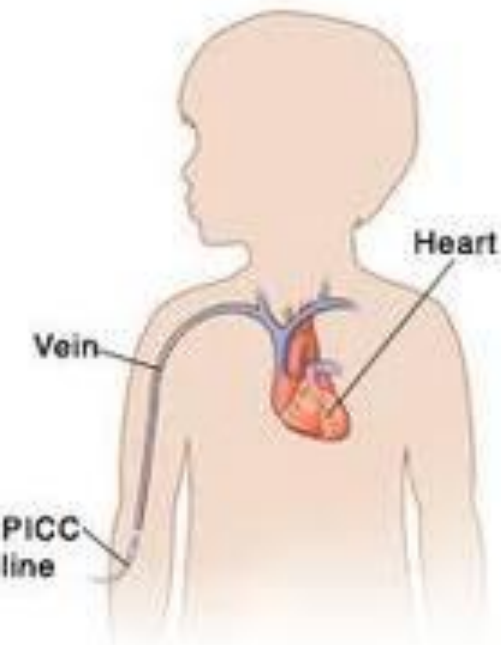


PICC or PO?

The Case for Rational Antimicrobial Transitions



James K. Todd, MD

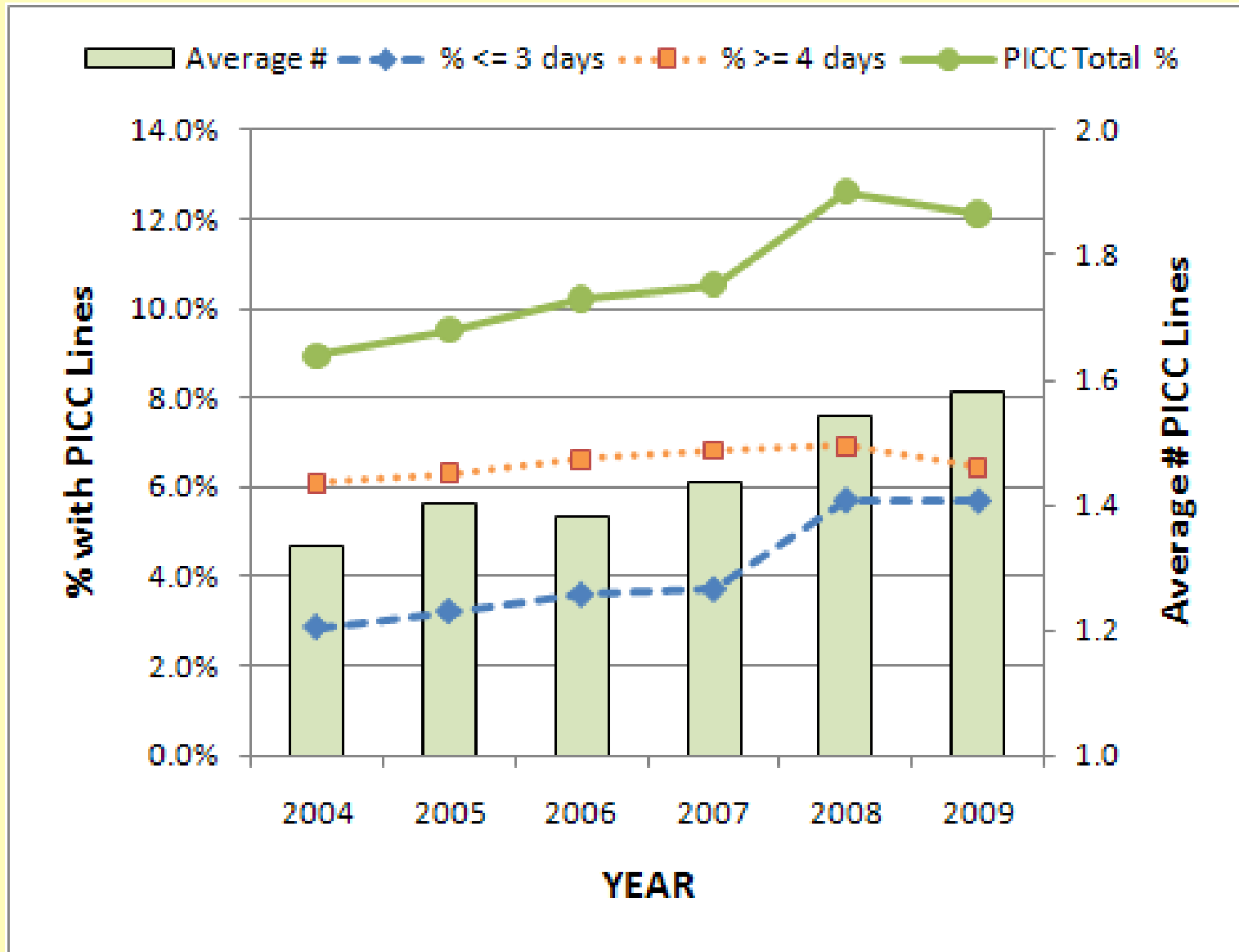
Disclosure: *“No conflicts ...
(except with the rest of my ID colleagues)”*



PICC-ing: An International Controversy



PICC Line Use at TCH



PICC Line (≤ 3 days) Correlates

Admission	Relative Risk	95% CI
Severity	1.93	1.84 – 2.0
# IV Drugs Day of Discharge	1.19	1.16 – 1.20
Year (2004 – 2009)	1.21	1.18 – 1.24
<i>Not significant (Length-of-stay, PO drugs)</i>		

Readmission Odds ratio = 1.20 (95% CI: 1.07 – 1.35)

ID Diseases “Discharged” with PICC Line (<= 3 days)

Principal Dx Code - Title (ICD-9)

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid				
0020 - Typhoid fever	1	.6	.6	.6
0038 - Salmonella infection NEC	1	.6	.6	1.2
0210 - Ulcerogland tularemia	1	.6	.6	1.8
0362 - Meningococcemia	5	3.0	3.0	4.8
0380 - Streptococcal septicemia	2	1.2	1.2	6.0
03811 - MSSA septicemia	1	.6	.6	6.6
03811 - Staph aureus septicemia	3	1.8	1.8	8.4
03812 - MRSA septicemia	1	.6	.6	9.0
03819 - Staph septicemia NEC	3	1.8	1.8	10.8
0382 - Pneumococcal septicemia	3	1.8	1.8	12.6
03840 - Gram-neg septicemia NOS	2	1.2	1.2	13.8
03841 - H. influenzae septicemia	1	.6	.6	14.4
03842 - E. coli septicemia	3	1.8	1.8	16.2
03843 - Pseudomonas septicemia	1	.6	.6	16.8
03849 - Gram-neg septicemia NEC	1	.6	.6	17.4
0388 - Septicemia NEC	3	1.8	1.8	19.2
0389 - Septicemia NOS	10	6.0	6.0	25.1
04082 - Toxic shock syndrome	5	3.0	3.0	28.1
05479 - H simplex comp NEC	3	1.8	1.8	29.9
0548 - H simplex w comp NOS	1	.6	.6	30.5
0654 - Mosquito-borne hemor fev	1	.6	.6	31.1
0785 - Cytomegaloviral disease	2	1.2	1.2	32.3
0790 - Adenovirus infect NOS	1	.6	.6	32.9
07989 - Viral infection NEC	1	.6	.6	33.5
07999 - Viral infection NOS	2	1.2	1.2	34.7
1125 - Disseminated candidiasis	2	1.2	1.2	35.9
1179 - Mycoses NEC & NOS	2	1.2	1.2	37.1
1369 - Infect/parasite dis NOS	2	1.2	1.2	38.3
7806 - Fever	4	2.4	2.4	40.7
78060 - Fever NOS	3	1.8	1.8	42.5
78552 - Septic shock	1	.6	.6	43.1
78559 - Shock w/o trauma NEC	1	.6	.6	43.7
7907 - Bacteremia	41	24.6	24.6	68.3
9583 - Posttraum WND infect NEC	2	1.2	1.2	69.5
99590 - SIRS NOS	1	.6	.6	70.1
99669 - Infect due to device NEC	1	.6	.6	70.7
99851 - Infected postop seroma	3	1.8	1.8	72.5
99859 - Postop infection NEC	46	27.5	27.5	100.0
Total	167	100.0	100.0	

• Major DRGs:

- Postop Infection 27.5%
- Bacteremia 24.6%
- Septicemia 6.0%

• Quickie Validation:

- Cases (most recent) 10
 - PICCs 9
 - Organism 6
 - No focal culture 3
 - PO Alternative 7

Summary of TCH's PICC Line Epidemiology

- TCH is putting an increasing number of PICC lines into an increasing number of children.
 - The number of PICC lines within 3 days of discharge is increasing. These children are more likely to:
 - Have a higher severity of illness
 - Have an infectious disease diagnosis
 - *Go home with a PICC line on IV antibiotics but ...*
 - *Have an oral alternative because an organism was isolated or they responded to a single initial antibiotic.*
 - Be readmitted

Antimicrobial Stewardship

- Since 2002, the Belgian Antibiotic Policy Coordination Committee (BAPCOC) has supported the development of AMTs in Belgian hospitals with policy guidance and federal funding for antibiotic managers.
 - Antibiotic stewardship tools used by AMTs included:
 - hospital antibiotic formulary (96.3%)
 - practice guidelines for antibiotic therapy and surgical prophylaxis (91.6% and 96.3%);
 - list of 'restricted' antimicrobial agents (75.9%);
 - concurrent review of antibiotic therapies (64.2%);
 - de-escalation of therapy after a few days (63.9%);
 - **sequential intravenous/oral therapy for antibiotics with equivalent bioavailability (78.7%);**
 - dedicated antimicrobial order forms (36.1%);
 - automatic stop of delivery (43.5%);
 - analysis of antibiotic consumption data (96.2%);
 - analysis of microbial resistance data (89.8%).

*Van Gastel, E, M Costers, et al. (2010). "Nationwide implementation of antibiotic management teams in Belgian hospitals: a self-reporting survey." J Antimicrob Chemother **65(3): 576-80.***

Osteomyelitis: PO as good as PICC

- Children aged 2 months to 17 years diagnosed with acute osteomyelitis between 2000 and 2005 at 29 freestanding children's hospitals in the United States
- RESULTS:
 - 1,969 children met inclusion criteria
 - 1,021 received prolonged intravenous therapy and 948 received oral therapy.
 - The use of prolonged intravenous therapy varied significantly across hospitals (10%-95%).
 - The treatment failure rate was:
 - 5% (54 of 1021) in the prolonged intravenous therapy group
 - 4% (38 of 948) in the oral therapy group.
 - Thirty-five (3.4%) children in the prolonged intravenous therapy group were readmitted for a catheter-associated complication.

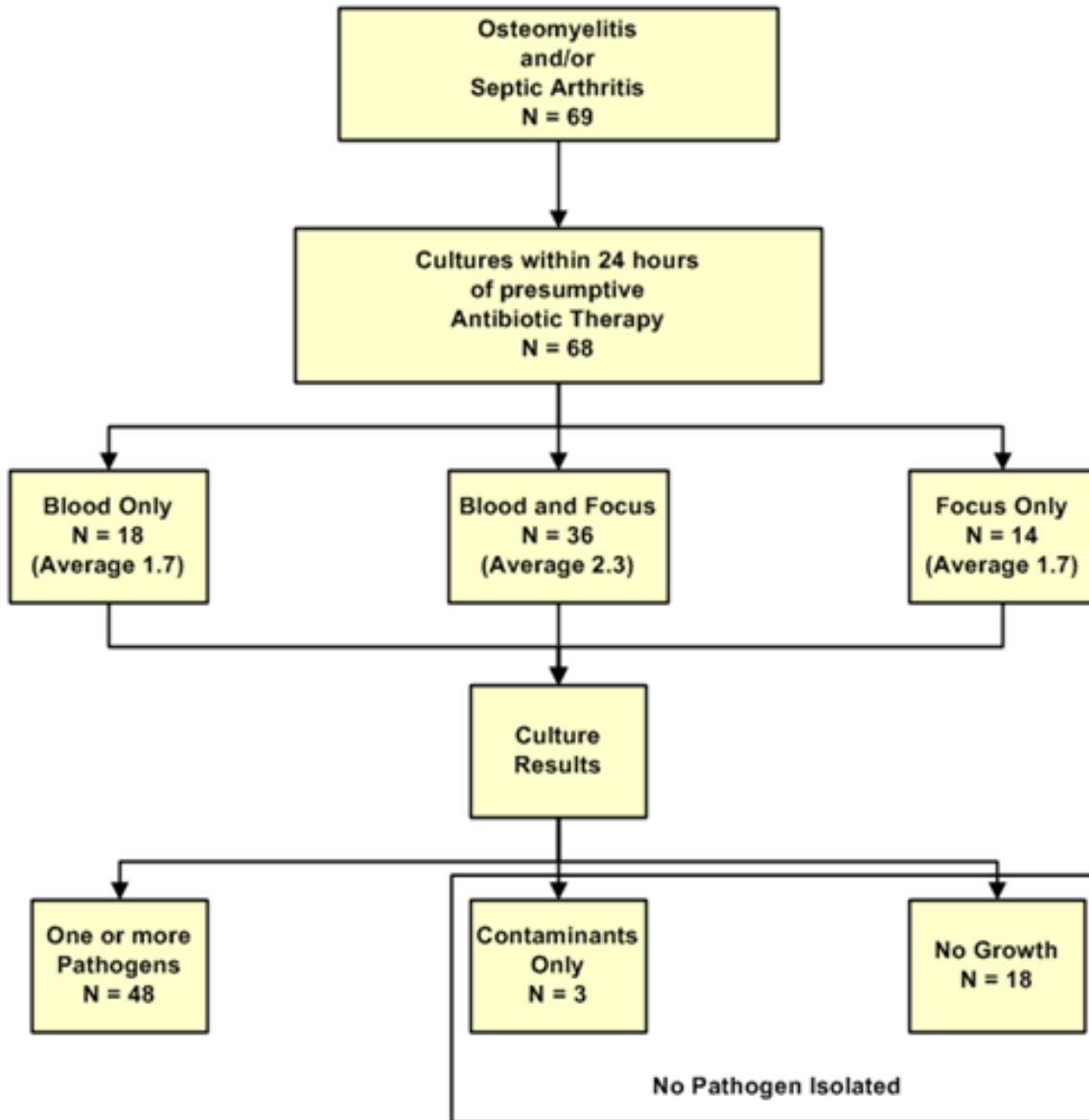
Zaoutis, T, AR Localio, et al. (2009). "Prolonged intravenous therapy versus early transition to oral antimicrobial therapy for acute osteomyelitis in children." *Pediatrics* **123(2): 636-42.**

PICC Risks

- A total of 441 PICCs were inserted in 390 children.
- Treatment of infectious disease (46%) was the most frequent reason for PICC insertion.
- One hundred twenty-nine (29%) PICCs were removed for complications.
 - Occlusion (7%),
 - Accidental displacement (8%),
 - Suspicion of sepsis (8%)
 - Only 2% of PICCs had documented catheter-associated sepsis.

Thiagarajan, RR, C Ramamoorthy, et al. (1997). "Survey of the use of peripherally inserted central venous catheters in children." Pediatrics 99(2): E4.

TCH Experience



Need to Get Blood and Focus Cultures

Culture Source	N	Pathogen Positive	No Pathogen
Blood Only	18	11 (61.1%)	7
Focus Only	14	10 (71.4%)	4
Blood and Focus:	36	26 (72.2%)	10
<i>Blood only</i>		4	
<i>Focus only</i>		17	
<i>Blood and Focus</i>		5	

Sensitivity for one or more pathogen, blood only: $20/54 = 37.0\%$ *

Sensitivity for one or more pathogen, focus only: $32/50 = 64.0\%$ *

* $P = 0.006$

Culture Effect

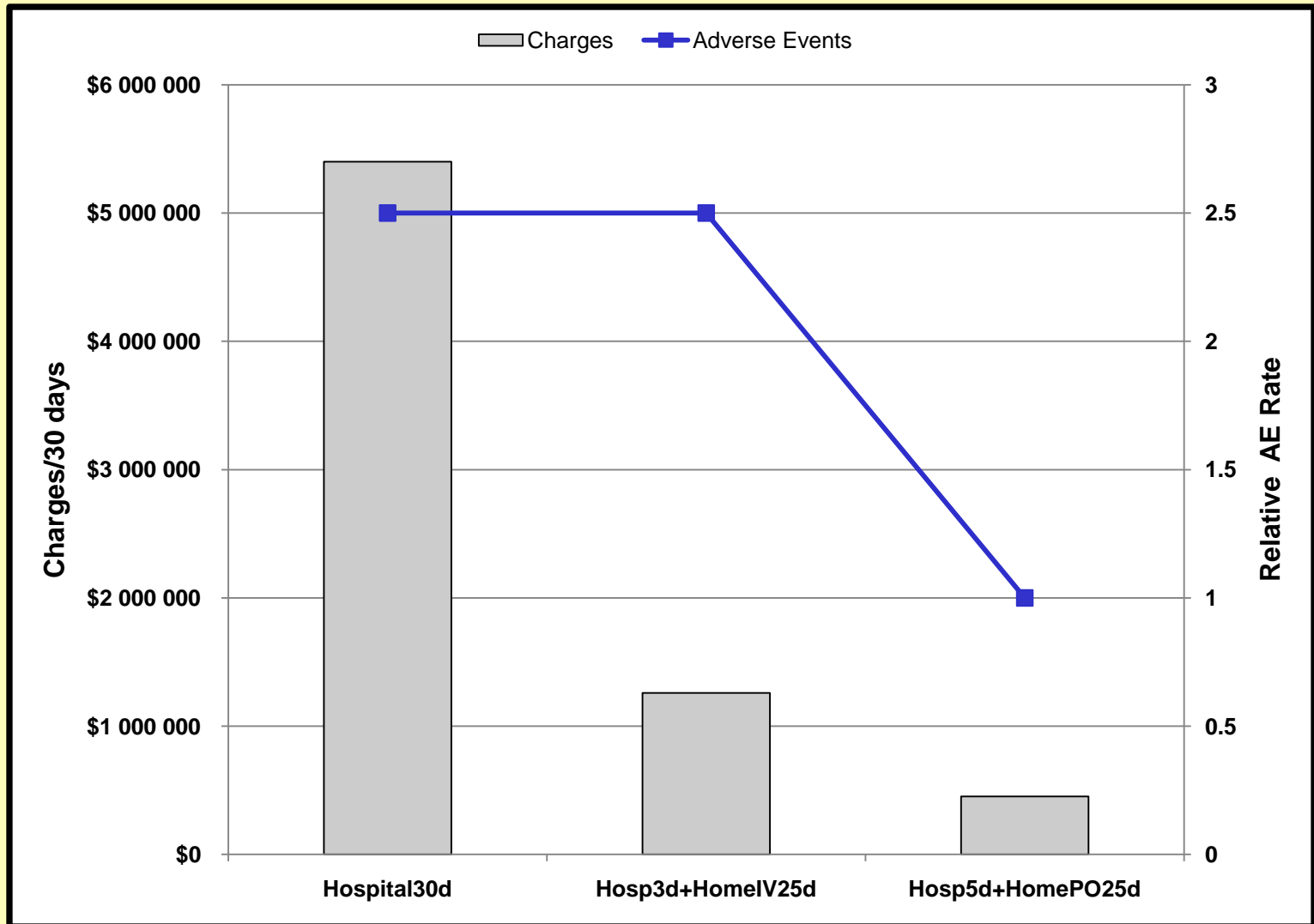
- 39 of 48 (81.3%) who grew a pathogen were sent home on a single antibiotic as compared to only 12 of 21 (57.1%) who did not grow a pathogen ($p = 0.036$, Chi-square).
- 29 of 48 (60%) who grew a pathogen went home on parenteral antibiotics even though 40 of those 48 (83.3%) grew a pathogen (MSSA, *S. pneumoniae*, GAS) potentially amenable to oral antibiotic therapy.
- No difference in outcome if bacteremia and treated orally

Home Therapy Outcomes

Home therapy	Route of AB			Number of Antibiotics		
	PO	IV	Significant Difference	Single	Multiple	Significant Difference
Number of Cases	37	32		52	17	
Rehospitalization, n (%)	3 (8.1%)	2 (6.3%)	ns	2 (3.8%)	3 (17.6%)	ns
Total Adverse Events, n (%):	7 (18.9%)	15 (46.9%)	2.5 (1.2, 5.3)*	13 (25%)	9 (52.9%)	2.1 (1.1, 4.1)*
Adverse Drug Reaction, n (%):	7 (18.9%)	8 (25.0%)	ns	9 (17.3%)	6 (35.3%)	ns
Adverse Catheter Events, n (%):	0	7 (21.9%)	@	4 (7.7%)	3 (17.6%)	ns
Duration of Antibiotics, days	52.7	81.4	28.7 (5.8, 51.6)**	63.9	73.8	ns
Duration of Hospitalization, days	5.9	7.3	ns	5.7	8.2	ns
Average number of antibiotics	1.2	1.4	ns	1.0	2.1	@

*Relative Risk Ratio (95% confidence Interval)
 ** Mean Difference (95% confidence interval) by t-test for independent samples
 @ Significantly different by definition

Estimated Charges: Osteomyelitis, 100 cases



IV to PO switch therapy

- Antibiotics ideal for oral administration are those that have the appropriate spectrum, high degree of activity against the presumed or known pathogen, and have good bioavailability.
 - Oral antibiotics with high bioavailability, that is $>$ or $=$ 90% absorbed, achieve serum/tissue concentrations comparable to IV administered antibiotics at the same dose.
- Initial IV therapy is appropriate in patients who are in shock/have impaired intestinal absorption, but after clinical defervescence, completion of therapy should be accomplished with oral antibiotics.
- The trend in treating serious systemic infections entirely with oral antimicrobial therapy will continue, and is clearly the wave of the future.

Childhood Pneumonia

- Multicentre, randomised, open-label equivalency study was undertaken at tertiary-care centres in eight developing countries in Africa, Asia, and South America.
 - Children aged 3-59 months with severe pneumonia were admitted for 48 h and, if symptoms improved, were discharged
 - Injectable penicillin and oral amoxicillin were equivalent for severe pneumonia.
- Potential benefits of oral treatment include decreases in (1) risk of needle-borne infections; (2) need for referral or admission; (3) administration costs; and (4) costs to the family.

Addo-Yobo, E, N Chisaka, et al. (2004). "Oral amoxicillin versus injectable penicillin for severe pneumonia in children aged 3 to 59 months: a randomised multicentre equivalency study." Lancet 364(9440): 1141-8.

Childhood Pneumonia

- 2037 children aged 3-59 months with severe pneumonia were randomly allocated to:
 - initial hospitalization and parenteral ampicillin (100 mg/kg per day in four doses) for 48 h, followed by 3 days of oral amoxicillin (80-90 mg/kg per day; n=1012)
 - home-based treatment for 5 days with oral amoxicillin (80-90 mg/kg per day in two doses; n=1025).
- There were 87 (8.6%) treatment failures in the hospitalized group and 77 (7.5%) in the ambulatory group (risk difference 1.1%; 95% CI -1.3 to 3.5) by day 6.
- Home treatment with high-dose oral amoxicillin is equivalent to currently recommended hospitalization and parenteral ampicillin for treatment of severe pneumonia without underlying complications, suggesting that WHO recommendations for treatment of severe pneumonia need to be revised.

Hazir, T, LM Fox, et al. (2008). "Ambulatory short-course high-dose oral amoxicillin for treatment of severe pneumonia in children: a randomised equivalency trial." *Lancet* **371(9606): 49-56.**

Pyelonephritis too!

- 306 children 1 to 24 months old with fever and urinary tract infection
- Oral cefixime for 14 days (double dose on day 1) or initial intravenous cefotaxime for 3 days followed by oral cefixime for 11 days.
- Treatment groups were comparable regarding demographic, clinical, and laboratory characteristics.
 - Repeat urine cultures were sterile within 24 hours in all children,
 - Mean time to defervescence was 25 and 24 hours for children treated orally and IV
 - Reinfections occurred in 4.6% of children treated orally and 7.2% of children treated IV,
 - Mean extent of scarring was approximately 8% in both treatment groups.
 - Mean costs were at least twofold higher for children treated IV (\$3577 vs \$1473).
- Oral cefixime can be recommended as a safe and effective treatment for children with fever and urinary tract infection. Use of cefixime will result in substantial reductions of health care expenditures

Hoberman, A, ER Wald, et al. (1999). "Oral versus initial intravenous therapy for urinary tract infections in young febrile children." Pediatrics 104(1 Pt 1): 79-86.

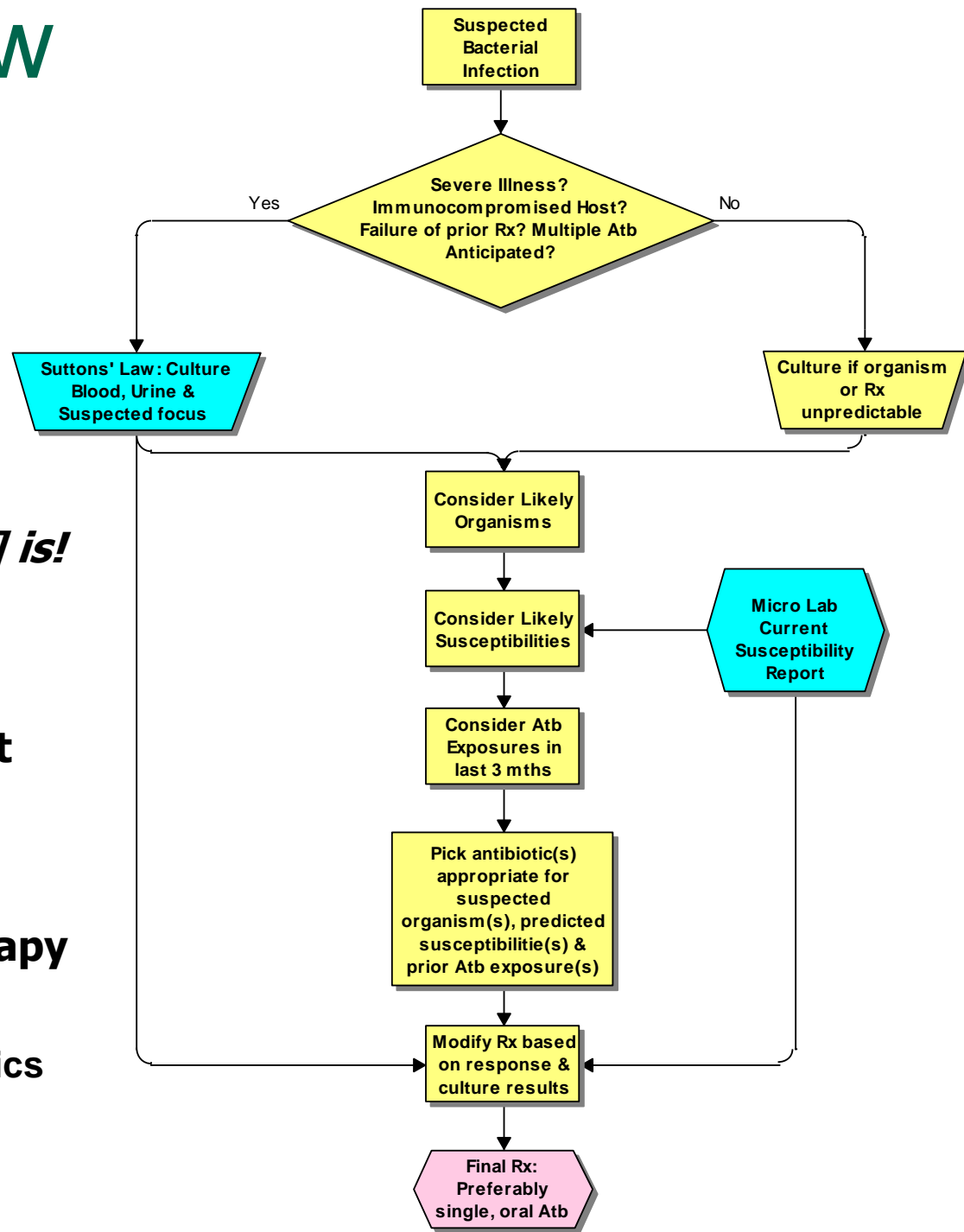
Sutton's Law



Culture where the [Infection] is!

- **Serious Infections**
- **Failure of prior treatment**
- **Immune compromised hosts**
- **Especially if empiric therapy includes:**

- **Broad-spectrum antibiotics**
- **Multiple antibiotics**



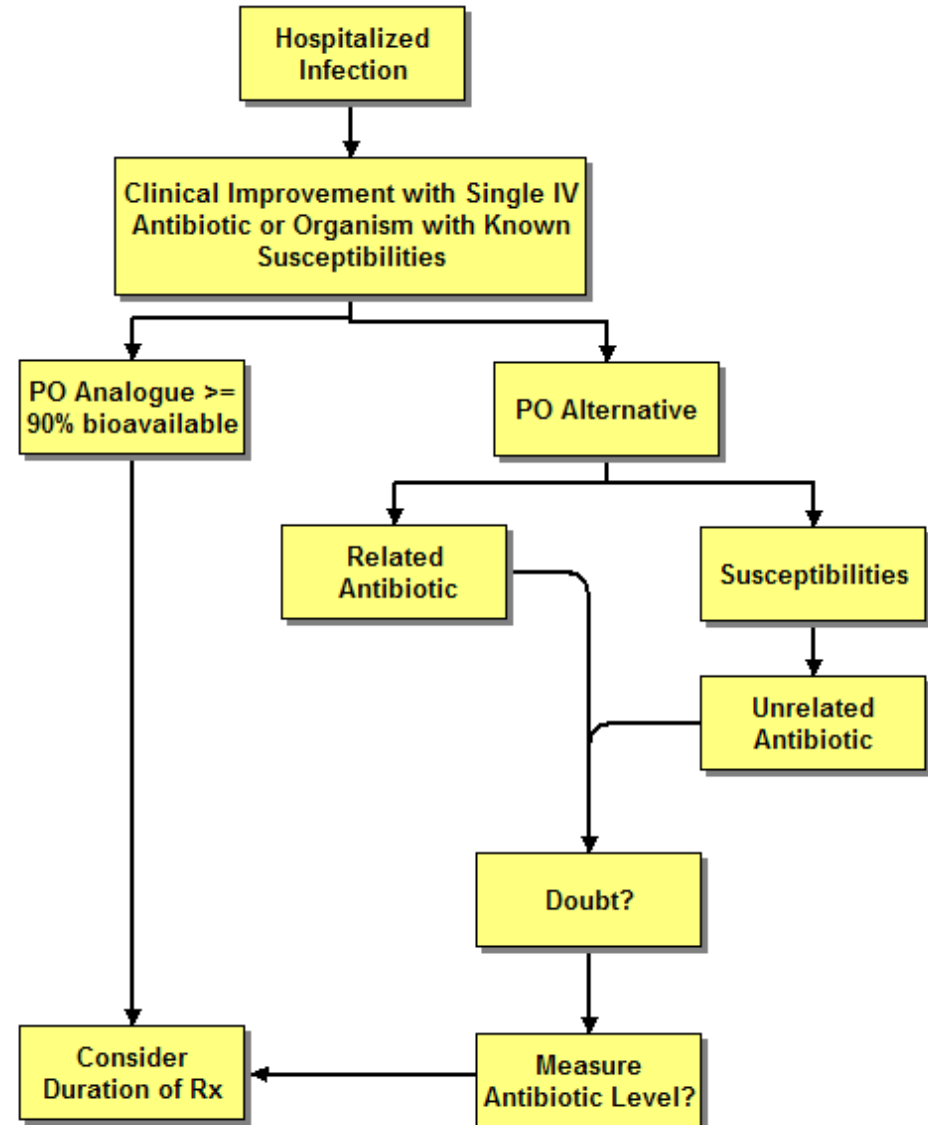
TCH “IV to PO” Policy

- Indications:

- Clinically improved
- Tolerating oral intake
- Able to obtain Meds
- Known organism or on single antibiotic

- Antibiotic IV to PO Options

- Analogue: same drug, PO formulation, $\geq 90\%$ bioavailability
- Alternative:
 - Related: same class, PO formulation, high bioavailability
 - Unrelated: different class, PO formulation, high bioavailability



Most Antimicrobials Have Oral Alternatives

Antimicrobial Formulations at Children's Hospital Colorado	IV	Oral			Monitor	DOSE Information		Antimicrobial Levels		
	IV Cost	Oral Cost	Adjust for Food	Bioavailability (Oral Alternatives)**		IV	PO	Level done at:	Turn-around time	Normal Levels
Antibiotics										
Miscellaneous										
AZTREONAM	\$\$\$\$\$			Check Susceptibilities	R	50 mg/kg/dose q8h, CF: 50 mg/kg/dose q6h (max 2 gm/dose)				
CLINDAMYCIN	\$\$\$	\$(cap) \$\$\$\$ (susp)		90%		10 mg/kg/dose Q6-8h (max 4.8 gm/day)	10 mg/kg/dose TID - QID (max 1.8 gm/day); 75, 150, 300 mg caps, 75 mg/5 ml sol	Focus	3-6 days	
LINEZOLID	\$\$\$\$\$	\$\$\$\$	w/wo	100%	CBC	Children less than 5 yrs: 10 mg/kg/dose q8h; 5 yrs and greater: 10 mg/kg/dose Q12h (max 600 mg/dose); Do not administer with MAOI's	Children less than 5 yrs: 10 mg/kg/dose q8h; 5 yrs and greater: 10 mg/kg/dose Q12h (max 600 mg/dose); 300, 600 mg tabs, 100 mg/5 ml susp	NJH	5-7 days	
METRONIDAZOLE	\$\$	\$	w/wo	100%	R,L,CBC	30-50 mg/kg/day divided TID-QID (max 1000 mg/dose)	30-50 mg/kg/day divided TID-QID (max 1000 mg/dose); 62.5, 125, 250, 500 mg tabs, 50 mg/ml susp	Focus	3-6 days	
QUINUPRISTIN-DALFOPRISTIN	\$\$\$\$\$			Check Susceptibilities	L	7.5 mg/kg/dose q8h				
RIFAMPIN	\$\$\$\$	\$\$	wo	95%	L	10-20 mg/kg/day divided QD-BID (max 600 mg/dose)	10-20 mg/kg/day divided QD-BID (max 600 mg/dose); 150, 300 mg caps, 50 mg/ml susp			
SULFAMETHOXAZOLE-TRIMETHOPRIM	\$\$-\$\$\$	\$	w/wo	90-100%	R,L,CBC	Minor infection: 6-10 mg/kg/day divided q12h; Serious infection: 15-20 mg/kg/day divided q6h	Minor infection: 6-10 mg/kg/day divided q12h; Serious infection: 15-20 mg/kg/day divided q6h; 100-20, 200-40, 400-80(ss), 800-160(dose)mg tabs, 200-	Mayo	2-8 days	> 2 ug/ml

Practical Magical Thinking

