# Rapid Diagnostics and Antimicrobial Stewardship

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# Rapid Diagnostics & Stewardship

- Procalcitonin
- Respiratory Viral Panels
- Bacteriological and Fungal Diagnostics
  - PCR based methods
  - MALDI-TOF
  - PNA-FISH

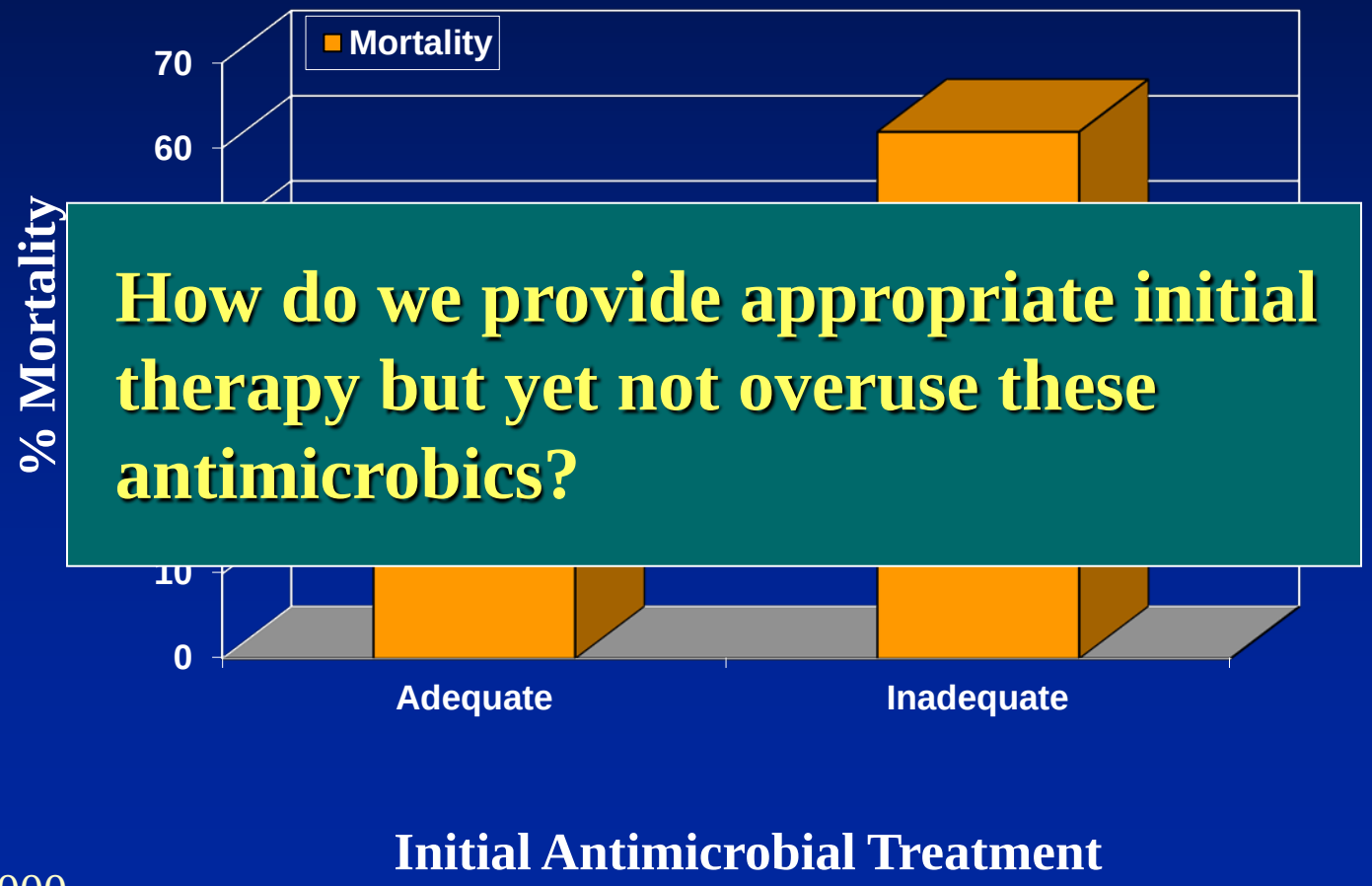
# Antimicrobial Stewardship

## Empiric Antimicrobial Therapy

- Study of 492 patients with BSI
- Mortality rate was associated with inadequate initial antimicrobial therapy (R.R. = 2.18)
- Most common organisms treated inadequately
  - VRE, *Candida* sp., MRSA, CNS, *P. aeruginosa*
- Candida, prior antibiotics, low serum albumin, increasing central catheter days all associated with inadequate antibiotics

Chest 2000;118:146

# Antimicrobial Stewardship




**How do we provide appropriate initial therapy but yet not overuse these antimicrobics?**

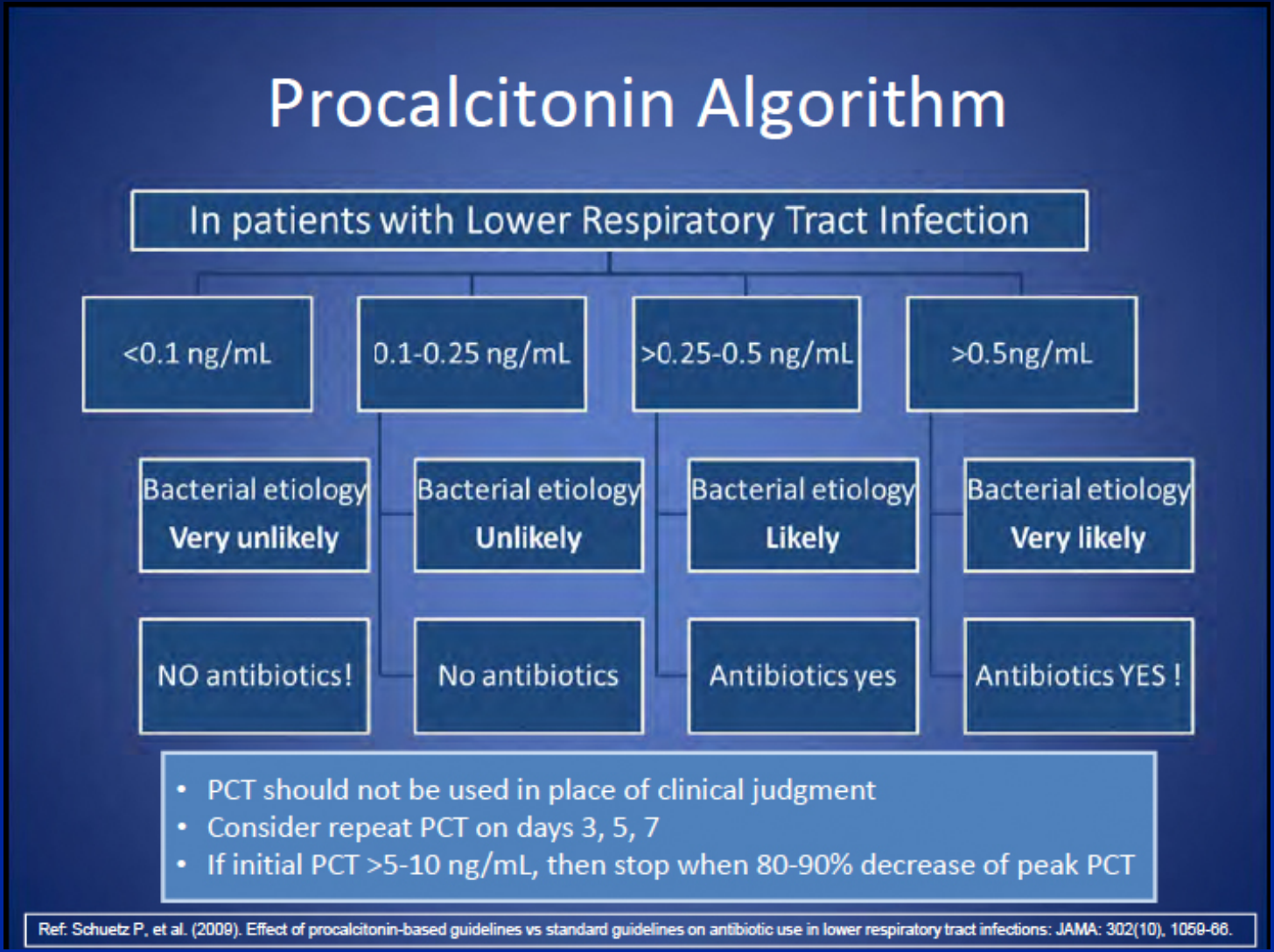
Chest 2000

# Rapid Diagnostics & Stewardship

## Use of Procalcitonin

- A calcitonin precursor hormone
- Marker for severe bacterial infection
  - Released in response to direct stimulation by cytokines
  - Suppressed by IFN-γ in viral infections
- Several studies demonstrate utility in antimicrobial stewardship program
- <1 ng/mL indicates absence of bacterial infection

# Rapid Diagnostics & Stewardship



# Rapid Diagnostics & Stewardship

- Multicenter, prospective, parallel-group, open-label trial (311 procalcitonin, 319 control, 9 excluded)
- The procalcitonin group had antimicrobials started and stopped based on predefined cut-offs
- Mortality was non-inferior to controls at day 28
- 2.7 days less of antimicrobials in the procalcitonin group ($p<0.0001$)

Lancet 2010;375:463-474

# Rapid Diagnostics & Stewardship

## Procalcitonin Use in Pneumonia

- Retrospective study of patients with pneumonia
- 66 in non procalcitonin, 50 P group

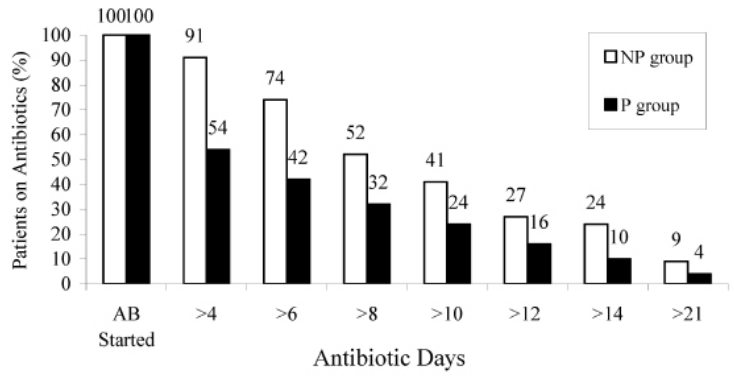



FIGURE 1. Percentage of patients on antibiotics from day 1 through 21 between the no procalcitonin (NP) and the procalcitonin (P) groups. AB, antibiotic.

ICHE 2012;33:424-426.

# Rapid Diagnostics & Stewardship

## Evidence and Use of PCT in Acute Respiratory Infections

| Outcome | PCT Group n = 2085 | Control n = 2126 | Adjust OR (95% CI) | P for interaction |
|---|---|---|---|---|
| **Overall** – Primary Care, Emergency Dept, ICU | | | | |
| Mortality (%) | 118 (5.7) | 134 (6.3) | 0.94 (0.71 to 1.23) | 0.754 |
| Treatment failure (%) | 398 (19.1) | 466 (21.9) | 0.82 (0.71 to 0.97) | 0.02 |
| Initiation of antibiotics (%) | 1341 (64) | 1778 (84) | 0.24 (0.2 to 0.29) | < 0.001 |
| Duration of antibiotics (days) | 7 (4 – 10) | 10 (7 – 13) | -2.75 (-3.12 to -2.39) | < 0.001 |
| Total exposure of antibiotics (days) | 4 (0 – 8) | 8 (5 – 12) | -3.47 (-3.78 to -3.17) | < 0.001 |

Ref: Schuetz, P et al. (2012). Cochrane Database of Systematic Reviews

# Rapid Diagnostics & Stewardship

## Evidence and Use of PCT in CAP

| Outcome | PCT Group n = 999 | Control n = 1028 | Adjust OR (95% CI) | P for interaction |
|---|---|---|---|---|
| **Community acquired pneumonia** | | | | |
| Mortality (%) | 92 (9.2) | 111 (10.8) | 0.95 (0.73 to 1.24) | 0.687 |
| Initiation of antibiotics (%) | 898 (90) | 1019 (99) | 0.07 (0.03 to 0.14) | < 0.001 |
| Duration of antibiotics (days) | 7 (5 – 10) | 10 (8 – 14) | -3.34 (-3.79 to -2.88) | <0.001 |
| Total exposure of antibiotics (days) | 6 (4 – 10) | 10 (8 – 14) | -3.98 (-4.44 to -3.52) | < 0.001 |

Ref: Schuetz, P et al. (2012). Cochrane Database of Systematic Reviews

# Rapid Diagnostics & Stewardship

## Procalcitonin – Cochrane Analysis

- 4221 patients in 14 trials of acute respiratory illnesses
- Antimicrobial consumption decreased
- No differences in mortality or treatment failures
- Further studies in ICU and other illnesses
- My comment: Adjunctive test

Schuetz et al Cochrane Review 2012

# Rapid Diagnostics & Stewardship

## Respiratory Viral Panels and Antibacterial Use

- 3 studies reviewed
- All demonstrated decreased use of antibacterial drugs
- Optimized use of oseltamivir
- No change in LOS or mortality

BMC Medicine 2011;9:44
J Ped Infect Dis 2013
ID Week 2014 Abstract 607

# Rapid Diagnostics & Stewardship

## RVP and Antibacterial Use

- 17 respiratory viruses with turn around time < 4 hours
- 50 patients with positive tests
- 100 patients with negative tests
- Most common organisms were influenza (34%), RSV (20%), metapneumovirus (20%) and rhinovirus (18%)

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# Rapid Diagnostics & Stewardship

| Outcomes | Negative RVP | Positive RVP | P |
|---|---|---|---|
| De-escalation at 24 hrs | 8 | 13 | 0.003 |
| DOT | 9(1-35) | 6 (1-53) | 0.03 |
| LOS Median (range) | 4.3 (0.4-39.9) | 3.6 (0.9-26) | 0.25 |
| In-hospital mortality | 3 | 2 | 0.75 |

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# Rapid Diagnostics & Stewardship

## Management of Bacterial Pneumonia

- Urine pneumococcal antigen
  - Sensitivity 74%, specificity 94%
  - 15 minutes to perform the test
- Urine Legionella antigen
  - Sensitivity ~70%, specificity >99%
  - 15 minutes to perform the test
- Most helpful if test is positive

# Rapid Diagnostics & Stewardship

**Table 1. Tests for Rapid Identification of Bloodstream Pathogens**

| Blood Culture Assay | Pathogens Detected | Resistance Markers | Turnaround Time (After Blood Cultures Turn Positive) |
|---|---|---|---|
| PNA-FISH | *Staphylococcus aureus*, CoNS, *Enterococcus faecalis*, other enterococci, *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Candida albicans, Candida parapsilosis, Candida glabrata, Candida krusei, Candida tropicalis* | No | 1.5–3 h |
| *Quick*FISH | *S. aureus*, CoNS, *E. faecalis*, other enterococci, *E. coli, K. pneumoniae, P. aeruginosa* | No | <30 min |
| MALDI-TOF[a] | Gram-positive and gram-negative bacteria, yeast, fungi, filamentous fungi, mycobacteria | In development | 10–30 min |
| Gene Xpert MRSA/SA | *S. aureus* | *mecA* | <1 h |
| Verigene gram-positive blood culture (BC-GP) | *S. aureus, Staphylococcus epidermidis, Staphylococcus lugdunensis, Streptococcus anginosus group, Streptococcus agalactiae, Streptococcus pneumoniae, Streptococcus pyogenes, E. faecalis, Enterococcus faecium, Staphylococcus* spp., *Streptococcus* spp., *Listeria* spp. | *mecA, vanA, vanB* | 2.5 h |
| Verigene gram-negative blood culture (BC-GN)[b] | *Escherichia coli, Shigella* spp., *K. pneumoniae, Klebsiella oxytoca, P. aeruginosa, Serratia marcescens, Acinetobacter* spp., *Proteus* spp., *Citrobacter* spp., *Enterobacter* spp. | KPC, NDM, CTX-M, VIM, IMP, OXA | 2 h |
| FilmArray blood culture identification (BC ID) | *S. aureus, Staphylococcus* spp., *S. agalactiae, S. pneumoniae, S. pyogenes, Streptococcus* spp., *Enterococcus* spp., *Listeria monocytogenes, Hemophilus influenza, Neisseria meningitides, Enterobacter cloacae* complex, *E. coli, K. pneumoniae, K. oxytoca, P. aeruginosa, Serratia marcescens, Acinetobacter baumanii, Proteus* spp., *C. albicans, C. glabrata, C. krusei, C. parapsilosis, C. tropicalis* | *mecA, vanA, vanB* | 1 h |
| Whole blood assays | | | |
| Light Cycler[c] SeptiFast | *S. aureus*, CoNS, *Streptococcus* spp., *S. pneumoniae, E. faecalis, E. faecium, E. coli, K. pneumoniae, K. oxytoca, P. aeruginosa, Enterobacter cloacae/aerogenes, S. marcescens, A. baumanii, Proteus mirabilis, Stenotrophomonas maltophilia, C. albicans, C. glabrata, C. krusei, C. parapsilosis, C. tropicalis, Aspergillus fumigatus* | No | 6 h |
| SeptiTest[c] | >300 pathogens | No | 8–12 h |
| T2 *Candida*[d] | *C. albicans, C. glabrata, C. krusei, C. parapsilosis, C. tropicalis* | No | 3 h |

Clin Infect Dis 2014;59:272

# Rapid Diagnostics & Stewardship

## Verigene BC-GP (Nanosphere)

- 74 patients with documented enterococcal bacteremia (28 post BC-GP)
- Median time to appropriate antimicrobial therapy was 23.4 hours shorter
- LOS shorter
- Cost less
- TAT post blood culture is 2.5 hours

J Clin Microbiol 2013; 51:408

# Rapid Diagnostics & Stewardship

## Xpert MRSA/SA – Blood Culture

- 2 studies including over 350 patients
- Shortened the time to switch to targeted antimicrobial β-lactam 40.8 – 44.6 hours
- Decreased treatment if negative
- LOS 6.2 days
- TAT < 1 hours post BC positivity

ICHE 2010;31:1043
Clin Infect Dis 2010;51:1074

# Rapid Diagnostics & Stewardship

## MALDI-TOF

- `1300 patients in 5 studies
- 20-46 hours shorter to optimal care
- Increased clinical cure (15-34%)
- Lowered mortality rate (21% v 8.9%)
- Shortened length of stay

Clin Infect Dis 2014;59:S134

# Rapid Diagnostics & Stewardship

## Blood culture Free Systems

- Light cycler
- T2 Biosystems

## Other Systems

- PNA-FISH

# Rapid Diagnostics & Stewardship

## Summary

- Multiple rapid systems are in use and being developed
- Consistently show benefit in relation to antimicrobial stewardship and optimizing clinical outcomes
- Useful but not ready to abandon traditional microbiology