

15-16 Antimicrobial Stewardship

25 Applicability of the CDC Campaign “12 Steps to Prevent Antimicrobial Resistance among Hospitalized Children” to the Neonatal Intensive Care Unit (NICU)

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Background: While infants hospitalized in the NICU have high rates of empiric antibiotic use due to high rates of hospital-acquired infections, there have been few studies examining inappropriate antimicrobial usage in this patient population.

Objective: To classify antibiotic prescribing in a level III, tertiary care NICU as appropriate or inappropriate based on the “12 Steps to Prevent Antimicrobial Resistance among Hospitalized Children”.

Methods: This retrospective observational study of intravenous antimicrobial usage was performed from September to December 2005 in our level III university affiliated NICU. Each usage of antibiotics given to 50 consecutive infants \geq 72 hours of age for any clinical indication was judged by two physician investigators as either appropriate or inappropriate and if inappropriate, which 12 Step recommendation was violated. Discrepancies were resolved by consensus.

Results: The mean gestational age and birth weight of the 50 subjects (48% female) was 36 weeks (range 24-42 weeks) and 2,690 grams (range 620-4,255), respectively. Nineteen (38%) of 50 underwent surgical, primarily cardiac, procedures. During the study period, these 50 infants received 104 courses (716 antibiotic-days) of antibiotics. Overall, 19 infants had at least one inappropriate antibiotic course; 34 (33%) of 104 courses (172 inappropriate antibiotic-days) were judged to violate one or more 12 Step recommendations. The most common violations were failure to ‘Target the pathogen’ (e.g., continued use of Vancomycin for methicillin-sensitive *Staphylococcus aureus* infections) with 66 inappropriate days, and ‘Practice antimicrobial control’ (e.g., post-operative prophylaxis $>$ 48 hrs) with 52 inappropriate days. In all, 55% (n=30 days) of carbapenem, 30% (n=84 days) of vancomycin, and 44% (n=44 days) of cefazolin antibiotic-days were inappropriate. No usage days of 2nd (n=17 days) or 3rd (n=25 days) generation cephalosporin agents were judged inappropriate.

Conclusions: Violations of the CDC 12 Step recommendations were common in our NICU and suggest that this framework could be used to improve antimicrobial stewardship in this patient population.

26 An Educational Intervention to Reduce Inappropriate Treatment of Asymptomatic Bacteriuria in a Long-Term Care Facility: The Critical Role of Nursing Staff

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Background: In long-term care facilities, treatment of asymptomatic bacteriuria (ASB) is common. However, randomized, controlled trials suggest that such treatment offers no benefit, and may promote antibiotic resistance.

Objective: To perform an educational intervention to reduce inappropriate treatment of ASB in a long-term care facility.

Methods: For 3 months before and 6 months after an educational intervention, we monitored the appropriateness of urine culture collection and antibiotic treatment based on published guidelines. The

intervention included education of nursing staff to discourage the collection of urine cultures in the absence of symptoms suggestive of urinary tract infection, and of primary care practitioners to not treat asymptomatic bacteriuria. Poisson analysis was used to compare rates of inappropriate urine culture submission and treatment of asymptomatic bacteriuria the pre- and post-intervention periods.

Results: In pre-intervention period, 23 of 38 (61%) antibiotic regimens were prescribed for treatment of ASB rather than for symptomatic urinary tract infection. After the intervention, inappropriate submission of urine cultures decreased significantly from 3.7 to 1.5 per 1,000 patient days (incidence rate ratio 0.41, 95% confidence interval 0.27-0.64, $P < 0.0001$). However, when inappropriate cultures were sent and ASB was identified, there was no significant decrease in the frequency of treatment in the pre- and post-intervention periods (68% versus 69%, respectively; $P = 0.94$). The overall rate of treatment of ASB in the long-term care facility was reduced from 1.75 to 0.65 per 1,000 patient days (incidence rate ratio 2.71, 95% confidence interval 1.4-5.32, $P = 0.0017$).

Conclusions: Educational interventions can significantly reduce treatment of ASB in long-term care. Education of the nursing staff regarding appropriate criteria for requesting urine cultures should be an important component of such interventions. Further research is needed to identify more effective strategies to reduce treatment of ASB by primary care providers.

27 Lost in Translation? Reliability of Assessing Antimicrobial Appropriateness Using Computerized Case Vignettes Assembled from Paper and Computerized Records

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Background: To remove biases and to review patient records for the appropriateness of antimicrobial use more efficiently, we created a two-step process of computer-assisted case vignette assembly by trained assistants and review by an infectious diseases (ID) MD.

Objective: To assess the reliability of this instrument.

Methods: For 35 inpatient antimicrobial recipients, computerized case vignettes were populated with entries from our computerized data warehouse, and 2 trained assistants independently added clinical data abstracted from paper charts to create 2 parallel sets of vignettes. We compared the vignettes for discrepancies that could alter expert reviewer assessments. Also, an ID MD reviewed the paper charts of 24 other inpatient antimicrobial recipients, randomly selected from a cohort of 539 computerized case vignettes reviewed previously, to compare the assessments of antimicrobial appropriateness by vignette vs chart review.

Results: Of the 35 case vignettes assembled independently by the 2 assistants, there were no discrepant entries for patient allergies; discrepancies in abstracted pre-admission antimicrobial use, comorbidities, symptoms and physical findings were rare; and abstracted peak temperature differed by more than 1° F in only 5 (14%) of 35. Abstracted indications for hospital admission were discrepant in 2 (6%); 7 (17%) of 41 abstracted indications for antimicrobial therapy were discrepant. Abstracted physician radiograph readings (when computerized radiologist readings were not available) were discrepant in 11 (44%) of 25 cases and the location in which antimicrobials were started (emergency department versus medical floor) was discrepant in 10 (29%) of 35 cases.

Of 24 cases reviewed by an ID MD using both computerized case vignette and chart review, assessments for appropriateness of antimicrobial starts agreed in 18 (75%); errors were found in 14 (58%) cases by vignette review and in 16 (67%) by chart review. Assessments of subsequent antimicrobial therapy were the same in both methods for 5 (21%) cases; prescribing errors were identified in 54 (52%) of 104 patient-days on antimicrobials by vignette review and in 69 (75%) of 92 patient-days on antimicrobials by chart review. Discrepancies were caused by discordant antimicrobial administration records (9 cases), abstractor failure to note events requiring data censoring (5 cases), enhanced timing or

description of key clinical events with chart review (3 cases), ID reviewer failure to note key vignette findings (2 cases), and ID reviewer inconsistency in applying appropriateness criteria (2 cases).

Conclusions: Our two-step process of computer-assisted case vignette assembly and review is acceptably reliable but improved technical, abstractor and reviewer performance are needed.

28 Does Delay Matter? The Importance of Comorbidities and Methicillin-Resistant Staphylococcus aureus (MRSA) in Assessing the Impact of Delay of Appropriate Antimicrobial Therapy (DAT) for Bacterial Bloodstream Infections (BSIs)

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Background: DAT of bacterial BSIs has been associated with increased in-hospital mortality, particularly in intensive care units (ICUs). This concern has led to a focus on broad empirical antimicrobial therapy to overcome the threat of bacterial antimicrobial resistance. There have been few studies involving non-ICU patients analyzing the effect of DAT on mortality.

Objective: To determine the association between DAT and inpatient death for bacterial BSIs in ICU and non-ICU patients.

Methods: We performed a case-control study using a prospectively-collected electronic database at a large urban hospital from August 2001 to February 2006. Patients with monomicrobial bacterial BSIs (excluding coagulase-negative Staphylococcus spp. and anaerobes), with antimicrobial use initiated after cultures, were selected. Patients who died within 24 hours of culture or with multiple episodes of BSIs in an admission were excluded. DAT was defined as not receiving active antimicrobial therapy until 24 hours after the index blood draw, as determined by in vitro susceptibility testing. Mortality, the primary endpoint, was defined as in-hospital death within 30 days of blood culture. Data were analyzed using chi-square for univariate and logistic regression for multivariate analyses.

Results: 1523 patients had an eligible BSI; 25% were in the ICU at the time of index blood culture and 35% had DAT. Mortality was 9% overall, 22% in the ICU cohort and 4% in the non-ICU cohort. In univariate analyses, age, Charlson score, ICU, vasopressor use, nosocomial onset, neutropenia, and MRSA were significantly associated with death ($P < 0.05$). In multivariate analysis, age, Charlson score, ICU, vasopressor use, nosocomial onset, neutropenia, and MRSA remained significant (Table). DAT was not significantly associated with mortality in univariate or multivariate analyses.

Table: Multivariate Analysis of Predictors of In-Hospital Death

Factor	Odds Ratio (95% CI)	P value
Delay of appropriate therapy (DAT)	1.07 (0.68-1.68)	0.771
MRSA infection	2.06 (1.21-3.51)	0.008
Age	1.02 (1.00-1.03)	0.009
Charlson ≥ 7	4.49 (2.46-8.19)	<0.001
Charlson 2-6	1.73 (1.09-2.74)	0.02
Charlson <2 (reference group)	-	
ICU at time of culture	2.95 (1.83-4.74)	<0.001
Vasopressor use at time of culture	5.60 (3.37-9.30)	<0.001
Neutropenia	4.38 (2.10-9.11)	<0.001
Nosocomial onset	2.53 (1.61-4.00)	<0.001

Conclusions: In a study involving both ICU and non-ICU patients, DAT for bacterial BSIs was not associated with increased risk for in-hospital 30-day mortality; rather, comorbidities, nosocomial onset, and MRSA BSI were more important predictors of mortality. Studies of the role of appropriate empirical

antimicrobial therapy in outcomes should account for the independent effects of organism types, resistance patterns, and comorbidities.

29 Lessons Learned from Surveillance of Antimicrobial Susceptibility of *Pseudomonas aeruginosa* at a Large Academic Medical Center, 2000 to 2006

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Background: The high morbidity and mortality associated with ineffective empirical therapy for *P. aeruginosa* infections emphasizes the need for reliable data on which to base the choice of empirical therapy. Periodic monitoring of resistance is therefore mandatory. For *P. aeruginosa*, significant declines in susceptibility to many antimicrobials, primarily cefepime, were noted over the last year at our institution. Cefepime is currently approved for intensive care unit (ICU) empiric therapy; while carbapenems are restricted to approval by the antibiotic stewardship program. Current evidence suggests that controlling antimicrobial resistance requires modifying antimicrobial usage within specific patient-care areas of the hospital.

Methods: Census, antimicrobial usage, and susceptibility data were collected on a semi-annual basis and defined daily doses per 1000 patient days were calculated from the years 2000 through 2006.

Relationships between antimicrobial usage and *P. aeruginosa* resistance were determined by univariate linear regression. A case-control study was performed to define various patient-specific risk factors for non-susceptible strains of *P. aeruginosa* to cefepime for non-ICU patients.

Results: Rates of susceptibility of *P. aeruginosa* to most antimicrobials have decreased by 10-15% over the last five years; however susceptibilities varied considerably by patient-care areas. Overall, susceptibility rates remain lower in the ICUs compared to the non-ICU patient-care areas, except for cefepime over the last time period. Cefepime and meropenem usage and *P. aeruginosa* susceptibility showed a significant relationship when individual ICUs were compared. Decreased meropenem exposure was associated with lower resistance rates relative to cefepime. Risk factors for non-susceptible *P. aeruginosa* isolates to cefepime were cystic fibrosis (OR = 4.6), initial ICU admission (OR = 4.4), third generation cephalosporin use within six months (OR = 5.5), and greater than three admissions in the last six months (OR = 8.73).

Conclusions: In order to control the spread of antimicrobial resistance, the pattern of antimicrobial susceptibilities and utilization in specific patient-care areas should be monitored and may lead to improved initial empiric therapy. In our non-ICU patient population, cefepime resistance was associated with patient-specific risk factors. Effective empiric antimicrobial therapy requires consideration of identified risk factors for *P. aeruginosa* resistance. In our adult ICU patient populations, increased cefepime exposure was associated with decreased activity against *P. aeruginosa*. Carbapenem resistance has remained low, secondary to decreased utilization. We feel at our institution antimicrobial stewardship does play a role in controlling drug resistance.

30 Effectiveness of a Sustained Campaign of Physician and Patient Education in Reducing Antibiotic Use for Upper Respiratory Infections

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Background: Antibiotic prescribing for uncomplicated upper respiratory infections is a common medical error that contributes to medical costs, adverse drug events, and antibiotic resistance. Few studies have demonstrated the effectiveness of programs for reducing this unnecessary use.

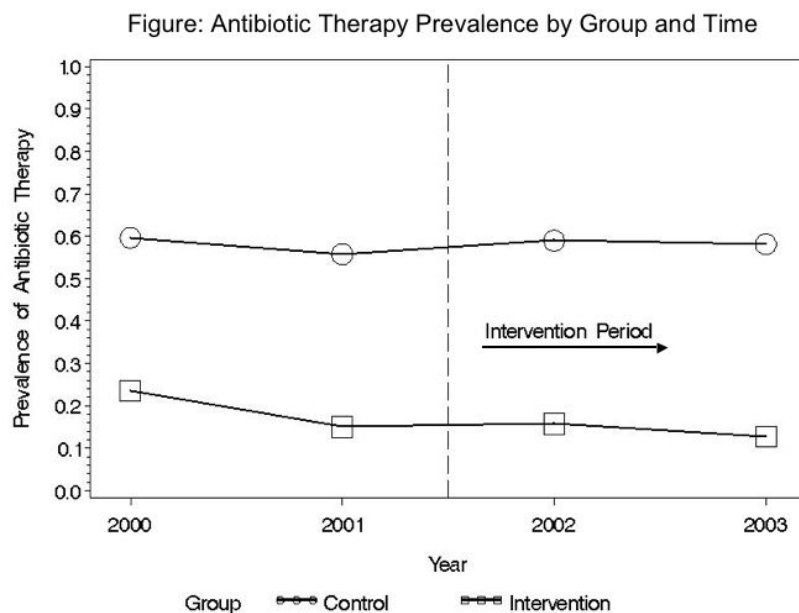
Objective: To determine the effectiveness of a sustained campaign of distributing patient-targeted

educational materials with physician involvement in reducing the frequency of antibiotic prescribing for uncomplicated upper respiratory infections.

Methods: A controlled, time-series design was used to test our intervention during a 4-year study period. The intervention and control physician groups (and their patients) were from multiple practices of a university, faculty-physician outpatient group and a university-affiliated outpatient group, respectively. In the latter 2 years of the study, the intervention group physicians received once-yearly educational mailings and approved patient educational materials for mailings to specific patients they had seen for upper respiratory infections in the prior year. The outcome was the proportion of visits for each physician for upper respiratory infections (excluding sinusitis, pneumonia, and chronic lung disease) in which antibiotics were prescribed.

Results: We abstracted 2,613 patient visits for 70 physicians. The prevalence of antibiotic prescribing in the intervention group decreased from 24% to 13% during the study, versus 60% to 58% in the control group (Figure). The ratio of odds ratios for change in slope with the intervention in the intervention group versus the control group was 0.76 (95% confidence interval 0.3-1.95, p value=0.57).

Conclusions: While the prevalence of antibiotic prescribing appeared to decrease more in the intervention group than the control group, the observed effect was not statistically significant. The low baseline prescribing rate in the intervention group may have been due to those practices being more academic, and may have limited the potential for further improvement. Alternatively, more multi-dimensional interventions may be necessary to change prescribing behavior.



31 Making the Case for Antibiotic Stewardship in a Small Tertiary Care Facility

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Background: We initiated an antibiotic stewardship program with a focus on fluoroquinolones (FQs).

Objective: Our goals were determine appropriateness of FQ use and costs, and effectiveness of intervention.

Setting: The New Mexico VA Healthcare System has 121 acute care beds and 26 long-term care beds,

plus over 716,000 outpatient encounters yearly. Levofloxacin and ciprofloxacin are available, with formulary use criteria (Table 1). A digital medical record allows abstraction of clinical, microbiological, and pharmacy data.

Baseline assessment: We collected diagnosis, drug and duration, prescribing physician and service, and culture results on all outpatients prescribed FQs over two weeks. Inpatient data were collected over two successive three-month periods, with an intervention in the second period. For inpatients, we calculated cost of IV therapy, and alternate cost of appropriate PO, non-respiratory FQ, or non-FQ therapy.

Inpatient Intervention: Post-prescription review was done for IV FQ orders generated by daily digital report. 99 patients received intravenous FQ; however, 45 either received a one time dose, or had therapy changed or discontinued before intervention. On 54 patients, providers were asked to consider changing therapy from IV to PO and/or non-respiratory FQ, or non-FQ therapy as indicated by guidelines.

Outpatient assessment: 160 FQ prescriptions were written, with 53% meeting criteria for FQ use. Only 11% of respiratory FQ prescriptions met criteria. Appropriate use of non-respiratory FQs alone could have saved an estimated \$33,500 per year.

Inpatient Baseline Assessment: 63% of 92 cases met criteria for FQ use. In 76% of cases, however, FQ could have been given orally instead of IV. 79% of respiratory FQ did not meet criteria. IV-to-PO switch and appropriate use of non-respiratory FQ could have saved an estimated \$30,016 per year.

Results of Intervention Period: In 54 patients, 41 were appropriate for IV-to-PO conversion; 37 patients were converted. 46 were appropriate for levofloxacin-to-ciprofloxacin conversion. After the intervention, 65 patients had their therapy changed to either a different drug class or discontinued altogether, including 11 patients who had their medications changed without active intervention. 54 patients total were converted from the respiratory FQ to non-respiratory FQ

Conclusions: Inappropriate use of IV and respiratory FQs is costly. Our intervention demonstrated the potential for a stewardship program in our institution, enabling us to develop proposals for expansion of

Table 1. Criteria for use of fluoroquinolones at NMVAHCS

Criteria for the Use of Fluoroquinolones

- Levofloxacin: indicated for inpatient therapy of beta-lactam allergic patients with community-acquired pneumonia and health care-associated pneumonia.
- Ciprofloxacin is FQ of choice for treatment of UTI, prostatitis, uncomplicated gonococcal urethritis or cervicitis, selected GI/skin/soft tissue/joint infections, or other gram negative infections as guided by microbiological data.
- Ciprofloxacin may be used in conjunction with an anti-pseudomonal beta-lactam as an alternative to an aminoglycoside.

the program.

32 Antibiotic Dispensement from Pharmacies and Antibiotic Resistance in Pratumthani, Thailand

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Objectives: To describe antibiotic dispensement (AD) by regional drug pharmacies associated with common syndromic illnesses and to correlate regional AD and antibiotic resistance.

Methods: Six internists trained as patients with common syndromic ailments for mock presentation to regional drug pharmacies in Pratumthani, Thailand. Presentations (and guideline treatments) were #1 acute fever, sore throat (no antibiotic [NA]), #2 acute fever, myalgia, rhinorhea, cough (NA), #3 acute fever, tender maxillary sinus with non-purulent discharge (NA), #4 acute watery diarrhea (NA), #5 skin abrasion without exudates (NA), #6 acute dysuria (quinolone). Antibiotic defined daily doses (DDD) per 1,000 inhabitants per day was correlated with regional rates of penicillin-resistant *Streptococcus pneumoniae* (PRSP), erythromycin-resistant *S. pneumoniae* (ERSP) and ciprofloxacin-resistant *Salmonella non-typhi* (CRSnT) using linear regression.

Results: Appropriate AD for all indications occurred at 56 of 280 (20%) pharmacies. AD for mock syndromic illnesses was 74%, 65%, 80%, 76%, 64% and 100% for #1-6, respectively. Tetracycline, amoxicillin, penicillin, erythromycin, amoxicillin-clavulanate, rifampicin and azithromycin were most commonly dispensed. By multivariate analysis, pharmacy proximity (<5kms) to hospital was the sole predictor of appropriate antibiotic use (aOR 34; 95% CI 15-83; $P<0.001$). From 2000-2005, there was a linear relationship between beta-lactam use (8.8-10.8 DDD/1,000 inhabitants per day) and PRSP (37-51%; $R^2 0.84$; $P=0.009$), erythromycin use (2.1-2.4 DDD/1,000 inhabitants per day) and ERSP (26-37%; $R^2 0.94$; $P=0.001$) and ciprofloxacin use (1.35-2.7 DDD/1,000 inhabitants per day) and CRSnT (2-4%; $R^2 0.82$; $P=0.01$).

Conclusion: Inappropriate AD from pharmacies for syndromic illnesses was common. Strategies to promote judicious AD in countries with over-the-counter antibiotic sales are warranted. Rates of PRSP, ERSP and CSnT, over time, correlated with inappropriate AD.

33 Factors Associated with Inadequate Antibiotic Therapy for Gram-negative Bacteremia Outside the ICU and Impact on Outcomes

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Background: A considerable number of Gram-negative bacteremias occur in non-critically ill patients (pts) admitted to regular wards. While inadequate antibiotic therapy in intensive care units (ICUs) has been associated with adverse outcomes, there are no prospective studies in non-ICU patients to examine the frequency of inadequate therapy and its impact on outcomes.

Objective: To study the epidemiology, treatment and outcome of Gram-negative bacteremia in non-ICU patients. Factors predisposing to inadequate antibiotic treatment and the impact of inadequate therapy on outcomes were determined.

Methods: A 3-month (8/1/06-10/31/06), prospective cohort study of adult non-ICU patients with Gram-negative bacteremia in a 1250-bed tertiary care hospital was performed. Inadequate empirical antibiotic therapy was defined as either not starting an antibiotic ≤ 24 hrs after the initial blood culture was drawn, or starting an antibiotic which the bacteria was not susceptible to.

Results:

111 non-ICU pts had Gram-negative bacteremia. Mean age=55.9 (± 15.7) years. The median Charlson comorbidity score at diagnosis was 4 (range 0-16). 48 (43%) had cancer & 18 (16%) were neutropenic. Most pts were admitted to general medical (n=38; 34%) or oncology wards (n=28; 25%). 69 (62%) bacteremias were hospital-acquired. The predominant bacteria in single organism infections were *E. coli* (28%), *K. pneumoniae* (19%), & *P. aeruginosa* (7%); 25 (23%) pts had polymicrobial bacteremia. 105 (95%) pts had sepsis, 45 (41%) sepsis-associated hypotension, 27 (24%) required ICU transfer, and 19 (17%) died.

37 (33%) had inadequate antibiotic therapy. These pts were more likely to have had a surgical procedure prior to the bacteremia [10 (27%) inadequate vs. 4 (5%) adequate therapy; $p=0.002$]. After the notification of bacteremia, the infectious diseases service was not consulted more frequently in pts with inadequate therapy [8 (22%) vs. 9 (12%); $p=0.26$]. These pts did not have a higher rate of sepsis [33 (89%) vs. 72 (97%); $p=0.09$], sepsis-associated hypotension [15 (41%) vs. 30 (41%); $p=1.0$], ICU transfer [8 (22%) vs. 19 (26%); $p=0.8$], post-bacteremia length of stay (median=6.5 vs. 5.4 days; $p=0.5$) or death [8 (22%) vs. 11 (15%); $p=0.4$].

Conclusions: A considerable proportion of non-ICU patients with Gram-negative bacteremia developed sepsis, sepsis-associated hypotension, and had subsequent ICU admission in this tertiary care hospital. One-third of pts received inadequate empirical antibiotic therapy, which is comparable to data from ICUs. There was no difference in adverse outcomes between pts receiving adequate or inadequate therapy in this study.

34 Methicillin-Susceptible *Staphylococcus aureus* (MSSA) Bloodstream Infection (BSI): Missed Opportunities to Optimize Antimicrobial Therapy

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Background: Antimicrobial therapy with a penicillinase-resistant semisynthetic penicillin or a first generation cephalosporin is considered optimal therapy for infections caused by MSSA. This is both due to superior clinical efficacy and to reduce unnecessary use of vancomycin.

Objective: As part of a pilot study to direct an antimicrobial stewardship program, to identify the rate of missed opportunities to optimize antimicrobial therapy for MSSA BSI.

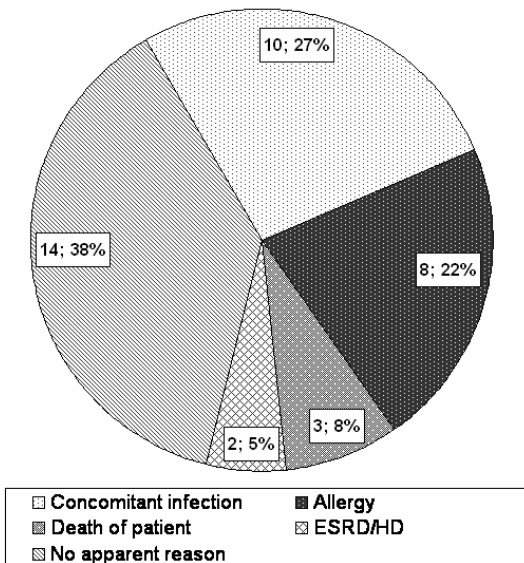
Methods: Medical record review was performed for 81 consecutive MSSA BSIs during an 18 month period to determine antimicrobial use from the time the blood culture was drawn until 72 hours after the release of antimicrobial susceptibility testing (AST) results. Optimal antimicrobial therapy was defined as use of a parenteral penicillinase-resistant semisynthetic penicillin or a first generation cephalosporin within the above mentioned timeframe. Chi-square test or Fisher's exact tests were used to determine if there were statistical associations between optimal antimicrobial therapy and admitting clinical service, an infectious diseases consult, or presence of vascular catheter when the blood culture was obtained. We also collected data on possible reasons to justify suboptimal therapy, and categorized them as follows: (1) beta-lactam allergy, (2) concomitant infection at another site, (3) end stage renal disease/hemodialysis, (4) death prior to availability of AST results, or (5) no apparent reason.

Results: Of the 81 MSSA BSI examined, 37 (46%) were determined not to have received optimal antimicrobial therapy within the first 72 hours after release of AST results. Among these 37 patients, a reason for not changing to optimal therapy could be identified for 23 (62%) (see figure). Fourteen (38%) had suboptimal therapy continued for no apparent reason and represent missed opportunities to optimize therapy. An infectious diseases consult was statistically associated with a change to optimal therapy ($p=0.0003$).

Conclusions: Although almost half of the patients with MSSA BSI did not receive optimal antimicrobial therapy, fewer than one-fifth may be easily amenable to a change to optimal therapy. A careful allergy evaluation may increase that proportion to closer to one-third. Evaluation by an expert in infectious diseases, either through formal infectious diseases consultation or by application of an antibiotic

stewardship program, may facilitate the change to optimal antimicrobial therapy for MSSA BSI.

Categorization of suboptimal therapy



35 Optimizing double coverage for gram negative (GN) infections in the ICU: utility of a combination antibiogram

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Background: The failure to administer appropriate initial antimicrobial coverage for treating GN infection in critically ill patients is associated with worsened outcomes. Because of the high frequency of resistance to single antimicrobial agents, it may be beneficial to expand coverage with a second agent to ensure that empirical therapy is adequate.

Objective: Based on a combination antibiogram, to quantify any benefit of the addition of a second antimicrobial agent to the empirical treatment of GN infection in adult ICU patients.

Methods: Based on the results of cultures from adult ICU patients collected between 1999 and 2005, the proportion of common GN isolates susceptible to monotherapy with each of 3 antimicrobial agents (imipenem, piperacillin/tazobactam, ceftazidime) was compared with the pairing of each single agent with 4 different second agents (gentamicin, tobramycin, amikacin, ciprofloxacin).

Results: In all, 5097 isolates were tested. The proportion of all GN isolates covered by monotherapy was 71.5% for ceftazadime, 74.3% for piperacillin/tazobactam and 84.0% for imipenem. When compared with monotherapy, addition of any second agent significantly increased ($p < .0001$) the proportion of isolates covered. The proportion of isolates covered by dual therapy ranged from 82.8% (ceftazidime + ciprofloxacin) to 95.0% (imipenem + amikacin). When considering specific pathogens individually, the added benefit of dual therapy was variable. The addition of a second agent to imipenem to treat *Klebsiella spp.*, *Acinetobacter baumannii*, and *Escherichia coli* was of no added benefit given the broad coverage of imipenem monotherapy. In contrast, for *Pseudomonas aeruginosa*, adding any second agent to imipenem significantly increased the proportion of isolates covered from 66.2% to a range of 75.7-91.4% ($p < .0001$). When compared to monotherapy with piperacillin/tazobactam, addition of any second agent significantly increased coverage for every species tested ($p < .0001$) except *A. baumannii*, for which aminoglycosides but not ciprofloxacin increased coverage. Adding any second agent to ceftazidime significantly increased coverage for *P. aeruginosa*, *Enterobacter spp.* and *Klebsiella spp.*, but dual therapy with ciprofloxacin did

not significantly increase coverage for *E. coli* or *A. baumannii*. Differences in coverage with or without addition of a second agent were comparable when analysis was limited to bloodstream isolates.

Discussion: Dual antimicrobial therapy for GN infection in ICU patients offers a significantly increased breadth of coverage when compared with monotherapy. However, the magnitude and clinical benefit of added coverage varies considerably between pathogens and specific antimicrobial agents. A combination antibiogram may help guide the choice of empirical therapy by quantifying the benefit of adding additional antimicrobial agents in specific circumstances.

36 Electronic Measures of Hospital Antimicrobial Utilization: A Multi-Center Pilot Assessment of Feasibility and Variability in Intensive Care Units

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Background: Accurate measurement of hospital antimicrobial use (AU) is the first step in developing strategies for control of AU and antimicrobial resistance. Rates of hospital AU are not routinely compiled or reported, perhaps because previously reported measures have used disparate data sources and units of measurement and were rarely validated. Variation in AU between and within intensive care units (ICUs) has received little attention.

Objective: Assess the feasibility of obtaining electronic measures of AU and assess the variation in AU among 14 ICUs in 4 US academic medical centers.

Methods: We measured aggregate, class- and drug-specific AU retrospectively for 2 years and prospectively for 1 year in 14 ICUs within 4 U.S. academic medical centers using computerized pharmacy and administrative databases and uniform definitions and units of measurement (antimicrobial days [ADs], patient-days on antimicrobials and defined daily doses [DDDs], all per 1000 patient-days). For each participating institution we also surveyed the systems for medication ordering, distribution and administration; the types of accessible electronic AU data (e.g., MD orders, pharmacy dispensing or charges, nursing medication administration records [MAR]); and the programming resources necessary to derive these measures.

Results: Systems for medication ordering, distribution and administration varied between and within institutions over the time of the study. Accessible computerized pharmacy data sources included pharmacy dispensing (3 institutions), nursing MAR (2 institutions) and MD orders (2 institutions); comparison of AU measures derived from 2 sources concurrently (e.g., MD orders and MAR) will be possible in 3 institutions. The necessary programming resources and personnel time have not been onerous and the measures are amenable to automated reporting. Preliminary data from a single institution show that aggregate AU in the medical ICU is about 50% higher than in the surgical ICU and 3-fold higher than in the coronary care unit (CCU), and, in the medical ICU, demonstrate more than 1.5-fold variation over time in aggregate AU and more than 3-fold variation over time in anti-pseudomonal and anti-MRSA AU. AU in this institution's MICU is substantially higher, while that of its CCU is lower, than that of their counterpart ICUs in a second medical center. Comprehensive data collection, validation and analysis are ongoing.

Conclusions: Collection and programming of computerized pharmacy data to report uniform measures of AU in hospitals is feasible. Preliminary data suggest substantial variation in AU among and within ICUs. If confirmed, the sources of this variation and its potential inclusion in interventional strategies merit further investigation.