anti-PCT

Will PCT level improve survival and reduce antibiotics exposure in ICU patients?

No big difference in survival between PCT and control

Lancet ID, 2013, 13: 426-435

Will PCT level help to reduce antibiotic exposure??

YES

PCT had 2.7 more days without antibiotic exposure

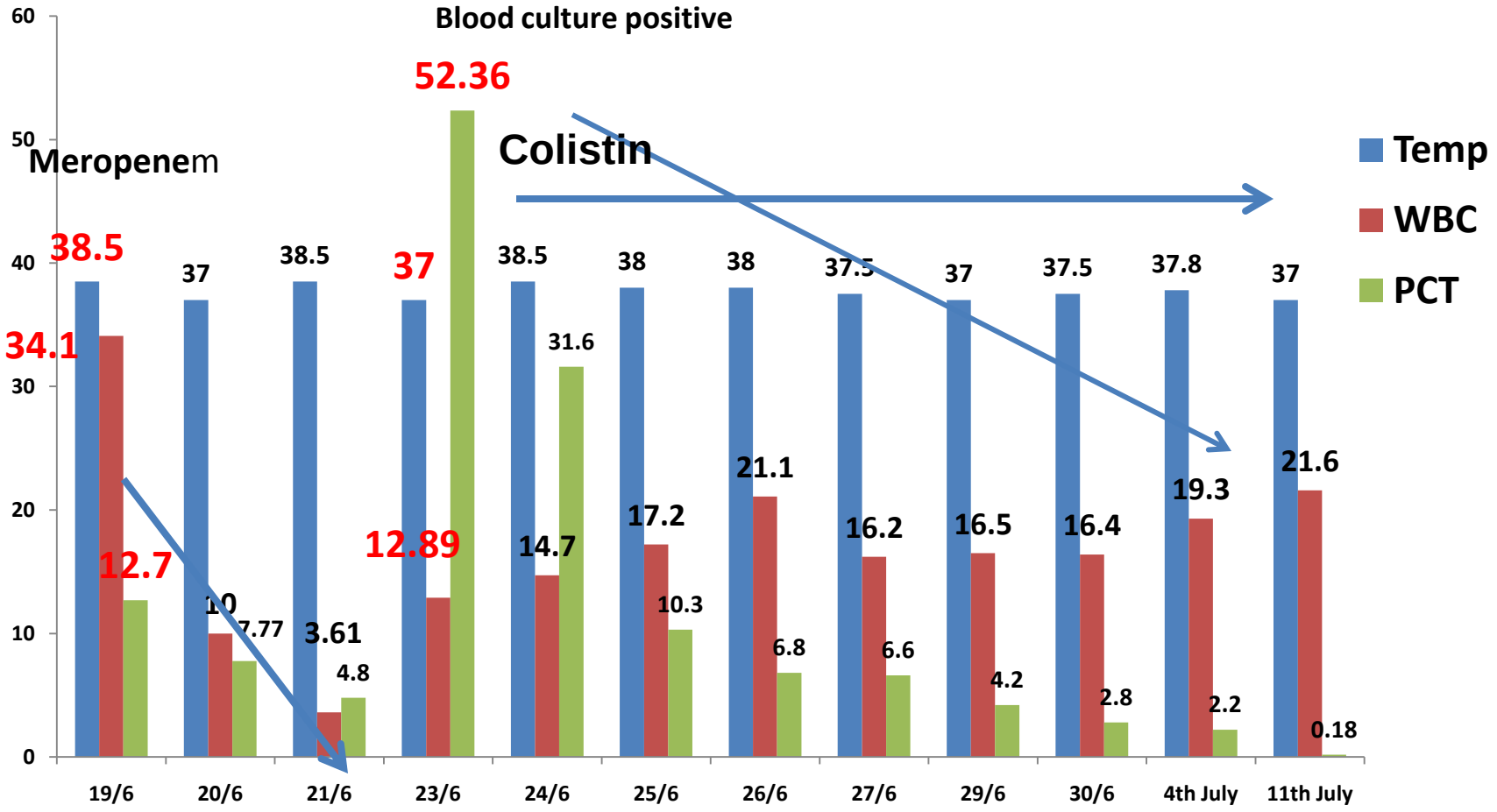
Limitation of the study:
53% PCT group were not treated according to protocoal??

Lancet ID, 2013, 13: 426-435

Case 1

- A 40 year-old male
- Admitted to the ICBU 35% burn on 18th June, 2013
- Severe hypotension
- Started on Meropenem immediately
- On the 23rd June blood grew MDR *Acinitobacter baumanii* sensitive to colistin only
- Same bacteria grew in Wound, ETT

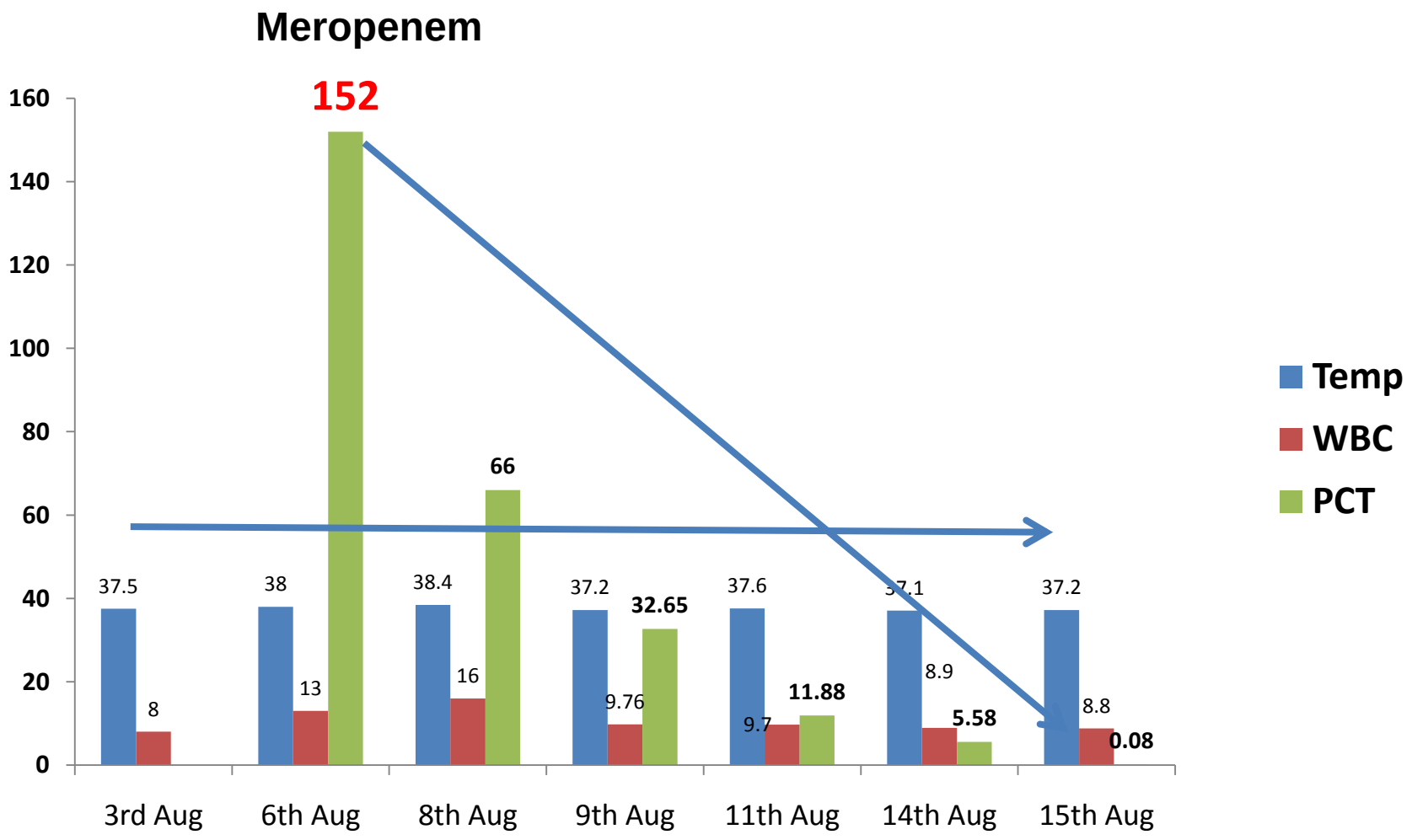
Case 1


Blood culture positive
Meropenem
Colistin
Temp
WBC
PCT
60
50
40
30
20
10
0
38.5
34.1
12.7
37
10
7.77
38.5
3.61
4.8
37
52.36
12.89
38.5
14.7
31.6
38
17.2
10.3
38
21.1
6.8
37.5
16.2
6.6
37
16.5
4.2
37.5
16.4
2.8
37.8
19.3
2.2
37
21.6
0.18
19/6
20/6
21/6
23/6
24/6
25/6
26/6
27/6
29/6
30/6
4th July
11th July

Case 2

- 57 year subdural hematoma
- MICU
- Sepsis:
- Started on Pip/Tazo
- ETT
- Blood Culture
  - Both grew *Klebsiella pneumoniae* ESBL
- Shifted to Meropenem

Case 2


Meropenem
152
66
32.65
11.88
5.58
0.08
160
140
120
100
80
60
40
20
0
37.5
8
38
13
38.4
16
37.2
9.76
37.6
9.7
37.1
8.9
37.2
8.8
3rd Aug
6th Aug
8th Aug
9th Aug
11th Aug
14th Aug
15th Aug
Temp
WBC
PCT

Prompt modification of therapy upon increase in PCT

Antimicrobial Stewardship

2. Role of new and rapid diagnostic tools in the early diagnosis of pneumonia

Pneumonia

Life-threatening acute infection of LRT

»incidence Germany 600.000 – 800.000 [1]

»up to 5% of patients admitted to a hospital for other causes develop a pneumonia [2]

»fast progressing disease

American Thoracic Society / IDSA classifies

»community-acquired pneumonia (CAP)

»acquired in the community without any history of medica intervention

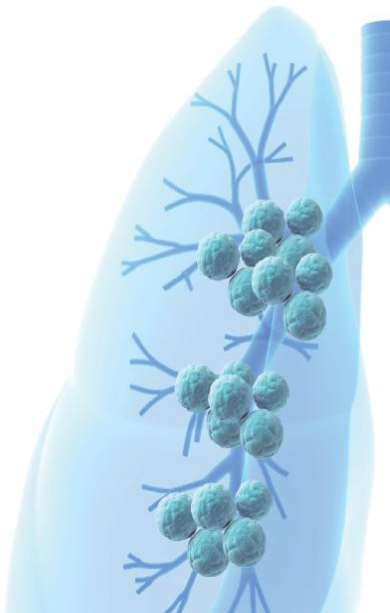
»healthcare-associated pneumonia (HCAP)

»occurs in a non-hospitalized patient with extensive health contact

»hospital-acquired pneumonia (HAP)

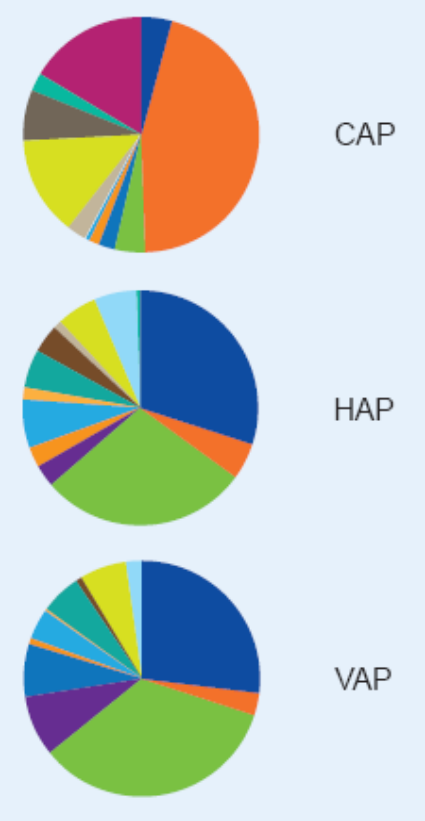
»occurs 48 hours or more after admission

»ventilator-associated pneumonia (VAP) after endotrachea

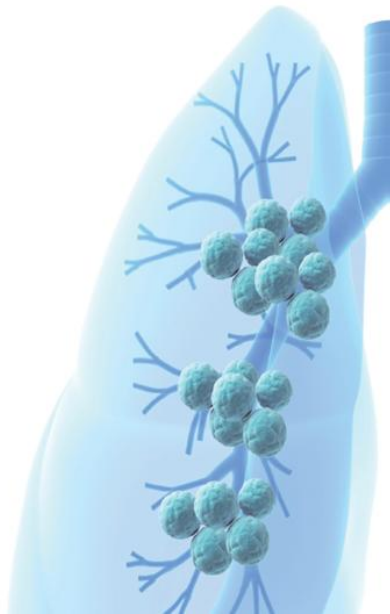


1 Höffken et al, S3 Leitlinie CAP (2009)
2 Talan et al, Clin Cour Vol25 (2007)

Microbial etiology of pneumonia

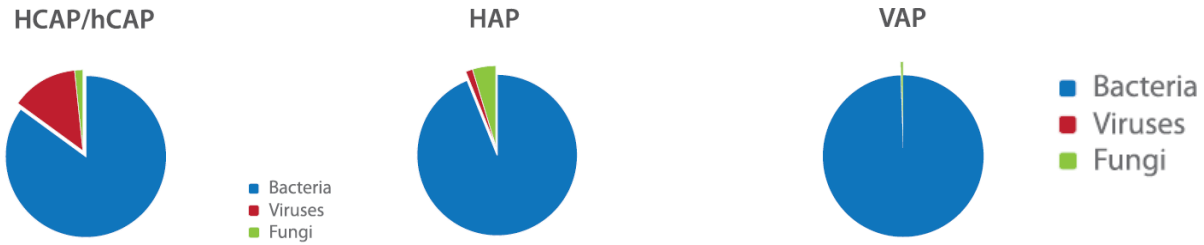


- *Staphylococcus aureus*
- *Streptococcus pneumoniae*
- *Chlamidophila pneumoniae*
- *Pseudomonas aeruginosa*
- *Enterobacteriaceae*
- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Proteus sp.*
- *Enterobacter sp.*
- *Serratia marcescens*
- *Legionella sp.*
- *Moraxella catarrhalis*
- *Haemophilus influenzae*
- *Stenotrophomonas maltophilia*
- *Acinetobacter baumannii*
- *Pneumocystis jirovecii*

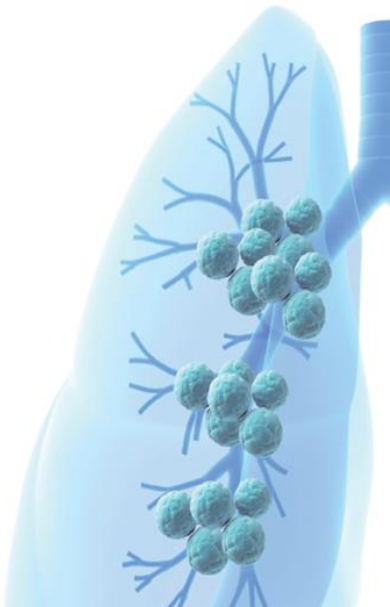


* CDC: Prevention of Healthcare-Associated Pneumonia, Management of mdr Organisms in Healthcare Settings , American Thoracic Society: HAP, VAP, HCAP II Guideline, CAP Guideline Paul-Ehrlich-Gesellschaft CAP-Leitlinie: Nosocomial pneumonia: prevention, diagnosis, treatment, European Respiratory Society: Lower Respiratory Tract Infections, British Society of Antimicrobial Chemotherapy:. HAP Guideline, Canadian Guideline Committee: VAP Diagnosis and Treatment.

Hospital-acquired pneumonia



- caused by a wide variety of pathogens
- spectrum depends on the circumstances pneumonia was acquired
- polymicrobial in 25 - 30%, depending on subtype [1]
- common pathogens include
  - aerobic gram-negative bacilli
  - gram-positive cocci
- **30 – 40 % false-negative cultures [1]**
- hospitalized pneumonia
  - due to viruses / fungi significantly less common, except in immune compromised patient
  - bacteria often drug-resistant



1 Fabregas, N Anesthelogy, Vol 4 Issue 4, 760 -771 (2009)

Clinical relevant resistance in pneumonia

–It is not just MRSA …..

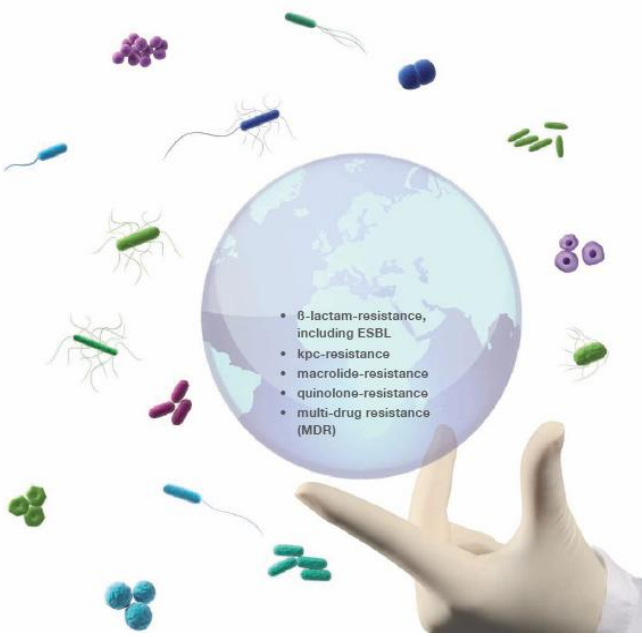
»ß-lactam-resistance, including ESBL

»KPC-resistance

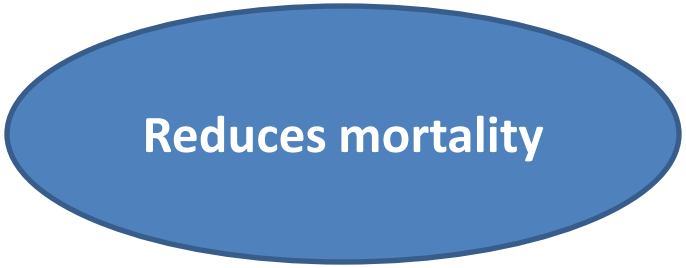
»Macrolide-resistance

»Quinolone-resistance

»Multi-drug resistance (MDR)



Challenges in testing respiratory tract infections



- Mortality rates reaches up to 36%
- Rapid a… …ffective initia…
- What i…
- Which antibi…
- Which antibiotic …

Empirical therapy for pneumonia

Inappropriate empiric therapy

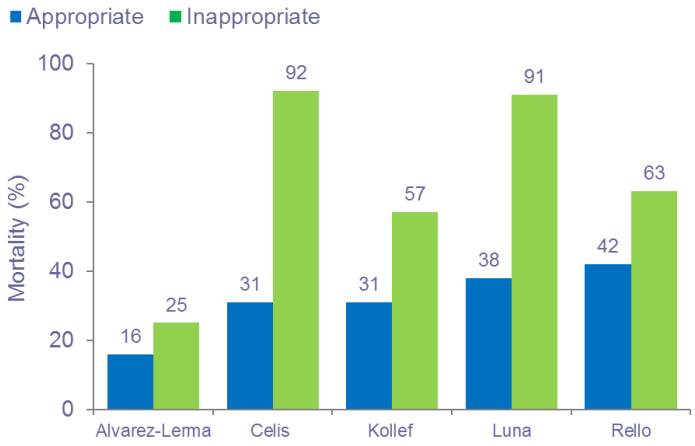
» empirically based initial regimen wrong in up to 40 – 50 % of cases [1]

» associated with increased mortality,

» adequate initial treatment significantly reduces

- **mortality**
- **LOS**
- **costs per patient**

- **outcome benefits from faster diagnostics [3]**

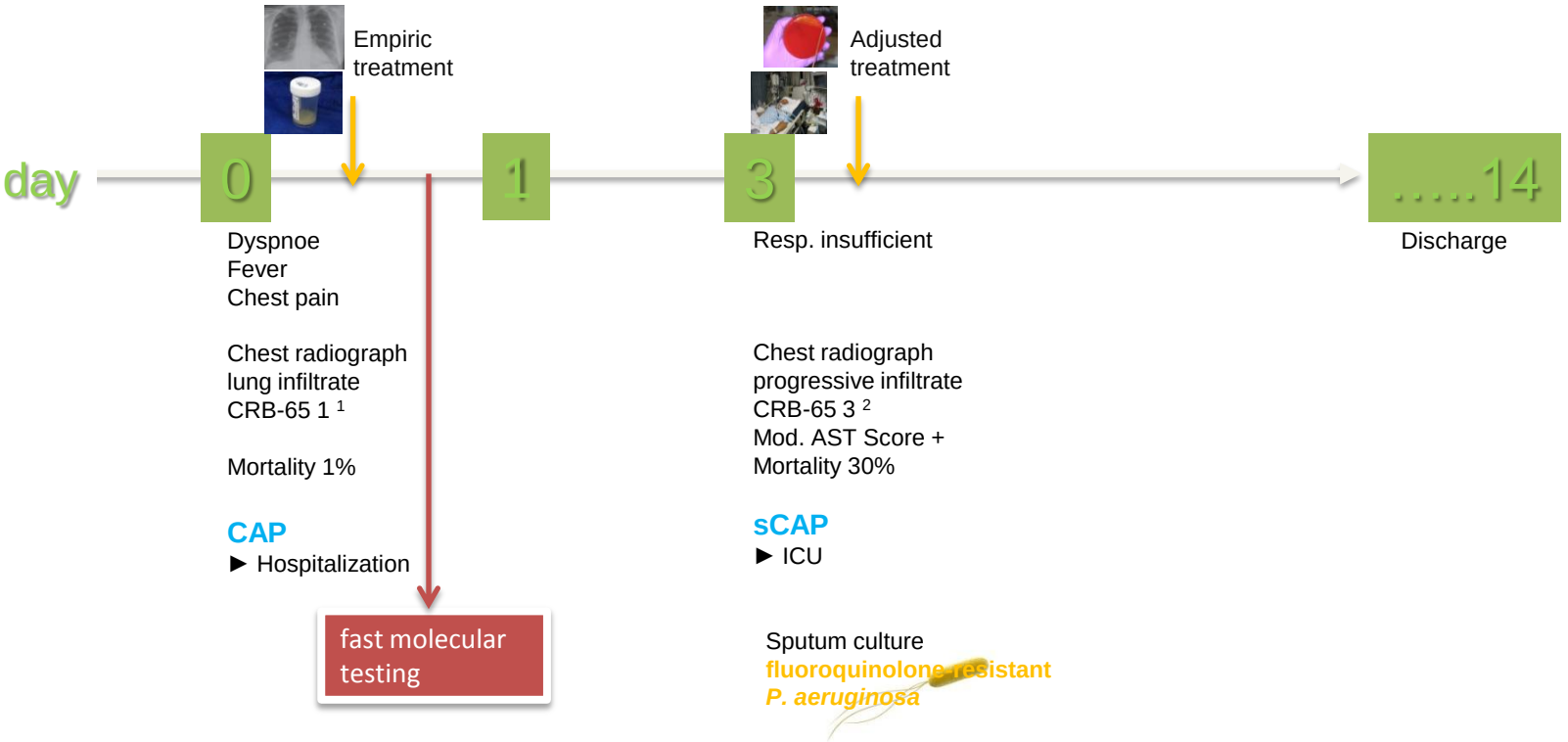


Alvarez-Lerma F. Intensive Care Med 1996; 22:387–94
Celis R, et al. Chest 1988; 93:318–24;
Kollef MH, Ward S. Chest 1998; 113:412–20
Luna CM, et al. Chest 1997; 111:676–85;
Rello J, et al. Am J Respir Crit Care Med 1997; 156:196–200.

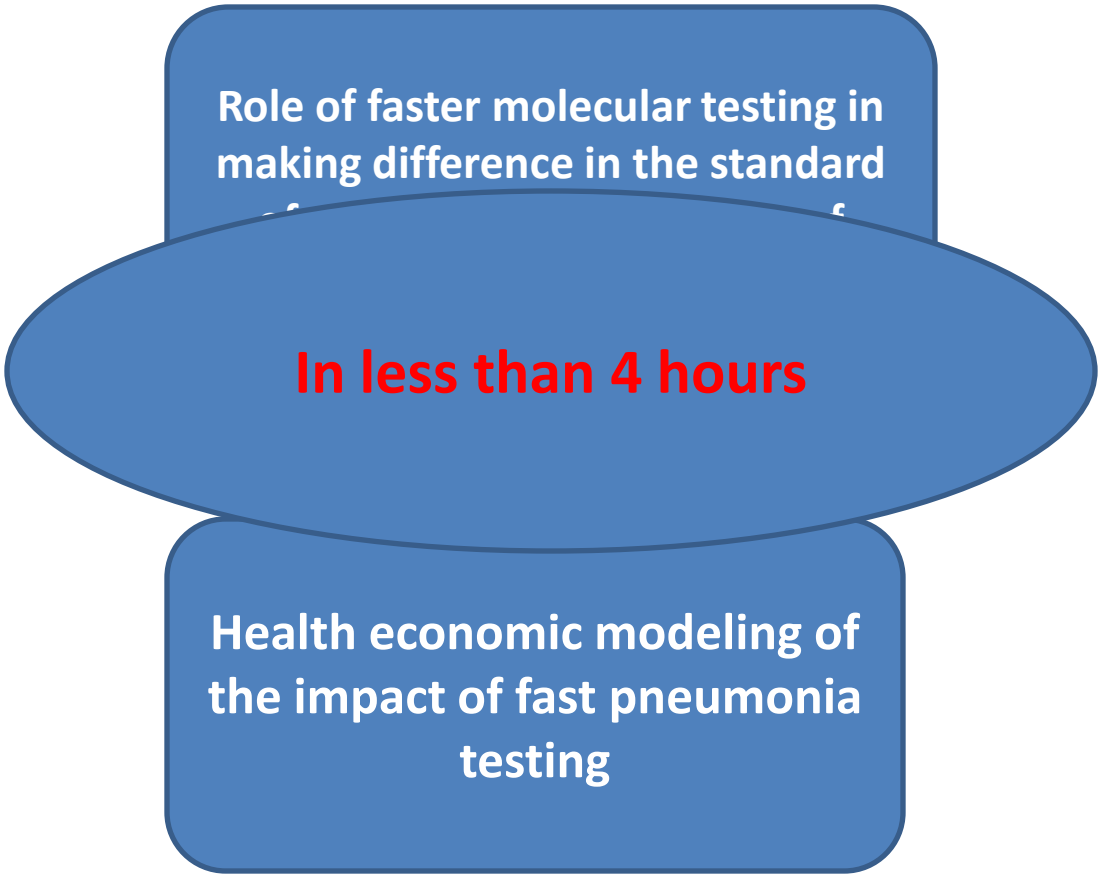
1 Kollef et al, Chest. 1999 Feb;115(2):462-74
2 Talan et al, Clin Cour, Vol 25 (2007)
3 Rello J et al, Am J Respir Crit Care Med 1997;156:196–200.

CASE STUDY

- Female, 73 y



1 Short inpatient hospitalization
2 Severe pneumonia


Role of faster molecular testing in making difference in the standard
In less than 4 hours
Health economic modeling of the impact of fast pneumonia testing

UNMET MEDICAL NEED

SUPPLEMENT ARTICLE IDSA PUBLIC POLICY

IDSA

An Unmet Medical Need: Rapid Molecular Diagnostics Tests for Respiratory Tract Infections

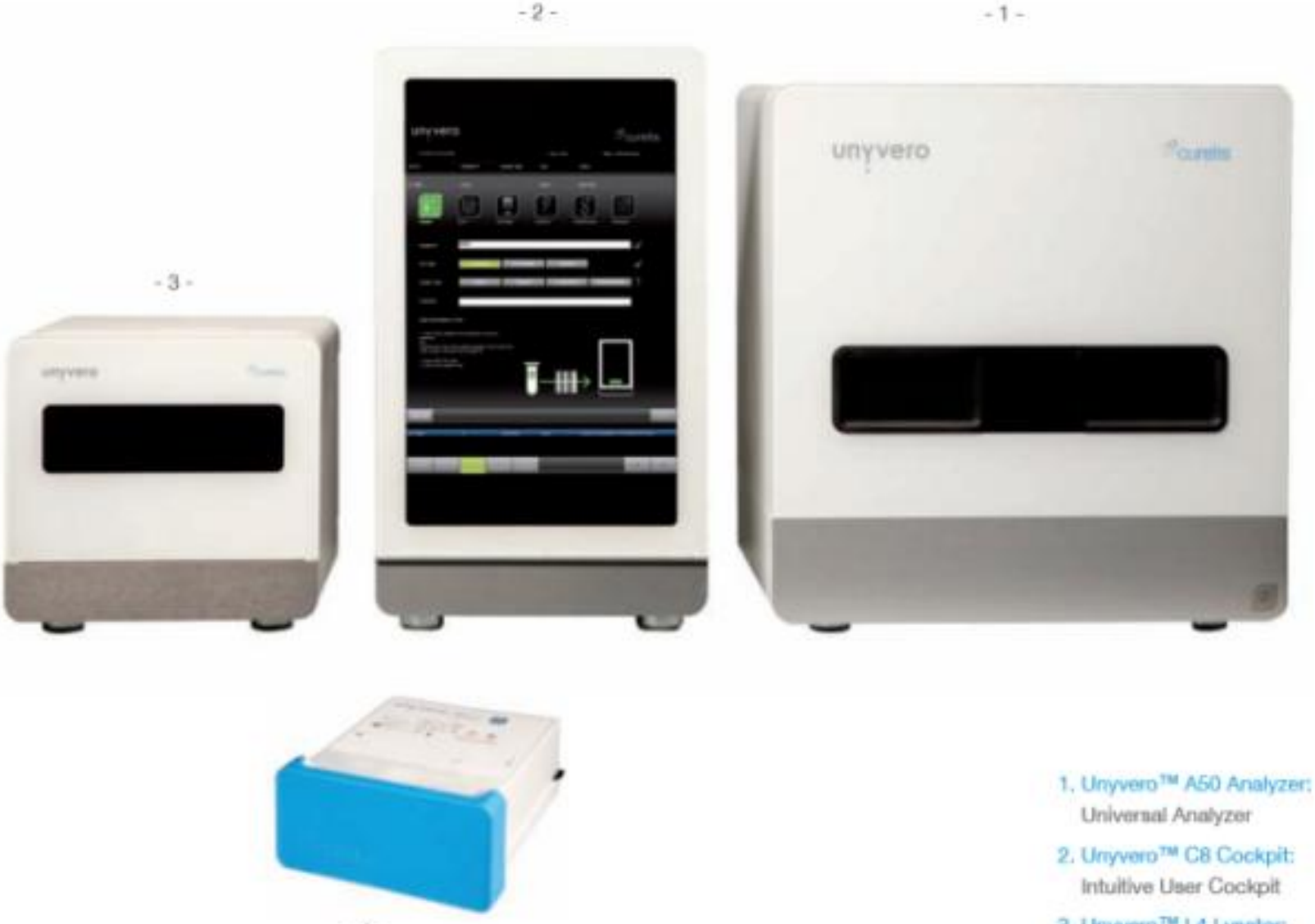
Infectious Diseases Society of America[a]

ISDA; CID 2011, 52 (Suppl 4)

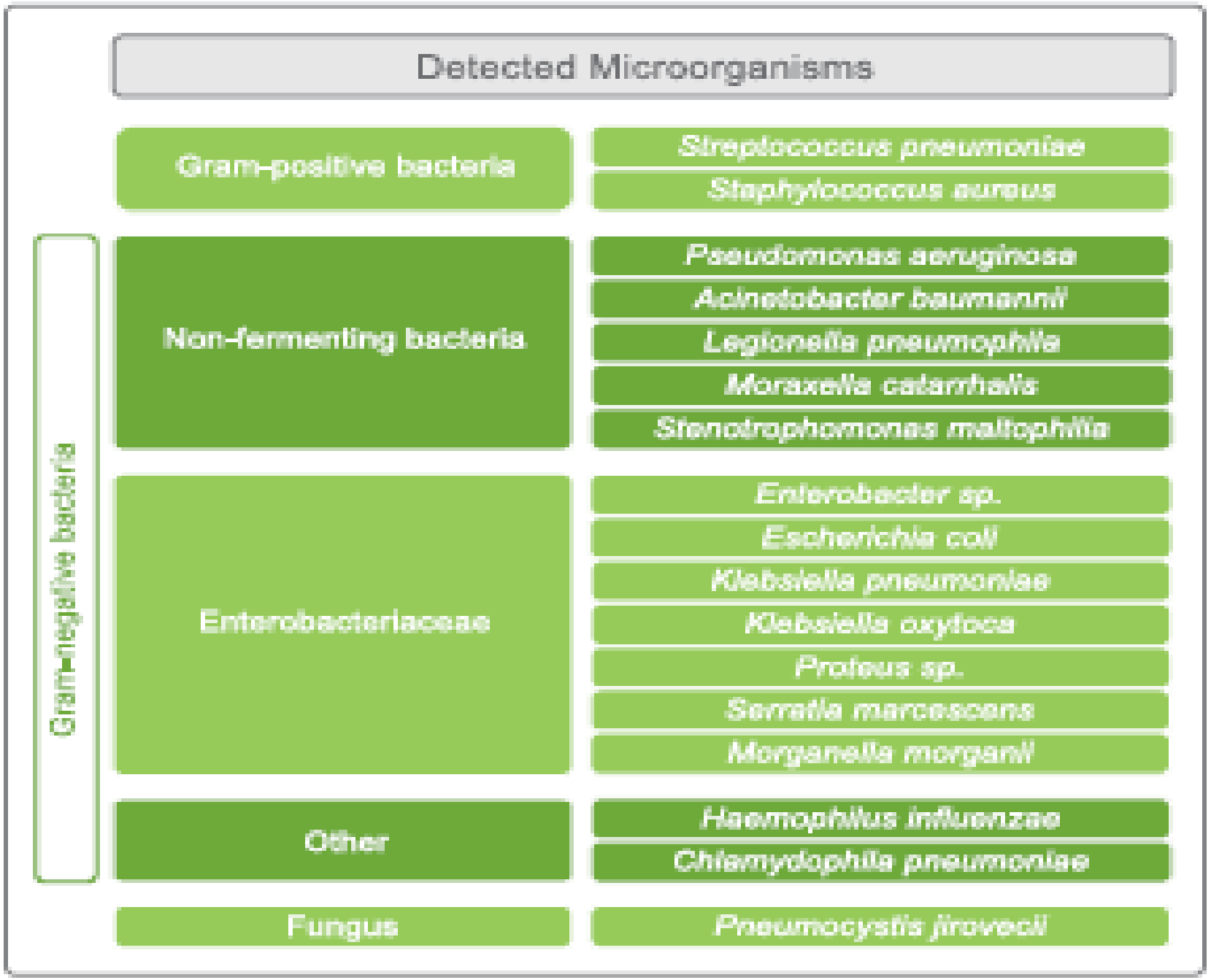
unyvero™

Evaluation of P50 Pneumonia Application in the rapid diagnosis of pneumonia in a tertiary-care hospital in Kuwait

Dr. Aneesa Abdulla
Dr. Shama Shatti
Dr. Ahmed Behbehani
Professor Eiman Mokaddas

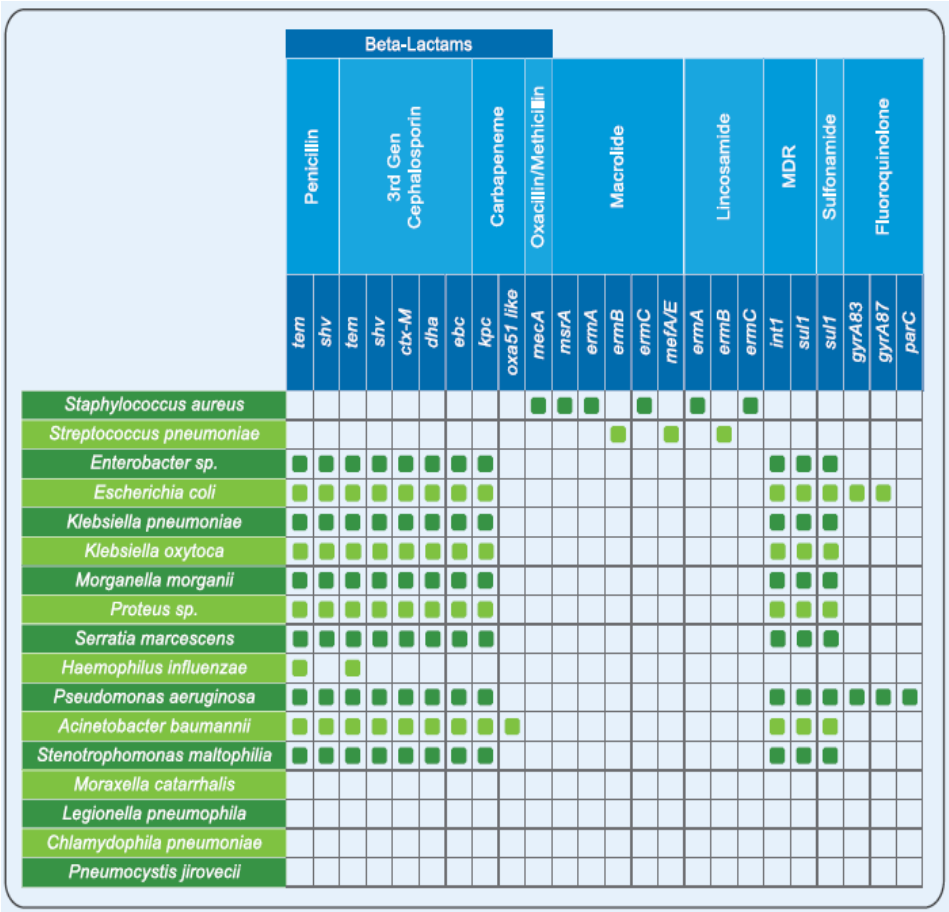


1. Unyvero™ A50 Analyzer: Universal Analyzer
2. Unyvero™ C8 Cockpit: Intuitive User Cockpit
3. Unyvero™ L4 Lysator: Universal Lysator
4. Unyvero™ Cartridge: Disposable for different clinical application


Detected Microorganisms
Gram-positive bacteria
Streptococcus pneumoniae
Staphylococcus aureus
Gram-negative bacteria
Non-fermenting bacteria
Pseudomonas aeruginosa
Acinetobacter baumannii
Legionella pneumophila
Moraxella catarrhalis
Stenotrophomonas maltophilia
Enterobacteriaceae
Enterobacter sp.
Escherichia coli
Klebsiella pneumoniae
Klebsiella oxytoca
Proteus sp.
Serratia marcescens
Morganella morganii
Other
Haemophilus influenzae
Chlamydophila pneumoniae
Fungus
Pneumocystis jirovecii

ANTIBIOTIC RESISTANCE MARKERS

Marker	Structure	Mechanism	Localization
tem	ß-Lactamase	Target inactivation/hydrolyzation	Plasmid
shv	ß-Lactamase	Target inactivation/hydrolyzation	Chromosome/ Plasmid
ctx-M	ß-Lactamase/ Cefotaximase	Target inactivation/hydrolyzation	Plasmid
dha	AmpC-ß-Lactamase	Target inactivation/hydrolyzation	Chromosome/ Plasmid
ebc	AmpC-ß-Lactamase	Target inactivation/hydrolyzation	Plasmid
kpc	Carbapenemase	Target inactivation/hydrolyzation	Chromosome/ Plasmid
oxa51 like	Carbapenemase	Target inactivation/hydrolyzation	Plasmid
mecA	Penicillin binding protein	Target alteration	Chromosome
msrA	Efflux pump	Target discharge	Chromosome
ermA	Erythromycin-methylase	Target modification	Chromosome and Plasmid
ermB	Erythromycin-methylase	Target modification	Chromosome and Plasmid
ermC	Erythromycin-methylase	Target modification	Chromosome and Plasmid
mefA/E	Efflux pump	Target discharge	Transposon
int1	Integrase	MDR marker	Chromosome and Plasmid
sul1	DHPS	Target alteration	Plasmid
gyrA83	Gyrase A	Target mutation	Chromosome
gyrA87	Gyrase A	Target mutation	Chromosome
parC	Topoisomerase	Target mutation	Chromosome



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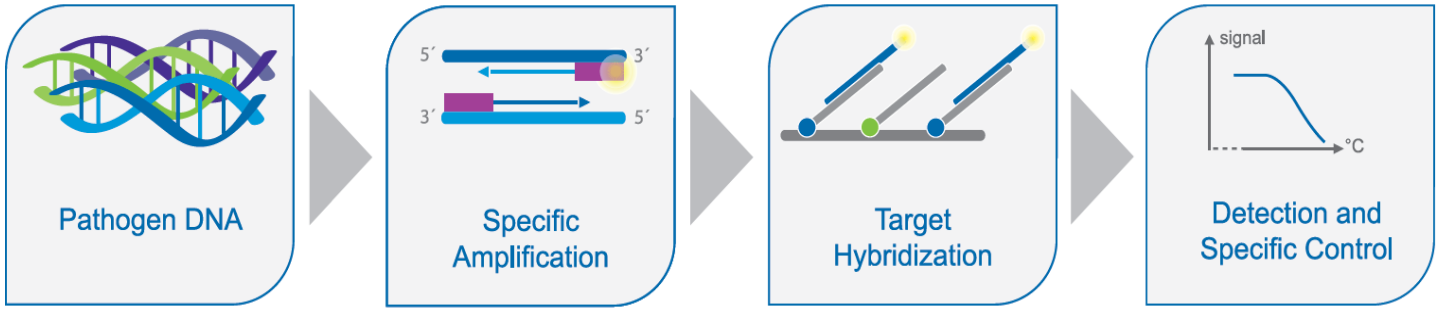
Multiplex PCR and array-based detection



a few, qick, manual steps

fully automated, unsupervised analysis

answers < 4h

Step 1 ~ 60 seconds:

Transfer the patient sample into the Unyvero™ Sample Tube.

Step 2 ~ 30 seconds:

Place the Unyvero™ Sample Tube into the Unyvero™ Lysator.

Step 3 ~ 30 seconds:

After taking the Sample Tube out of the Lysator insert it and the Unyvero™ Master Mix Tube into the Unyvero™ Cartridge.

Step 4 ~ 20 seconds:

Load the Cartridge into the Unyvero™ Analyzer for further fully automated processing.

Answers:

Comprehensive results are available in < 4 hours and will be displayed on the Unyvero™ Cockpit screen without any further operator interaction.

Objectives

- To evaluate the role of unyvero™ in the rapid diagnosis of pneumonia (Both CAP and HAP) and the detection of resistance markers in comparison with the conventional culture techniques
- To evaluate the impact of **rapid molecular diagnosis of pneumonia on the management of patients**

Methods

- All patients with the clinical diagnosis of pneumonia both CAP, HAP and VAP from 3 ICU's, one Organ Transplant Department, and KCCC/ Shaikha Badria Center for Cancer and Chemotherapy admitted to the hospital from November 2012 till April 2013 were included in the evaluation.
- 6 patients on mechanical ventilation with no evidence of pneumonia were included as surveillance
- All relevant clinical data were collected
- Sputum, ETT's or BAL were inoculated into cartridge and processed as well by conventional culture technique

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Results

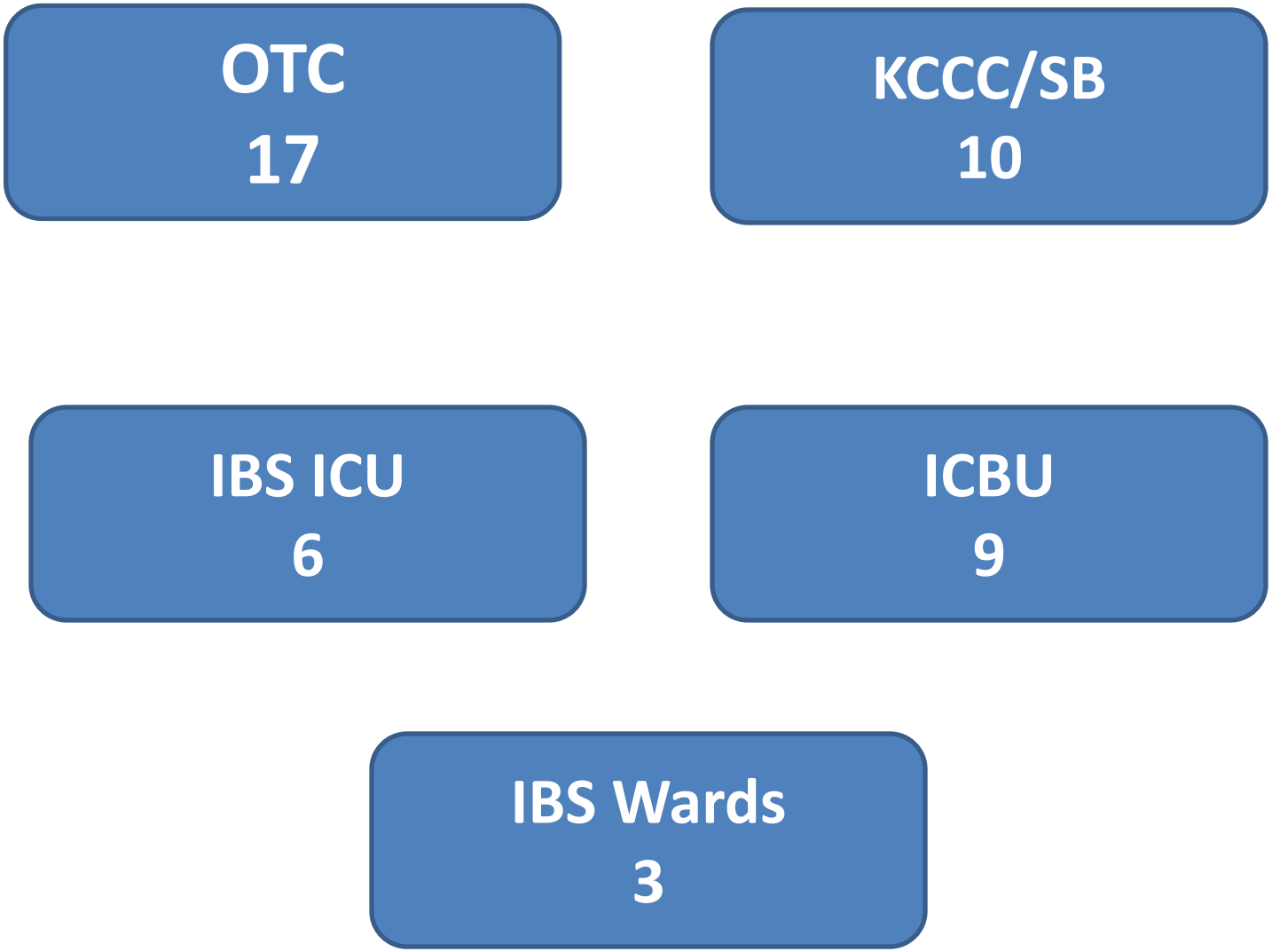
A total of 45 patients were included in the evaluation

VAP
18

HAP
10

CAP
11

6 surveillance cases


OTC
17
KCCC/SB
10
IBS ICU
6
ICBU
9
IBS Wards
3

- **The detailed data on all the patients:**
  - Underlying conditions
  - Clinical diagnosis
  - Signs of infection (e.g. fever, WBC, PCT)
  - Microbiology diagnostic findings by Unyvero compared to the conventional culture techniques for both ID as well as antimicrobial susceptibility testing results
  - Empirical antibiotic therapy
  - **Modification of antibiotic therapy based on Unyvero results in 4 hrs**
  - The final outcome of the patients.

Comparision between Unyvero and Conventional culture in the detection of different microrganisms

Organism	Unyvero	Conventional Culture
S.pneumoniae	13	1
Haemophius influenzae	6	2
S.aureus	4	0
Pseudomonas aeruginosa	6	4
Acinitobacter baumanii	7	5
Stenotrophomonas maltophilia	8	4
Klebsiella pneumoniae	6	1
E.coli	4	3
Maroxella catarallis	2	0
Proteus spp.	3	2
Enterobacter spp.	0	2
Pneumocyctis jerovesii	1	0
Pantonia	0	1
Legionella pneumoniae	4	0
Chamydia pneumoniae	1	0
Enterococcus spp.	0	2
Candida spp.	0	13
Not detected/ No growth	4	3
Commensals	0	3

TAT for Unyvero
4hrs
For both ID and AST

TAT for the conventional culture technique is 48-72 hrs

Comparison of the detection of antibiotic resistance between Unyvero System and the conventional Culture

TAT 4 hrs

Organism			ional culture
Pseudomonas aerug.			1
Klebsiella spp.	2	1	1
Acinitobacter baumanii	4	4	4
Proteus spp.	1	1	1
E.coli	1	1	1

Impact of Rapid diagnosis of Pneumonia on the management of pneumonia cases

In 12 cases
6 VAP, 4 CAP, 2 HAP

Empirical AB X modified either the same day or within 24 hrs according to Unyvero results for both ID and resistance markers

With significant improvement after the modification

4 patients all immunocompromised *Legionella pneumophila* detected and treated accordingly

One *Chlamydia pneumoniae* detected in one cancer patient and treated accordingly

Case 1

- 52 years Kidney transplant
- Case of CAP (hospitalized)
- Unyvero in 4hrs:
  - *S.pneumoniae*
  - *Hemophilus influenzae*
- Empirical therapy:
  - Respiratory quinolone
  - No improvement
- Modification:
  - Add ceftriaxone
- Marked improvement

Conventional tculture After 48 hrs *Haemophilus influenzae*

Case 2

- 57 years Kidney transplant
- A case of VAP
- Unyvero in 4 hrs:
  - *Acinitobacter baumani*
  - *Pseudomonas aerugino*
- Resistance Markers:
  - Int1, sul1 AND Oxa 51
- Empirical therapy:
  - Meropenem
- Modification upon resistance markers the same day:
  - Add colistin

Conventional culture after 72 hrs *Acinitobacter baumanii*
Resistant to meropenem
Sensitive to colistin

Case 3

- 27 years patient in neurology ward
- A case of HAP
- Unyvero in 4 hrs:
  - *S.pneumoniae*
  - *Pseudomonas aeroginosa*
  - *Legionella pneumophila*
  - *Stenotrophomonas maltophilia*
  - *S.aureus*
- Resistance markers:
  - None
- Empirical therapy:
  - Tazocin
- Modification of therapy
  - Add respiratory quinolone for *Legionella pneumophila*

Conventional culture after 72 hrs
Proteus mirabilis
Pseudomonas aeruginosa
Sensitive strain

Case 4

- 53 years patient in SB
- A case of lymphoma
- Unyvero in 4 hrs:
  - *Acinitobacter baumanii*
  - *Stenotrophomonas maltophilia*
  - *Pneumocystis jerovrci*
- Resistance Markers:
  - Oxa 51
  - CTX-M
  - Tem
- Empirical therapy:
  - Meropenem
- Modification:
  - Add colistin
  - Cotrimoxazole

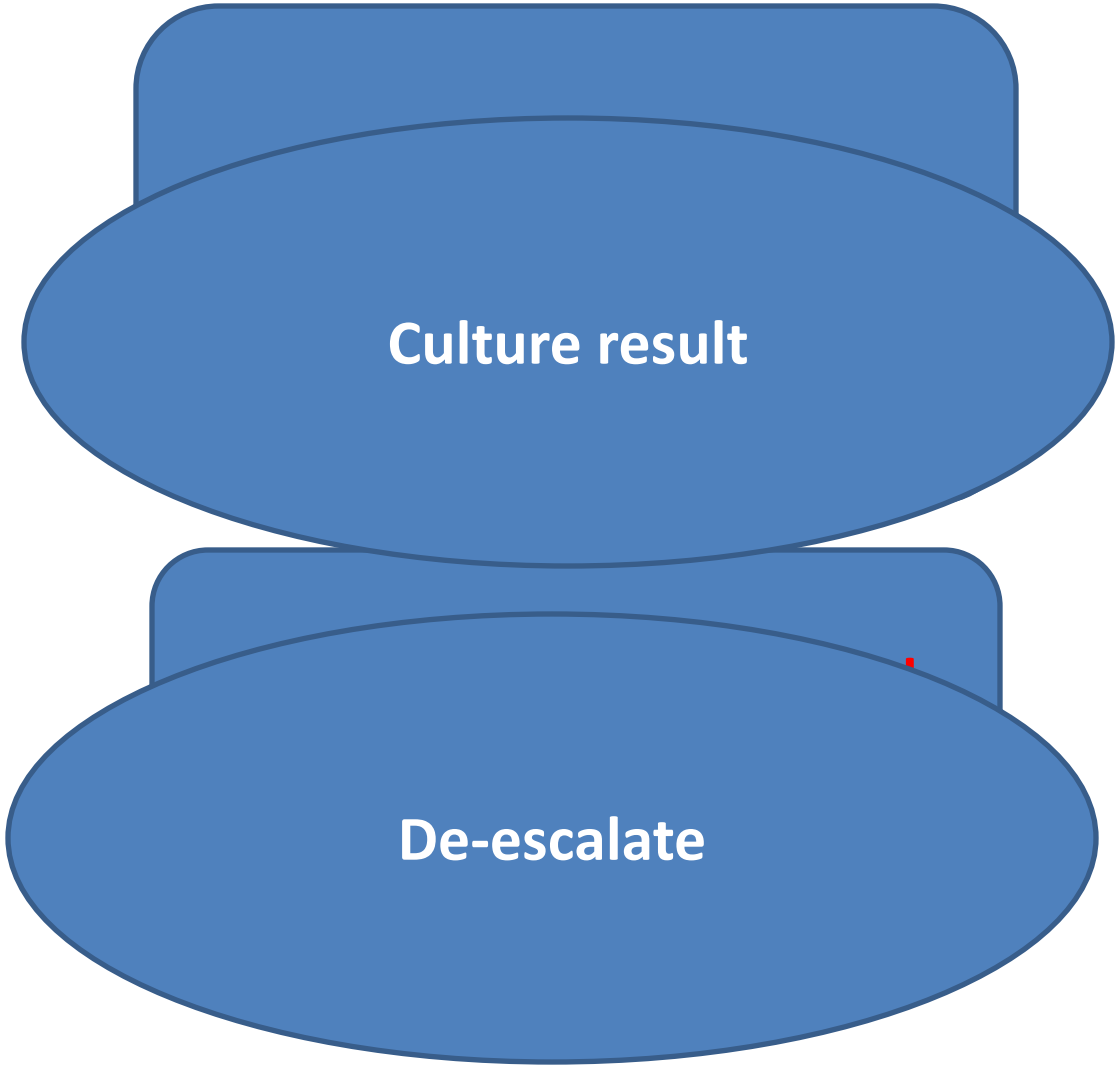
Conventional techniques After 72 hrs *Acinitobacter baumanii* only Sensitive to meropenem

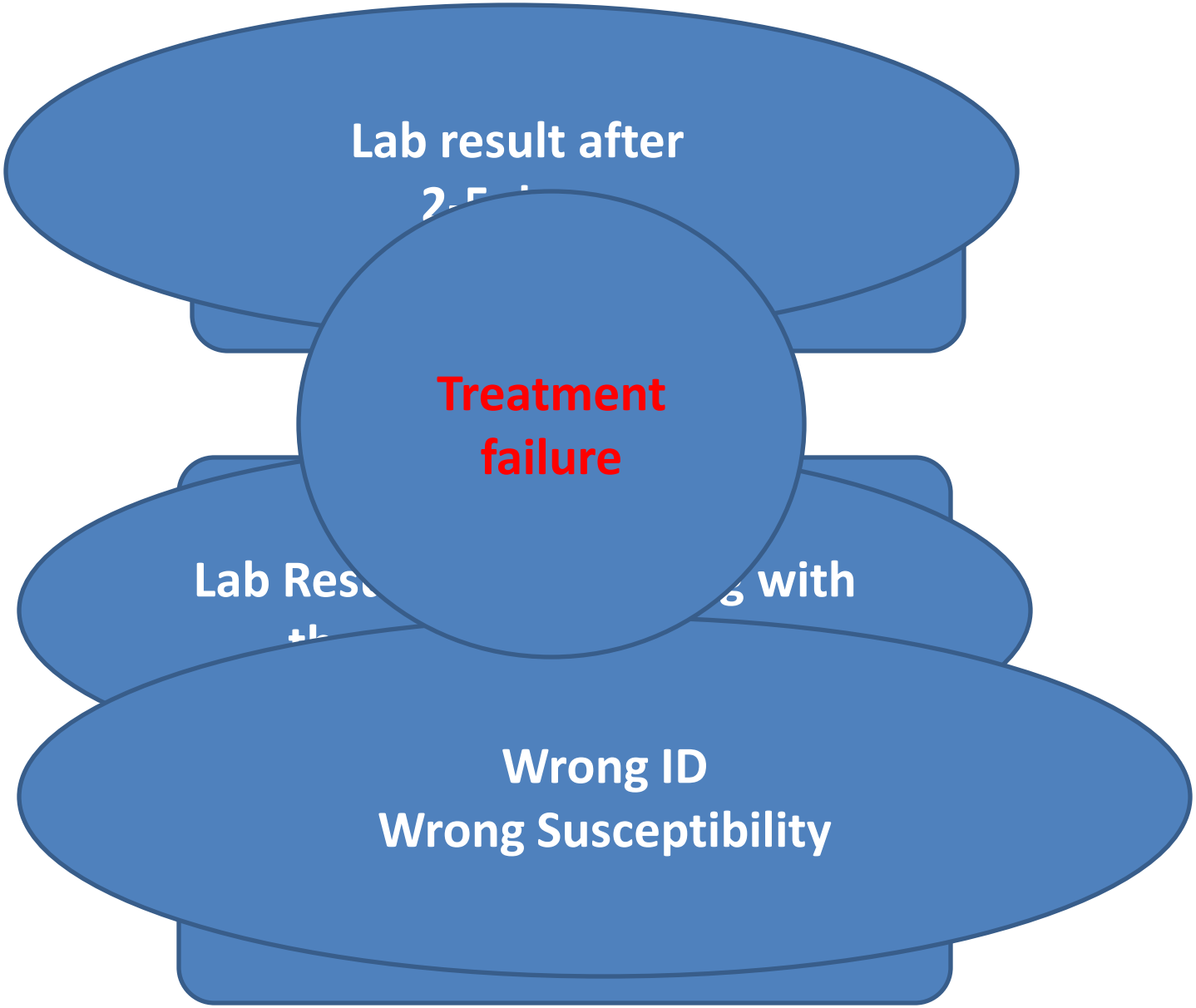
Acknowledgement

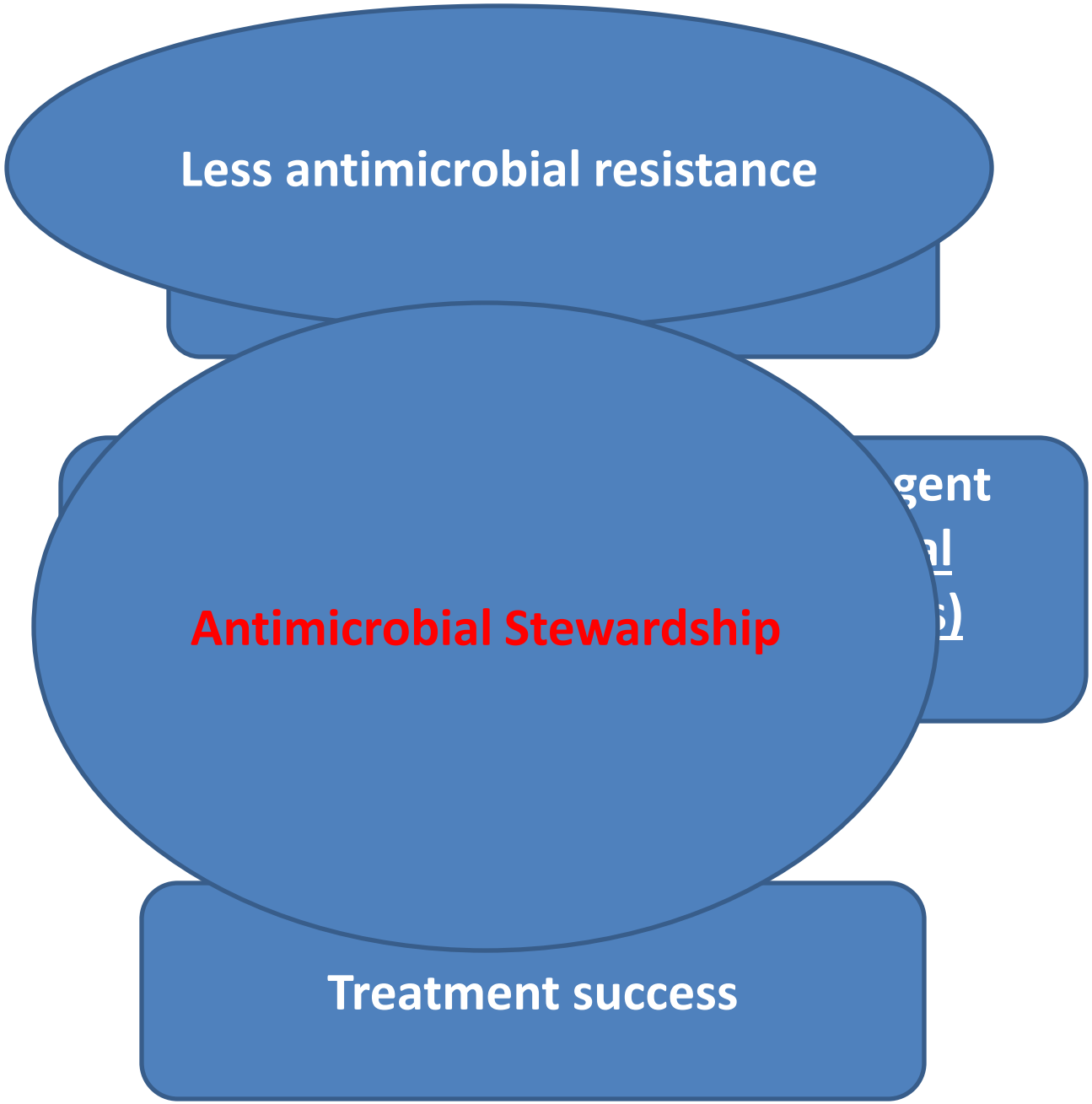
Conclusion

Management of Infectious Diseases

In the era of antimicrobial resistance, are new antibiotics the solution???


Culture result
De-escalate


Lab result after
Treatment
failure
with
Wrong ID
Wrong Susceptibility


Less antimicrobial resistance
Antimicrobial Stewardship
Treatment success

Timing Line

Diagnosing Sepsis and Pneumonia

Time waits for no body

Tomorrow is too late

Thank You