Impact of Rapid Diagnostics on Antimicrobial Stewardship

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Learning Objectives

- Identify the ways in which clinicians can engage in antimicrobial stewardship
- Discuss a plan for community engagement across all healthcare providers
- Review Joint Commission standards and accountability initiatives
- Analyze the impact and application of rapid POC diagnostics in antimicrobial stewardship

Agenda

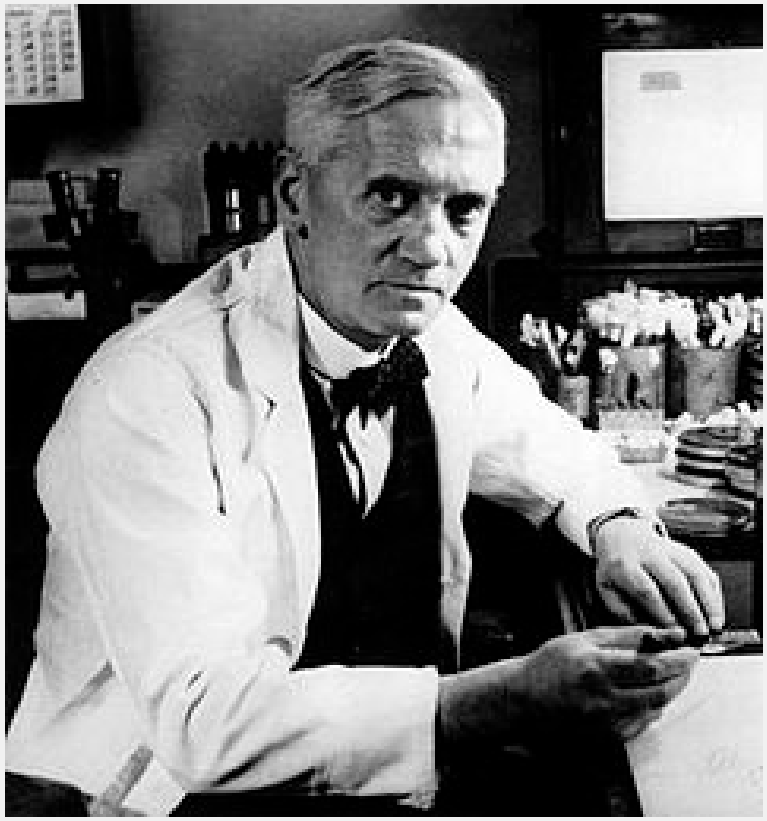
- Introduction
- National Action Plan
- Goals of an Effective Antimicrobial Stewardship Program
- Review of current rapid diagnostic tests: Pros and Cons
- Examples
- Conclusions


Crisis
Success
strategy

Birth of Antimicrobial Stewardship

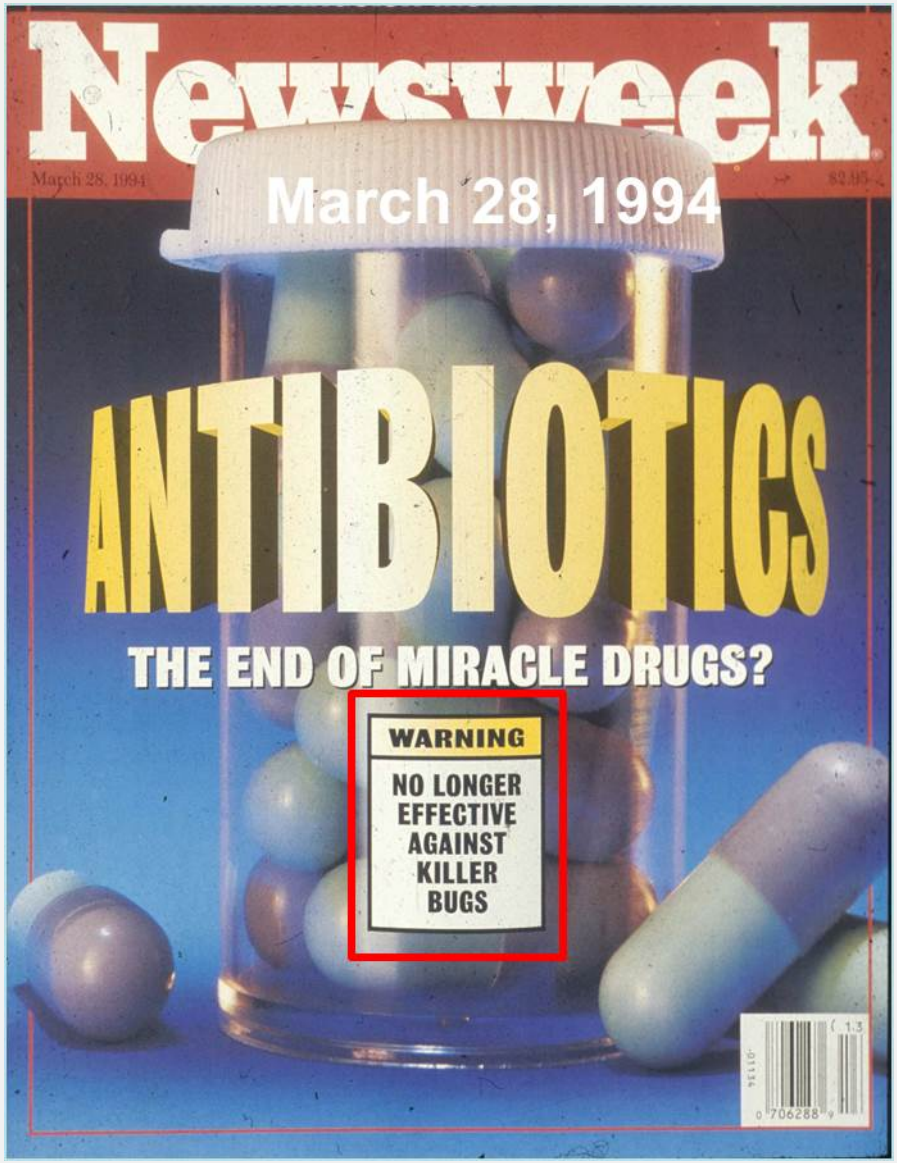
"Microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out…

In such cases, the thoughtless person playing with penicillin is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted."



Fleming A. New York Times. 26 June 1945:21

1994


Newsweek
March 28, 1994
March 28, 1994
ANTIBIOTICS
THE END OF MIRACLE DRUGS?
WARNING
NO LONGER EFFECTIVE AGAINST KILLER BUGS

2015


STRONGER, SMARTER, SEXIER YOU?
WE EVALUATE ANTI-AGING PRODUCT CLAIMS
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ConsumerReports
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HOW TO STOP A
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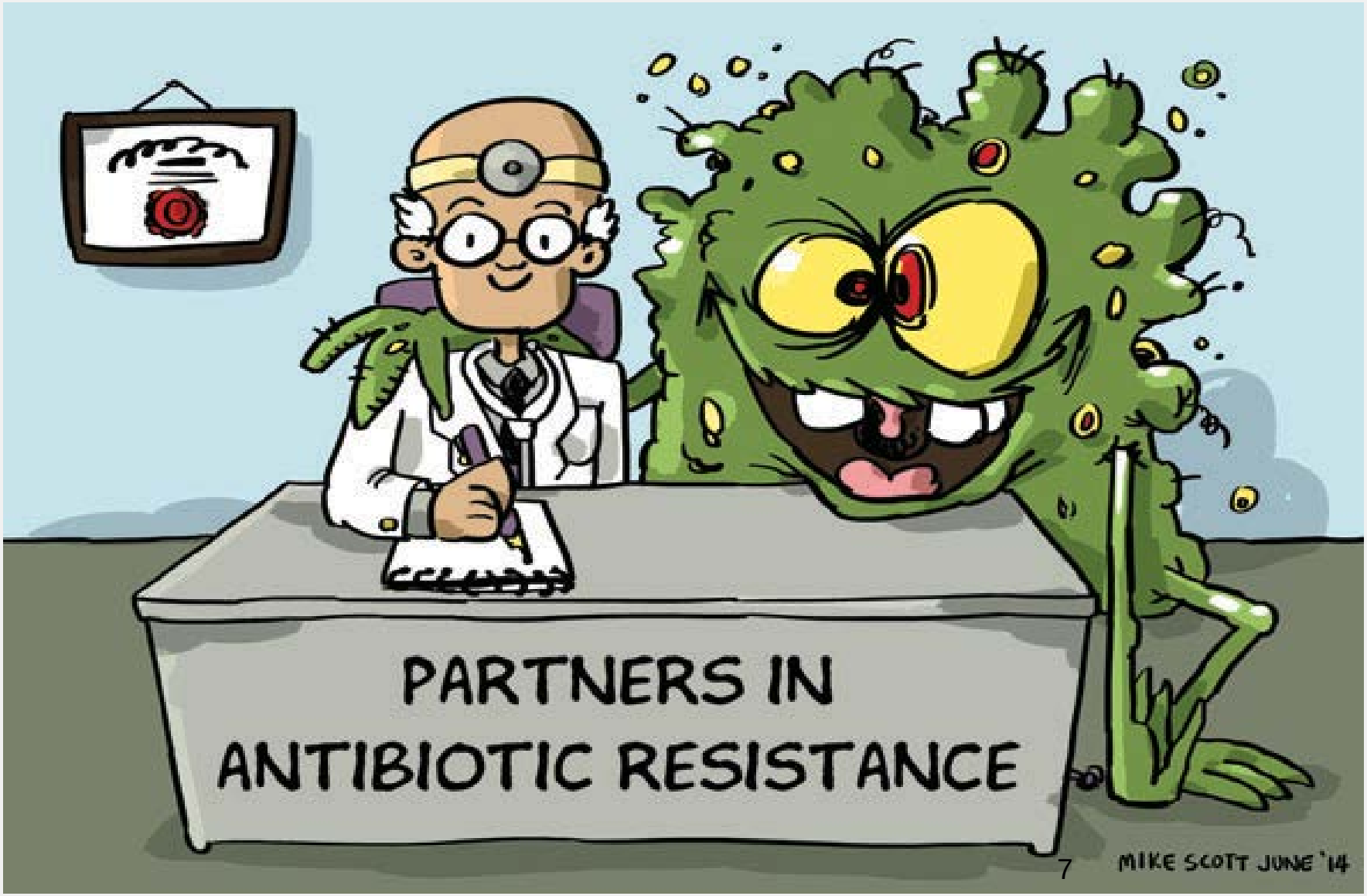
Don't Outlive Your Money: Here's How
More and more antibiotics no longer work, and dangerous bugs are making us sicker. What can we do about it before it's too late?
PLUS
TV, YOUR WAY A GUIDE TO PICKING THE BEST PLAN
AUGUST 2015
CONSUMERREPORTS.ORG


PARTNERS IN
ANTIBIOTIC RESISTANCE
MIKE SCOTT JUNE '14

Texas A&M Health Science Center

Complex problem

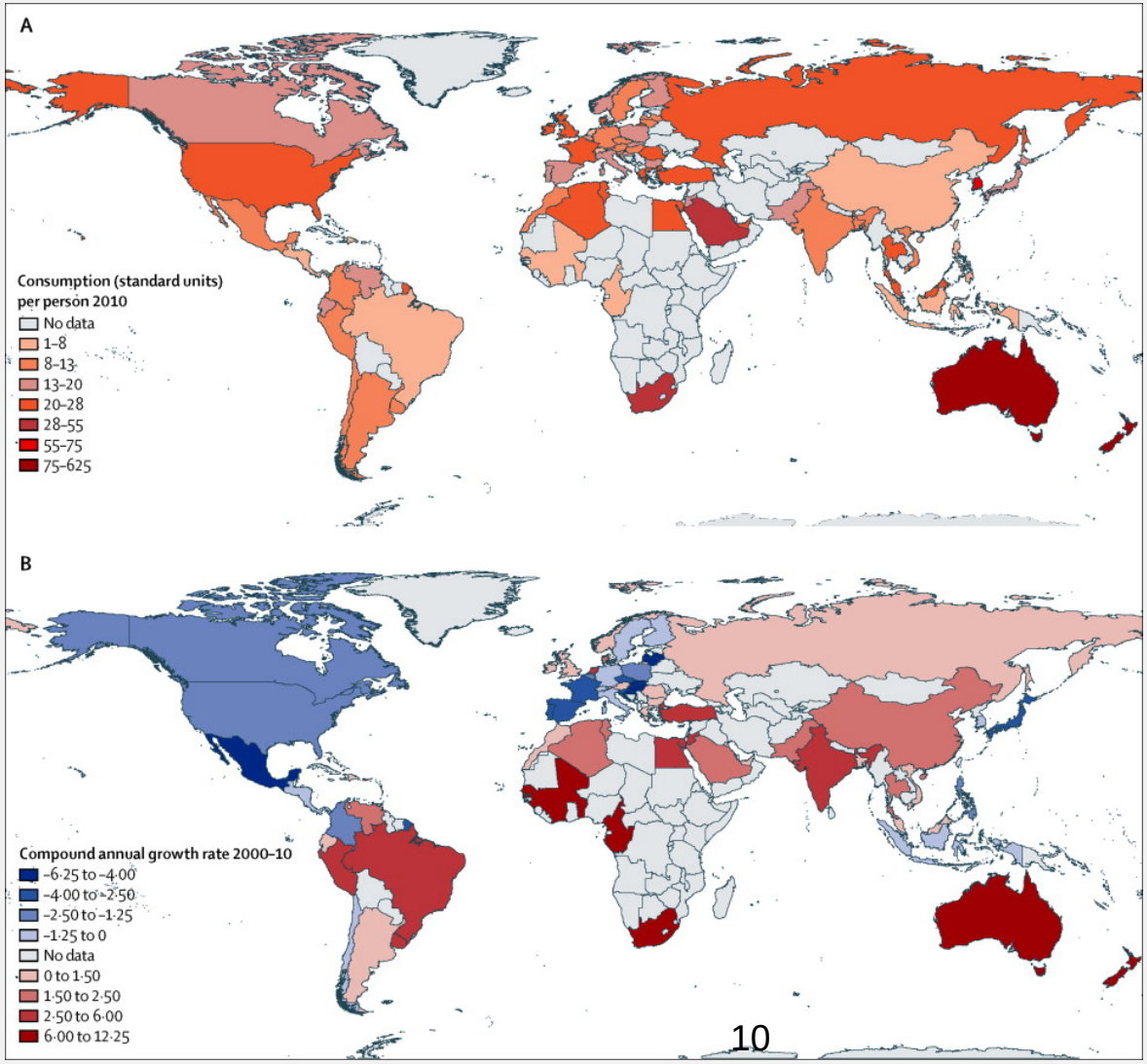
Why We Need to Improve Antibiotic Use

- Antibiotics are misused across the continuum of care
  - Studies indicate that up to 50% of antibiotic use is either unnecessary or inappropriate across all type of health care settings [1]
- Use of antibiotics in animals-~80% of antibiotics sold in US are used in animals primarily to promote growth and prevent infection [2]
  - Molecular methods have confirmed that resistant bacteria in animals are consumed by humans resulting in infection
  - Up to 90% of antibiotics used in animals are excreted in urine and stools and can disperse in fertilizer, groundwater, and surface runoff
- Antibiotic misuse adversely impacts patients and society
  - ↑Antimicrobial resistance(AR) and *C difficile infections*
- In 2011 a national survey found that 60% of infectious diseases physicians had seen a pan-resistant, untreatable infection in the last year [3]
- Improving antibiotic use improves patient outcomes and saves money
- Improving antibiotic use is a public health imperative-WHO considers AR an emerging threat to global stability

1. Clin Infect Dis 2007; 44:159-177 | *2. Clin Infect Dis* 2013; 56:1445-1450 | 3. *Clin Infect Dis 2014; 59:S17-S75*

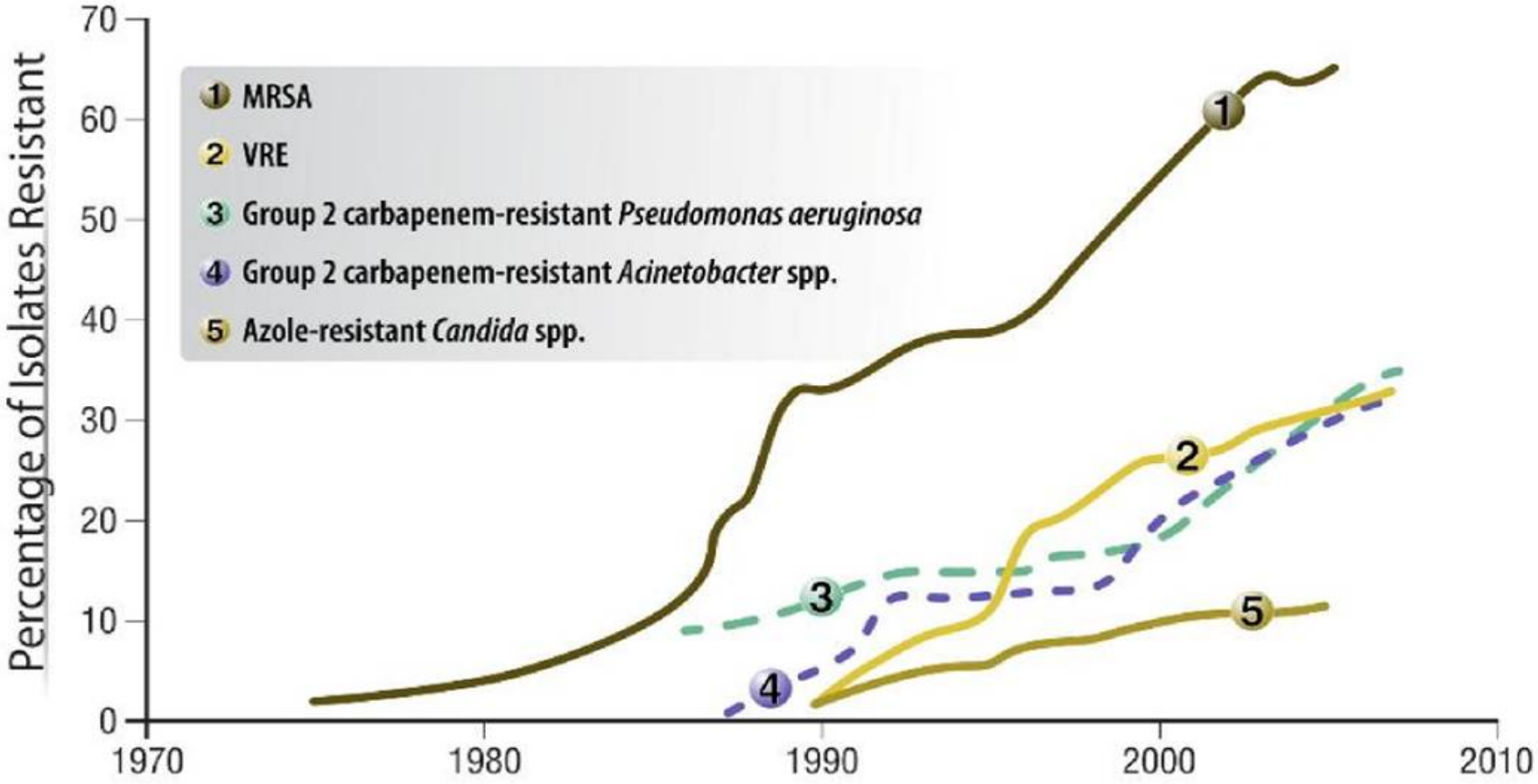
We are using a lot of antibiotics worldwide!!

Consumption of antibiotics in 2010 per person (A), and compound annual growth rate of antibiotic drug consumption between 2000 and 2010 (B)

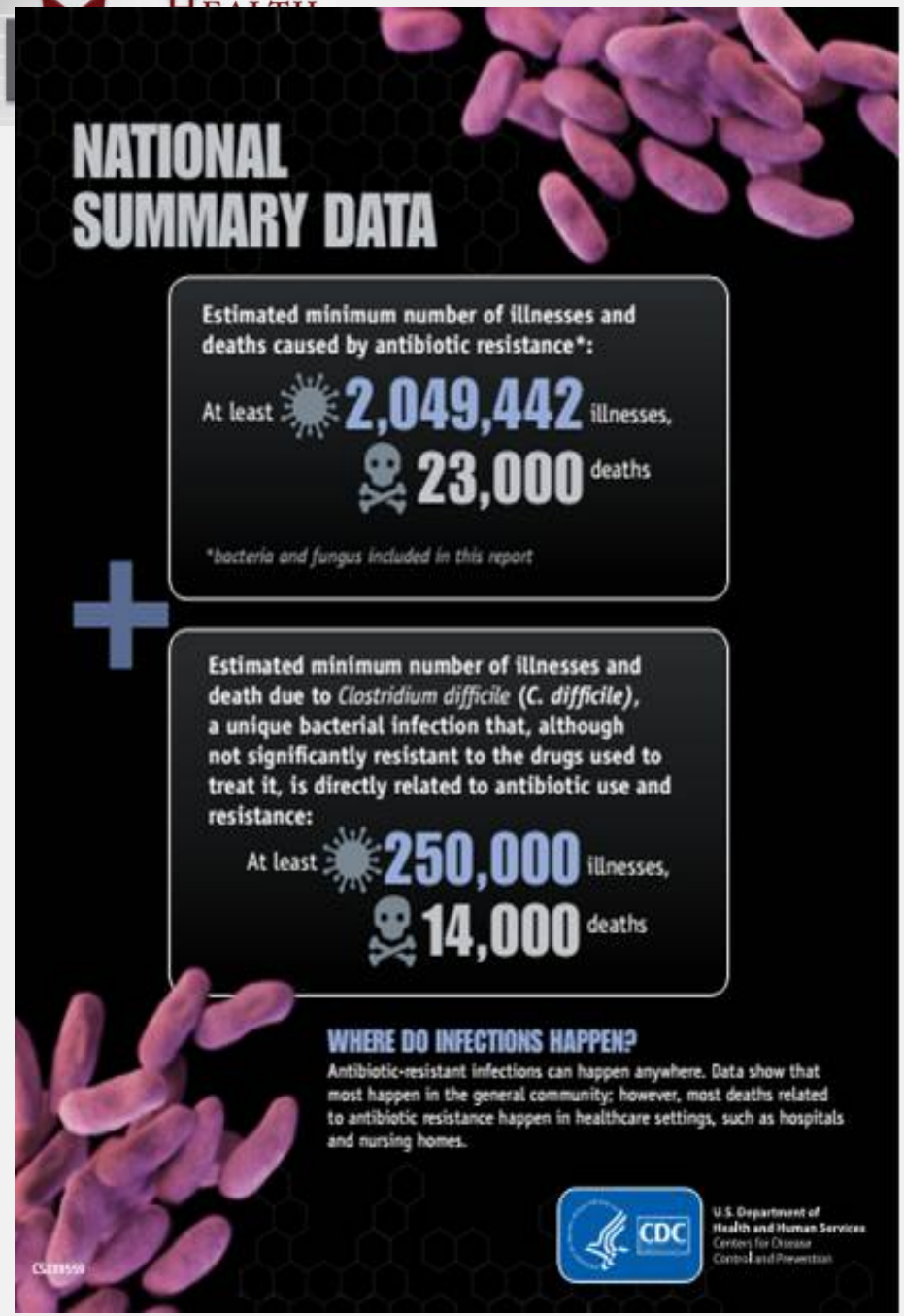


Lancet Infect Dis. 2014;14:742-50.

Trends in Antimicrobial Resistance



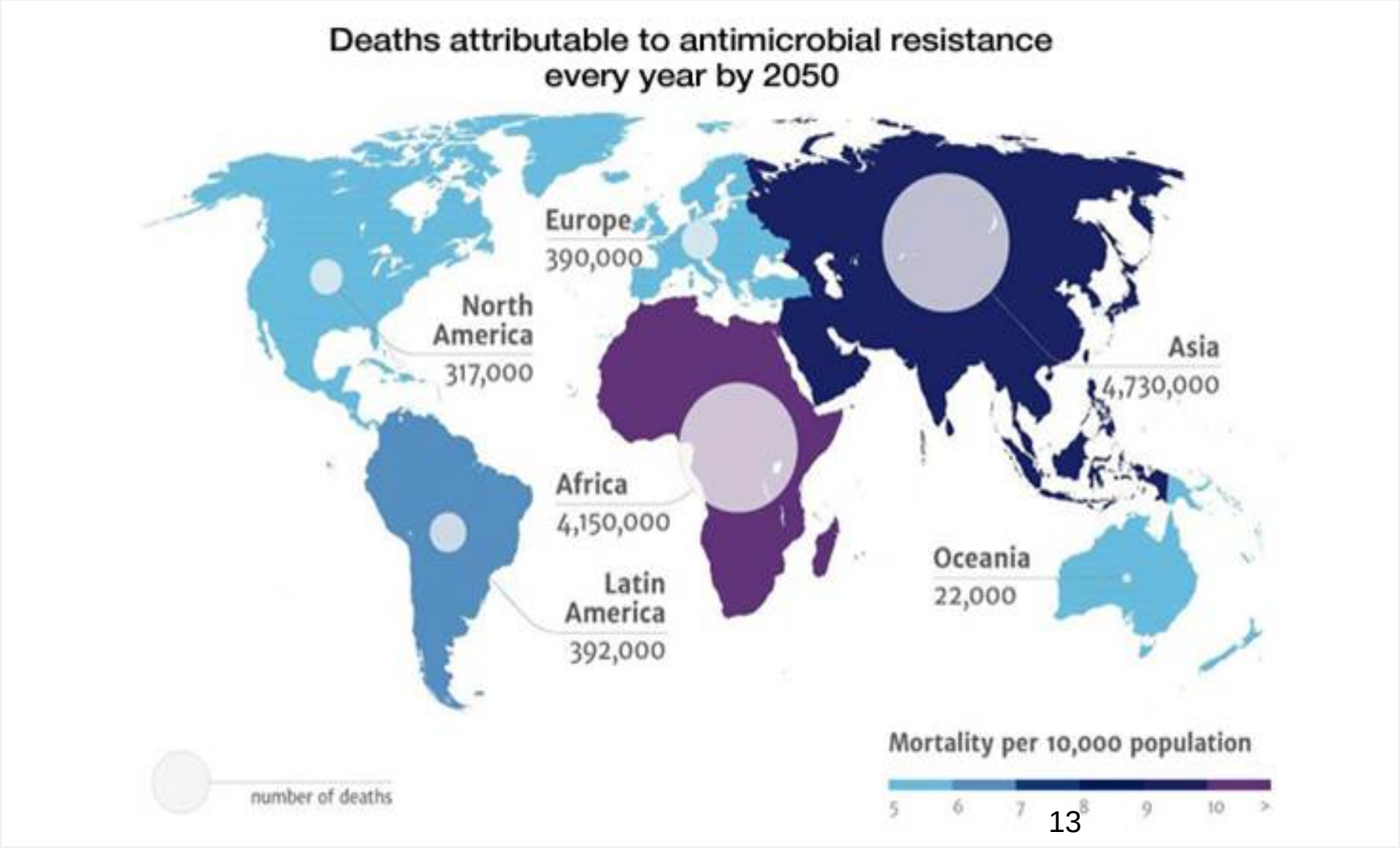
Adapted from Wenzel RP, et al. *Infect Control Hosp Epidemiol.* 2008;29:1012-1018.

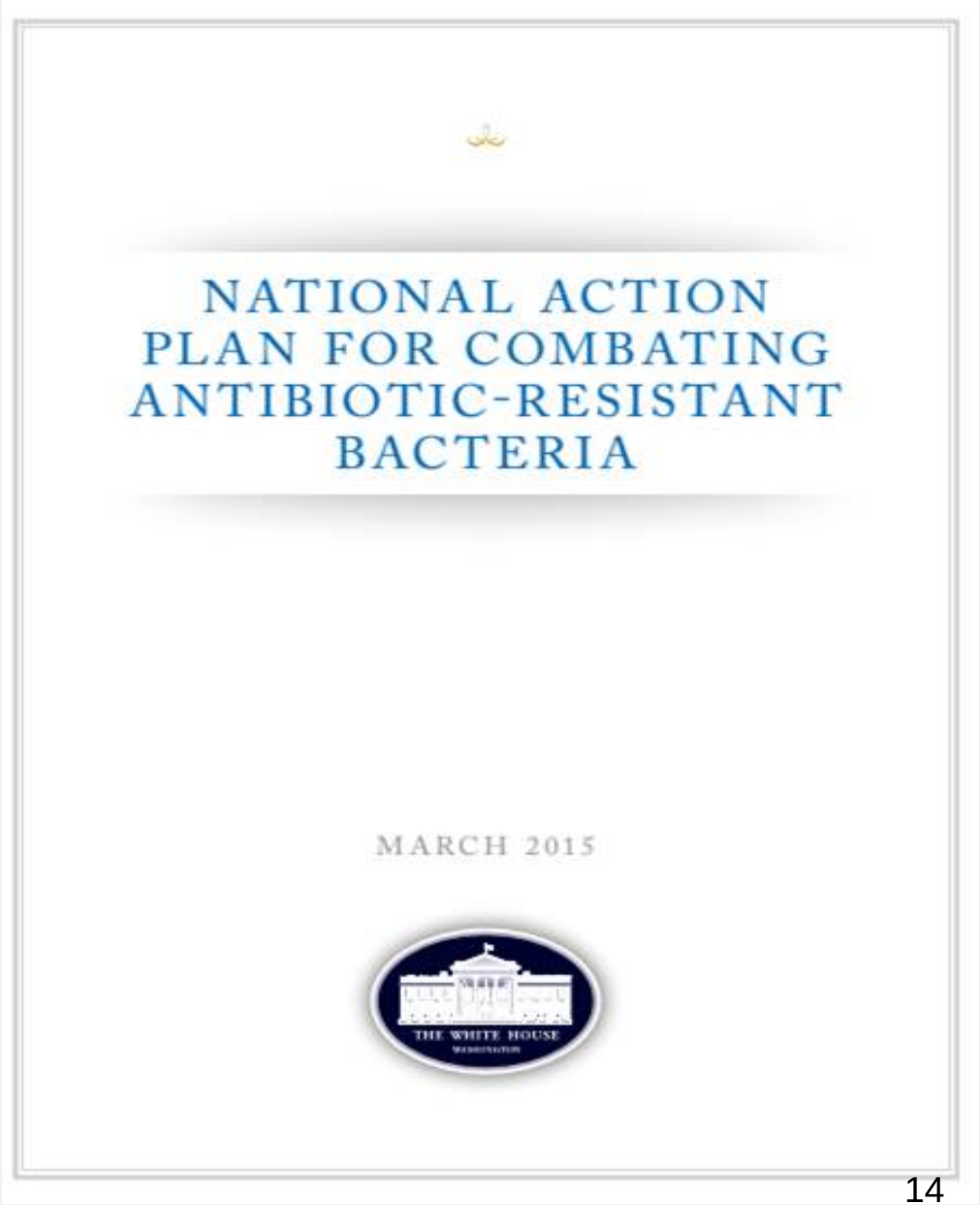


- $20 billion in excess direct healthcare costs
- costs to society for lost productivity as high as $35 billion a year (2008 dollars)
- The use of antibiotics is the single most important factor leading to antibiotic resistance
- ↑ ***C. difficile*** **infections**[1]
  - **453,000 case 2011**
  - **29,000 deaths 2011**

1. N Engl J Med 2015;372:825-834

UK Review on AR 2016




NATIONAL ACTION
PLAN FOR COMBATING
ANTIBIOTIC-RESISTANT
BACTERIA
MARCH 2015
THE WHITE HOUSE

Proposed Policy Changes

- Strengthen antibiotic stewardship in inpatient, outpatient, and long-term care settings
  - **Alignment with CDC Core Elements**
  - **Compliance with Conditions of Participation and The Joint Commission (TJC) Accreditation requirements**
- Implement annual reporting of antibiotic use in inpatient and outpatient settings and identify variation at geographic, provider, and patient levels
- Establish and improve antibiotic stewardship programs across all healthcare settings
- Reduce inappropriate antibiotic use by 50% in outpatient settings and 20% in inpatient settings
- Establish State Antibiotic Resistance (AR) Prevention (Protect) Programs in all 50 states

National Action Plan highlights

- The plan sets 1-, 3-, and 5-year targets in each of the five overarching goals, which are to:
  - slow the emergence of resistant bacteria and prevent the spread of resistant infections
  - strengthen national one-health surveillance efforts to combat resistance (the "one-health" approach to disease surveillance integrates data from multiple monitoring networks, according to the White House)
  - advance development and use of rapid and innovative diagnostic tests for the identification and characterization of resistant bacteria;
  - accelerate basic and applied research and development for new antibiotics, other therapeutics, and vaccines; and
  - improve international collaboration and capacities for antibiotic resistance prevention, surveillance, control, and antibiotic research and development

National Action Plan continued

- The plan sets goals for eradicating pathogens that have been labeled urgent or serious threats by the Centers for Disease Control and Prevention (CDC). The 2020 targets include:
  - 50% reduction from 2011 estimates in the incidence of *Clostridium difficile*
  - 60% reduction in hospital-acquired carbapenem-resistant Enterobacteriaceae infections
  - 35% reduction in hospital-acquired multidrug-resistant *Pseudomonas* species infections
  - 50% reduction from 2011 estimates in methicillin-resistant *Staphylococcus aureus* bloodstream infections
  - 50% reduction in inappropriate antibiotic use in outpatient settings and a 20% reduction in inpatient settings,
  - The development and wide dissemination of rapid diagnostic tests that can be used in a physician's office or at the hospital bedside to distinguish between viral and bacterial infections, and thus help ensure more appropriate use of therapeutics.

Antimicrobial Stewardship

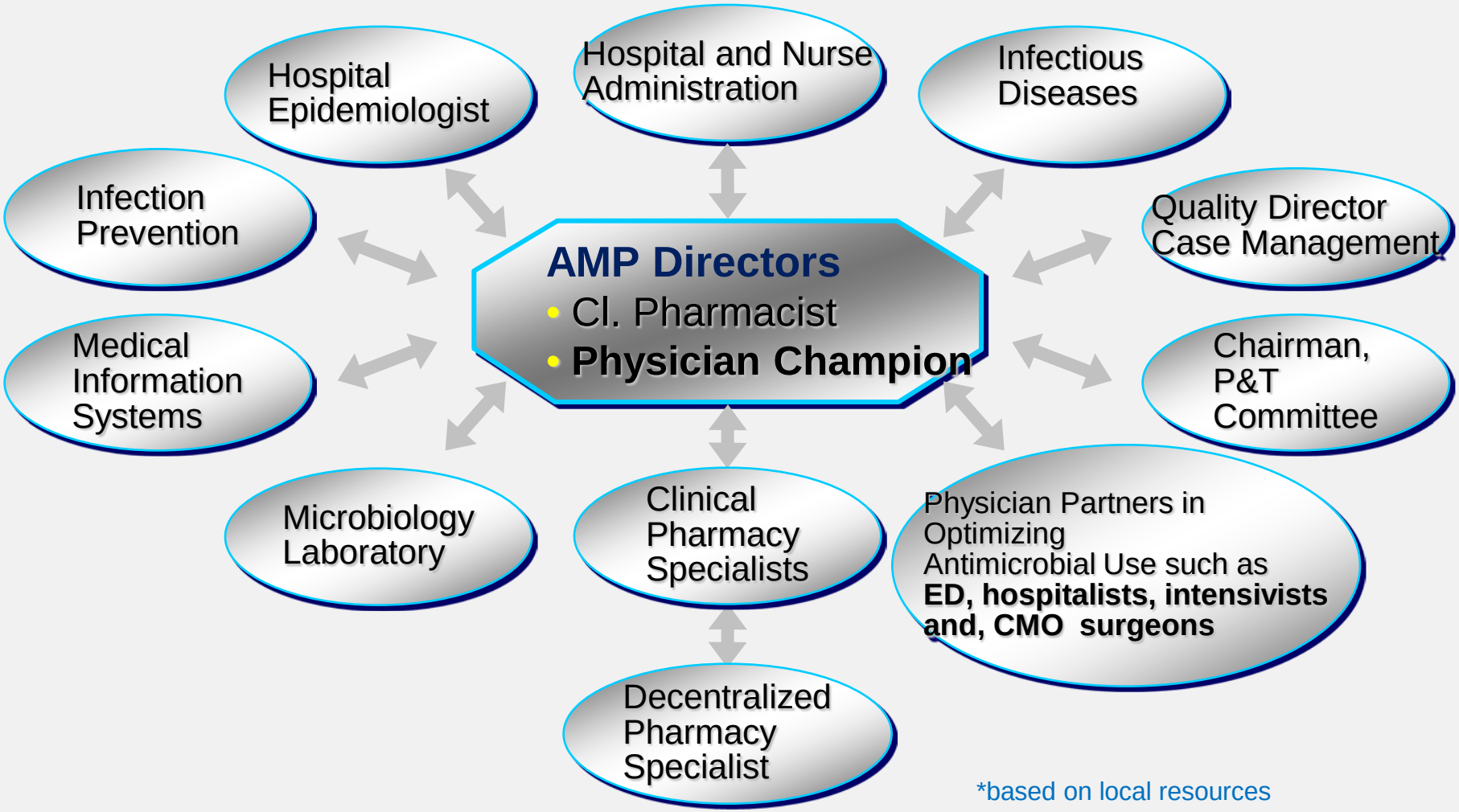
- Antimicrobial stewardship (AS) aims to optimize use of antimicrobials to improve patient outcomes and reduce collateral damage
- AS interventions use different strategies (both persuasive and restrictive) to change the prescribing behaviors of frontline clinicians
  - Passive education-limited impact
  - Audit and Feedback-
    - with and without real-time “academic detailing”
  - Restricted Formularies
  - Prior Approval
  - EBOS based on local epidemiology

Engaging the Staff in the Work: Building the Team

- Champion(s)
- Supporters(stakeholders)
- Leadership

Antimicrobial Stewardship Team

Multidisciplinary Team Approach to Optimizing Clinical Outcomes*



*based on local resources

Modified: Dellit et al. ClD 2007;44:159-177.

Physician To Do List

- Stewardship is every physician's responsibility
- Select physician champion
- Develop an effective antimicrobial stewardship team
- Partner with clinical pharmacy
- Education the medical staff and administration about the urgency and value of an effective antimicrobial stewardship team
- Program must be approved by the Physician Executive Committee-program should be physician directed
- Comply with infection prevention especially hand hygiene
- Assure that microbiology is aware of how to detect new resistance mechanisms (e.g. CREs, NDM1) and new CLSI break points

What can the individual physician do?

- Obtain appropriate cultures before starting antibiotics
- Review antibiotic use in past 48-72 hours – can we de-escalate? or
- Stop antibiotic in patients with alternative noninfectious diagnosis
- Optimize dosing and duration of antibiotic therapy
- Avoid unnecessary use, especially viral URIs (75%)*

***Must implement across the continuum of care community wide**

Pharmacy Responsibility

- Identify ASP Pharmacist lead
- Work with facility leadership to redistribute pharmacy resources to ASP
- Establish staff development plan to elevate staff competence
  - ASP site- Competency- Pharmacy
  - External (MAD-ID and SIDP)
- Establish **partnership** with Physician Champion
- Complete Gap Assessment
- Utilize Clinical Interventions
- Collect, report and track assigned program metrics monthly

Role of Infection Prevention

- Timely communication to team when MDROs are identified
- Prevention of MDRO in health care facilities
- Monitor trends in antimicrobial resistance
- Educate team about NHSN definitions of HAIs
- Collaborate with microbiology, pharmacy, medical staff, and administration to plan and implement effective interventions

Are nurses underutilized in ASP?

	RN	PharmD	ID-MD
Patient triage and isolation	X		
Accurate allergy history	X	X	
Timely antibiotic initiation*	X		X
Daily progress monitor and report	X	X	X
Preliminary antibiotic dosing	X	X	X
Adverse event monitoring	X	X	
Change in patient condition	X		X
IV to PO adjustment	X	X	X
Patient education	X	X	X

Olans RN et al. *Clin Infect Dis*. 2015 Aug 11. pii: civ697. [Epub ahead of print]
*make sure cultures obtained first

Defining a Role for Nursing Education in Staff Nurse Participation in Antimicrobial Stewardship.
Olans RD et al. *J Contin Educ Nurs*. 2015; 46:318-21.
"Identified a need for more education and also an interest in the area for practicing nurses."

Microbiology Competency Items

- Specimen Collection and Testing
- Identification and susceptibility testing for clinically significant pathogens
- Basic, confirmatory and specialized resistance testing methods
- Use of CLSI standards
- Cumulative antibiograms
- Timely notification of MDRO findings
- Evaluate rapid diagnostics testing appropriate for your population-must be actionable and impact patient care

Lessons Learned for Successful Stewardship

- Although ASP interventions have had limited success at some facilities, we can do better
  - Direct (passive)educational approaches generally do not result in sustained reductions in prescribing[1]
  - Restrictive policies can be circumvented
    - "Stealth dosing"[2]
    - Misrepresenting clinical information [3,4]
  - Audits can be "gamed"[5]
- To bring about lasting change, clinicians need to hard wire new culture about what is considered prudent antimicrobial prescribing[6]

1. Arnold et al. Cochrane Database of Systematic Reviews 2005:4
2. LaRosa et al. ICHE 2007:28
3. Calfee et al. J Hosp Infect 2003:55
4. Linkin et al. ICHE 2007:28
5. Szymczak et al. ICHE 2014:35
6. Bosk et al. Lancet 2009:374

Lessons Learned for Successful Stewardship continued

Prescribing drivers

- Lack of conclusive microbiology
- Diagnostic uncertainty
- Insecurity

Getting appropriate cultures **before** starting antibiotics is critical to enhancing identification of the pathogen

Is there a role for rapid diagnostics?

Traditional Method of Infectious Disease Diagnosis

- Clinical history/exam
- Is the patient infected?
- Is the infection viral or bacterial?
- Gram stain?
- Which virus or bacterium?
- Treatment decision

Historical Perspectives

- Cultivation of bacteria
  - Joseph Lister, ~1880

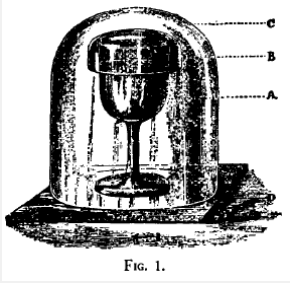
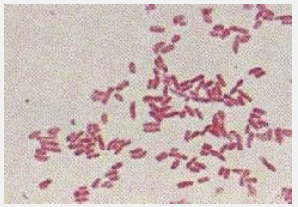
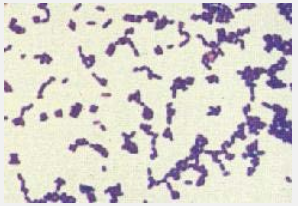


FIG. 1.

- New method of staining bacteria
  - Hans Christian Gram, 1884





- New container for cultivation
  - R. J. Petri, 1887

Traditional Method Suspected Infection

- Fluid or Tissue Sample
- Gram's Stain
  - Bacteria present? If so, Gram - or +
  - Results in minutes
- Sample incubated in culture media
  - Usually 24-72 hours for growth
- Biochemical testing to determine the organism
  - Minutes to 24 hours
- Susceptibility testing
  - Another 24-48 hours

Traditional Culture Methods

PROBLEMS

- Usually takes ~ 48 - 72 hours
- Requires a sufficient number of bacteria
  - Often not possible if antibiotics given prior
- May be difficult in mixed infections
- Fastidious organisms won't grow or require specialized media
- Viral, Fungal, and Mycobacterial cultures
  - technically more difficult
  - take longer (up to 6 weeks)

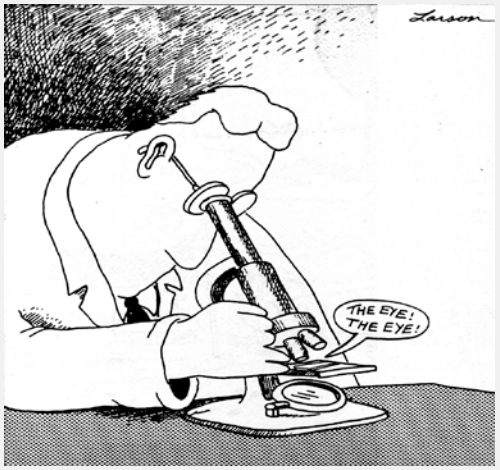
Other Traditional Methods

- Rapid Antigen Tests
  - Group A Streptococcus
    - Sensitivity/Specificity

    86%/92% in children, 91%/93% in adults
  - Influenza EIA
    - Sensitivity/Specificity 50-70%/90-95%[2]
- Serology
  - Measurement of host antibodies to a suspected pathogen
  - Lack sensitivity & specificity
  - Requires 1 - 2 weeks to get results, 8-10 weeks for diagnosis

[1]*PLoS One* 9(11):e111727, 2014
[2]*www.cdc.gov/flu/professionals/diagnosis/rapidclin*

Rapid Molecular Methods



- Various technologies available
  - Urinary Antigens
    - *Legionella, S pneumoniae*
  - Influenza A/B, RSV antigens
  - Polymerase chain reaction (PCR)
  - Multiplex PCR
  - Nanoparticle Probe Technology
  - Peptide Nucleic Acid Fluorescent In Situ Hybridization (PNA FISH)
  - Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS)

PNA FISH

- Uses synthetic, neutrally charged oligonucleotides molecules to act as probes
- These molecules hybridize with RNA specific for certain species
- The hybridization of the probe molecule with the RNA is detected via fluorescence
- One of the first rapid technologies utilized for bloodstream infections
  - *S aureus* vs CoNS
  - *E. faecalis* vs faecium
  - *E coli* vs *K penumoniae* vs P *aeruginosa*
  - *C albicans* vs *C parasilosis* vs *C grabrata*

Polymerase Chain Reaction

- Uses a fluorescently labeled probe with two primers
- These primers target DNA that is specific to a species or resistance mechanism
- The primers detect and then amplify target gene sequences
- Multiplex PCR uses many primers
- Several devices commercially available for bloodstream infection detection

Rapid detection of MRSA/MSSA From blood cultures or nares samples

Method	TAT	Sens	Spec	Equipment	Per test
PCR (various)*	1-4	90-98	91-99	30-150K	25-50
Bacteriophage**	5-6	92	98	n/a	?
Chromogenic agar	18-48	60-90	90-100	n/a	5

*Commonly used commercial assays: home brew PCR is far less expensive
**blood culture only, nares test in development
***TAT is analytic TAT only!**

Bhowmick, et al. 50th ICAAC, Boston, MA, 2010, Abstract D-155.
Carroll KC. Mol Diagn Ther 2008;12:15
Malhotra-Kumar et al. J Clin Microbiol 2010;48:4598.
Reyes RC, et al. Diagn Microbiol Infect Dis 2008;60:225
Pape J, et al. J Clin Microbiol 2006;44:2575.

Infect Control Hosp Epidemiol. 2010 Oct;31(10):1043-8. doi: 10.1086/656248.

Impact of an assay that enables rapid determination of Staphylococcus species and their drug susceptibility on the treatment of patients with positive blood culture results.

Parta M[1], Goebel M, Thomas J, Matloobi M, Stager C, Musher DM.

- PCR MRSA/SA BC system
  - Group 1 – immediate determination and notification of GPC in BC
  - Group 2 – historical cohort with standard micro

	Group 1	Group 2	P-value
Non-SA species receiving no anti-staph. Tx	**76%**	**55%**	**<.01**
MRSA Tx received	**6%**	**25%**	**<.01**
Mean time to appropriate Tx for MSSA	**5.2 h**	**49.8 h**	**.007**

Duration of unnecessary drug ↓ 61 hours / patient

Bacterial PCR Tests Routinely Used in Clinical Practice

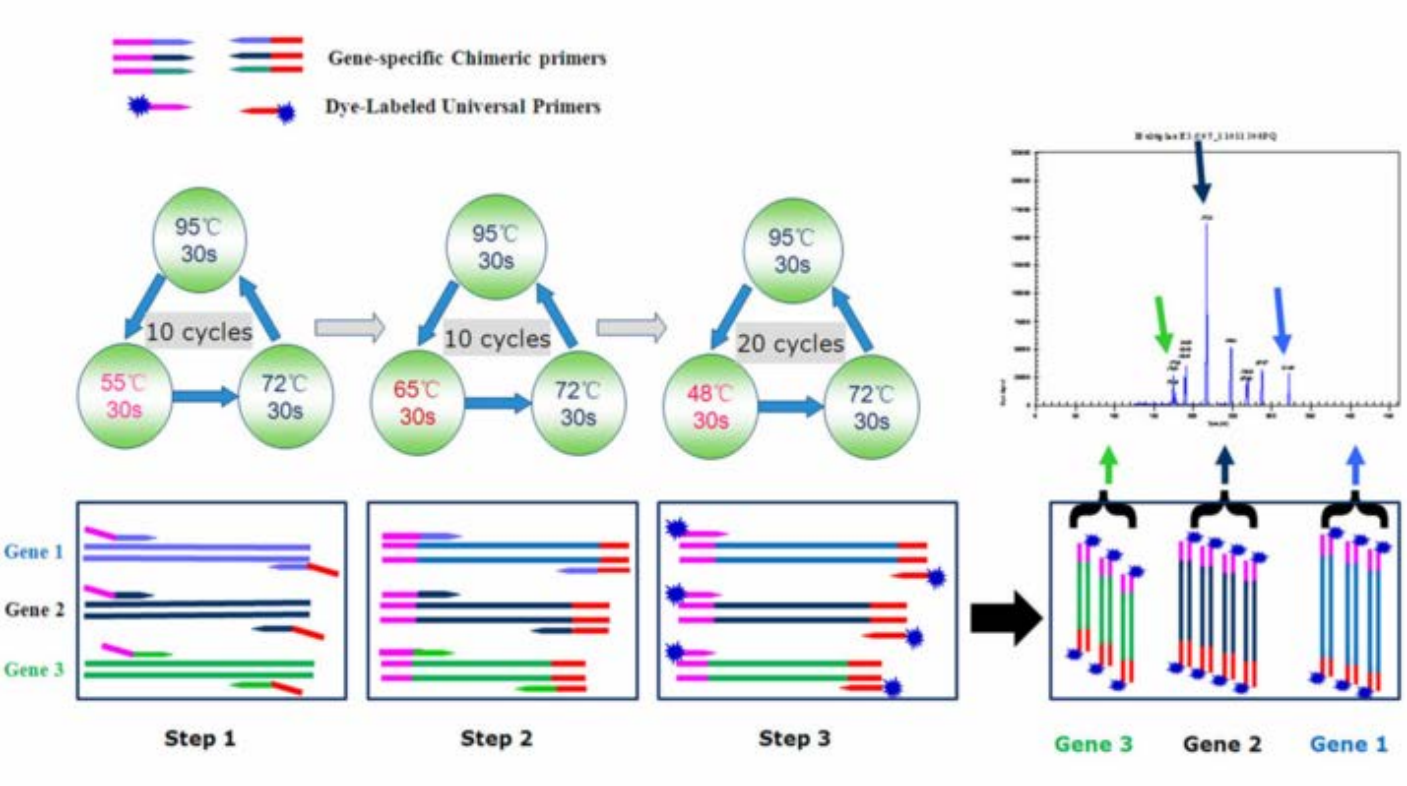
- Gonorrhea, Chlamydia
- Tuberculosis
- Ehrlichiosis *(Ehrlichia chaffeensis)*
- Lyme Disease (*Borrelia burgdorferi*)
- Whipple's Disease (*Tropheryma whippelii*)
- Pertussis (*Bordatella pertussis*)
- C. diff (*Clostridium difficile*)

Viral PCR Tests Routinely Used in Clinical Practice

- Human Immunodeficiency Virus (HIV)
- Hepatitis B
- Hepatitis C
- Cytomegalovirus (CMV)
- Herpes Simplex Virus (HSV)
- Varicella Zoster Virus (VZV)
- Enterovirus
- Epstein-Barr Virus
- Influenza
- Human Pappilomavirus (HPV)

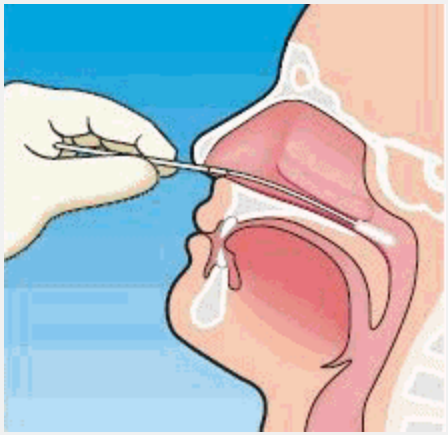
Multiplex PCR

- Multiple primers for various DNA targets done simultaneously



BMC Microbiol 13:58, 2013

PCR Panels in Current Use



- Respiratory Panel (FDA approved 2008)
- GI panel (FDA approved 2012)
- Blood culture panel (FDA approved 2014)
- Meningitis panel (FDA approved 2015)

Rapid Identification of Positive Blood Cultures (N=118)

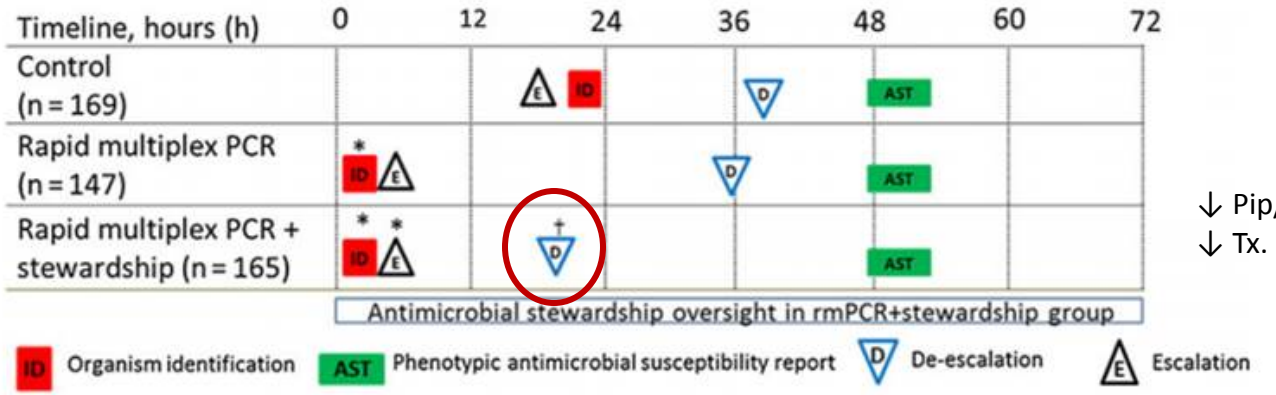
Panel	Targets	Accuracy Rate, %
FilmArray BCID Panel, Biofire Diagnostics, Salt Lake City, Utah	• Detects 19 bacterial targets, 3 resistance genes, and 5 yeast targets	91-92
Verigene BC-GP and BC-GN-RUO, Nanosphere, Inc., Northbrook, IL	• BC-GP test has 12 bacterial targets and 3 resistance markers • BC-GN-RUO test has 9 bacterial targets and 6 resistance markers	90-96 94-98

J Clin Microbiol. 2014;52:3433–3436.

Randomized Trial of Rapid Multiplex Polymerase Chain Reaction–Based Blood Culture Identification and Susceptibility Testing

Ritu Banerjee,[1,a] Christine B. Teng,[2,a] Scott A. Cunningham,[3] Sherry M. Ihde,[3] James M. Steckelberg,[4] James P. Moriarty,[5] Nilay D. Shah,[5] Jayawant N. Mandrekar,[6] and Robin Patel[3,4]

[1]Division of Pediatric Infectious Diseases, Mayo Clinic, Rochester, Minnesota; [2]Department of Pharmacy, National University of Singapore and Tan Tock Seng Hospital, Singapore; [3]Division of Laboratory Medicine and Pathology, [4]Division of Infectious Diseases, [5]Division of Health Care Policy and Research, and [6]Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota



↓ Pip/T use
↓ Tx. contaminants

Figure 2. Comparison of time to organism identification, availability of phenotypic antimicrobial susceptibility results, and first appropriate modification of antimicrobial therapy for the subset of study subjects with organisms represented on the rapid multiplex polymerase chain reaction (rmPCR) panel (n = 481). Time 0 is when the positive Gram stain result was reported. Median time in hours (interquartile range [IQR]) to organism identification: control 22.3 (17–28), both rmPCR and rmPCR + stewardship 1.3 (0.9–1.6); de-escalation: control 39 (19–56), rmPCR 36 (22–61), rmPCR + stewardship 20 (6–36); escalation: control 18 (2–63), rmPCR 4 (1.5–24), rmPCR + stewardship 4 (1.8–9). *$P < .05$ vs control; †$P < .05$ vs control and rmPCR groups.

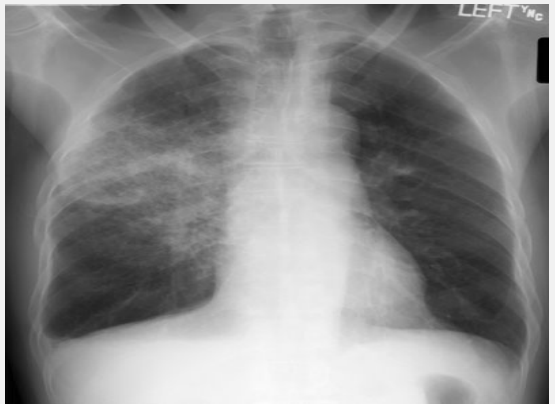
Clinical Impact of Blood Culture PCR in Gram-negative Bacteremia (with Antibiotic Stewardship)

- **<u>Decreased</u>**
  - Time to optimal antibiotic therapy 80.9h to 23.2h p<0.001)
  - Length of stay from 22.3 to 15.3 days (p=0.001)
  - Mortality from 21% to 8.9% (p=0.01)
  - Hospital cost (per inpatient survivor) by $26,298 (p=0.002)

J Infection 69(3):216-25, 2014

PCR Panel – Coming Soon

- Lower Respiratory Tract Infection (LRTI)
  - Sputum sample pathogen detection in 87% of patients vs. 39% by culture
  - Regardless of antibiotic therapy (72% vs. 32%)
  - Potential to de-escalate antibiotics in 77%



Clin Infect Dis 62(7):817-23, 2016

Limitations of PCR

- False Positives
  - Due to contamination (sensitivity)
  - Need for specialized equipment
- False Negatives
  - Due to inhibitors (Blood, Urine, Sputum)
- Colonizer vs. Pathogen
- Cost
- Antibiotic Susceptibility Testing

PCR Results Management

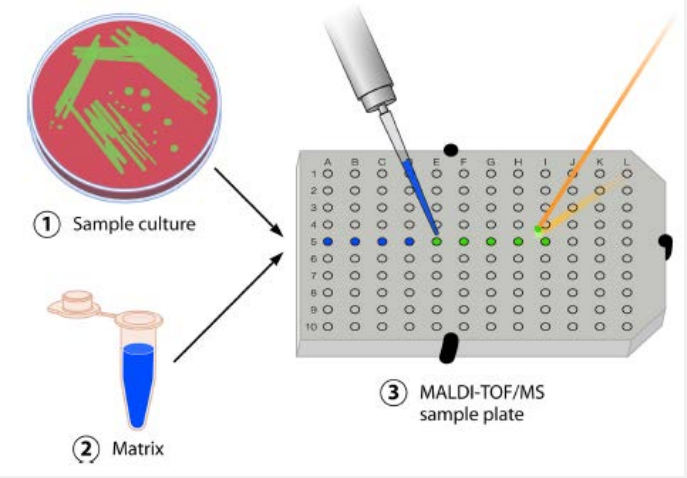
- Interpretation and clinical judgment remain critical
  - Determine the significance of a positive result
    - e.g. *Clostridium difficile* colonization
  - Understand nuances
    - e.g. the mecA gene in *S. aureus* may be present but not expressed
  - Knowing what is on the panels and what is not
  - Knowing which panel to order and when

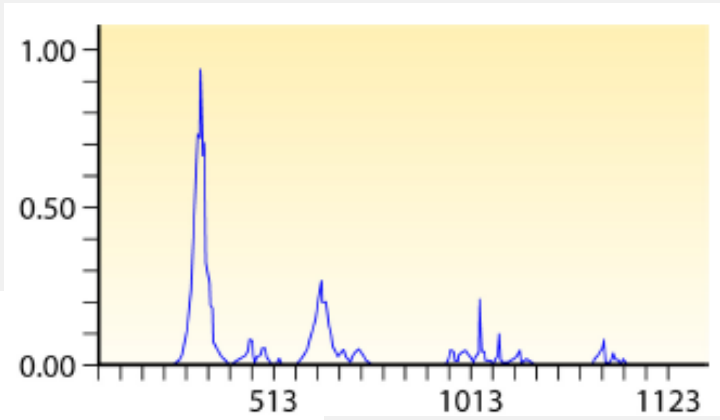
Texas A&M Health Science Center

Matrix-Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry

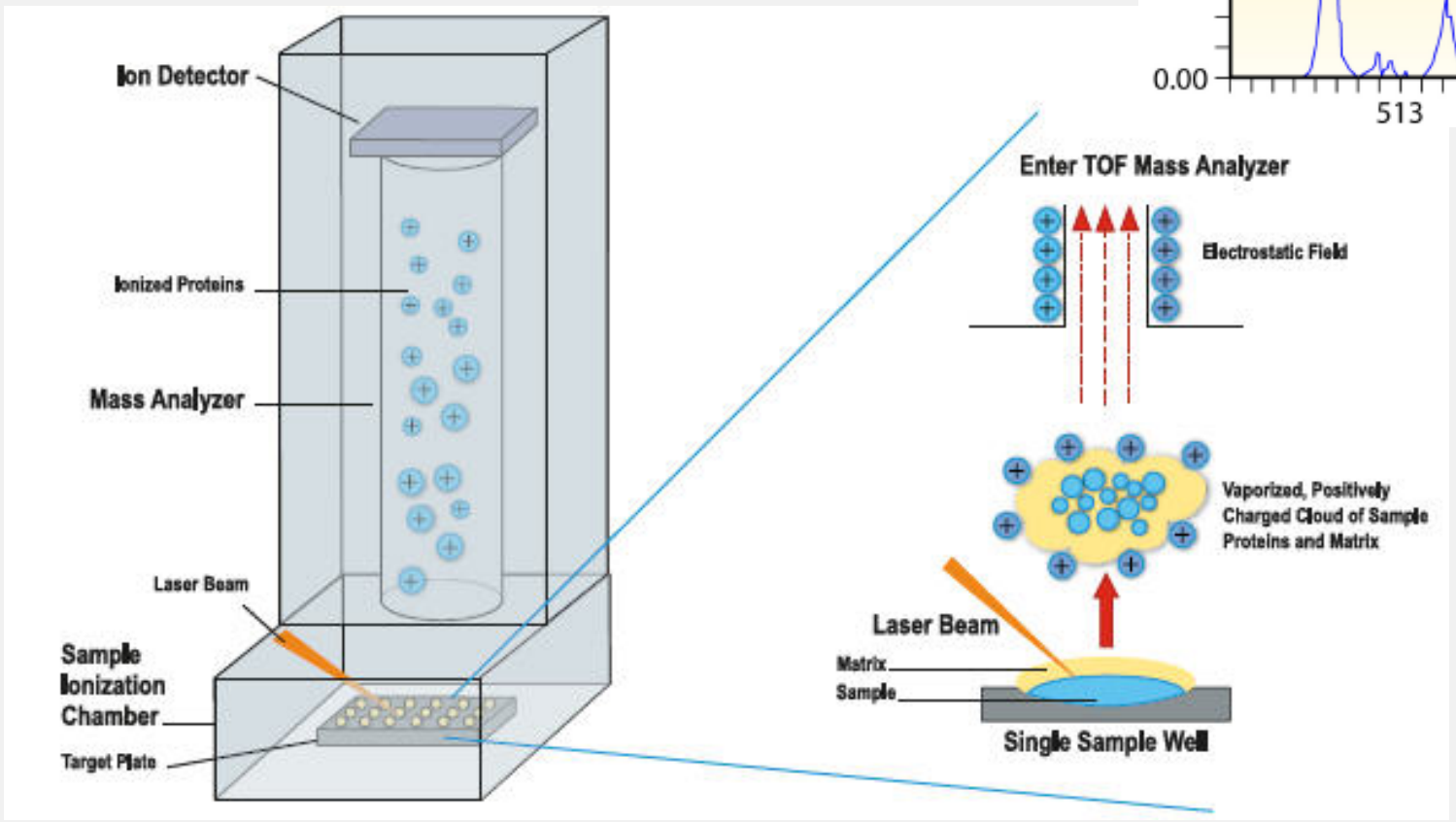
MALDI TOF MS

MALDI TOF MS

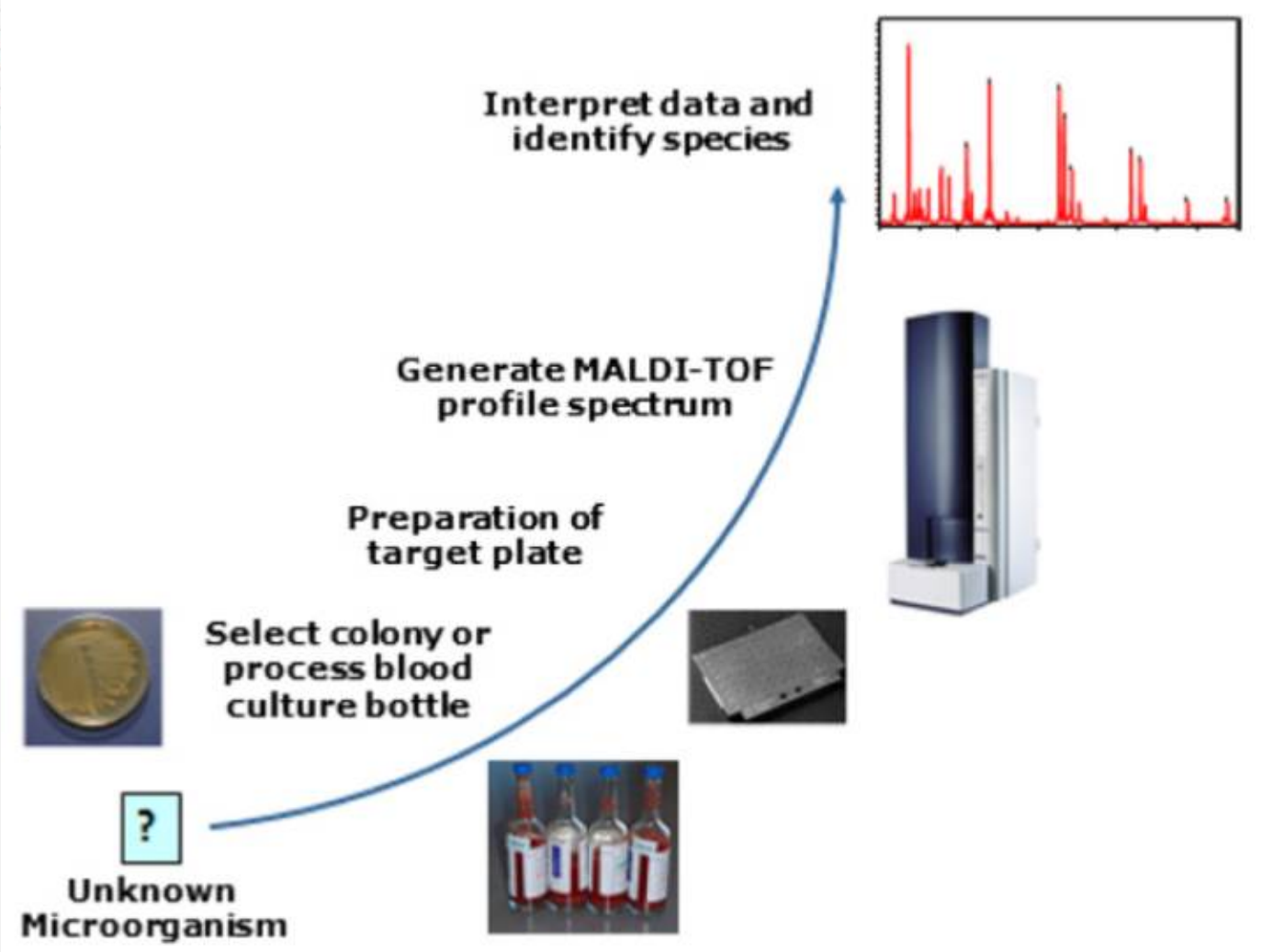




MS Profile
(match to database)



Clin Micro Rev 26(3):547-603 ,2013



Results in ~1 hour

Cost of machine and software $200,000
Cost of reagents $0.5
Tech time 5 min

J Molecular Diagnostics 14(5):419-23, 2012

J Clin Micro 49(4):1614-6, 2011

MALDI TOF Performance

- Correctly identified 93.2% of organisms to the species level and 5.3% to the genus level (1.5% unidentified)[1]
- Study of 501 pts with bacteremia/candidemia[2]
  - With antibiotic stewardship
  - Improved time to effective therapy from 30.1 to 20.4h
  - Decreased length of stay by 2.8 days
  - Reduced mortality from 20.3% to 14.5%

[1] *J Clin Micro* 48(5):1549-54, 2010

[2] *Clinical Infectious Diseases* 57(9):1237-45, 2013

MALDI-TOF Vs Multiplex PCR

Automated mass spectrometry microbial identification system for identification of bacteria, fungi, and mycobacteria isolated directly from clinical samples in clinical microbiology laboratories

System	Advantages	Disadvantages
MALDI-TOF	• Fast • Accurate • Less expensive per test than molecular and immunological-based detection methods • Not technically complex	• High initial cost of the MALDI-TOF equipment • Identification of new isolates possible only if found in available database • Does not identify resistance genes • May require culture of organism
Multiplex PCR	• Culturing of the organism not required • Specific, sensitive, rapid, and accurate • Closed-tube system reduces risk of contamination • Can detect many pathogens simultaneously • Can identify fastidious and uncultivable microorganisms	• Highly-precise thermal cycler is needed • Highly-trained laboratory personnel may be required to perform the test, depending on the test platform • Initial cost of the equipment is less than MALDI-TOF, but the cost per run is more

Front Microbiol. 2015;6:1-16.

Rapid Diagnostic Test and Invasive Candidiasis

- Invasive candidiasis (IC) including candidemia and deep-seated candidiasis is associated with up to 50 % overall mortality and up to $80,000.
- Blood cultures are the most common method used to diagnose IC but miss up to half of all IC cases.
- Blood cultures typically take 2–3 days to isolate yeast in the blood and an additional 2–3 days to identify Candida to the species level

Curr Fungal Infect Rep 2016

Rapid Diagnostic Test and Invasive Candidiasis (continued)

- Eight studies were identified of which five had sufficient information to be included in the review.
- PNA-FISH, MALDI-TOF, Multiplex PCR, T2 Candida were included
- Compared to conventional methods and baseline stewardship activities, the integration of RDTs for IC and real-time decision support, mainly through antifungal stewardship, was associated with decreased mortality, more optimal use of antifungals, and reduced healthcare costs.

Curr Fungal Infect Rep 2016

EXAMPLES

Case

- Ms Jones 26 weeks pregnant presents on February 2nd with a 2-day history of low-grade fever, sore throat, and mild arthralgias.
- T-100.4, P-80, mild erythema post pharynx, lungs clear, no rash
- WBC 6400, POC influenza A/B negative
- Disposition symptomatic care
- Patient returns 2 days later with SOB, bilateral infiltrates, hypoxic, requires intubation. Bal PCR+ influenza A

Other Traditional Methods

- **Influenza EIA**
  - **Sensitivity/Specificity 50-70%/90-95%[1]**
- **National Action Plan**
  - The development and wide dissemination of rapid diagnostic tests that can be used in a physician's office
- **There is now a POC Molecular approved for influenza**

If this was available for this patient would the outcome had been different?

[1]*www.cdc.gov/flu/professionals/diagnosis/rapidclin*

Diagnosis of *C. difficle*

Two questions:

1. What are the clinical characteristics that best identify a patient to test for *C. diff*?

2. What test or combination of tests best identifies patients who are symptomatically infected with toxigenic *C diff?*

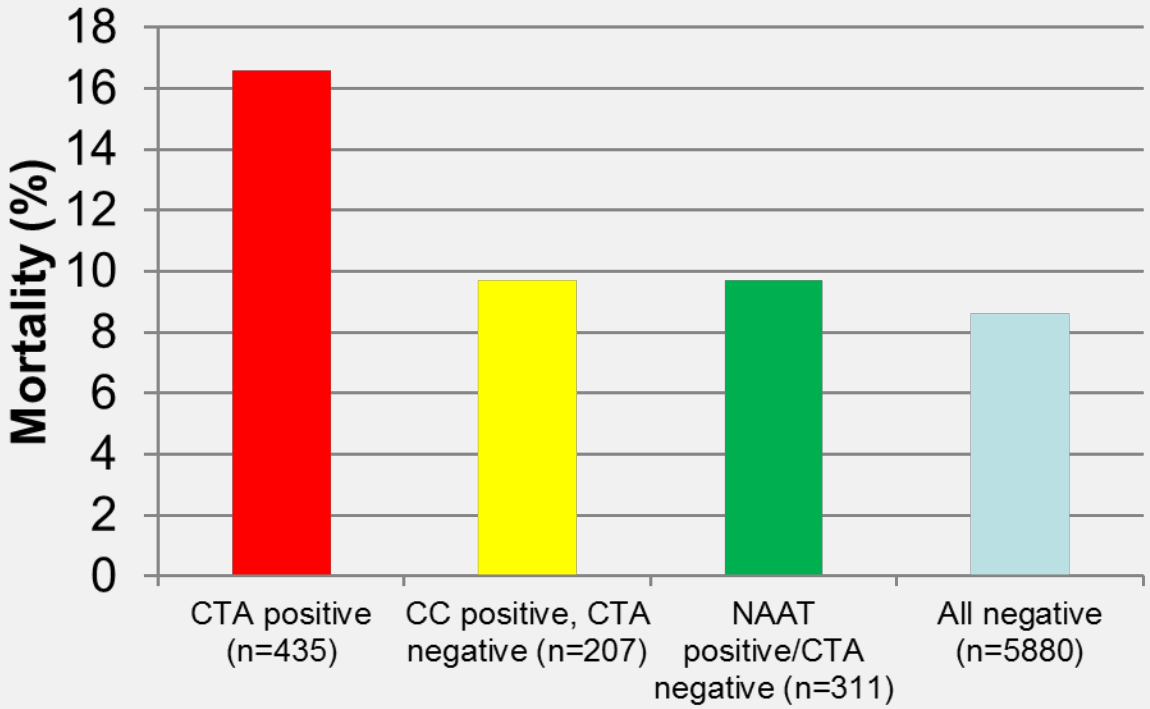
Microbiology

- Ubiquitous anaerobic, Gram-positive, spore-forming rod
- Common cause of antibiotic-associated diarrhea
- Can produce toxins causing colitis
- Associated with extended hospital stay and increased resource utilization
- When the normal gastrointestinal (GI) flora is disrupted, exposure to C. *difficile* may result in CDI
- Colonization Rates
  - **Healthy adults: 3%–5%**
  - **Inpatients: 16%–35%**

Lancet Infect Dis. 2005;5:549-557.
Med Clin North Am. 2006;90:1141-1163.

PCR diagnostic strategies may detect patients colonized with CDI but not infected

UK: prospective, multicenter study of suspected CDI patients tested for cytotoxicity assay (CTA), cytotoxigenic culture (CC), or nucleic acid amplification test (NAAT).



Mortality increased significantly in CTA positive patients (OR 1·61, 95% CI 1·12–2·31)

Lancet Infect Dis 2013;13:936-45

C. difficile Testing

Testing Option	Result	Interpretation
EIA Toxin Test (A&B)	Toxin Pos (high specificity)	**Presume CDI**
EIA Toxin-No longer recommended as stand alone test	Toxin Neg (low sensitivity)	Perform PCR/NAAT
GDH and Toxin A&B Combo Test	GDH Neg (high sensitivity)	**No CDI, no further testing**
	GDH Pos, Toxin Pos	**Presume CDI**
	GDH Pos, Toxin Neg (GDH has low specificity)	Perform PCR/NAAT
PCR/NAAT	PCR/NAAT Pos (high sensitivity but only mod specificity, does not distinguish true CDI from asymptomatic carriers)	CDI or possible carriage; perform clinical assessment
	PCR/NAAT Neg	**No CDI, no further testing**

- **Test only liquid specimens that conform to shape of the cup (except ileus)**
- **PPV dependent upon disease prevalence**
- **Test methods with higher sensitivity and PPV reduces repeat testing**

Case

- Mr. Smith is a 57 year-old male who presents with fever, a productive cough, and SOB. Mr Smith had a viral-like illness last week and was improving when he suddenly developed worse cough and high fever (102)
- On exam T-103, P-110, RR 24, BP 100/60 tubular breath sounds and crackles t right base
- CXR right lower lobe lobar pneumonia

Case cont

- WBC 18,000 with 14% bands, creat 1.5, lactate 3.2
- After cultures patient was given azithromycin, vancomycin, and ceftriaxone
- An MRSA nasal screen by PCR was negative
- Blood cultures were negative, sputum revealed “normal flora”
- A diagnostic test was performed

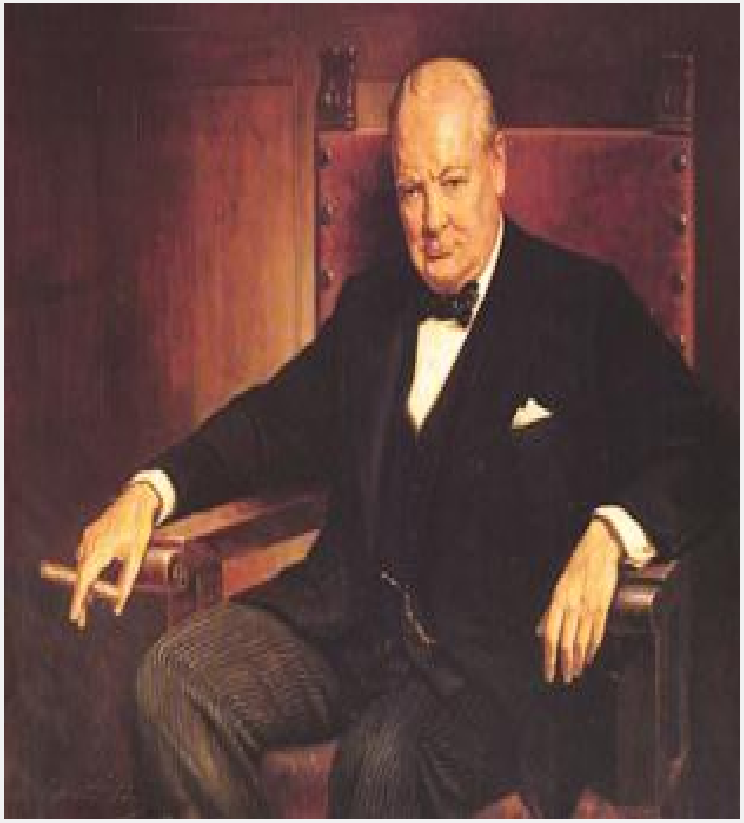
Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults

- Urinary antigen tests for pneumococcus, was responsible for the majority (67%) of pneumococcal detections in our study.
- These tests are more sensitive than blood culture and improve the detection of nonbacteremic pneumococcal pathogens with a reported sensitivity of 70 to 80% and a specificity of more than 90%.
- *Note-urine Ag does not predict susceptibilities

N Engl J Med 2015; 373:415-427

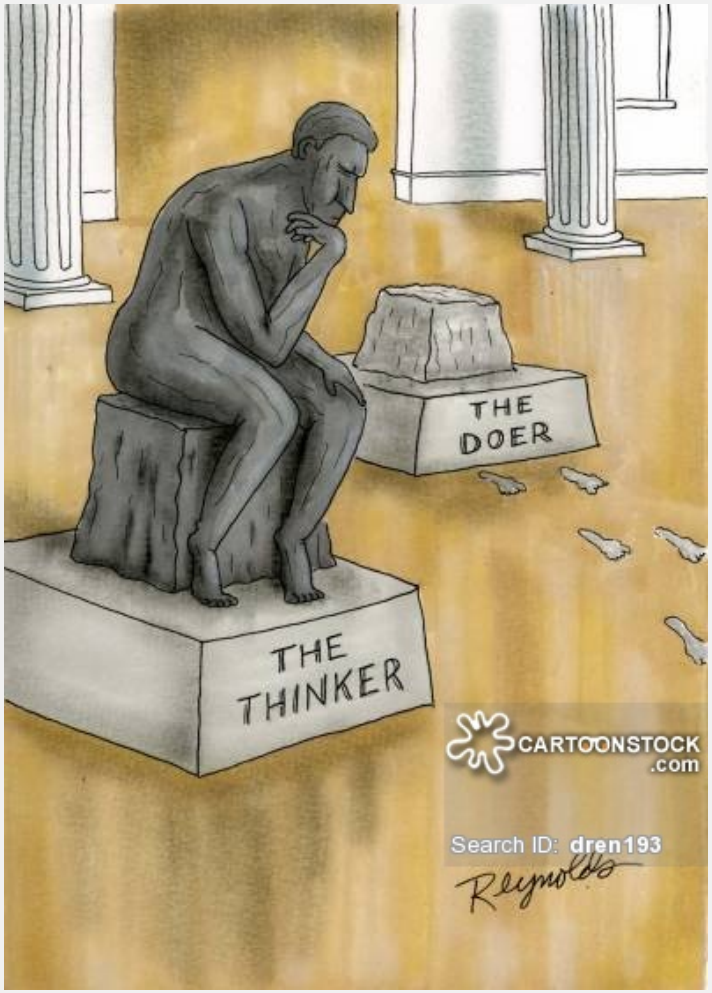
Key Takeaways

- No one rapid diagnostic platform meets all needs: select test(s) based on work flow and patient population
- Rapid diagnostics can decrease diagnostic uncertainty
- To be effective, rapid diagnostics have to actionable and tied to local stewardship program
- Monitor for unintended consequences
- Testing must be correlated with overall clinical condition of the patient



A pessimist sees the difficulty in every opportunity, an optimist sees the opportunity in every difficulty

Winston Churchill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