Nasal MRSA PCRs for the de-escalation of empiric pneumonia treatment

By: Sierra Detwiler

Objectives

- Understand the current guidelines and recommendations for empiric CAP, HAP, and VAP
- Identify the data behind MRSA PCRs for de-escalation of vancomycin
- Make confident recommendations for de-escalation to providers
- Answer questions and provide the data behind those answers

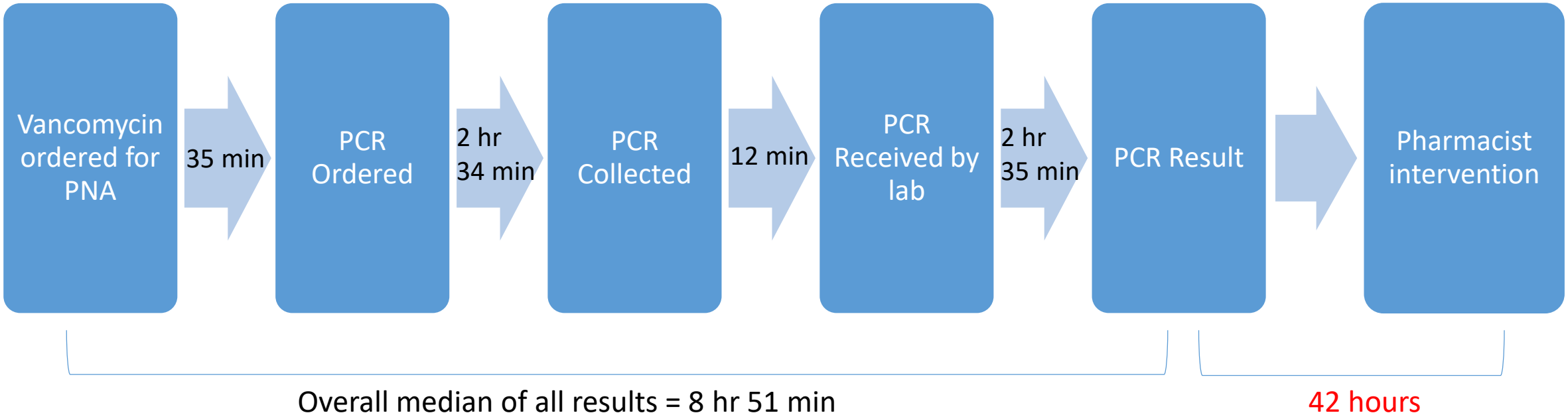
MUE results

	Pre-intervention (n=51)		Post-intervention (n=62)	
Duration of Vancomycin (Days) Based on days of open I-vent	Median Mean	4 4.61	Median Mean	4 4
Duration of Vancomycin (Days) Based on days of Vancomycin admin.	Median Mean	4 4.67	Median Mean	4 4.17
# of levels drawn	Median Mean	1 1.43	Median Mean	1 1.18
LOS (Median Days)	Median Mean	10 12.31	Median Mean	9 11
Time to Pharmacist Intervention (Hr)*	Median Mean	N/A	Median Mean	42 56.98
*Calculated based on the time from PCR result to time ivent entered				

	Pre-intervention		Post-intervention	
% of PCRs Ordered	56.86%	29/51	91.93%	57/62
% of PCRs Ordered by MD	100%	29/29	47.37%	27/57
% of Respiratory Cultures	56.86%	29/51	52.61%	32/62
% of Interventions Made (made/opportunity)	25.00%	5/20	56.52%	26/46
% of Physician Acceptance	80.00%	4/5	76.92%	20/26
% of abx re-escalation	5.88%	3/52	1.61%	1/61

*opportunities were defined as a MRSA (-) nasal swab result
*abx re-escalation: defined as re-starting vancomycin after previously being discontinued

Review PCR process



Things Identified: Survey results

Pharmacist Education and Support

- Review current guidelines
- Answer and develop a FAQ sheet
- Assist educating/making recommendations when encountering a difficult physician or case

Physician Education

- Attend Hospitalist meetings this month
- Best education is one-one education on a case-by-case basis

Evaluate the current guidelines and recommendations for CAP, HAP, and VAP

“HCAP” at Memorial

- Many patients receiving vancomycin & cefepime/pip-tazo **do not need it**

- The most consistently strong individual risk factors for respiratory infection with MRSA or *P. aeruginosa* are:
  - **Prior isolation** of these organisms, especially from the respiratory tract, and/or
  - Recent hospitalization and exposure to parenteral antibiotics

CAP Guidelines – Removal of HCAP

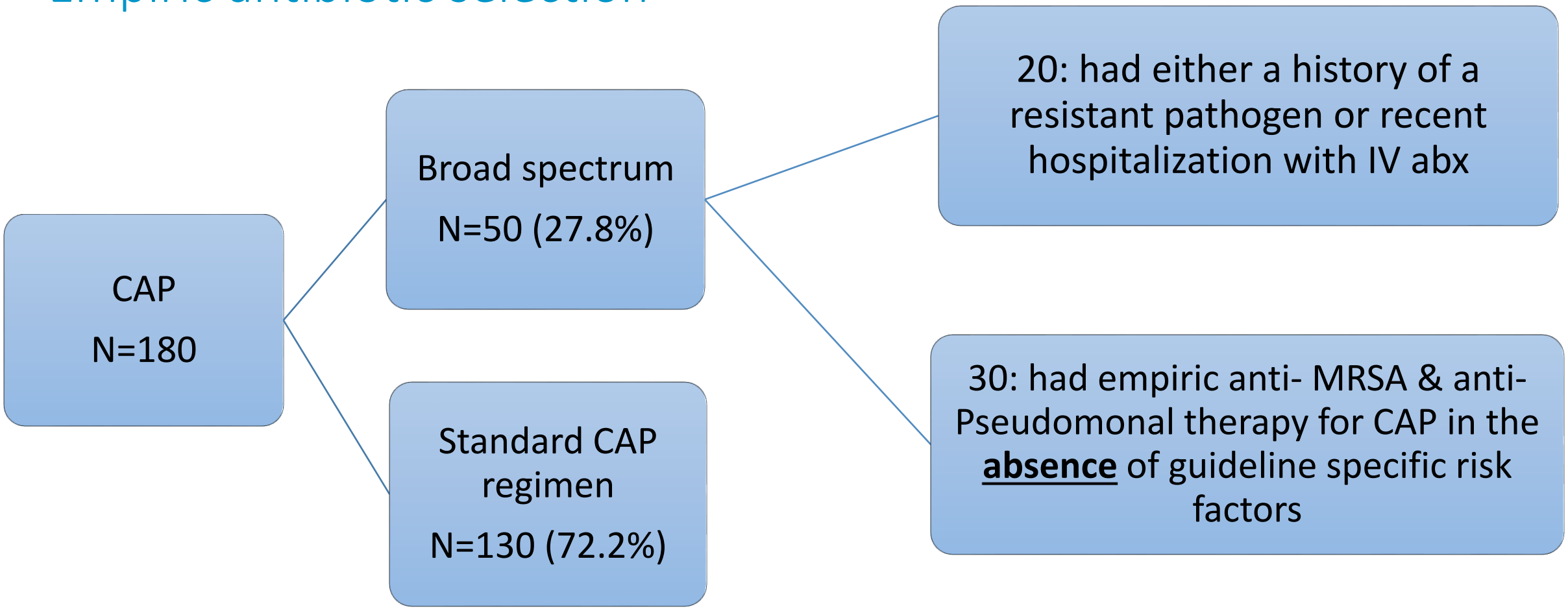
Table 2. Differences between the 2019 and 2007 American Thoracic Society/Infectious Diseases Society of America Community-acquired Pneumonia Guidelines

Recommendation	2007 ATS/IDSA Guideline	2019 ATS/IDSA Guideline
Sputum culture	Primarily recommended in patients with severe disease	Now recommended in patients with severe disease as well as in all inpatients empirically treated for MRSA or *Pseudomonas aeruginosa*
Blood culture	Primarily recommended in patients with severe disease	Now recommended in patients with severe disease as well as in all inpatients empirically treated for MRSA or *P. aeruginosa*
Macrolide monotherapy	Strong recommendation for outpatients	Conditional recommendation for outpatients based on resistance levels
Use of procalcitonin	Not covered	Not recommended to determine need for initial antibacterial therapy
Use of corticosteroids	Not covered	Recommended not to use. May be considered in patients with refractory septic shock
Use of healthcare-associated pneumonia category	Accepted as introduced in the 2005 ATS/IDSA hospital-acquired and ventilator-associated pneumonia guidelines	Recommend abandoning this categorization. Emphasis on local epidemiology and validated risk factors to determine need for MRSA or *P. aeruginosa* coverage. Increased emphasis on deescalation of treatment if cultures are negative
Standard empiric therapy for severe CAP	β-Lactam/macrolide and β-lactam/fluoroquinolone combinations given equal weighting	Both accepted but stronger evidence in favor of β-lactam/macrolide combination
Routine use of follow-up chest imaging	Not addressed	Recommended not to obtain. Patients may be eligible for lung cancer screening, which should be performed as clinically indicated

Pneumonia Antibiotic Recommendations

CAP Standard Regimens:	• Ceftriaxone 1g IV q24 + azithromycin 500mg IV/PO daily x 5 days OR • Levofloxacin 750mg IV/PO q24
CAP w/ previous (within 1 year) isolation of MRSA:	• Standard Regimen + IV vancomycin pharmacy to dose
CAP w/ previous (within 1 year) isolation of *Pseudomonas spp*:	• Cefepime 1g IV q6 or Pip/tazo 3.375/4.5g IV q8 extended infusion + azithromycin 500mg IV/PO daily x 5 days
CAP w/ hospitalization & IV abx in past 90 days:	• Nonsevere: Standard CAP regimen • Severe: Cefepime 1g IV q6 + IV vancomycin pharmacy to dose + azithromycin 500mg IV/PO daily x 5 days

Empiric antibiotic selection



Microbiology

- Total respiratory cultures submitted: 68/180 (37.8%)
  - Total encounters with organism identified → 18 (10%)
  - Patients with a pathogen R to standard CAP regimen → 6 (3%)

Patients	Pathogen	Risk Factor(s)	Notes
1	ESBL E.coli	1. Hospitalized with IV abx (90 d) 2. CKD 3. COPD 4. Diabetes 5. Cerebrovascular disease 6. Gastric acid suppression	Escalated to merrem
2	MRSA	1. Hx of MRSA in past year 2. COPD 3. Immunosuppression 4. Cerebrovascular disease 5. Gastric acid suppression	Was already on vanco/cefepime

Microbiology

Patients	Pathogen	Risk Factor(s)	Notes
3	MRSA K. Pneumoniae (pan sens)	1. COPD 2. Gastric acid suppression	Felt colonization (did not escalate therapy)
4	Pseudomonas Acinetobacter	1. History of MDR Pseudomonas in past year 2. Nursing home (Standifer Place) 3. CKD 4. Diabetes 5. Cerebrovascular disease 6. Tube feeding 7. Gastric acid suppression	Was already on vanco/zosyn; switched to cefepime
5	Pseudomonas	None	Escalated to Vanco/Cefepime
6	ESBL E.coli	1. Hospitalized with IV abx (90 d) 2. COPD	Escalated to merrem

Respiratory cultures both campuses (Jan-Oct 19)

Total inpatient respiratory cultures submitted: 1576

Pathogen	Number	Overall Percentage
MRSA	92/1576	**6%**
P. aeruginosa	93/1576	**6%**
Ceftriaxone R gram negative	135/1576	**9%**

CAP Summary

- **Standard CAP Regimen**
  - Ceftriaxone + Azithromycin or Levaquin

- **Risk factors for resistant pathogens:**
  - Prior isolation
  - Recent hospitalization with IV antibiotics

- There are still encounters where empiric broad spectrum anti-MRSA and anti-pseudomonal coverage is initiated and **unneeded**

HAP/VAP – Guideline Recommendation

Standard: Cefepime or Zosyn or Levaquin

Recommend MRSA coverage in HAP/VAP if:

- Prior IV abx use within 90 days

  OR
- Pt without risk factors for antimicrobial resistance, who are being treated in ICUs where >10%–20% of S. aureus isolates are methicillin resistant

HAP/VAP at Memorial

- Our Empiric Regimen:
  - Cefepime + Vancomycin

- In addition:
  - Obtain cultures and/or nasal MRSA PCR to allow for de-escalation.

↑24%

Regimens	Sensitive (%)
CPM	70
CPM + VANC	94
CPM + VANC + FQ	99
CPM + VANC + TOB	99

HAP/VAP Summary

- **Our empiric regimen**: Cefepime + Vancomycin

- ****Obtain MRSA PCR and cultures to allow for de-escalation****

- **MDR Risk Factors:**
  - Prior IV abx use within 90 days

    OR
  - Pt without risk factors for antimicrobial resistance, who are being treated in ICUs where >10%–20% of S. aureus isolates are methicillin resistant

Identify the data behind MRSA PCRs for de-escalation of vancomycin

Nasal MRSA PCR Clinical Efficacy

Study	Design	Results		
Parente DM, et al. (2018)	Meta-analysis N = 5163	**All – PNA** Sensitivity 70.9% Specificity 90.3% PPV 44.8% NPV 96.5%	**CAP/HCAP** Sensitivity 85.0% Specificity 92.1% PPV 56.8% NPV 98.1%	**VAP** Sensitivity 40.3% Specificity 93.7% PPV 35.7% NPV 94.8%
		Conclusion: High specificity and NPV for ruling out MRSA pneumonia→ Especially CAP/HCAP		

Nasal MRSA PCR Clinical Efficacy

Study	Design	Results
Giancola SE, et al. (2016)	Retrospective N=200	Sensitivity 90.5% Specificity 79.9% PPV 34.5% **NPV 98.6%** Conclusion: Nasal swab MRSA PCR test may be used to guide discontinuation of anti-MRSA antibiotics in patients with clinically confirmed pneumonia in the intensive or intermediate care units
Dangerfield B, et al. (2014)	Retrospective Cohort N=435	Sensitivity 88.0% Specificity 90.1% PPV 35.4% **NPV 99.2%** Conclusion: Pts treated empirically with anti-MRSA activity, a nasal swab negative for MRSA by PCR can be reasonably used to guide antibiotic de-escalation

Pharmacist-Driven Protocols

Study	Design	Results
Woolever NL, et al. (2020)	Retrospective N= 355	Duration of Vanc: **14.3 vs 24 h (p<0.001)** Conclusion: A pharmacist-driven protocol effectively **reduces** the duration of vanc therapy for patients with LRTI
Dunaway S, et al. (2018)	Retrospective N=196	Duration of vancomycin therapy **49 vs 18 h (p < 0.001)** No change: All cause mortality, LOS, 30-day readmission Conclusion: **Shorter** duration of empiric vancomycin therapy by ~31 h per patient without increasing adverse clinical outcomes
Willis C, et al. (2017)	Retrospective N=300	Duration of Vanc: Median **2.1-day reduction (2.1 vs 4.2 days, p < 0.0001)** Conclusion: Pharmacist-driven protocol using a MRSA PCR nares assay to guide vancomycin de-escalation → **reduction** in vancomycin utilization without compromising clinical outcomes

Efficacy and Impact Summary

- MRSA nasal PCR swabs have a 95-99% NPV.
- Pharmacists can make a huge impact on de-escalation and reduce the duration of vancomycin by **days**!
- **Order MRSA nasal swabs and de-escalate ASAP for all pneumonias**

Review patient cases

80 YO Male

9/5

- Vancomycin initiated for PNA
- PCR ordered @ 1843 – Collected @ 2038 Received @ 0955 – Resulted @ 0955

9/6

- New culture/radiology results: “SCr trending down, WBC trending down”
- Plan: “MRSA nasal PCR not detected, high negative predictive value for MRSA pneumonia - Blood cx in progress, no growth to date.”
- PCR Received @ 0955 – Resulted @ 0955

9/7

- New culture/radiology results: Respiratory profile negative. Nasal PCR negative. No growth at 3 days on blood culture. Covid negative.
- Plan: “Per MD note - Will probably d/c vancomycin after 4-5 day course if no cxs are positive for MRSA. Send sputum cx if possible."

9/8

- New culture/radiology results: GPC and GPR on gram stain of Lower respiratory culture. Respiratory profile negative. Nasal PCR negative. No growth at 4 days on blood culture.
- Plan: “Per MD note - Will d/c vancomycin tomorrow if no cxs have MRSA tomorrow."
- Vancomycin DC’d @1205

Vitals and Culture Report

Vancomycin IV (mg)	1,750	1,500	1,500	1,500
Cultures				
Cultures				
Labs				
WBC	9.2	8.5	9.9	12.0
Creatinine	1.27	1.16	1.22	1.30
BUN	30	31	40	49
Sed Rate				
Vitals				
Temperature	98.5 (36.9)	98.3 (36.8)	98.5 (36.9)	98.2 (36.8)
Heart rate	88	83	76	89
Resp rate	18	15	28	24
Pulse oximetry	92	96	98	97
R Oxygen device		BIPAP	Hi/Flo He...	Heated Hi...
R Oxygen flow rate	10	40	40	40
R IP vent mode				
R FIO2		40	40	65

09/11/2020	Occult Blood, Stool	Final result	Normal
09/10/2020	Lower Respiratory Culture	Final result	
09/10/2020	SARS-CoV-2 (COVID19)	Final result	
09/07/2020	Lower Respiratory Culture	Final result	
09/06/2020	Respiratory Profile, PCR	Discontinued	
09/06/2020	MRSA MSSA by PCR	Final result	Normal
09/06/2020	Respiratory Profile, PCR	Final result	Normal
09/05/2020	MRSA MSSA by PCR	Final result	Normal
09/03/2020	SARS-CoV-2 (COVID19)	Final result	
09/03/2020	Blood Culture #2	Final result	
09/03/2020	Blood Culture #1	Final result	

Revisit to see where and what we could have done

9/5

- Vancomycin initiated for PNA
- PCR ordered @ 1843 – Collected @ 2038

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- Plan: “Per MD note - Will d/c vancomycin tomorrow if no cxs have MRSA tomorrow."
- Vancomycin DC’d @1205

68 YO Female

8/24

- Vancomycin initiated for PNA
- PCR ordered @ 1148

8/25

- New culture/radiology results: “blood Cx x2 NGTD, Urine Cx no growth”
- Plan: “If source is pneumonia: MRSA nasal PCR ordered. (Called nurse for reminder to collect)”
- PCR Collected 8/25 @ 1219 – Received @ 1236 – Resulted @ 1434

8/26

- Recommended Dcing Vancomycin secondary to negative PCR
- NP Accepted
- No compromise to clinical outcomes and not re-started

Vitals and Culture Report

24 Hrs:	CHI... C CHI Memorial Hospital 600 North 08/23 0000	08/24 0000	08/25 0000	08/26 0000
Antimicrobial				
ampicillin sodium/sulbactam Na 3 gr...	6,000	1,500		
piperacillin sodium/tazobactam 3.37...		3.375	10.125	10.125
piperacillin sodium/tazobactam 4.5 g...		4.5		
Vancomycin IV (mg)		1,500	1,000	1,250
Cultures				
Cultures				
Labs				
WBC	27.9	28.1	25.2	19.7
Creatinine	1.31	1.14	0.95	0.88
BUN	43	35	23	14
Sed Rate				
Vitals				
Temperature	100.2 (37...	98.7 (37.1)	97.9 (36.6)	98.9 (37.2)
Heart rate	90	88	88	88
Resp rate	20	22	20	20
Pulse oximetry	92	94	97	95
R Oxygen device	OxyMask	Not on O2	Not on O2	OxyMask

08/25/2020	MRSA MSSA By PCR	Final result	Normal
08/22/2020	SARS-CoV-2 (COVID19)	Final result	
08/22/2020	Urine Culture	Final result	
08/22/2020	Blood Culture #2	Final result	
08/22/2020	Blood Culture #1	Final result	

Review Interventions

8/24

- Vancomycin initiated for PNA
- PCR ordered @ 1148 (Call nurse once PCR is first ordered)

8/25

- New culture/radiology results: “blood Cx x2 NGTD, Urine Cx no growth”
- Plan: “If source is pneumonia: MRSA nasal PCR ordered. (Called nurse for reminder to collect)”
- PCR Collected 8/25 @ 12.19 – Received @ 12:36 – Resulted @ 14:34

8/26

- Recommended Dcing Vancomycin secondary to negative PCR
- NP Accepted
- Vancomycin DC’d @1424
- No compromise to clinical outcomes and not re-started

Address current questions regarding MRSA PCRs

What if the patient is COVID (+)?

- Continue with current pneumonia recommendations and de-escalate if nasal MRSA PCR result is negative

Study	Design	Results
Punjabi CD, et al. (2020)	Retrospective Cohort N=472	**PCR result**: 12/122 test were positive • Of those 2 patient had a corresponding positive respiratory culture for MRSA **NPV 100%**

Days from Admission	Day 3	Day 7	Day 14	Day 28
Total patients with respiratory cultures obtained, no.	158	285	405	472
Patients with MRSA in respiratory cultures, no	1	7	18	27
Prevalence, %	0.6	2.4	4.4	5.7

What if the patient has sepsis secondary to PNA?

- If it is secondary to PNA and the nasal MRSA PCR is negative, then it is unlike the pathogen is MRSA and vancomycin is not needed.

What if there are multiple possible infections?

- The nasal MRSA PCR is to help guide de-escalation for empiric pneumonia treatment only – not other indications.

- Still evaluate critically:
  - Ex. Pt started on vanc – empiric for two possible infections PNA and intra-abdominal → should you get a PCR?

Maybe → Vancomycin Use Criteria

	Empiric	Recommend DC in 48-72 hr

Abdominal Infections	• Abdominal Infections Healthcare-associated secondary peritonitis
	  • Known colonizer of MRSA
	  • Recent abdominal surgery
	  • Recent broad spectrum antibiotic use
	• Severe secondary peritonitis
	  • Patient hemodynamically unstable
	• Peritoneal dialysis related peritonitis
		• Patient clinically stable &
		• No microbiologic evidence of drug resistant gram positive infection

What if the respiratory cultures have not resulted yet?

- Still make the recommendation – no need to wait
- Referring back to the meta-analysis mentioned earlier → The NPV ranges from ~95-99%
- Call Micro

All – PNA	CAP/HCAP	VAP
NPV 96.5%	**NPV 98.1%**	**NPV 94.8%**

What if the patient still looks sick? (Elevated WBC, fever, ventilated, etc.)

- Still make the recommendation.
- As mentioned in the two pharmacist-driven studies – there was **no** compromise in clinical outcomes.
- ICU patients: Be cautious if this is not a solid PNA case.
  - If bacterial PNA is primary/official clinical problem → make recommendation
  - ICU patients have multiple sites for a possible infection

What if the patient decompensates after discontinuing? Would you restart it?

- Unlikely. Unless there was an independent factor that pointed to MRSA or if another source was of concern.
- If it was specifically PNA → would look at PNA coverage
  - Ex. Possibly escalate ceftriaxone to cefepime for increased GN coverage

When not to use MRSA PCR results?

- Empyema
- Prior mupirocin decolonization (this admission)
- Anti-MRSA Abx for >48 hours

Questions?

References

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Aspiration Pneumonia

- Aspiration pneumonia
  - Aspirate on gastric contents = aspiration pneumonitis
    - Resolution of symptoms within 24 to 48 hours and require ONLY supportive treatment, WITHOUT antibiotics
  - Do not routinely add anaerobic coverage unless lung abscess or empyema suspected
    - More recent studies have shown anaerobes are uncommon in patients hospitalized with suspected aspiration