Respiratory Specimens:
From collection to clinical decision-making

Dr Tina Law
Senior Clinical Microbiologist, Ampath Laboratories
MBChB (UCT), DTM&H (Wits), FC Path (SA) (Microbiology), MMed (Microbiology) (Wits)

AMPATH LABORATORIES

OVERVIEW

1. Specimen selection & collection
2. Basic concepts (MC&S)
   - Microscopy/Culture/Sensitivity
3. Lower respiratory tract cultures
4. Molecular Diagnostic Tests
5. Mycobacterial Diagnostics
6. Blood cultures
7. CRP
8. PCT

1. Specimen selection & collection

- At a basic level, the doctor needs answers to 3 very basic questions from the laboratory:
  1. Is my patient's illness caused by an infection?
  2. If so, what microbe (bacteria, virus, parasite, fungus)?
  3. What is the susceptibility profile of the organism so therapy can be targeted?

- **A properly selected & collected specimen is the single most important step in the diagnosis of any infectious disease**

- General rules for all specimens:
  1. The **quantity** of the specimen must be adequate
  2. It should be **representative** of the infectious process
  3. **Avoid** specimen **contamination** by using sterile containers & observing aseptic technique
  4. Take samples **before** administering **antibiotics**
  5. **Prompt transportation** to the laboratory

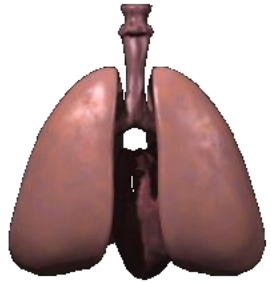
Miller JM, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2018 update by the Infectious Diseases Society of America and the American Society for Microbiology. CID 2018;67(6):e1-e94.

AMPATH LABORATORIES

Lower Respiratory Tract Infections

- Respiratory tract infections are among the most common infectious diseases
- The list of causative agents continues to expand as new pathogens & syndromes are recognised
- **Clinical microbiology is a science of interpretive judgement that is becoming more complex, not less**

- Key points for the laboratory diagnosis of lower respiratory tract infections:
  - PCRs have largely replaced rapid antigen tests & culture for respiratory virus detection
  - First morning expectorated sputum is always best for bacterial culture
  - Blood cultures may occasionally be helpful, particularly in hospitalised patients with pneumonia
  - In the immunocompromised host, a broad diagnostic approach based upon invasively obtained specimens is suggested
  - Bronchoscopy with washings is the optimal diagnostic specimen in paediatrics

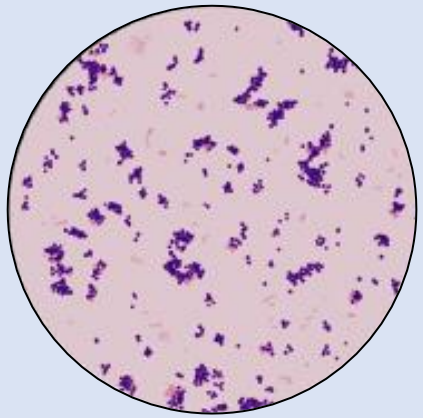


Miller JM, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2018 update by the Infectious Diseases Society of America and the American Society for Microbiology. CID 2018;67(6):e1-e94.

2. MC&S Basic Concepts – Microscopy (Gram Stain)

Gram +

e.g. *Staphylococcus aureus*



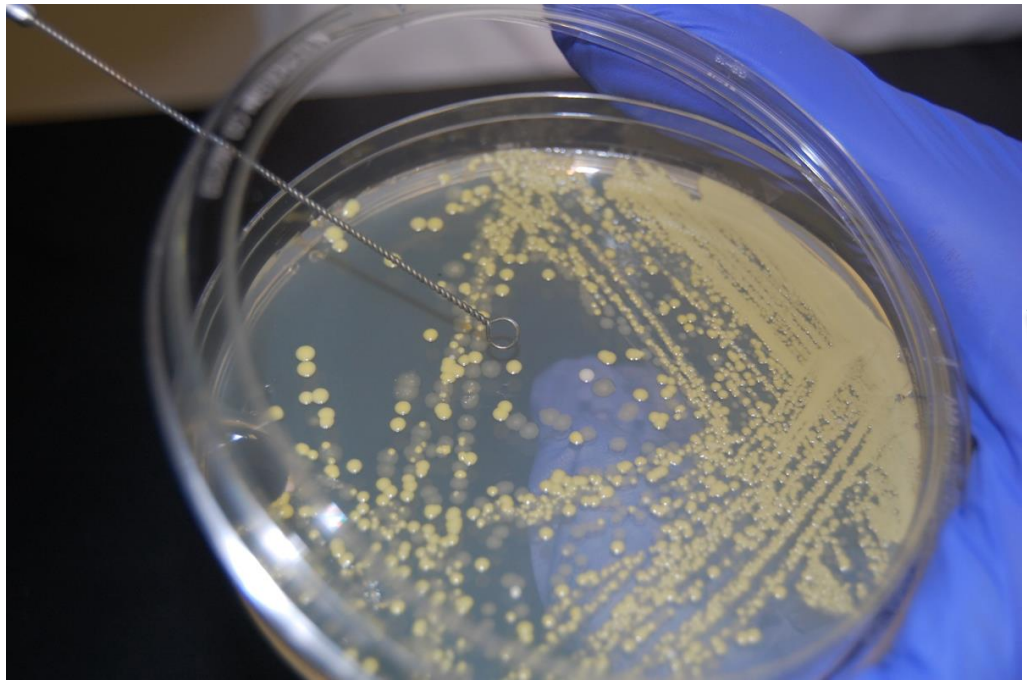
Gram -

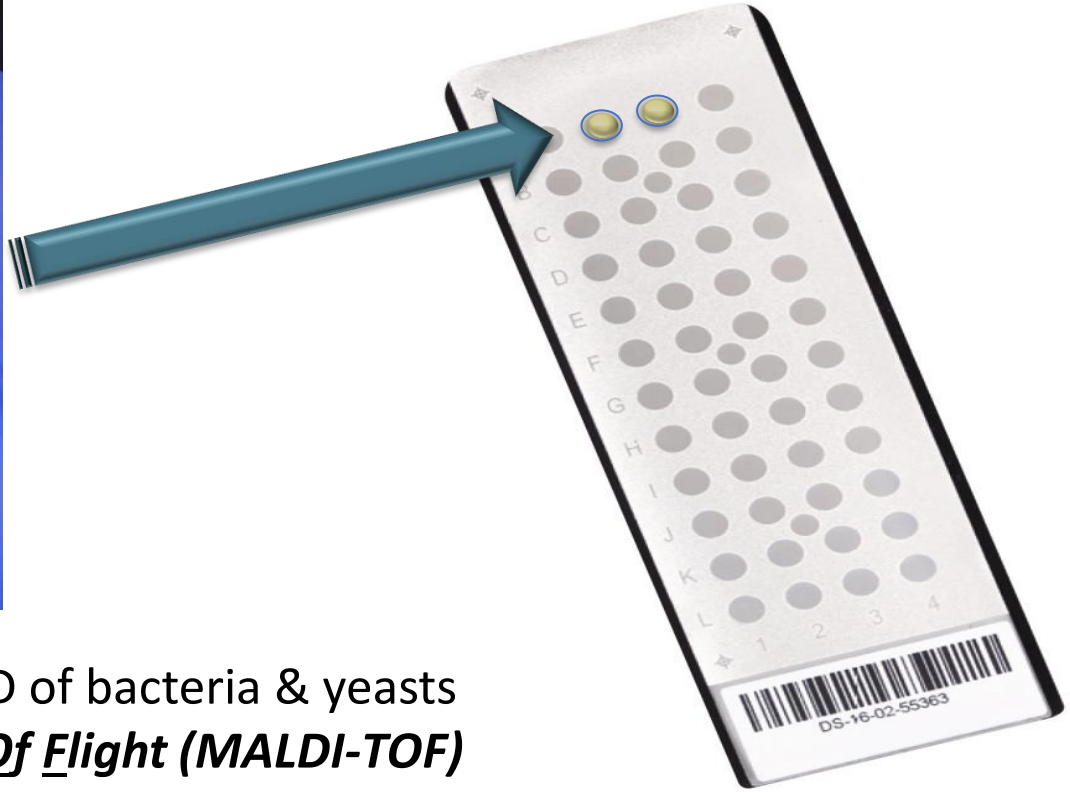
e.g. *Klebsiella pneumoniae*

Basic Concepts - Culture Media

Miller JM, et al. CID 2018;67(6):e1-e94.

Basic Concepts – Organism Identification





- One of the most important advances in post-culture ID of bacteria & yeasts is ***Matrix-Assisted Laser Desorption Ionization-Time Of Flight (MALDI-TOF) Mass Spectrometry (MS)***
- Based on ID of characteristic protein patterns

AMPATH LABORATORIES

Singhal N, et al. Front Microbiol 2015;6:791.

MALDI-TOF MS

BIOMÉRIEUX

Biomérieux Vitek® MS

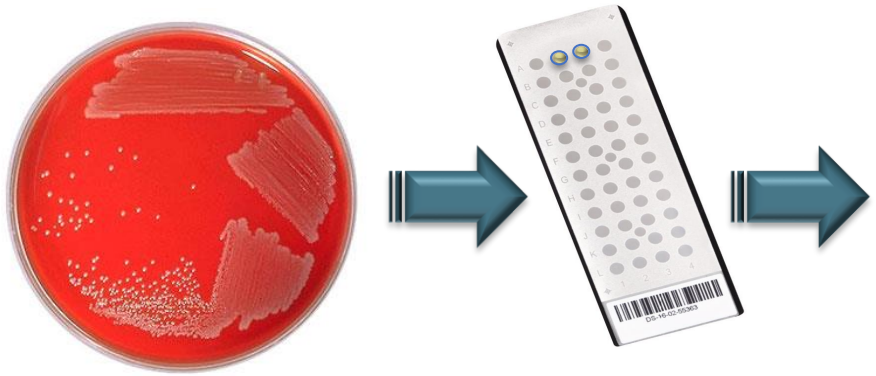
BRUKER

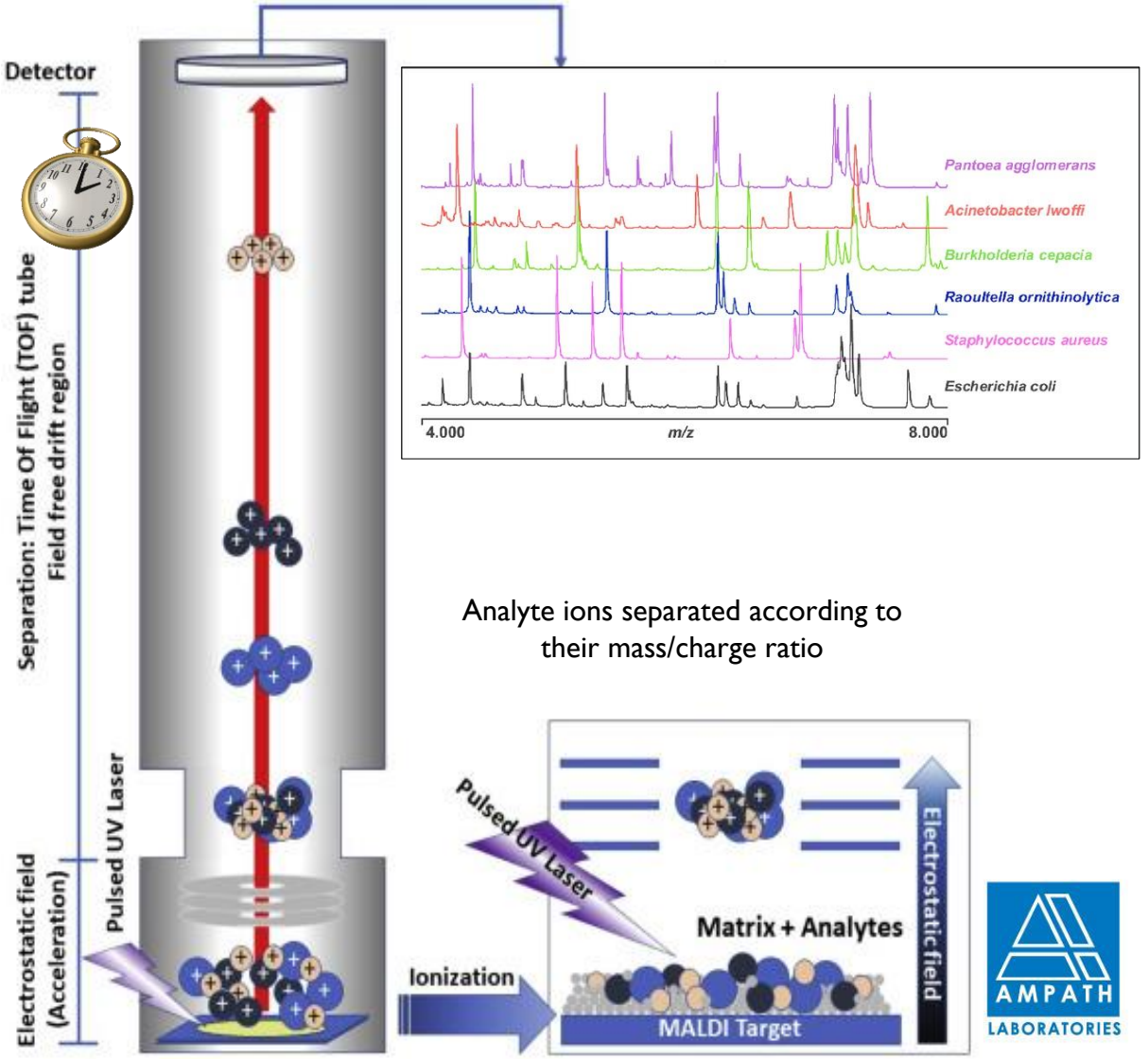
Bruker MALDI Biotyper®

AMPATH LABORATORIES

Principle of MALDI-TOF MS

- A pulsed UV-laser is used to evaporate the matrix & the analyte into the gas phase
- In addition to desorption support, the matrix ionizes the analyte molecules by proton transfer
- The ions are then accelerated by an electrical field & enter the field-free flight tube of the mass spectrometer
- By simple measurement of the TOF of the analyte ions, their mass to charge ratio can be determined



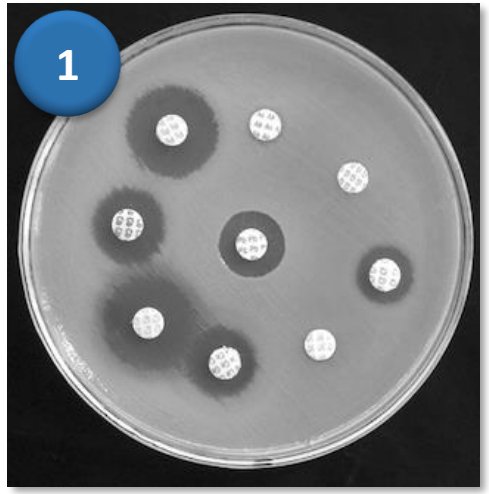


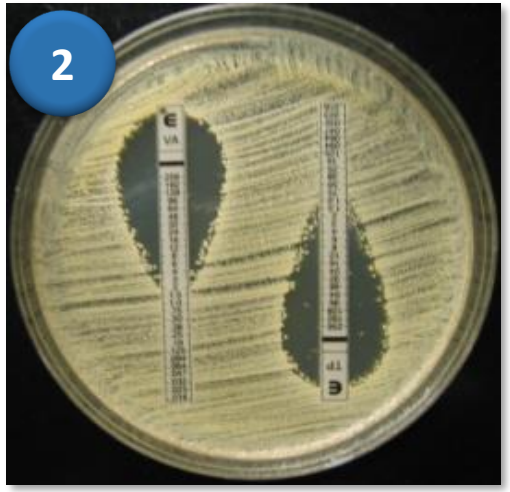
Singhal N, et al. Front Microbiol 2015;6:791.

Basic Concepts - Antimicrobial Susceptibility Testing (AST)

- AST can be carried out using a variety of methods
- The methods most commonly used are:

1. Disk diffusion (Kirby-Bauer)
2. Antibiotic gradient strips (Etest®)
3. Automated systems (Vitek®)
4. Broth microdilution





Miller JM, et al. CID 2018;67(6):e1-e94.

Basic Concepts - Minimum Inhibitory Concentration (MIC)

- **MIC is the lowest concentration of the antibiotic that results in inhibition of visible growth** (*i.e.* colonies on a plate or turbidity in broth culture)
  - under standard conditions
  - with a standard inoculum

- The MIC is the main pharmacodynamic parameter that quantifies susceptibility against an antibiotic

- Categorise bacteria as:
  - S = Susceptible
  - I = Susceptible, increased exposure (i.e. higher dose)
  - R = Resistant

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

AMPATH LABORATORIES

Miller JM, et al. CID 2018;67(6):e1-e94.

3. Lower Respiratory Tract Specimens

- **Interpretation of culture results must take the following into consideration:**
  1. **QUALITY of the specimen on microscopy**
  2. **Quantitation of growth (heavy, moderate, or light)**
  3. **ALWAYS correlate clinically and radiological for significance**

- Rates of true pathogen detection vary among studies:
  - Good quality specimens: 73% (95% CI 26-96%)
  - Lower quality specimens: 36% (95% CI 22-53%)

Good Quality vs. Bad Quality

- ***Candida* spp. does NOT cause pneumonia**
- *Candida* spp. is a respiratory coloniser

Important!

Klompas M. UpToDate 2022.

Interpretation of Lower Respiratory Tract Cultures

1. QUALITY of the specimen on microscopy

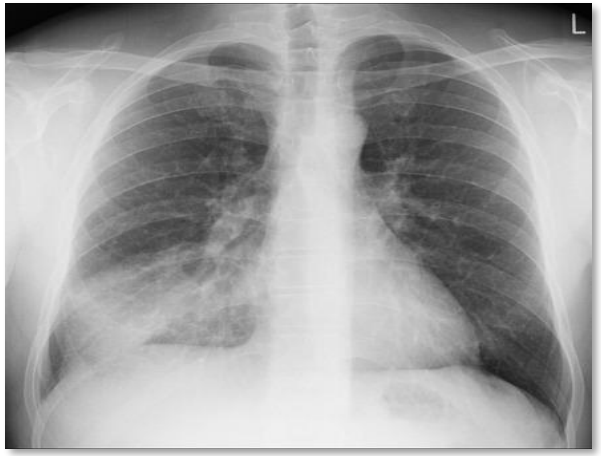
- Few/no polymorphic white cells & many epithelial cells (from mucous membrane of the mouth) indicate specimen consists of or contains saliva ➡ **culture results will therefore not be reliable** ➡ send repeat specimen
- Numerous polymorphs with only scanty epithelial cells & culture results that correlate with Gram stain ➡ indicate a 'good' specimen
- The presence of >25 epithelial cells indicates a sputum with oropharyngeal contamination and therefore grounds for rejection for bacterial culture

Bartlett's Grading System for Assessing Quality of Sputum Specimens	
No. of neutrophils per 10X low power field	Grade
< 10	0
10 – 25	+ 1
> 25	+ 2
Presence of mucus	+ 3
No. of epithelial cells per 10X low power field	Grade
< 10	0
10 – 25	- 1
> 25	- 2

1. Quantitation of growth (heavy, moderate, or light)

- True pathogens are generally present in moderate or heavy amounts

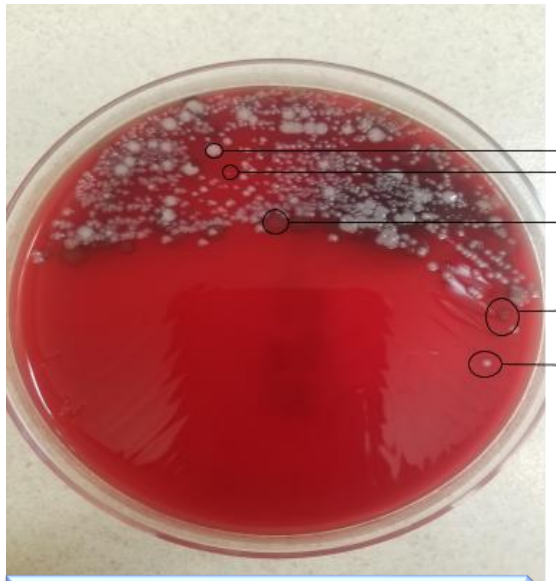
3. ALWAYS correlate clinically and radiological for significance



Klompas M. UpToDate 2022.

AMPATH LABORATORIES

Example: Sputum culture



Few growth of at least 5 different colony types:

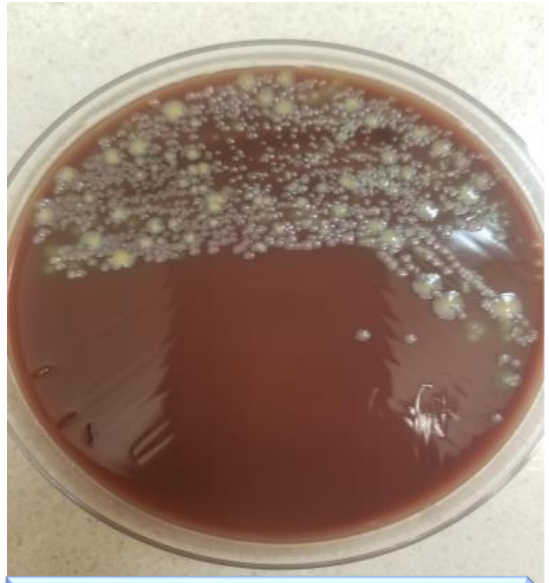
(1) Large white
(2) Small clear
(3) Large spreading alpha
(4) Smaller coining alpha
(5) smaller white

Blood agar

Rare lactose-fermenting Gram negative rod

Rare pinpoint non lactose-fermenting Gram negative rod

MacConkey agar



Same as blood agar: few growth of 5 or more colony types

Chocolate agar

AMPATH LABORATORIES

Sputum Cultures

AMPATH LABORATORIES

Drs Du Buisson, Kramer, Swart, Bouwer Inc.
Registration number: 2007/018337/21
PR0520005200431

Pathology Report

24hr Contact No. 011 709 1000

Patient:
[redacted]

Doctor:
Dr T Law
8 Sturdee Avenue
Ground Floor
Rosebank, JHB 2021

FINAL REPORT
Req: [redacted]
Specimen: 20:RE0037817S

[redacted]

Collected: 2020-10-10 01:07
Received: 2020-10-11 01:07
Printed: 2021-11-17 10:26
Batch: Email 436671 I-STD

Copy Doctor: Ward Solomon Stix Morewa Rehab Ward, Solomon Stix Infection Control
Ordered: Sputum MCS, Sputum microscopy comment
Comments: No collection date/time on the request form
Sputum MCS

PROCEDURE		RESULT
Specimen: Sputum		**Description:**
>MACROSCOPY		
Appearance	:	Mucoid
>MICROSCOPY		
Pus cells	:	< 10 cells / LPF
Squamous epithelial cells	:	> 25 cells / LPF
Gram pos cocci	:	Numerous
Gram neg bacilli	:	Numerous
Gram neg cocci	:	Numerous
Gram neg coccobacilli	:	Moderate
Yeast cells	:	Absent
>MYCOBACTERIUM MICROSCOPY		
Acid fast bacilli		Absent
>AEROBIC CULTURE		
Acinetobacter nosocomialis		
Growth	:	Scanty
Id sens	:	Final

1. Quality of specimen

2. Quantitation of growth

AMPATH LABORATORIES

Drs Du Buisson, Kramer, Swart, Bouwer Inc.
Registration number: 2007/018337/21
PR0520005200431

Pathology Report

24hr Contact No. 011 709 1000

[redacted]

Doctor:
Dr T Law

FINAL REPORT
Req: [redacted]
Specimen: 20:RE0037817S

Collected: 2020-10-10 01:07
Received: 2020-10-11 01:07
Printed: 2021-11-17 10:26
Batch: Email 436671 I-STD

>AEROBIC CULTURE

A.noso

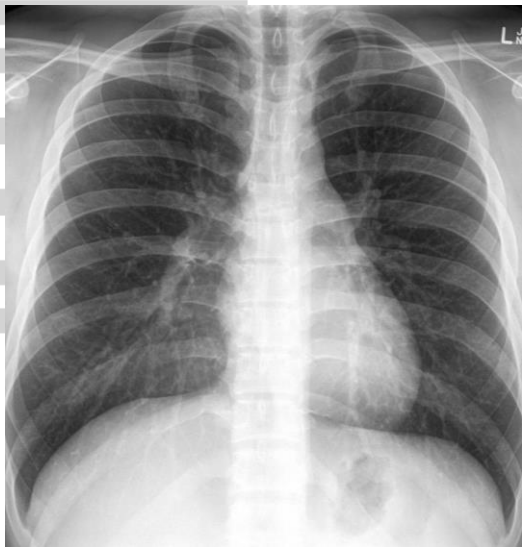
BETA-LACTAMS	
Ceftazidime	R
Cefepime	R
Imipenem	R
Meropenem	R
Doripenem	R
AMINOGLYCOSIDES	
Amikacin	R
Gentamicin	R
QUINOLONES	
Ciprofloxacin	R
OTHER	
Colist/Polymyx	S
Col/Poly MIC 2	S
Cotrimoxazole	R
Tigecycline	S

>COMMENT
Acinetobacter nosocomialis

Acinetobacter nosocomialis
This is an extensively drug-resistant isolate. Strict isolation, contact precautions and dedicated nursing of colonised and/or infected patients are advised. Please contact your local microbiologist regarding possible treatment options or if further advice if needed.

>COMMENT
The presence of >25 epithelial cells per LPF indicates a sputum with probable oropharyngeal contamination.

3. Correlate with CXR



No new infiltrates on CXR
Coloniser!

AMPATH LABORATORIES

Tracheal Aspirate Culture

AMPATH LABORATORIES

Drs Du Buisson, Kramer, Swart, Bouwer Inc.
Registration number: 2007/018337/21
PR0520005200431

Pathology Report

24hr Contact No. 011 789 1000

Patient:

Doctor:
Dr T Law
8 Sturdee Avenue
Ground Floor
Rosebank, JHB 2021

FINAL REPORT
Req:
Specimen: 21:RE0028998S

Collected: 2021-07-23 14:00
Received: 2021-07-23 15:55
Printed: 2021-11-17 10:39
Batch: Email 436692 I-STD

Copy Doctor: Dr T Law, Rosebank Clinic Infection Cont, Rosebank Clinic ICU
Ordered: Tracheal MCS, Fungal culture, Carbapenemase Cult Screening, Pneumocystis jiroveci PCR, Mycobacterium PCR

PROCEDURE		RESULT
Specimen: Tracheal aspirate		**Description:**
>MACROSCOPY		
Appearance	:	Mucoid
>MICROSCOPY		
Pus cells	:	> 25 cells / LPF
Squamous epithelial cells	:	< 10 cells / LPF
Gram neg bacilli	:	Numerous
Yeast cells	:	Absent
>MYCOBACTERIUM MICROSCOPY		
Acid fast bacilli	:	Absent
>AEROBIC CULTURE		
Klebsiella pneumoniae		
Growth	:	Profuse
>COMMENT		
Klebsiella pneumoniae		

This isolate tested positive for carbapenemase production with PCR. Strict isolation with contact precautions, screening of patient contacts, co-horting of colonised and/or infected patients and dedicated nursing are advised. Treatment with two active drugs is recommended. Please contact your local microbiologist for further advice if needed.

1. Quality of specimen

2. Quantitation of growth

AMPATH LABORATORIES

Drs Du Buisson, Kramer, Swart, Bouwer Inc.
Registration number: 2007/018337/21
PR0520005200431

Pathology Report

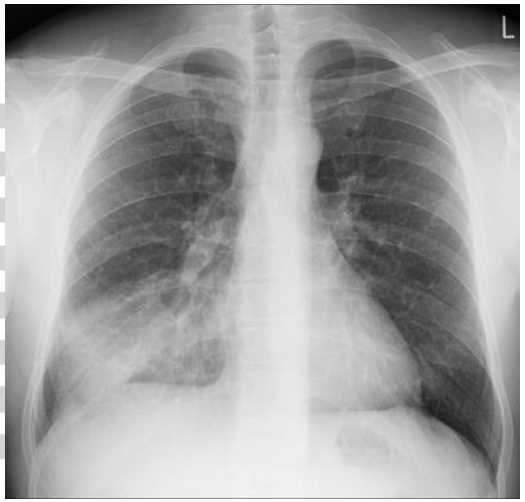
24hr Contact No. 011 789 1000

Doctor:
Dr T Law
FINAL REPORT
Req:
Specimen: 21:RE0028998S

Collected: 2021-07-23 14:00
Received: 2021-07-23 15:55
Printed: 2021-11-17 10:39
Batch: Email 436692 I-STD

>AEROBIC CULTURE	K.pneumo
BETA-LACTAMS	
Ampi/Amox	R
Amox+Clav	R
Pip+Taz	R
Cefuroxime	R
Ceftriax/Cefota	R
Ceftazidime	R
Cef+Avi	S
Cefepime	R
Cef+Taz	R
Imipenem	R
Imipenem MIC 16	R
Meropenem	R
Meropenem MIC 32	R
Ertapenem	R
Doripenem	R
Doripenem MIC 32	R
AMINOGLYCOSIDES	
Amikacin	S
Gentamicin	R
QUINOLONES	
Ciprofloxacin	R
OTHER	
Colist/Polymyx	S
Col/Poly MIC 1	S
Cotrimoxazole	R
Tigecycline	S
CARB	+

3. Correlate with CXR



New infiltrates on CXR

Pathogen – needs treatment!

AMPATH LABORATORIES

4. Molecular Testing of Respiratory Pathogens

	Core respiratory virus multiplex PCR	Comprehensive respiratory pathogens multiplex PCR	Triplex respiratory virus multiplex PCR
Components	**Viruses** SARS-CoV-2 Influenza A&B RSV A&B Adenovirus Metapneumovirus Parainfluenza 1-4 Rhinovirus	**Viruses** SARS-CoV-2 Influenza A&B RSV A&B Adenovirus Metapneumovirus Parainfluenza 1-4 Rhinovirus Enterovirus Coronavirus 229E Coronavirus NL63 Coronavirus OC43 Bocavirus **Bacteria** *B. pertussis* *B. parapertussis* *C. pneumoniae* *M. pneumoniae* *Legionella* spp.	**Viruses** SARS-CoV-2 Influenza A&B RSV A&B
Mneumonic	RVCORPCR	RPCOMPCR	COVTRIPCR

- Highly sensitive & specific viral PCRs have become the diagnostic "gold standard" in clinical virology
- Several of the newest assays also detect & identify the most common causes of "atypical" bacterial pneumonia
- **NB: Not all positive results indicate current active infection**
- **These results do not reflect on the microbiology cumulative reports as they are not from culture**

AMPATH LABORATORIES

Biofire® FilmArray® Pneumonia Panel plus

- Multiplexed PCR for simultaneous detection of multiple respiratory viral & bacterial pathogens in respiratory specimens (sputum, endotracheal aspirate & bronchoalveolar lavage)
  - 18 bacteria
  - 7 antibiotic resistance markers
  - 9 viruses
- Run time: Approximately 1 hour from loading on the instrument
- **Utility of the panel is most relevant to ICU admissions**
- The 15 typical bacteria are semi-quantified to the nearest whole log as DNA copies/mL: 10^4, 10^5, 10^6, and $\geq 10^7$
  - Can assist in distinguishing between an actual pathogen versus a coloniser

BIOFIRE® BY BIOMÉRIEUX

- Few limitations:
  - Nosocomial pathogens not covered: e.g. *S. maltophilia*, *Aspergillus* spp. & *Pneumocystis jirovecii*
  - Detection of DNA doesn't imply the presence of a viable pathogen
  - Susceptibilities of the organisms not known

Gastli N, et al. Multicentric evaluation of BioFire FilmArray Pneumonia Panel for rapid bacteriological documentation of pneumonia. CMI 2020. doi.org/10.1016/j.cmi.2020.11.014

AMPATH LABORATORIES

Biofire® FilmArray® Pneumonia Panel plus

Semi-Quantitative Bacteria

Gram Negative Bacteria

- Enterobacteriales:
  - *Enterobacter cloacae* complex
  - *Escherichia coli*
  - *Klebsiella pneumoniae* group
  - *Klebsiella oxytoca*
  - *Klebsiella aerogenes*
  - *Proteus* spp.
  - *Serratia marcescens*
- Non-lactose fermenters:
  - *Acinetobacter calcoaceticus-baumannii* complex
  - *Pseudomonas aeruginosa*
- *Haemophilus infuenzae*
- *Moraxella catarrhalis*

Gram Positive Bacteria

- *Staphylococcus aureus*
- *Streptococcus agalactiae*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*

Atypical Bacteria

- *Legionella pneumophila*
- *Mycoplasma pneumoniae*
- *Chamydophila pneumoniae*

Viruses

- Infuenza A
- Influenza B
- RSV
- Hyman Rhinovirus/Enterovirus
- Human Metapneumovirus
- Parainfluenza virus
- Adenovirus
- Coronavirus (endemic)
- MERS

Antimicrobial Resistance Genes

- Methicillin resistance:
  - *mecA/C & MREJ* → **MRSA**
- ESBL:
  - *CTX-M* → **ESBL**
- Carbapenemases:
  - *OXA-48-like*
  - *NDM*
  - *VIM* → **CRE**
  - *KPC*
  - *IMP*

BIOFIRE BY BIOMÉRIEUX

AMPATH LABORATORIES

Gastli N, et al. Multicentric evaluation of BioFire FilmArray Pneumonia Panel for rapid bacteriological documentation of pneumonia. CMI 2020. doi.org/10.1016/j.cmi.2020.11.014

Molecular Testing of Other Respiratory Pathogens

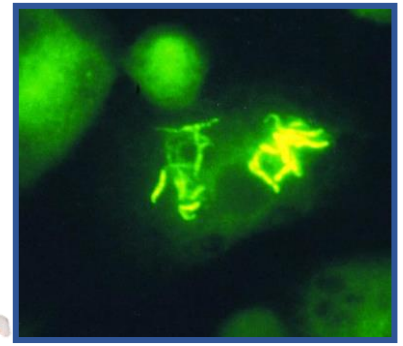
- Additional highly sensitive and specific PCRs are also available for testing of the following respiratory pathogens:

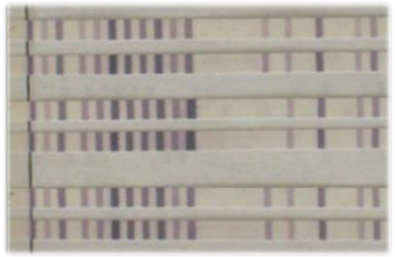
  - *Pneumocystis jirovecii*
    - BD MAX: MSG multicopy gene
    - Sensitivity 98%, specificity 96%
  - ***Mycobacterium tuberculosis* complex**
  - ***Mycobacterium* spp. (NTM)**
  - *Aspergillus* spp.
  - CMV

AMPATH LABORATORIES

5. Mycobacteria Diagnostic Tests

- **Microscopy**
  - Conventional light microscopy (Ziehl Neelsen stain)
  - LED fluorescent microscopy (Auramine O stain)
- **Molecular testing**
  - Xpert MTB/RIF Ultra assay
  - Direct TB PCR (pulmonary specimens): BD Max
  - Direct TB PCR (non-pulmonary specimens): ELITe InGenius
  - Hain Line Probe Assays (1st- and 2nd-line)
  - Non-tuberculosis Mycobacteria PCR (Direct & culture)
- **Culture**
  - Culture with specialised liquid culture systems (Mycobacteria Growth Indicator Tube (MGIT) & Myco/F Lytic)
- **Drug susceptibility testing (DST)**
  - 1st-line agents & 2nd-line agents
- **LF-LAM Urine test**
- **QuantiFERON-TB Gold** – Latent TB

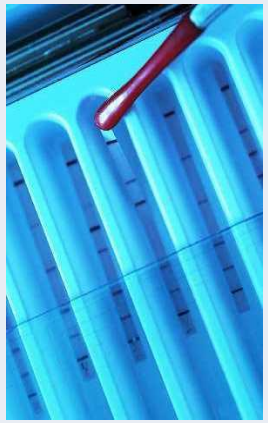




AMPATH LABORATORIES

MTB: Sensitivity & Limit of Detection

WHY IS TB CULTURE STILL THE GOLD STANDARD?

	Microscopy	MTBDR*plus*	Xpert MTB/RIF	Xpert MTB/RIF Ultra	Culture
Limit-of-detection	**5,000-10,000** bacilli/ml	≈**160** bacilli/ml	≈**114** bacilli/ml	**16** bacilli/ml	**10-100** bacilli/ml
					

Steingart KR, et al. Expert Rev Anti Infect Ther 2007;5:327-31.
Parsons LM, et al. CMR 2011;24(2):314-50.

AMPATH LABORATORIES

6. Blood Cultures

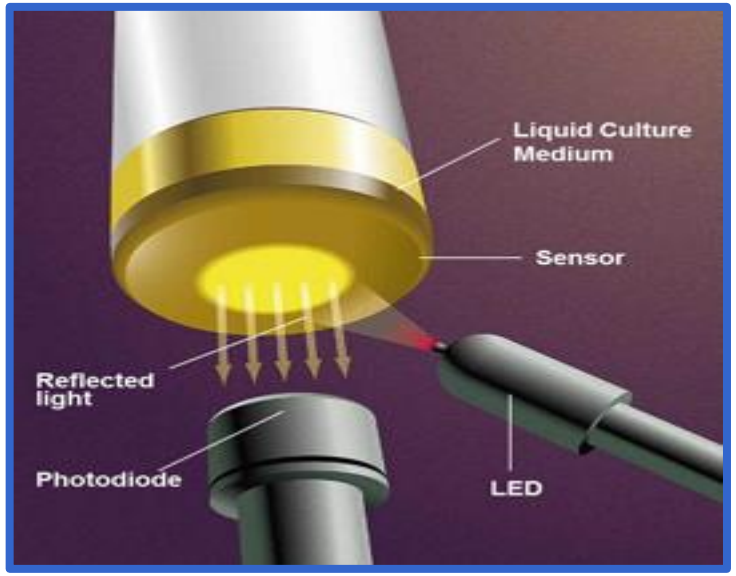
- **The major downside of doing blood cultures in patients with pneumonia, is their low diagnostic yield (positive cultures in 4.7-16%)**
- Ideally, send two sets of blood cultures for optimal yield (adults) in hospitalised patients only
- Blood cultures are incubated in automated, continuous-monitoring systems
- Once cultures become positive, an alarm & flashing light alert the lab staff
- A Gram stain is done immediately on a positive blood culture – this is useful in determining the possible aetiology of the bloodstream infection

Miller JM, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2018 update by the Infectious Diseases Society of America and the American Society for Microbiology. CID 2018;67(6):e1-e94.

AMPATH LABORATORIES

Blood Cultures

- CO_2 sensor bonded to bottom of blood culture bottle & separated from the broth by a semi-permeable membrane
- Sensor is impregnated with H_2O vapour when bottles are autoclaved during manufacturing process
- Unidirectional membrane is permeable to CO_2 only
- Micro-organisms multiply in the media, generate CO_2 which diffuses across the membrane into the sensor & dissolves in the water, thereby generating H^+ ions
- Free H^+ ions interact with the sensor: **green (alkaline)** ➔ **yellow (acidic)**
- As the sensor becomes lighter green & eventually yellow, it results in an increase of red light reflected by the sensor
- Once cultures become positive, the bottle is ejected from the Virtuo
- A Gram stain is done immediately – this is useful in determining the possible aetiology of the bloodstream infection



AMPATH LABORATORIES

Blood Culture Bottles

	Bottle Type	Purpose	Specimen Type
SA	BacT/ALERT SA	Standard Aerobic	Blood or SBF
SN	BacT/ALERT SN	Standard Anaerobic	Blood or SBF
FA	BacT/ALERT FA	FAN® Aerobic	Blood or SBF
FN	BacT/ALERT FN	FAN® Anaerobic	Blood or SBF
PF	BacT/ALERT PF	Paediatric FAN®	Blood only

SBF = Sterile body fluid

Fill window and volume markers

<u>For patient's on antibiotics</u>

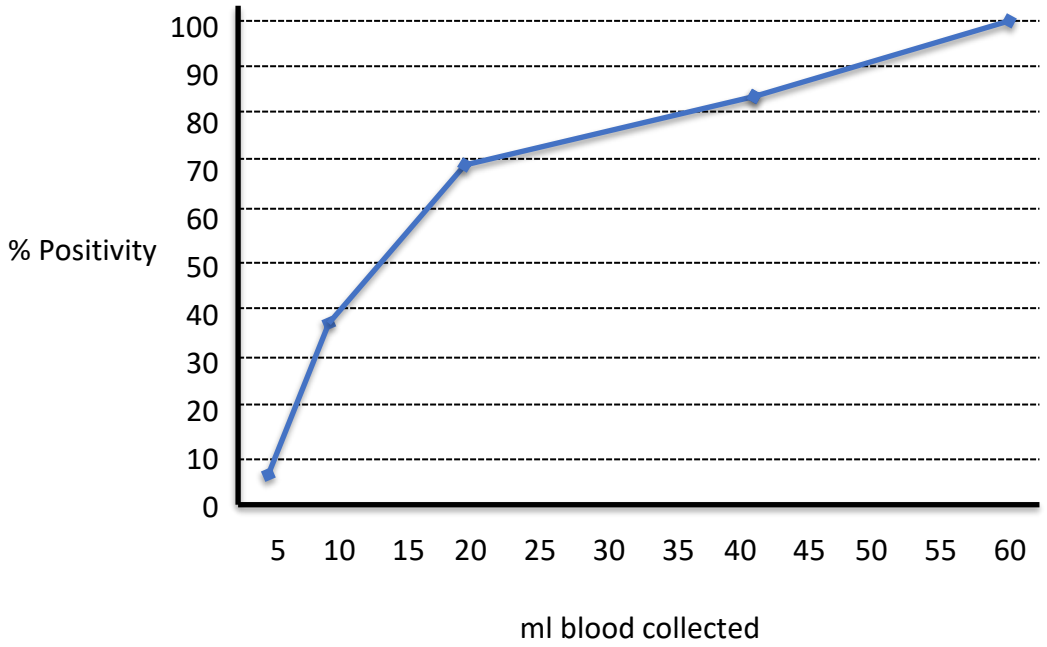
FAN® = Fastidious Antimicrobial Neutralization

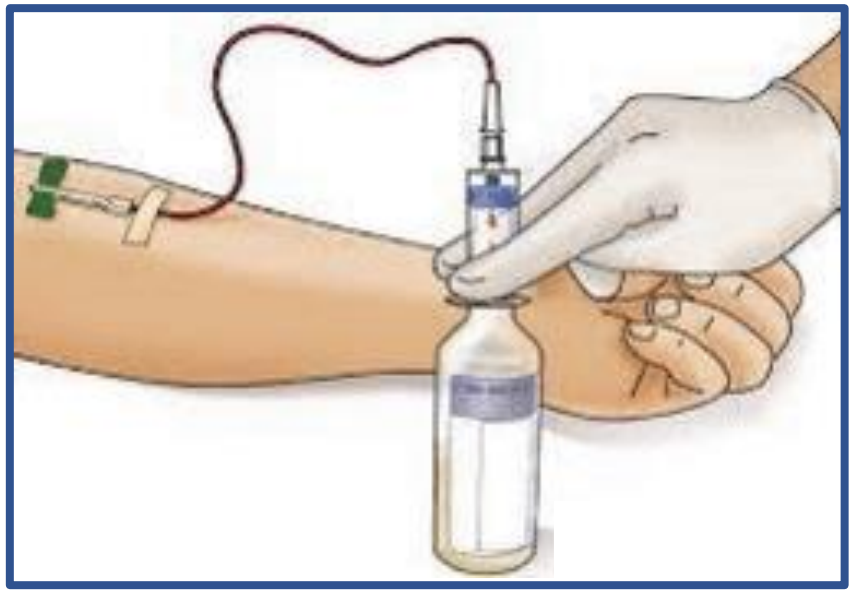
- Adsorbent Polymeric Beads (APB) to neutralize antimicrobials

AMPATH LABORATORIES

Blood Cultures

- **The volume of blood obtained for each blood culture is the most important variable** in recovering pathogens from patients with bloodstream infections
- **Adults: 20 - 30 mL of blood per culture set is recommended - requires 2 - 3 bottles (i.e. 10mL per bottle)**
- ***For adults it is always inappropriate to send a single yellow paediatric blood culture bottle***





Miller JM, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2018 update by the Infectious Diseases Society of America and the American Society for Microbiology. CID 2018;67(6):e1-e94.

AMPATH LABORATORIES

Blood Cultures

- **Children:** Weight-appropriate volume of blood should be cultured

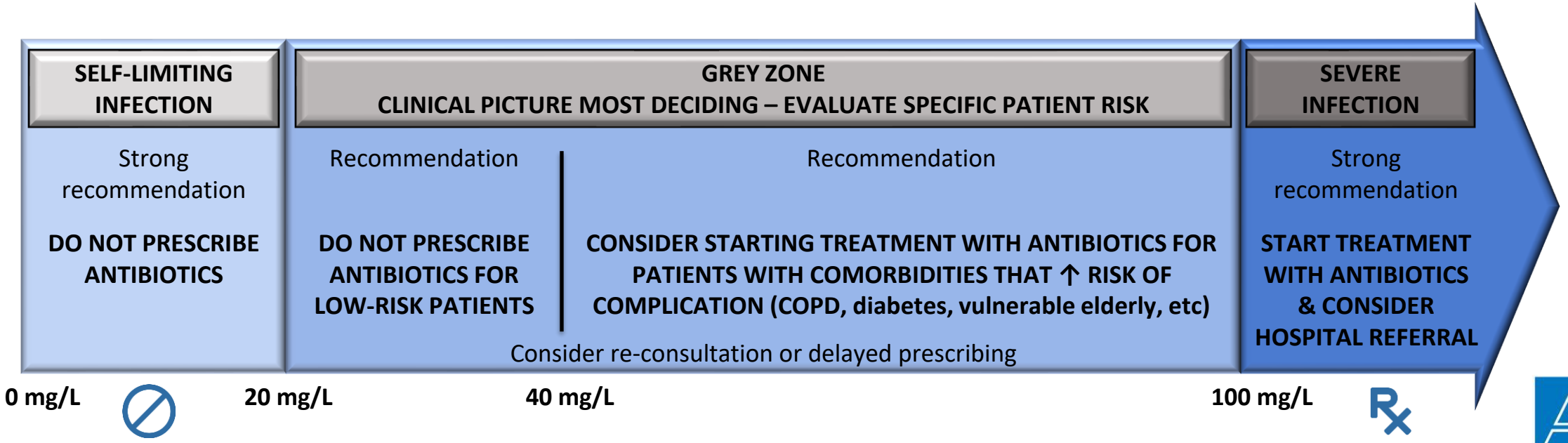
Recommended Volumes of Blood for Culture in Paediatric Patients			
Weight of patient	**Culture set No. 1**	**Culture set No. 2**	**Total Volume for culture**
≤ 1 kg	2 ml	-	2 ml
1.1 – 2 kg	2 ml	2 ml	4 ml
2.1 – 12.7 kg	4 ml	2 ml	6 ml
12.8 – 36.3 kg	10 ml	10 ml	20 ml
> 36.3 kg	20-30 ml	20-30 ml	40-60 ml
When ≤ 10 ml blood is collected, it should be inoculated into a single aerobic culture bottle			

Miller JM, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2018 update by the Infectious Diseases Society of America and the American Society for Microbiology. CID 2018;67(6):e1-e94.

AMPATH LABORATORIES

7. C-reactive protein (CRP)

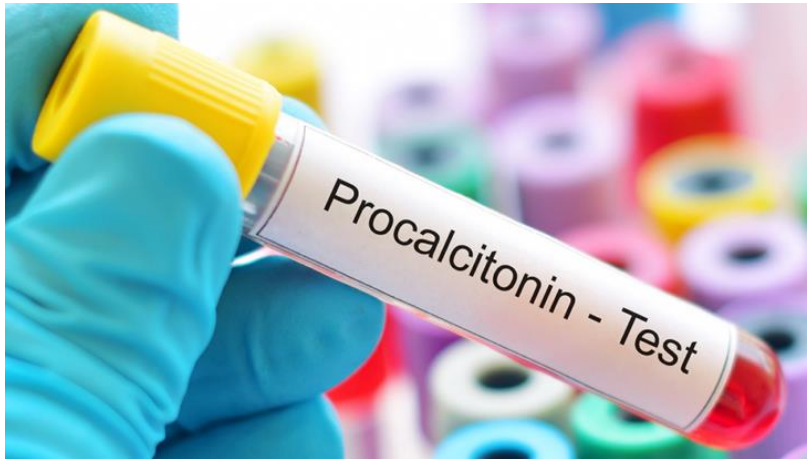
- A relatively **non-specific marker of inflammation** & therefore sepsis
- Levels are increased to some extent in most conditions associated with inflammation
- It is a cheap & widely available test & when levels are raised in a patient with signs suggestive of sepsis, it provides useful supporting evidence
- CRP increases slowly with a peak after 48-72 hours & a slow decrease thereafter



1. Noviello S, Huang DB. The basics and the advancements in diagnosis of bacterial lower respiratory tract infections. Diagnostics 2019;9:37. 2. https://www.enaspoc.com/consensus-statements

8. Procalcitonin (PCT)

- **PCT is a more reliable marker of sepsis than CRP**
- It is useful in distinguishing bacterial from other forms of infection
- PCT levels rise within 2-4 hours
- PCT kinetics then mirror the severity of infection
- **Evidence has shown that PCT is a useful method in guiding the initiation & duration of antibiotic treatment**
- PCT levels drop by ± 50% daily when infection is controlled & responds adequately to antibiotics



PCT can be elevated by non-bacterial-infectious causes[2]

Physiologic stress

- Newborns (<48-72 hours; after 72 hours interpret levels as usual)
- Massive stress (severe trauma, surgery, cardiac shock, burns, pre-eclampsia
- Prolonged, severe cardiogenic shock or organ perfusion abnormalities

Nonbacterial cytokine activation

- Some forms of vasculitis & acute graft vs. host disease
- Pancreatitis, chemical pneumonitis, mesenteric infarction, pulmonary aspiration
- Invasive fungal infections (e.g. candidiasis, aspergillosis) or acute *P. falciparum* malaria
- Chronic renal disease (≈2X increase in baseline levels), peritoneal dialysis or hemodialysis treatment
- Acute or chronic viral hepatitis, decompensated severe liver cirrhosis (Child-Pugh Class C) &/or acute liver failure
- Kawasaki, Still's Disease or Bell's Palsy

Dysregulated PCT production

- Treatment with agents that stimulate cytokines (OKT3, OK-432, TNF-alpha, antilymphocyte globulins, alemtuzumab, IL-2, granulocyte transfusion)
- Paraneoplastic syndromes due to medullary C-cell carcinoma, small cell lung carcinoma, or bronchial carcinoid

1. Noviello S, Huang DB. The basics and the advancements in diagnosis of bacterial lower respiratory tract infections. Diagnostics 2019;9:37.
2. Samsudin I, et al. Clinical Utility and Measurement of Procalcitonin. Clin Biochem Rev 2017;38(2):59-68.

How to Use PCT

LRTI

1 EVALUATE
Determine if antibiotics are necessary

< 0.1 ng/mL	Antibiotics are strongly discouraged
0.1-0.25 ng/mL	Antibiotics are discouraged
0.26-0.5 ng/mL	Antibiotics are encouraged
> 0.5 ng/ml	Antibiotics are strongly encouraged

2 MONITOR
Assess therapy effectiveness over time

Test follow-up samples once every 1-2 days, to support decision to discontinue antibiotic therapy

3 DISCONTINUE
Assess when to discontinue antibiotics

≤ 0.25 ng/mL OR ΔPCT > 80%	Discontinuation of antibiotics is encouraged

SEPSIS

1 EVALUATE
Assess sepsis risk & severity

< 0.5 ng/mL	Low risk for progression to severe sepsis &/or septic shock
0.5-2.0 ng/mL	Sepsis should be considered
> 2.0ng/ml	High risk for progression to severe sepsis &/or septic shock

2 MONITOR
Assess risk over time

Test follow-up samples once every 1-2 days, to support decision to discontinue antibiotic therapy

3 DISCONTINUE
Assess when to discontinue antibiotics

≤ 0.5 ng/mL OR ΔPCT > 80%	Discontinuation of antibiotics is encouraged

In a nutshell

Poor-quality specimens lead to misleading results, inappropriate antimicrobial therapy & delay in diagnosis

The quality of specimens is interpreted according to the microscopy & culture findings

Organisms from non-sterile sites may be colonisers & not necessarily the cause of infection

If the patient does not respond to antibiotic therapy chosen according to the microbiological susceptibility profile, consider:

- inadequate therapy for the infection site
- inadequate dosage
- poor source control
- possible selection of resistant mutants
- different organism is causing the infection

AMPATH LABORATORIES

Communication

- To determine significance of results requires knowledge of the patient's clinical status
- The microbiology report should encourage communication between the clinician, pharmacist & the medical microbiologist
- **Good communication makes a huge difference to patient management**


Thank You
?
Fisherbrand
AMPATH
LABORATORIES