Strategies for Stewardship and Tool for Implementation

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Main actions to prevent and control antimicrobial resistance

Prudent use of antimicrobials (only when needed, correct dose, dose intervals, duration)

Infection control (hand hygiene, screening, isolation)

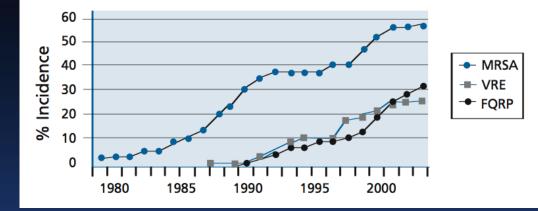
New antibiotics (with a novel mechanism of action, research, development)







Get Smart 2010



Each year

- 2 million patients develop bacterial HAI
- 90,000 people die
- More than 70% of these infections are resistant to at least one class of antibiotics

Antibiotic resistance is associated with:

- Increased risk of hospitalization
- Increased length of stay
- Increased hospital costs
- Increased risk of ICU transfer
- Increased mortality
- Decreasing inappropriate antibiotic use is the best way to control the development of resistance

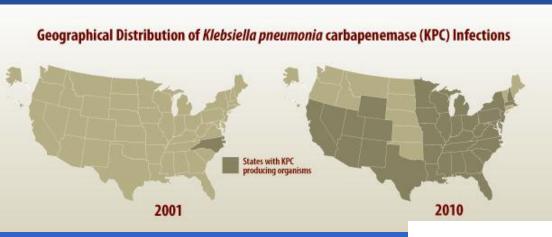
Antimicrobial Resistance: A local, national, and international problem....

Massachusetts:

-Between 2000 and 2007, 3-fold increase in *C. diff* as a primary diagnosis for hospitalization and >4-fold increase in deaths

-Over 1/3 of *Streptococcus pneumoniae* isolates in MA are resistant to penicillin and 20% could not be treated with other common antibiotics

- State DPH reported 67 cases of fluoroquinolone-resistant *N. gonorrheae* in 2006, up from 2 cases in 2001



HOME / NEWS / LOCAL / MASS.

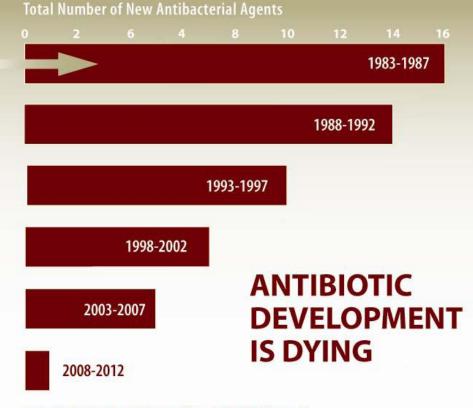
The Boston Globe

'Superbug' patient treated at MGH

Arrival of the germ in US casts a spotlight on global spread of drug-resistant bacteria

Bad Bugs: No Drugs, No ESKAPE

- Enterococcus
- S. aureus
- Klebsiella spp.
- Acinetobacter
- P. aeruginosa
- Enterobacter spp.



Source: The Epidemic of Antibiotic-Resistant Infections, CID 2008:46 (15 January)

What is Antimicrobial Stewardship?

 Antimicrobial stewardship involves the <u>optimal</u> <u>selection, dose and duration</u> of an antibiotic resulting in the cure or prevention of infection with <u>minimal unintended consequences</u> to the patient including emergence of resistance, adverse drug events, and cost.

Ultimate goal is improved patient care and healthcare outcomes

Dellit TH, et al. CID 2007;44:159-77, Hand K, et al. Hospital Pharmacist 2004;11:459-64 Paskovaty A, et al IJAA 2005;25:1-10 Simonsen GS, et al Bull WHO 2004;82:928-34

Get Smart: Know When Antibiotics Work

Goals:

- promoting adherence to appropriate prescribing guidelines
- decreasing demand for inappropriate antibiotics
 National campaign to target five conditions that accounted for >75% of all office based antibiotic prescribing:
 - Otitis media
 - Sinusitis
 - Pharyngitis
 - Bronchitis
 - The common cold



Get Smart 2010 Targeting Healthcare settings

Mission: To optimize the use of antimicrobial agents in inpatient healthcare settings Goals:

 Improve patient safety through better treatment of infections

- Reduce the emergence of antimicrobial resistant pathogens
- Encourage better use of antimicrobials in healthcare settings

Get SMART about Stewardship

- Starting off choosing the appropriate empiric regimen
 - "front end"
- Maintenance of therapy: Targeting, de-escalating, and discontinuing therapy
 - "back end"
- Are you treating infection or colonization?
 - Using current quality measures to promote ASP
- Route: IV or PO
 - Empowering your pharmacist
- Time: Stop antibiotics as early as possible
 - Harnessing your resources

Antimicrobial Stewardship Strategies at Tufts Medical Center

- Prospective audit with intervention and feedback
- Formulary restriction and preauthorization (pg 6858)
 Supplemental Strategies
 - Education: "AMT Question of the Week"
 - Antimicrobial guidelines and disease management
 - Dose optimization via PK-PD: extended dosing of Zosyn
 - De-escalation/Streamlining: MR/pages to change treatment
 - Antimicrobial order forms/order sets if CPOE
 - IV-PO switch: automated by pharmacy
 - Computerized decision support (Sentri7 and Safety Surveillor)

Starting off - "Front End"

- Also referred to as "preauthorization" or "pre-prescription approval"
- Restriction at the time the antimicrobial is prescribed:
 - Formulary vs. non-formulary
 - Target specific antimicrobials associated with high rates of resistance or \$\$\$
 - May target a specific disease or indication
- In order to receive restricted antibiotics, a prescriber must have clearance from a member of the stewardship team
- Performed by either an infectious diseases physician, a clinical pharmacist with infectious diseases training, or a member of the antimicrobial support team
- Requires resources early in the intervention process

ADULT ANTIMICROBIAL ORDER SHEET				
ALL SECTIONS MUST BE COMPLETED BEFORE DRUG CAN BE DISPENSED				
	our Clock)			
Patient Allergies: Wt (Kg): Serum	Creatinine:	Must be calculat		
			age) x IBW (Kg) *SCr x 72	mL/min
Suspected Infection Suspected/Known Site of Infection	tion:	Female = 0.85 x		
Decumented Infection Bone/Joint Respire	atory	IBW Calculations:		
List pathogen(s) isolated: CNS Skin/Sc Bacteremia Urine	oft Tissue	IBW (male) = 50 kg + {2.3 x (every inch above 5 feet)} IBW (female) = 45 kg + {2.3 x (every inch above 5 feet)}		
Febrile Neutropenia		*For patients > 60 years with an actual SCr < 0.7 mg / dL, u:		
Other			L for estimating Cri	
Drugs that may be prescribed without restriction.				
DRUG	Dose	Route	Frequency	Duration
Ampicillin/Sulbactam (Unasyn)	1.5g	IV	,	
	-			
Cefazolin		IV		
Ceftriaxone	1g	IV	Q24h	
Ciprofloxacin				Doses D
Clindamycin				Doses D
Ertapenem	1g	IV	Q24h	Doses D
Fluconazole		PO	Q24h	Doses 🛛 D
Gentamicin		IV		Doses D
Metronidazole				Doses D
Moxifloxacin	400mg	_	Q24h	Doses D
Oxacillin	_	IV		Doses D
Trimethoprim/sulfamethoxazole (Bactrim)		IV		
Vancomycin (see back for dosing recommendations)				Doses D
Drugs for which <u>RESTRICTIONS MAY APPLY</u> : SEE OTHER SI	_			
DRUG	Dose	Route	Frequency	Duration
Ampicillin/Sulbactam (Unasyn)	3g	IV		Doses D
Cefepime		IV		
Ceftriaxone		IV	Q24h	
Fluconazole		IV	Q24n	
Meropenem Piperacillintazobactam (Zosyn) (Net Indiastad for estimate who are			┨───┤──	
Piperacillin/tazobactam (ZoSyn) (Not indicated for patients who ar neutropenic, on HD, CAPD, have a CrCl <20 milmin, have CF, or hav had an organ transplant or BMT)	3.375g	IV, over 4h	Q8h	🗆 Doses 🗌 D
Piperacillin/tazobactam (Zosyn)		IV, over 30 min		Doses D
Voriconazole				Doses D
				Doses D
				Doses D
		_		
			├ ──┤──	
	1		I	Doses D

Maintenance of therapy: Targeting, de-escalating, and discontinuing therapy

- Empiric regimen is often NOT the regimen that needs to be continued for the full treatment course
- GET CULTURES and use the data to target therapy using the most narrow spectrum agent possible.
- Take an "Antibiotic Time Out" reassess after 48-72 hours

"Back end"

- Also called "post prescription review"
- Prescribers are allowed to order antibiotics upon admission
- Antibiotic orders are reviewed at specified intervals after initiation
- May be restricted to particular patient populations
 - Ex: Cefepime and Zosyn in ICU for up to 72 hours
 - Ex: Echinocandins in candidemia
- May be restricted to formulary drugs or by using a clinic pathway or protocol
 - Ex: Pneumonia or ABSSTI protocol

Getting started is as a easy as 123 and ABC

Getting Started...

- 1. Review Blood and urine cultures that grow organisms
- 2. Review of Key "Never" Combinations
 - 1. Metronidazole and Zosyn
 - 2. Cefazolin and cefepime
 - 3. Levofloxacin and azithromycin
- 3. Align the formulary with Local susceptibility data

Focus on the basics...

- A. Appropriate indication, dose, and duration
 - Guidelines
 - Order sets
- B. Take an antibiotic Break
 - Review of all orders after
 48 hours to asses for
 appropriate therapy
- C. Get Cultures

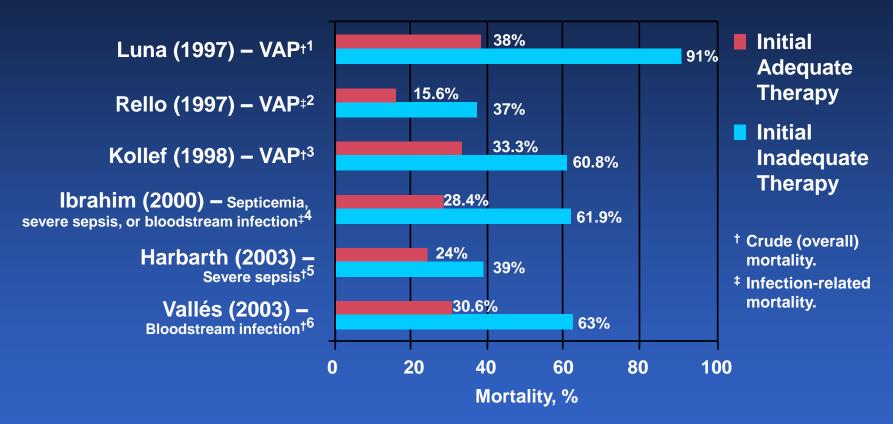
Antimicrobial Stewardship Care Bundle

- Prospective audit system
 - Stewardship program
 - Outcomes
 - Reason for treatment, cultures, empirical, and deescalation
 - LOS, mortality, and % interventions accepted

	With		
Indicator	Control Phase	Intervention Phase	р
Documented indication for			
antibiotic therapy	76/80 (95)	80/80 (100)	0.12
Appropriate cultures			
collected	70/80 <mark>(</mark> 87)	76/80 (95)	0.09
Appropriate empirical			
therapy	55/80 (69)	65/80 (81)	0.06
Appropriate deescalation ^a	41/57 (72)	52/58 (90)	0.01
All indicators concurrently	13/80 (16)	43/80 (54)	<0.001

Fraction (%) Courses Compliant

Mortality Associated With Initial Inadequate* Therapy in Critically III Patients With VAP or Septicemia, Severe Sepsis, or Community-Acquired Bloodstream Infection



* Based on the 2005 ATS/IDSA guidelines for VAP, HAP, and HCAP (*Am J Respir Crit Care Med.* 2005; 171:388–416), "inappropriate" refers to the inadequate therapy noted on this slide.

Luna CM et al. *Chest.* 1997;111:676–685.
 Rello J et al. *Am J Respir Crit Care Med.* 1997;156:196–200.
 Kollef MH et al. *Chest.* 1998;113:412–420.
 Ibrahim EH at al. *Chest.* 2000;118:146–155.
 Harbarth S et al. *Am J Med.* 2003;115:529–535.
 Vallés J et al. *Chest.* 2003;123:1615–1624.

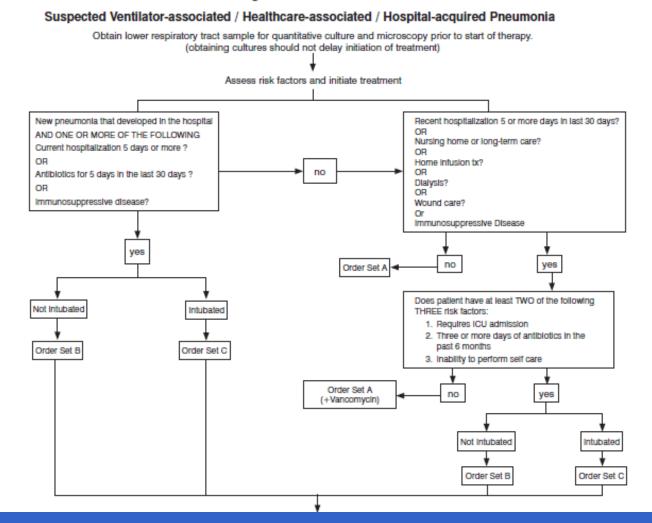
Tufts Medical Center

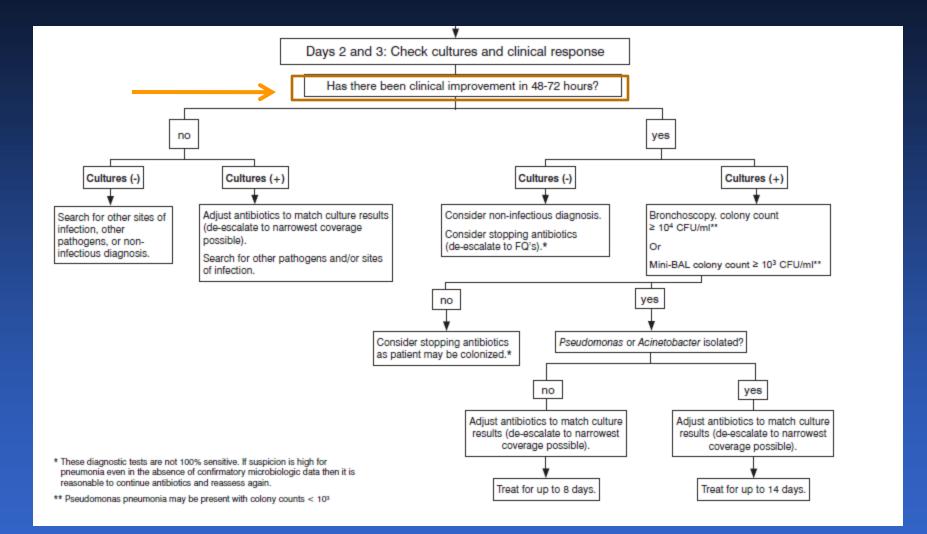
Ventilator-associated/Healthcare-associated/ Hospital-acquired pneumonia ORDER SHEET for ADULT PATIENTS

DATE:	TIME:	(24-hour clock)	L
Patient Allen	ties:	Weight (Kg):	Serum

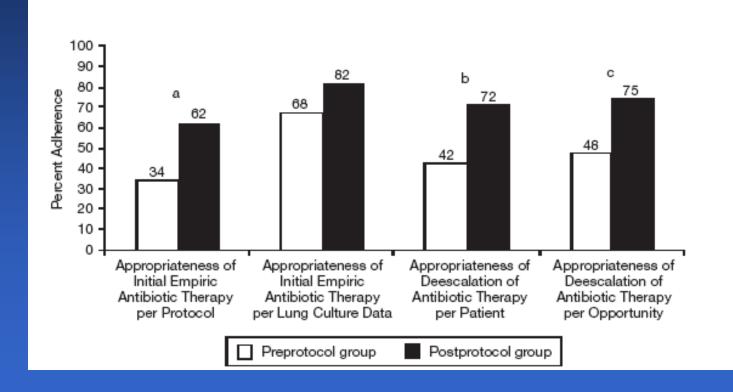
DATE: TIME:	(24-hour clock)			
Patient Allergies:	Weight (Kg):	Serum Creatin		Creatinine Clearance (mL/min):
MEDICATION ORDERS (INCLUDES IV MEDICATIO			PHYSICIANS (EXCLUDES MEDIC	ATION ORDERS)
Inter Ser Å. No Risk factors for Multi-drug Res (see Risk Assessment for Multi-dru Conflaxone 1g IV 024 hours x 72 hours OR Mostfloxacin 400 mg IV or PO 024 ho Consider adding Vancomycin If history of Ink MRSA Vancomycinmg IV o Consider adding Arithromycin for oreverage o Arithromycin 500 mg IV or PO 024 h Inter Ser B. Risk factors for Multi-drug Resis (see Risk Assessment for Multi- Organisms) AND not Intubated Drug 1: Cotagimeg IV 0 OR If patient has recent history of hives, ana Johnson syndome to penicillin or cophia	ag Resistant Organisms) urs x 72 hours totion or colonization with totion or colonization with talypical organisms inug Resistant xb x 72 hours b phytaxis or Stavans- laceportin:	Sputum grai laboratory in in "new prev fr patient is in bronchoscool Mini Bronch (Page rospin standard mik and attach d Laboratory On Biood cultur Legionella u Other Orders: Chest X-ray Check a tob AFTER the l	pecimen Order (select of n stain and outure (if a s the last 72 hours, use s unonia") hubated and no antibiot s (ohanges made in the i py cannot be performed: noalwoolar Lawage (Mini atory to perform, do not i oro requisition but write i usignated sticker) dens: ss x 2 finary antigen pulse oximetry ORPL n A.M. PALAT ORC stamycin serum concentivus	ane) putum has been processed by the tandard micro regulation but write to changes have been made in the ast 6 hours are acceptable) and -BAL) for quantitative culture hold antibiotics until obtained, use n'quantitative mini-BAL outsure" ise codmetry Qhours less X-ray in A.MC portable tration 2 hours and 6 hours is compiled and contact
	hours x 72 hours		or further dosing assist sment for Multi-dru	ance Ig Resistant Organisms
Inter Ser C. Risk factors for Multi-drug Resis (see Risk Assessment for Multi- Organisms) AND Intubated: Drug 1: Categoine g N OB hours x 72 hours Categoine g N O OR If patient has recent history of hives, and Johnson syndrome to periolilli or cophalocy Attroonam 2 g N OB hours x 72 hours Attroonam 2 g N OB hours x 72 hours Attroonam 2 g N OB hours x 72 hours Attroonam 7 g N OB hours x 72 hours Attroonam 9 g N OB hours x 72 hours or dosing weight) AND Drug 2: Classification of the State FOOTNOTES Adjust dose for renal dystanction. See Tufts-MC Tuft-MC Pharmacy website. Patient recontly received a B lactamer og throis considered as a second agent; however gran r frequently quincione restant. Prease call ANT for ourseleant requently quincione restant. Prease call ANT for the State Call and the renal failure and or CND considered as a second agent; however gran r	Ing Resistant Ab X 72 hours b bytwais or Stovens- orin: s kbhours x 72 hours b E rval dose (8 mg/kg, use ing (3 mg/kg, use idealhours x 72 hours b ours x 72 hours a Antibiotic Guidebook or ne or has history of any largeting ESBLs, optoficacin may be ogathe organisms are	hospital AND: Is courrent Has rood Has rood Has rood If answer is Yi if not intu- if intubati If NO – go to s Step 2: My pair Step 2: My pair Step 2: My pair Step 2: My pair Step 2: My pair Rocent h Recipient Has imme AND Criteria 2: TW 1. Requir 2. Three o 3. Inability Does NOT m Criteria 1 and Criteria 1 an	ty hospitalizad for 5 days wad antibiotics for 5 day unosuppressive disease 55 (lo 1 or more), then. balad – Order Set B ad – Order Set C dep 2 below lisent has pnoumonia an r drug resistant organis ospitalization 5 or more (s or more in the last 50 days OR or therapy
	with questions.			

Treatment algorithm for HAP/VAP/HCAP

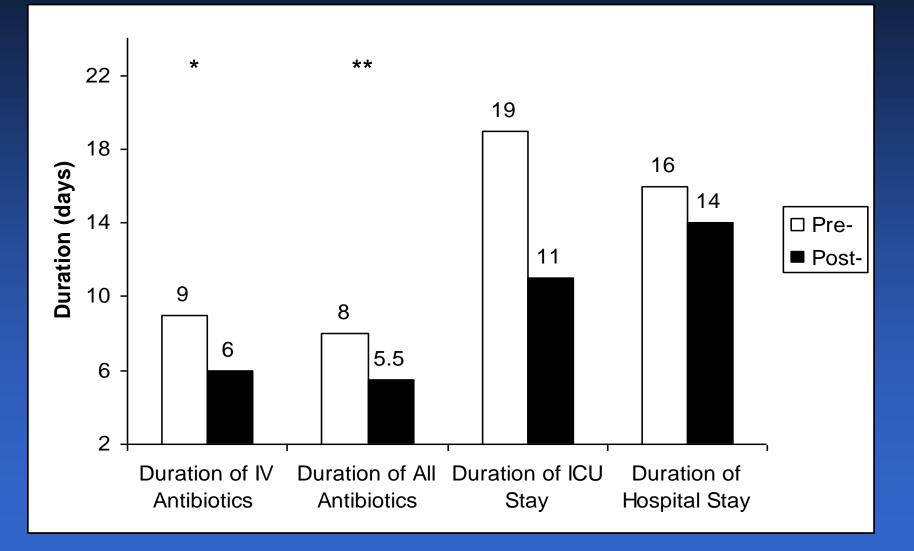




Benefits of a VAP/HAP Protocol at Tufts Medical Center



Duration of antibiotic use and hospital stay



(*) p=0.024, (**) p=0.01. Duration of ICU (p=0.97) and hospital (p=0.41) stay were not statistically different

Are you treating infection or colonization?

- Colonization = bacteria are present at the site sampled, but are not causing disease
- Contamination = bacteria are present in the laboratory sample, but not at the site
- NEITHER requires antibiotics!
- Cultures drawn through a central line should be avoided
- WBCs in the urine ≠ UTI; NO WBCs in the urine = NO UTI
- Candida is a frequent colonizer

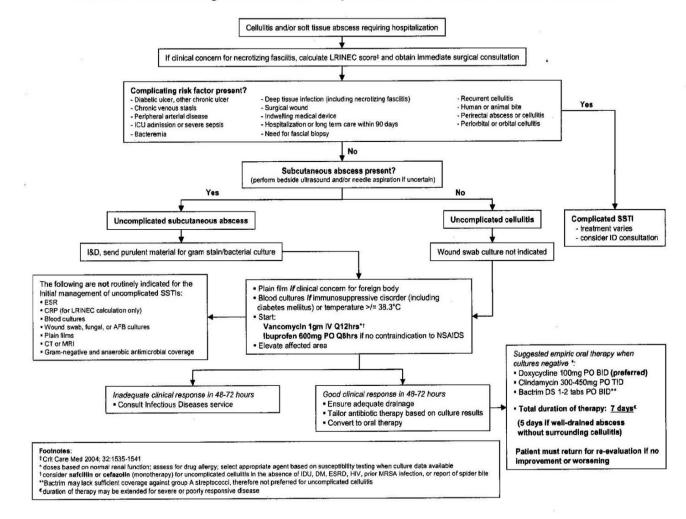
The government vs. the microbes Center for Medicare and Medicaid Services (CMS) Non Payment Conditions

- Object inadvertently left in after surgery
- Air embolism
- Blood incompatibility
- Catheter associated urinary tract infection
- Pressure ulcer (decubitus ulcer)
- Central line associated blood stream infection
- Surgical site infection- Mediastinitis after CABG, post orthopedic surgery, post bariatric surgery
- Certain types of falls and trauma

Working with ...

- Surgical Care Improvement Project (SCIP) to develop pre/post antibiotic guidelines
- Collaborate closely with Infection Control on the development of bundles for the prevention of HAIs
- Work with hospitalists and nursing specialists (i.e. wound care nurses, ostomy nurses, etc) to develop understanding of colonization vs infection

Guideline for the Management of Adults Hospitalized with Cellulitis or Cutaneous Abscess



Jenkins TC, Knepper BC, Sabel AL, et al. Decreased antibiotic utilization after implementation of a guideline for inpatient cellulitis and cutaneous abscess. *Arch Intern Med.* 2011;doi:10.1001/archinternmed.2011.29.

Route: IV or PO

- Many drugs are highly available in the PO form
- The oral route is less expensive, allows for earlier removal of lines and decreased length of stay
- Patients on oral antimicrobials with clearly documented reasons for continued hospital stay are not at risk for claims rejection by payors

Tufts Pharmacy IV to PO switch program

 Pharmacists may dispense, and nurses may administer to inpatients equivalent oral doses of certain highly bioavailable IV medications

Criteria:

- Functioning GI tract (taking oral fluids and medications or enteral feeds)
- No evidence of severe nausea, diarrhea, GI bleeding, high NG output, etc
- Normal stable vital signs
- WBC between 4,000 and 11,000 cells /microliter
- No life threatening infection

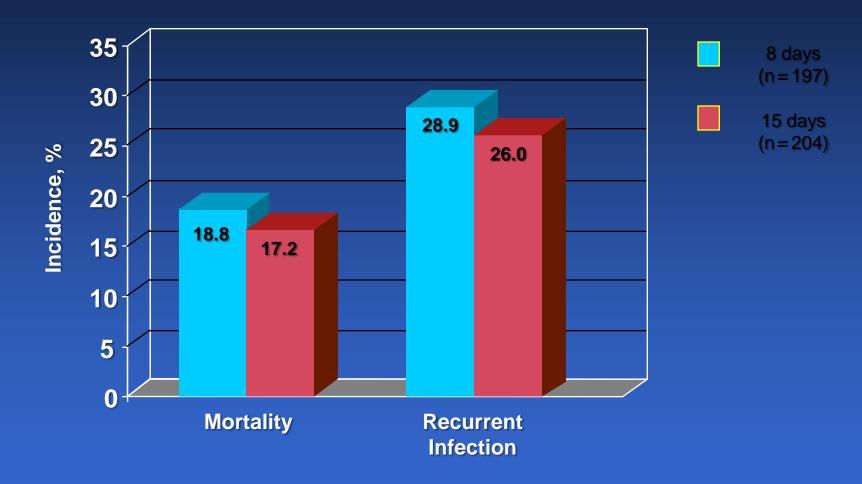
Pharmacists driven initiatives

- Pharmacokinetic dosing or monitoring of aminoglycosides or vancomycin
 - automatic dosing of AG's and vanco by pharmacy rather than clinicians
- Automatic Drug conversion
 - Ex: transfers from outside hospital automatically transitioned to formulary drugs
- Alternative dosing regimens
 - Continuous or prolonged infusions of ß-lactam
 - Increased frequency of dosing (e.g., meropenem)

Time: Stop antibiotics as early as possible

- "We know everything about antibiotics except how much to give."— Maxwell Finland (one of the forefathers of antibiotic therapy)
- Longer is not better
- CAP guidelines and clinical trials suggest good results with 5 days of antibiotics if patient meets clinical criteria
- Intra-abdominal infection guidelines: 4-7 days unless difficult to control the source of infection

Comparison Between 8-Day and 15-Day Treatments for VAP



Chastre J et al. JAMA. 2003;290:2588-2598.

Diagnostic and Pathogen Identification Techniques

- Biomarkers
 - Procalcitonin
 - CRP
- PNA FISH
- PCR
- E-test of patient samples

Decision Support for Antimicrobial Stewardship

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Med Rec Pilot Program *		
Keppra IV *	Q	
Anticoagulation * Argatroban or Lepirudin *	Q.	
Warfarin Daily Monitoring - TEST *		
Vitamin K Use *		
Heparin Dosing Study *		
Antimic Stewardship *	Q	
Daptomycin without CK Check *	Q	
Vanco Trough > 20 or < 10 *	Q	
Metronidazole AND Other Drugs with Anaerobic Activ *	Q	
C diff patients *	Q.	
Prolonged Antibiotic Therapy *	Q	
Antimicrobial Therapy *	Q	
Daptomycin and Linezolid Patients * Fluoroquinolone Patients *	, and the second s	
Cefepime and Ceftriaxone Patients *		
Antifungal Patients *		
Carbepenem Patients *	Q	
Zosyn Patients *	Q	
Med/Surg *	Q	
Enoxaparin and Fondaparinux Dosing *	Q	
IV to PO - Anti-infectives *	Q.	
IV to PO - Other *	Q.	~
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🖉 Order picklists -- Webpage Dialog

		57. M MD#0000/		
		57y M MR#22885	44	Session Details StartDateTime
Selected Visit	Discharge			
Other Visit				
No Visit				Ordering Dr.
Common	Patient Based	Order Sets	Search	Lisa Davidson (159085)
				Written
	Common Medica			Ordering Device
		crobials - No Restrictions		LAPTOPDAVIDSON1
All Meds Labs		crobials - Restricted Medications		TargetCosigner1
Favorites		Jobiais - Resulcted Medications		
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1 - MEDICINE ORDER SETS				
Adolescent				
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Allergy	Diuretics			
Cardiac Transplant				
Cardiology Adult		hloride Oral Preps		
CT Surg		Diabetic Medications		
СТИ	Taper Dosing	-		
CVVH Orders	Vitamin & Mir	Vitamin & Mineral Medications		
Dermatology	Stess Ulcer Prophylaxis Medications			
Diabetes	Bowel Management Medications			
ED	Lidocaine Medications			
Endocrine	-			
Endocrinology Pedi				
Specialty				
				The completed details will be applied to a
Add to Order Session	Close		Help	applicable orders.

Computer Surveillance and Decision Support in Antimicrobial Stewardship

- Sentri7
- SafetySurveillor
- TheraDoc
- Computerized physician order entry
- Benchmarking and local antimicrobials point prevalence surveys (state may consider doing this)

Behind the scenes: Infection Control and AMT

PREMIER SafetySurveillor™ Infection Control • Pharmacy

- Web-based infection control surveillance system/antimicrobial management program
- ADT, Microbiology, and Pharmacy data interfaces
 - OR data and Radiology data are in progress
- Ability to alert AMT to inappropriate antimicrobial use in real time and evaluation of antibiotic use trends.

Conclusions

- Antimicrobial resistance is a major patient safety and patient care issue, LIVES are at stake.
- Healthcare providers have a moral obligation to ensure that the currently available antimicrobials, as well as those yet to be developed remain the powerful tools that penicillin was in the 1940
- Antimicrobial stewardship strategies are the best way to achieve this goal.

The Future of Stewardship = YOU

- Appropriate antibiotic use is a patient safety priority
- Antibiotics are a shared resource and becoming a scarce resource.
- Inappropriate antibiotic use and resistant infections = Billions of \$\$ in excess healthcare costs
- To combat resistance: Think globally, act locally