My needs and expectations from the (microbiology) lab

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Consultant in Infectious Diseases
Group Lead in HIC

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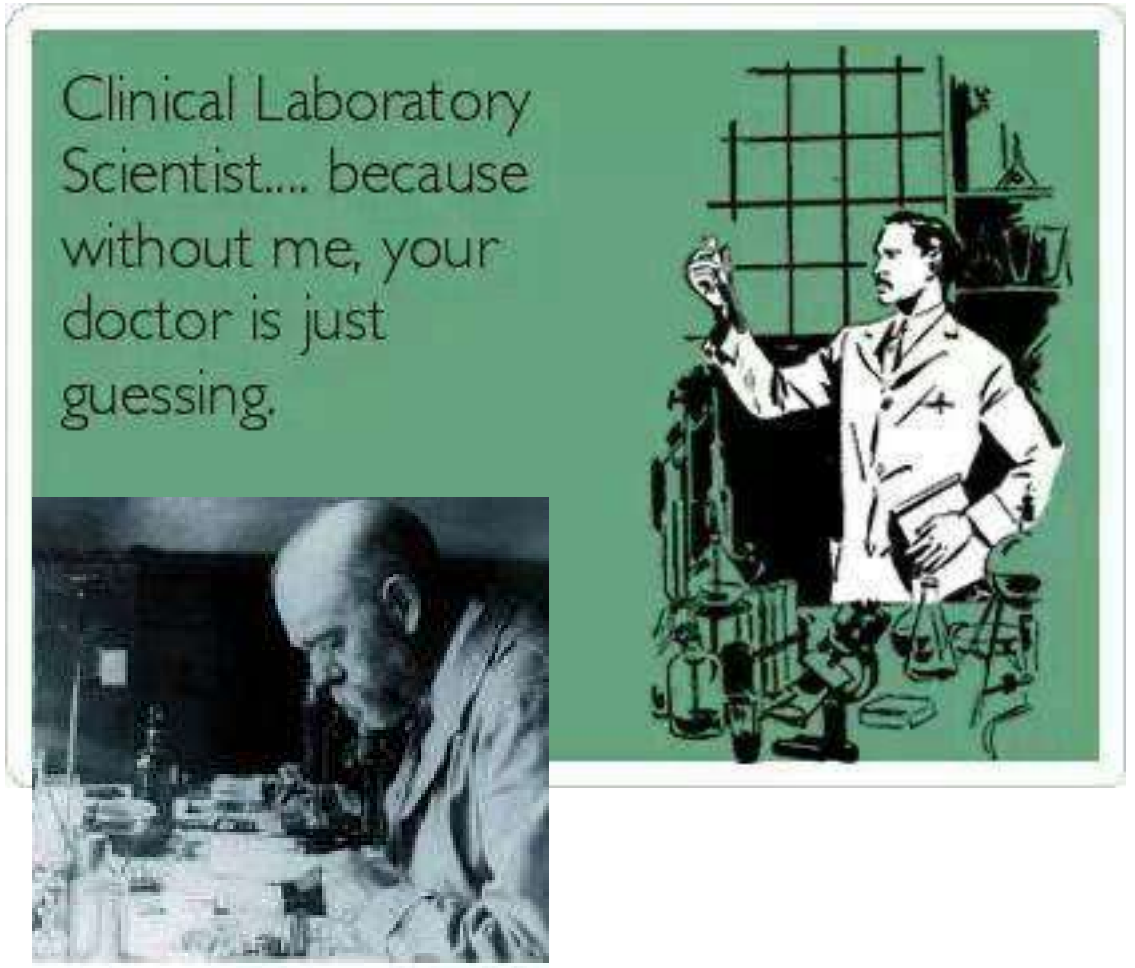
Disclosures

- I believe that diagnostics is a powerful tool
- Empowers clinicians to make treatment decisions
- Needs and expectations from a microbiologist > clinician



Talk from ID specialist perspective

Infectious diseases

1. Systematic
2. Error free
3. Newer, relevant tests
4. TAT- RDT
5. Communication
6. Bench to bedside
7. Research

IC, AMSP, QIP

1. Sampling
2. Training
3. Cascade Reporting
4. Antibiogram / CASR
5. Outbreak detection
6. Resistance trends
7. Hospital epidemiology

1. Systematic - don’t skip basic tests

- Gram stain precedes culture
- Gram stains that needs immediate reporting - for CSF and other critical specimens
- Create algorithm
  - don’t report urine culture without a dipstick or urine routine
  - liaise with biochemistry lab
  - CDI – testing based on algorithm
  - reduces unwanted tests and antibiotic use

2. Error free- accurate identification (expertise)

- Gram stain
- AFB stain

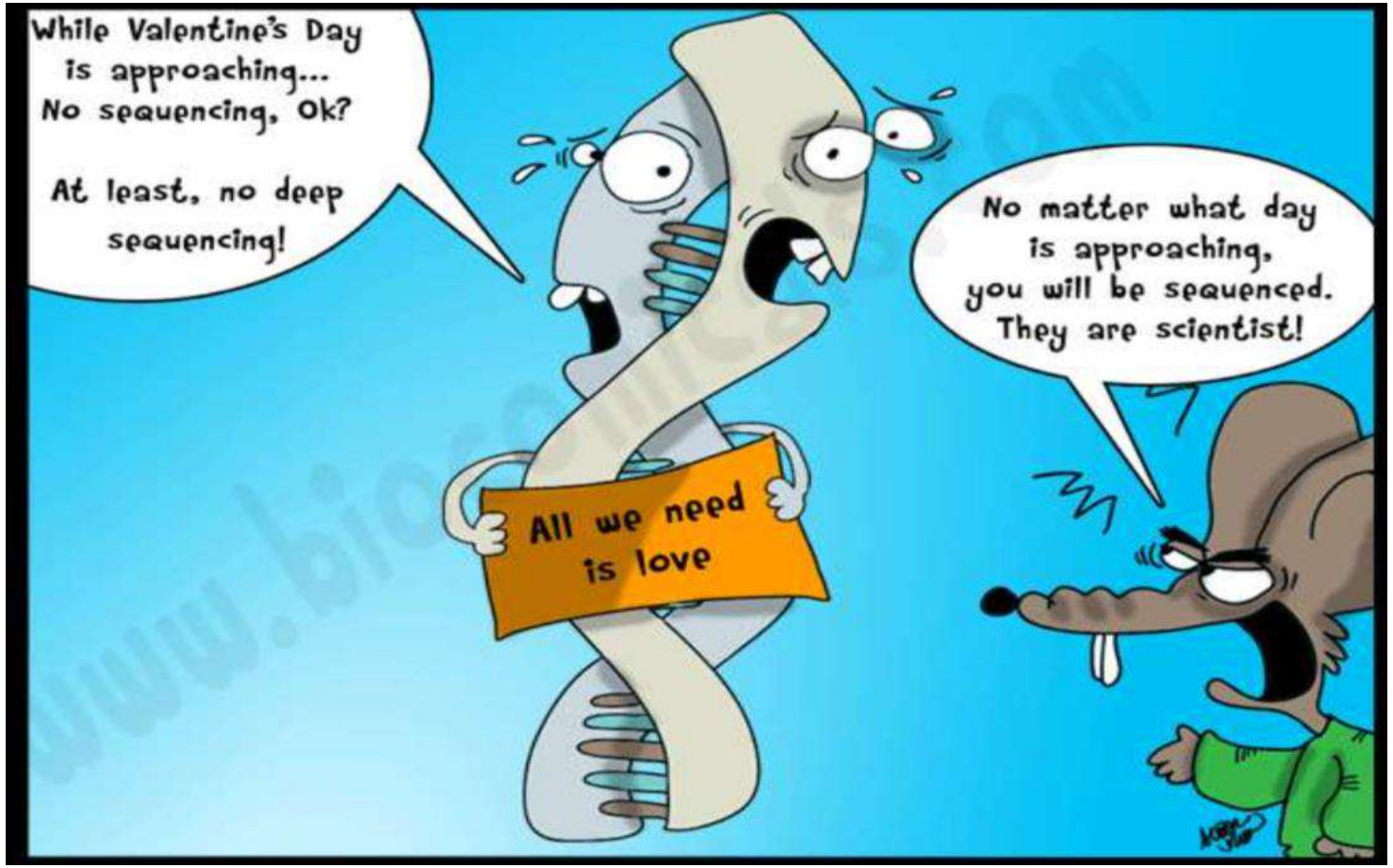
} Trained technical staff

- Organisms was isolated in pure or mixed culture
- Species identification
- Reporting of susceptibility

} Expertise and Updated

3. Newer, relevant diagnostics

Era of PCR



Boon, not bane

Clinical Infectious Diseases

IDSA GUIDELINE

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[a]

J. Michael Miller,[1] Matthew J. Binnicker,[2] Sheldon Campbell,[3] Karen C. Carroll,[4] Kimberle C. Chapin,[5] Peter H. Gilligan,[6] Mark D. Gonzalez,[7]

3. Newer relevant diagnostics

- **Multiplex PCR** for ID syndrome, endemic viruses (meningitis, hemorrhagic fever)
- **PCR** – CMV, JC, BK, PCP PCR, COVID-19
- **Resistance gene testing-** CARBA-R, mec A, van A
- **MALDITOF** –
  - for correct identification - on isolates grown in routine cultures
  - direct MALDITOF from blood are available, await FDA clearance
- **16srRNA, WGS, NGS-** for culture negative critical tissues
- **Serology** - BDG, GM, Histo Ag, Legionella Ag, parasitic and many others

4. TAT – RDT

- Accumulating samples and run the test = valuable time lost, empiricism will continue
- Liaise with a lab with fast TAT

- POC testing- dengue antigen, Rapid Strep Antigen, Rapid malaria card test, Cryptococcal Ag -lateral flow

Film-Array – syndromic panels

- Multiplex PCR
- FDA approved

1. Blood culture identification panel (BCID), BCID2
2. Respiratory pathogen panel
3. Pneumonia panel
4. GI pathogen panel
5. Meningo-encephalitis panel

- Eliminate guesswork
- Resistant genes identified
- Resistant genes identified
- Short TAT
- Targeted therapy in hours

Conventional method - approx 72-80 hours

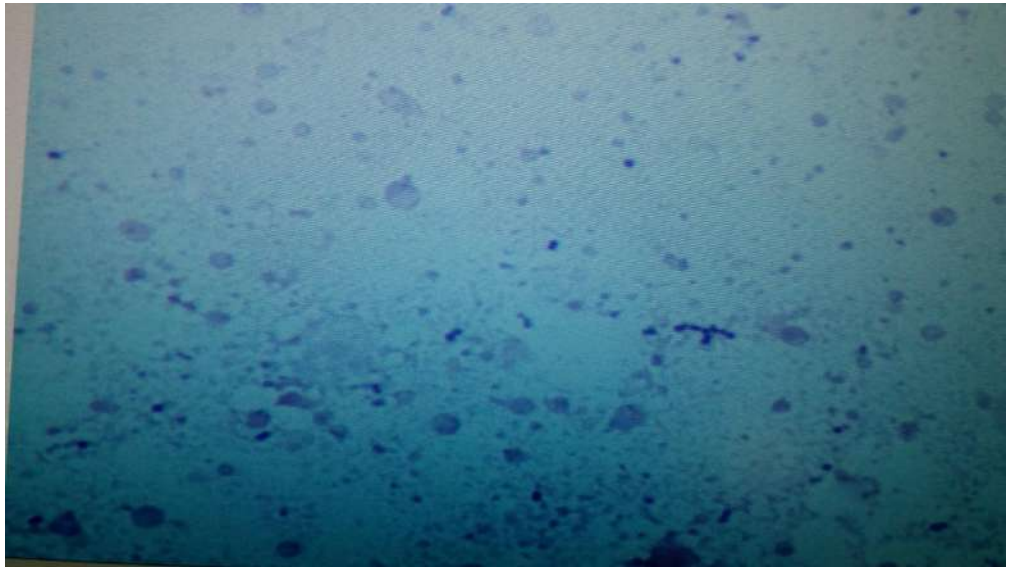
Blood culture flags = 24 hours
Gram stain= GPC

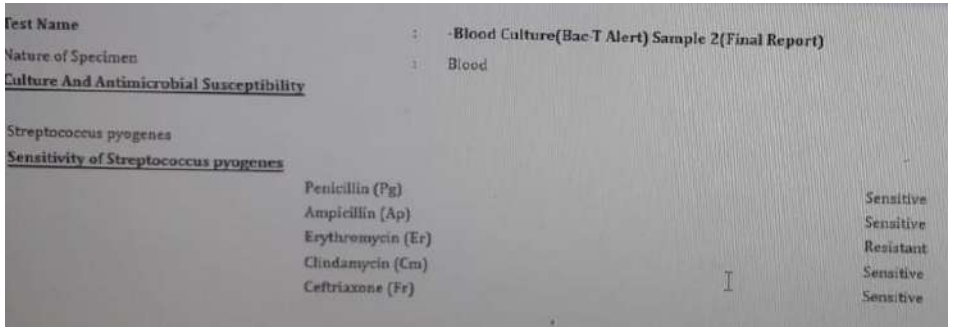
→

Culture growth
= 24- 48 hours

→

Identification and
DST = 8-16 hours





Test Name : -Blood Culture(Bac-T Alert) Sample 2(Final Report)
Nature of Specimen : Blood
Culture And Antimicrobial Susceptibility

Streptococcus pyogenes
Sensitivity of Streptococcus pyogenes

Penicillin (Pg)	Sensitive
Ampicillin (Ap)	Sensitive
Erythromycin (Er)	Resistant
Clindamycin (Cm)	Sensitive
Ceftriaxone (Fr)	Sensitive

BCID 2

Comprehensive: Simultaneously tests for 43 targets and identifies pathogens

TAT: 2 hours from culture flag

Accuracy:
Positive agreement rate (or sensitivity) across all pathogens on the BCID2 panel is 99%

Negative agreement rate (or specificity) is 99.8%

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

Multiplex polymerase chain reaction (PCR) for rapid bacterial identification from blood cultures: ready for prime time in India?

Yamunadevi Vellore Ramanathan[1,], Rajalakshmi Arjun[2], Vidya Krishna[3], Anil Tarigopula[4], Ram Gopalakrishnan[5]*

Abstract

Introduction Early identification and determination of antimicrobial susceptibilities of microorganisms growing in blood cultures is crucial as delay can lead to increased mortality, morbidity and cost. This study was done to evaluate the usefulness of the FilmArray blood culture identification (FA-BCID) in comparison with conventional techniques in early identification and antimicrobial initiation.

Methods This was a single centre, prospective study conducted in a 24-bed critical care unit (CCU) of a tertiary care hospital at Chennai, India between October 2016 and December 2016. Patients whose blood culture bottles were flagged using the BACTEC-FX system were included. The blood culture was processed by FA-BCID and by conventional method and the results were compared.

Results A total of 36 positive blood cultures were analyzed by both FA-BCID and conventional method from patients admitted in the CCU. FA-BCID accurately identified 80% of the organisms. Of 32 isolates identified by FA-BCID, 50% (16/32) showed isolated growth of Gram negative bacteria (GNB), 37.5% (12/32) showed isolated growth of Gram positive (GP) bacteria, whereas 12.5% (4/32) showed >1 micro-organism in the same culture bottle. Overall, sensitivity, specificity, positive predictive value and negative predictive

The turnaround time of FA-BCID was a median of 2 hours compared to 2 days for the conventional method. Antibiotics were de-escalated or escalated in 47.2% of patients based on FA-BCID within a median time of 3 hours.

Conclusion FA-BCID is a significant advance in the early identification and escalation or de-escalation of treatment for bacteremia in critically ill patients, with a high sensitivity for Gram positive bacteria as compared to Gram negative bacteria. Incorporation of probes for prevalent pathogens and resistance genes would make this panel more useful in Indian settings.

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology

Benefits of Adding a Rapid PCR-Based Blood Culture Identification Panel to an Established Antimicrobial Stewardship Program

Shawn H. MacVane,[a,b] Frederick S. Nolte[c]

Department of Pharmacy,[a] Division of Infectious Diseases,[b] and Department of Pathology and Laboratory Medicine,[c] Medical University of South Carolina, Charleston,

sequential time periods in a pre-post quasiexperimental study in 3 groups in the following categories: conventional organism identification (controls), conventional organism identification with ASP (AS), and BCID with ASP (BCID). Clinical and economic outcomes were compared between groups. There were 783 patients with positive blood cultures; of those patients, 364 (115 control, 104 AS, and 145 BCID) met inclusion criteria. The time from blood culture collection to organism identification was shorter in the BCID group (17 h; $P < 0.001$) than in the control group (57 h) or the AS group (54 h). The BCID group had a shorter time to effective therapy (5 h; $P < 0.001$) than the control group (15 h) or AS group (13 h). The AS (57%) and BCID (52%) groups had higher rates of antimicrobial de-escalation than the control group (34%), with de-escalation occurring sooner in the BCID group (48 h; $P = 0.034$) than in the AS group (61 h) or the control group (63 h). No difference between the control group, AS group, and BCID group was seen with respect to mortality, 30-day readmission, intensive care unit length of stay (LOS), postculture LOS, or costs. In patients with BSI, ASP alone improved antimicrobial utilization. Addition of BCID to an established ASP shortened the time to effective therapy and further improved antimicrobial use compared to ASP alone, even in a setting of low antimicrobial resistance rates.

Faster the diagnosis + ‘act upon it’, better the outcome

23 targets at once

TOP

The BIOFIRE® FILMARRAY® Respiratory 2.1 *plus* Panel is incredibly comprehensive, with **simultaneous testing for 23 of the most common pathogens, including SARS-CoV-2, involved in RTI.**

Viruses		Bacteria
Adenovirus	Influenza A	*Bordetella pertussis*
Coronavirus 229E	Influenza A/H1	*Bordetella parapertussis*
Coronavirus HKU1	Influenza A/H1-2009	*Chlamydophila pneumoniae*
Coronavirus OC43	Influenza A/H3	*Mycoplasma pneumoniae*
Coronavirus NL63	Influenza B	
Middle East Respiratory Syndrome CoronaVirus (Mers-CoV)	Parainfluenza 1	
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	Parainfluenza 2	
Human Metapneumovirus	Parainfluenza 3	
Human Rhinovirus/Enterovirus	Parainfluenza 4	
	RSV	

Sensitivity – 88-100%
Specificity – 90-100%

Patient selection
Sampling technique

CHEST Congress 2020 | ITALY Bologna | 25-27 June

Chest Infections

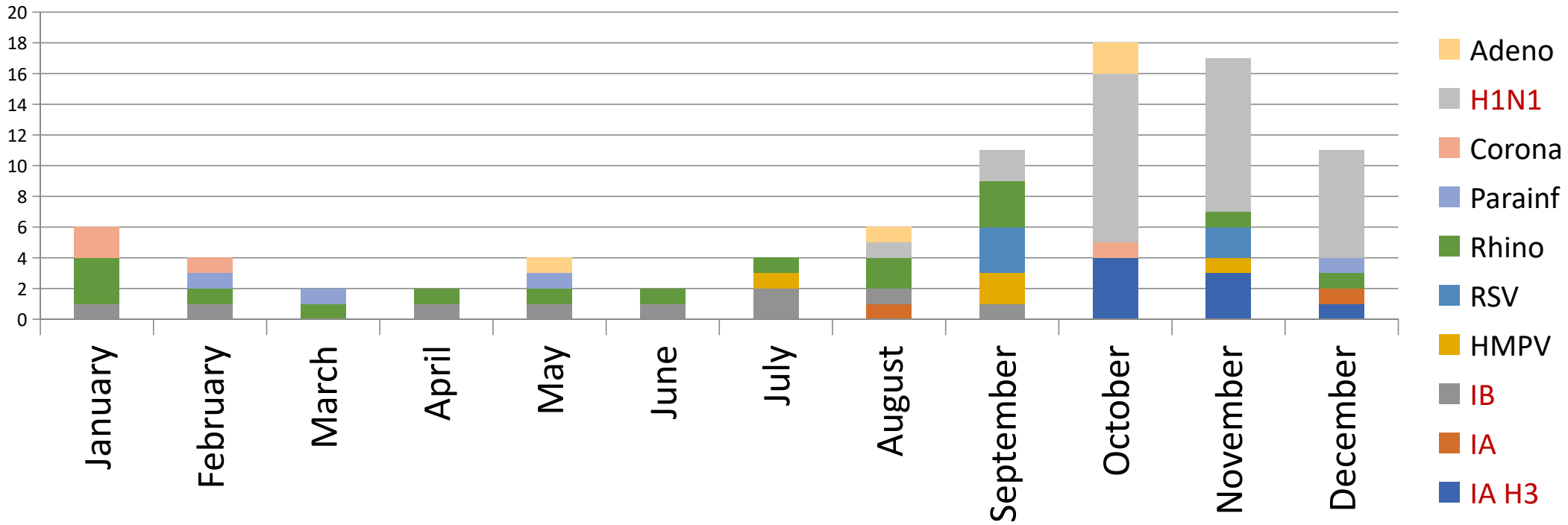
TYPE: Abstract Publication

TOPIC: Chest Infections

ETIOLOGICAL AND CLINICAL PROFILE OF VIRUS-ASSOCIATED COMMUNITY-ACQUIRED PNEUMONIA IN ADULTS

B. PONNUTHURAI*[1] A.K. A[1] A. PADMAMABHAN[1] AND R. ARJUN[2] [1]KERALA INSTITUTE OF MEDICAL SCIENCES, RESPIRATORY MEDICINE, TRIVANDRUM, INDIA [2]KERALA INSTITUTE OF MEDICAL SCIENCES, INFECTIOUS DISEASES, TRIVANDRUM, INDIA

- 217 adults, 2017-2018
- 66.4% - viral pathogen
- Influenza most common- 32%
- Seasonality for flu- Sept- Dec
- Timing of vaccine



ORIGINAL ARTICLE

Clinical Performance of FilmArray Meningitis/Encephalitis Multiplex Polymerase Chain Reaction Panel in Central Nervous System Infections

Sarath Chandran[1], Rajalakshmi Arjun[2], Aswathy Sasidharan[3], Vettakkara KM Niyas[4], Suresh Chandran[5]

Abstract

Introduction: Early identification of etiology is very important for initiating appropriate therapy promptly in patients with meningoencephalitis (ME). BioFire FilmArray® meningitis/encephalitis (FA-ME) panel is a fully automated multiplex polymerase chain reaction (PCR) that detects 14 pathogens simultaneously in an hour. There is a dearth of studies highlighting its usefulness in ME syndrome in Indian patients.

Methods: We performed a retrospective analysis of patients, admitted to the Kerala Institute of Medical Sciences Hospital, Thiruvananthapuram, Kerala, South India, with meningitis/encephalitis syndrome who underwent the multiplex PCR test on cerebrospinal fluid (CSF) over a period of 2 years from 2016 to 2018. Patients presenting with clinical diagnosis of acute meningitis, encephalitis, or ME who underwent CSF FA-ME panel were studied. The performance of the FA-ME panel was compared to CSF bacterial culture.

Results: Two-hundred and fifty-nine patients between December 2016 and December 2018 underwent the FA-ME test in CSF. FA-ME test detected pathogens in 61 (23.6%) out of 259 patients with ME syndrome. Among the pathogens detected by FA-ME panel, enterovirus was the commonest accounting for 29 cases (47.5%), followed by varicella in 11 patients (18%) and pneumococci in 9 (14.8%). CSF bacterial culture yield was low, positive only in 8 (3%) out of 259 cases, and matched with FA-ME panel in only one sample that grew *Streptococcus pneumoniae*. Bacterial culture yielded seven pathogens in those whose FA-ME panels were negative.

Conclusion: FA-ME panel improves diagnostic yield as compared to bacterial culture (26.3 vs 3%). FA-ME test helps in the early initiation of targeted antibiotic therapy and greater antibiotic de-escalation.

- Majority were due to enteroviruses and showed seasonal occurrence
- De-escalation in FA-ME was 49% vs 32% in conventional, $p<0.042$

Indian Journal of Critical Care Medicine, Volume 26 Issue 1 (January 2022)

Open Forum Infectious Diseases

Open Forum Infect Dis. 2020 Oct; 7(Suppl 1): S410–S411. PMCID: PMC
Published online 2020 Dec 31. doi: 10.1093/ofid/ofaa439.912

720. Clinical Performance of Film Array Gastrointestinal Pathogen Panel in Diarrhea

Rajalakshmi Ananthanarayanan, DNB Internal Medicine, Fellowship in ID, Niyas Vettakkara Kandy Muhammed,

6% by stool culture as compared to
39% by multiplex PCR

Table 1: Pathogens in FA GI pathogen panel

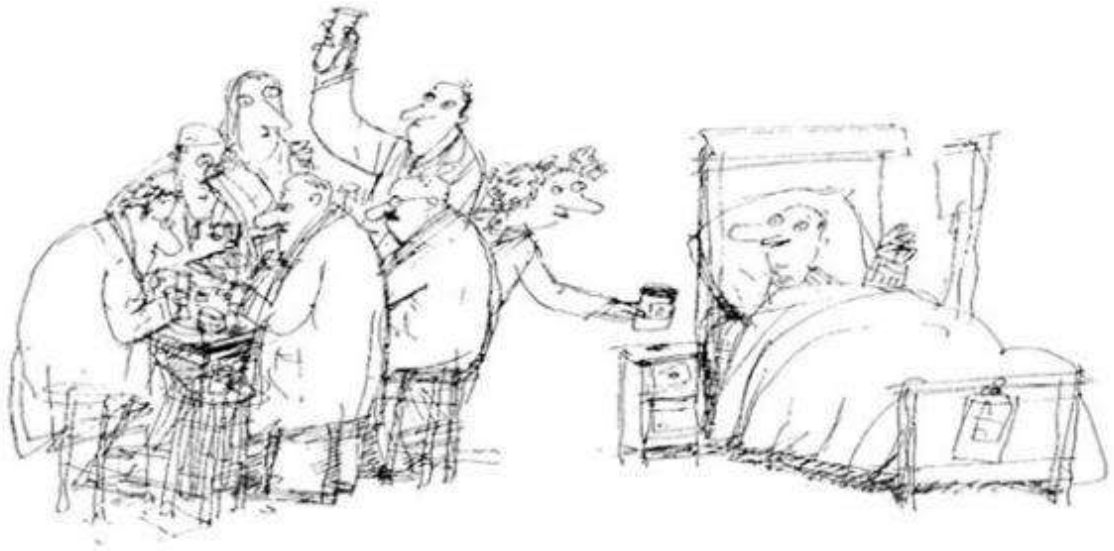
FA GI pathogen panel results	Frequency	As part of multiple organisms	Total frequency, (%)
EPEC	3	2	5 (12.8%)
ETEC (Enterotoxigenic *E. coli*)	1	2	3 (7.7%)
EAEC	5	4	9 (23%)
Salmonella	12	5	17 (43.5%)
Campylobacter	0	3	3 (7.7%)
Norovirus	2	1	3 (7.7%)
STEC E coli	1	0	1
EIEC	0	1	1
Shigella/ EIEC	2	0	2
Plesiomonas shigelloids	1	0	1
Clostridium difficile toxin A and B	0	2	2
More than one organism	12		

5. Communication – two way

- Patient details through request form – electronic or check box
- Critical values – blood culture, CSF, AFB, CDI, MDRO, rare pathogen
- CRE- guidance for further testing and therapy
- Clinical relevance of samples when in doubt
  - specimens of poor quality must be rejected
  - call physicians to clarify and resolve problems with specimen submissions

6. Bench to bedside

- Clinical rounds – understand factors that determine treatment, other than culture result
- Prioritize and process specimens from OR and IR, as soon as they arrive
- Understand IC practices
- **Familiarize and build trust among colleagues**



7. Research

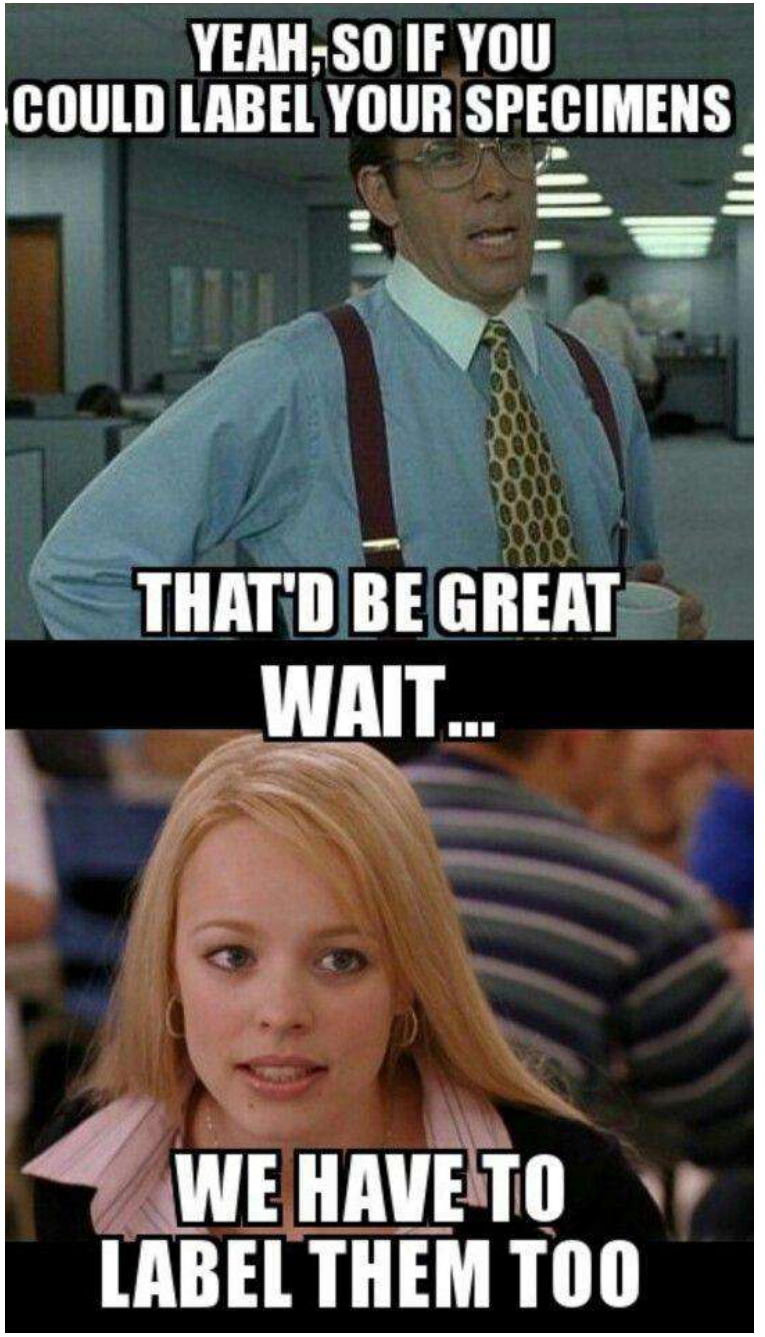
- Organism storage
- Serotyping, molecular diagnostics
- Hospital epidemiology
- Resistance trends

Pure culture is the foundation for all research on infectious diseases
- Robert Koch

IC, AMSP, QI

1. Sampling - pre-analytical

- The sample quality (appropriate site, timing, volume) = quality of the results.
- TAT of samples reaching the lab
- Proper storage if delay in processing
- Labelling- such as “wound” is not helpful - specify site and clinical information (eg, dog bite wound right forefinger).



2. Training reduces “Background noise”

- **Training for sampling** – link with nursing quality, residents, audit and feedback
- Blood and urine culture
  - aseptic technique is linked with contamination rate and antibiotic use
  - specimen should be collected prior to administration of antibiotics.
- Pus, fluid, tissue biopsies are preferred
- Drain samples usually reflect colonization
- Specimens like sputum, sinuses, wounds, fistulae require care in collection - commensal microbiota that can easily contaminate and complicate interpretation.

Don’t accept swabs (except naso/ oro-pharynx)

- A swab is not the specimen of choice for many specimens
  - swabs pick up extraneous microbes
  - hold extremely small volumes of the specimen (0.05 mL)
  - difficult to get bacteria or fungi away from the swab fibres and onto media,
  - the inoculum from the swab is often not uniform across several different agar plates.

- Flocked swabs - more effective than dacron, rayon, and cotton swabs. The flocked nature of the swab allows for more efficient release of contents for evaluation.

3. Reporting – not to report all that grows

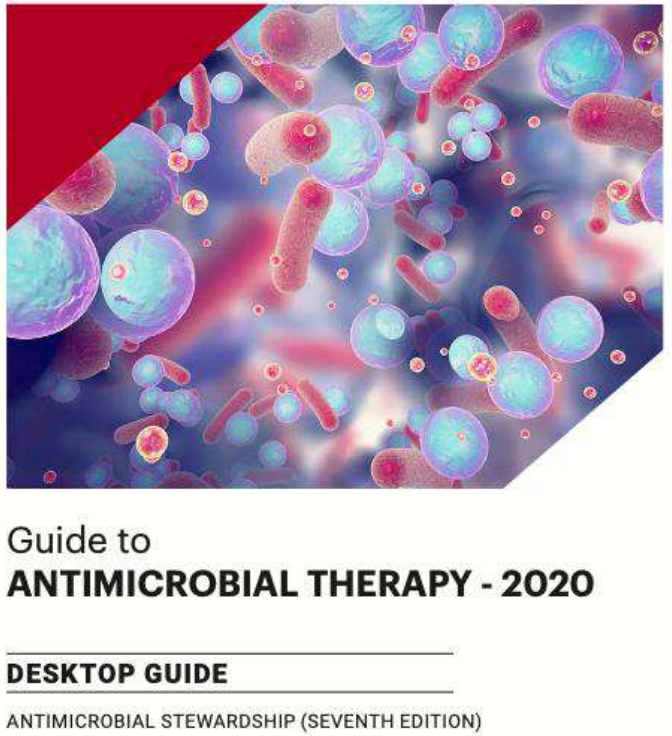
- **Cascade/ selective reporting** - do not report carbapenem susceptibility when a pathogen is susceptible to narrower-spectrum drugs

- **Therapy related comments** - e.g. Citrobacter freundii if susceptible in vitro to cefotaxime, ceftriaxone or ceftazidime, THEN note that the use in monotherapy of above should be discouraged, owing to the risk of selecting resistance

- **Supplementary testing** for susceptibility to new drugs if MDRO
- **Repeat testing** and promptly send to reference lab unusual susceptibility profiles
- **Additional comments** about colonization/ contaminants

4. Cumulative Antimicrobial susceptibility report (CASR)- antibiogram

- Bi-annual or at least annually
- WHOnet
- Help formulate empiric therapy



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5. Outbreak

- Recognition- first to identify the cluster or outbreak
- Quickly formulate a team and proceed
- Investigation
- Molecular typing

> Infez Med. 2021 Sep 10;29(3):427-433. doi: 10.53854/liim-2903-14. eCollection 2021.

Achromobacter spp. bacteremia outbreak related to contaminated furosemide ampoules

Rajalakshmi Arjun [1], Kalpana E John [2], Vettakkara Kandy Muhammed Niyas [1], Sreerekha R Nair [3], Viji Mohan [2], Raveendran Sarala Ratheesh [2]

6. Resistance trends

- Location of hospital
- Correlate with AUR
- IC measures

7. Hospital epidemiology

- Surveillance is the cornerstone – early warning system, electronic alerts

- “typing” or “fingerprinting” of epidemiologically related isolates to confirm the existence of an outbreak

Cross talk

Clinicians

- If adequate clinical information is lacking
- Alert in real time- bacteria, fungi, parasite, virus- on critical samples

Nursing/ training/ quality

- If blood contaminants are increasing
- Blood culture volume is low

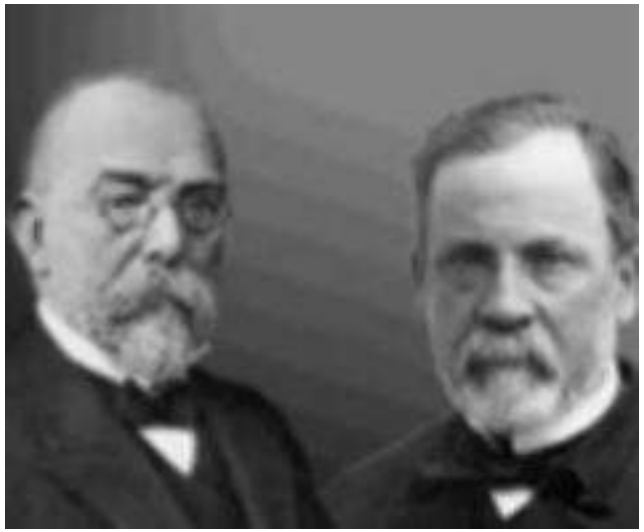
HIC/ Admin

- Outbreak

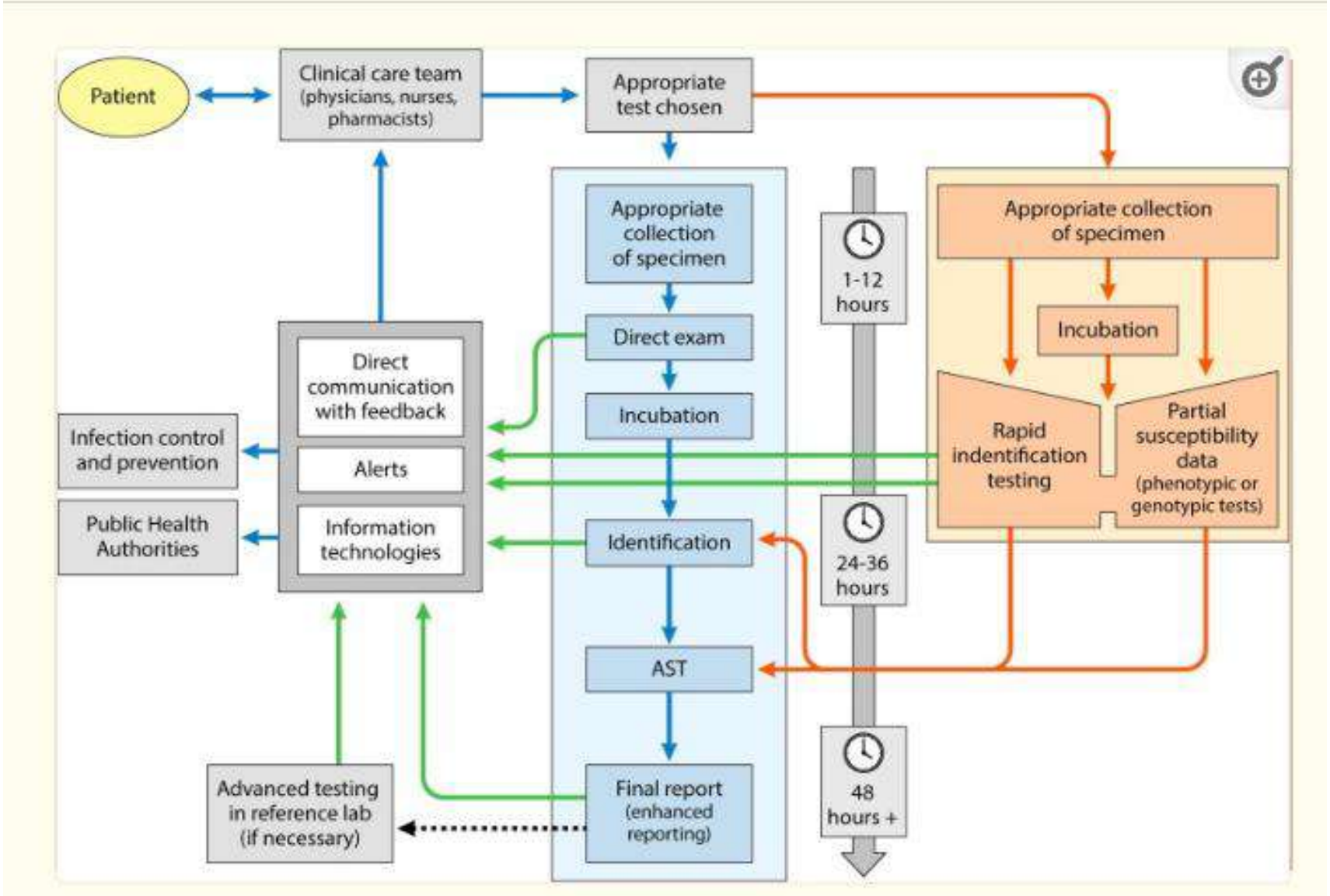
Clinical microbiology seems at a crossroads

- Downside- clinical utility of traditional methods, pressure to cut costs
  - outsourcing to off-site commercial or centralized laboratories
  - increasing the isolation from the clinician colleagues
  - consigning to increasingly technical roles

- Look forward - boost the clinical relevance
  - your expertise in conventional and innovative RDT
  - communication, bench to bed-side
  - levels unseen since the time of Koch and Pasteur



Roadmap- to seize emerging opportunities, reassert in patient care and AMSP



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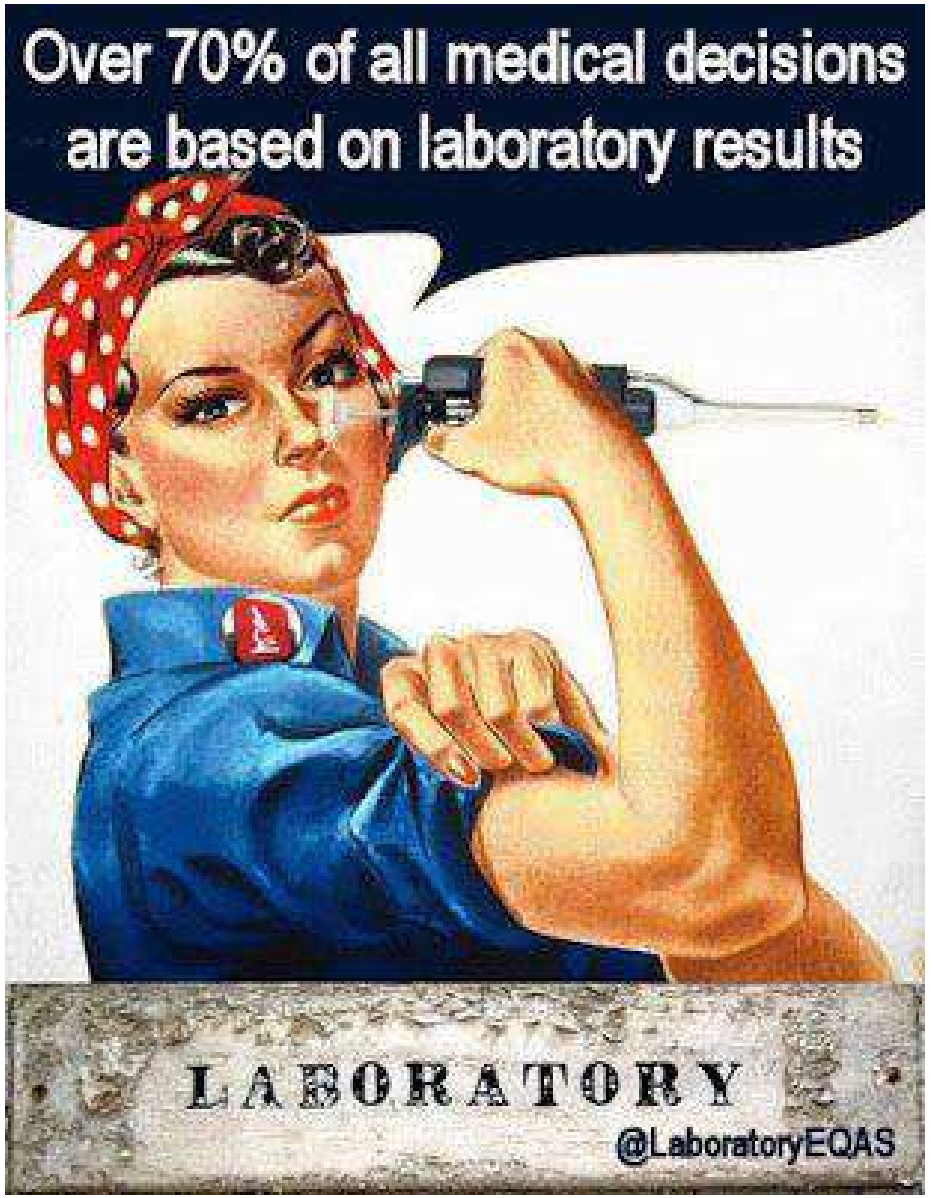
To the clinicians out there…

- Know your lab and interact regularly
- Order tests which have good literature support
- Appropriate sampling
- Don’t demand to report “everything that grows.”
- Develop the culture of cultures


Love a Microbiologist, they're well-cultured


Over 70% of all medical decisions are based on laboratory results
LABORATORY
@LaboratoryEQAS

Are you an MD/DNB and interested in an ID career?

- DM (Infectious Diseases) -Three year program
  - **Kottayam medical college, Kottayam, Kerala**
  - CMC, Vellore
  - AIIMS, New Delhi
  - AIIMS, Jodhpur
- FNB (National Board of Examinations) - Two year program
  - **KIMSHealth, Trivandrum, Kerala**
  - Apollo Hospitals, Chennai
  - Apollo, Hyderabad
  - Hinduja Hospital, Mumbai
  - Sterling Hospital, Ahmedabad
  - Sher-I-Kashmir, Kashmir
  - Manipal Hospitals, Bangalore