

## Prevention of Surgical Site Infections (SSI): Beyond SCIP

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## Topics to Discuss: BEYOND SCIP

- Dose Optimization
  - Obesity
  - Surgical duration
- Surgical checklist
- Chlorhexidine antiseptics
- Supplemental oxygen
- Mechanical Bowel Prep



## Dose Optimization

Pharmacokinetics 101

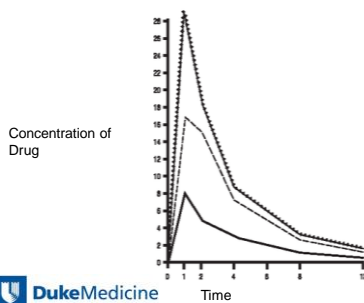


## What is a “Half-Life” ( $t_{1/2}$ )”

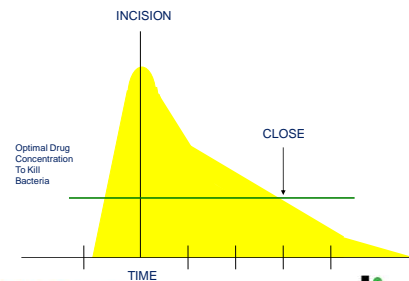
- The period of time required for the concentration or amount of drug in the body to be reduced by one-half
  - Marker for duration of action of a drug
- Typically considered in relation to the amount of the drug in plasma
- A drug’s plasma half-life depends on how quickly the drug is eliminated
  - Clearance: removal of a drug from plasma
  - Volume of distribution: distribution of the drug in various body tissues



## Half-Life



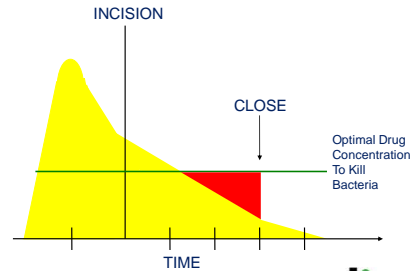
## Prophylaxis: Ideal Scenario



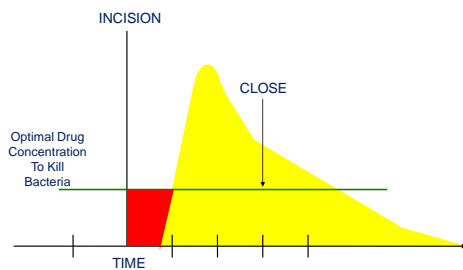
## Common Problems (Review)

- The antibiotic is given too soon before the incision is made
- The antibiotic is not initiated until after the incision is made, or not until after the operation is complete

## Prophylaxis: Too Early



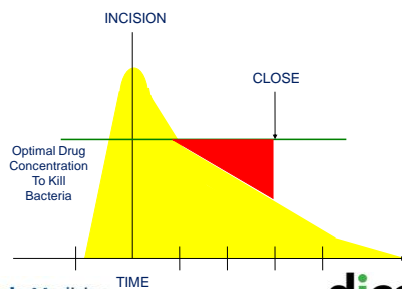
## Prophylaxis: Too Late



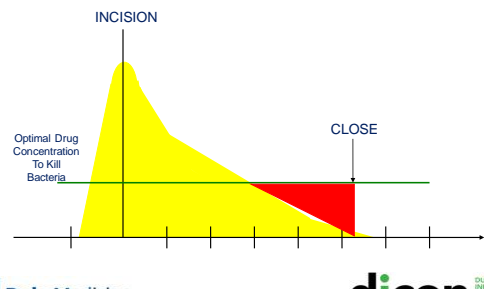
## Obesity and Surgical Duration

- Both significantly impact antibiotic levels in tissue
- Obesity is a risk factor for SSI
- Prolonged surgical duration is risk factor for SSI

## Prophylaxis: Obesity



## Prophylaxis: Long Procedure



# Overcome Obesity



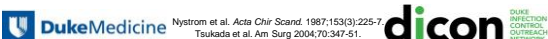
## Obesity is a Risk Factor for SSI

- Numerous studies have shown that obesity is an independent risk factor for SSI
  - Increased rates of SSI of 2 to 6 times higher than non-obese patients
- Patients often have other co-morbid illnesses such as diabetes mellitus and CV disease



## Obesity is a Risk Factor for SSI

- Why? Likely combination of technical and pharmacologic factors
  - Poorly vascularized tissue
    - Strong correlation between amount of SQ/intra-abdominal fat and risk of SSI
    - Decreased tissue oxygenation among obese patients
  - Creation of dead space
    - Fat > 3.4 cm
  - Inadequate dosing of peri-operative antimicrobial prophylaxis




## Obesity is a Risk Factor for SSI

- Case-control study of patients undergoing laminectomy

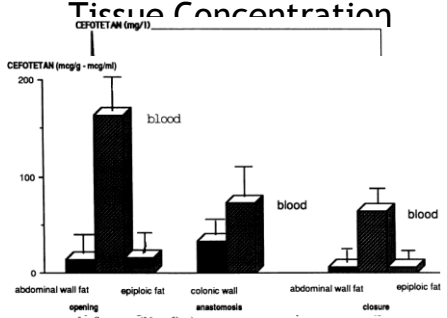
Factors in model	OR (95% CI)	P
Nonwhite race	2.5 (0.88-7.1)	.08
BMI >35	7.1 (1.8-28.3)	.005
Diabetes	4.2 (1.1-16.3)	.04
Noncervical laminectomy	6.7 (1.4-33.3)	.02

NOTE. BMI, body mass index; CI, confidence interval; OR, odds ratio.

- Obesity was an independent risk factor for SSI (risk 7-fold higher)



### Tissue Concentration



CEFOTETAN (mg/g - mg/ml)


abdominal wall fat opening for *S. aureus* (16 mg/liter)

epiopic fat

colonic wall anastomosis

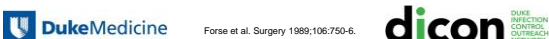
abdominal wall fat closure

epiopic fat



## Impact of Increasing Dose

- Trial comparing 1g cefazolin v. 2g cefazolin among obese patients undergoing bariatric surgery
- Baseline rates of infection
  - 16.5/100 in obese
  - 2.5/100 in non-obese (undergoing other clean-contaminated surgery)
- Tissue and serum concentrations were lower in patients who received 1g (p<0.0001)
- Rate decreased to 5.6/100 procedures in obese patients



## Dosing: Expert Recommendations

- SIP/SCIP: “The drug should be given in an adequate dose based on patient weight, adjusted dosing weight, or body mass index”

## Re-Dosing

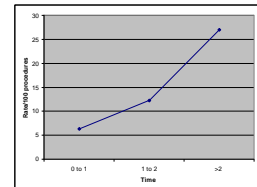
### Filling the Tank

## Surgical Duration is a Risk Factor for SSI

- Direct relationship between operative time and risk of SSI
- Risk greatly increases after 2 hours
  - In general, rate doubles with each additional hour of operative time
- NHSN uses “T-time” to denote when high risk period begins
  - 75% of average time for a specific procedure
- More data to support re-dosing than weight-based dosing

## Correlation between Time and Risk

- Multicenter, prospective study
- Abdominal surgery in 4700 patients
- Rates depended on length of procedure:
  - <1 hour - 6.3/100
  - 1-2 hours - 12.2/100
  - >2 hours - 27.7/100 procedures



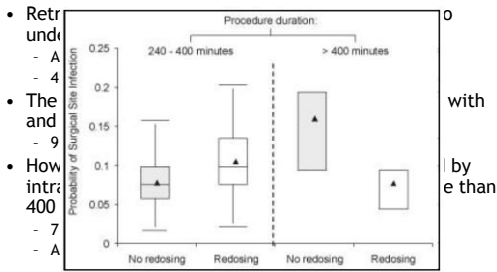
## Correlation between Time and Risk

- Recent trial looking at ertapenem vs. cefotetan for colorectal surgery
  - RCT, double blind
  - 1002 patients
- In multivariable analysis, “increased duration of surgery” associated with risk of SSI
  - aOR 1.34 (1.11-1.62); p=0.003

## Re-Dosing: Data Show it Works

- Review of published literature
- Analysis of 801 patients undergoing clean-contaminated operations:
  - 1g cefazolin
  - 1g cefazolin + 1g 3 hours later
- If procedure > 3 hours, then rate of SSI reduced from 6.1 to 1.3

## Re-Dosing: Cardiac Surgery?



## Re-Dosing: Expert Recommendations

- SIP/SCIP: "administration should be

Antimicrobial	Half-life normal renal function (h)	Half-life end-stage renal disease (h)	Recommended infusion time (min)	Standard intravenous dose (g)	Weight-based dose recommendation* (mg)	Recommended re-dosing interval (h)
Aztreonam	1.5-2	6	3-5†	1-2	Maximum 2 g (adults)	3-5
Ciprofloxacin	3.5-5	5-9	60	400 mg	400 mg	4-10
Cefazolin	1.2-2.5	40-70	3-5†	1-2	20-30 mg/kg 1 g < 80 kg; 2 g ≥ 80 kg	2-5
Cefuroxime	1-2	15-22	3-5†	1.5	2 g ≥ 80 kg 50 mg/kg	3-4
Cefamandole	0.5-2.1	12.3-18†	3-5†	1	15-60g	3-4
Cefoxitin	0.5-1.1	6.5-23	3-5†	1-2	20-40 mg/kg	2-3
Cefotetan	2.8-4.6	13-25	3-5†	1-2	20-40 mg/kg	3-6
Clindamycin	2-5.1	3.5-5.0†	10-60 (Do not exceed 30 minutes)	600-900 mg	<10 kg: at least 37.5 mg ≥10 kg: 3-6 mg/kg	3-6

## Surgical Safety Checklist

## Surgical Safety Checklist

- Checklists
  - Proven method for prevention of complications
    - Change system AND individual behavior
  - CLABSI
- New checklist for surgical care
  - 19 item surgical safety checklist
    - Sign in, Time out, Sign out
  - 8 institutions throughout world
  - Prospective, quasi-experimental study of patients before (n=3733) and after (n=3955) implementation
  - Non-cardiac surgery
  - During "Time-Out," OR team had to confirm that prophylactic antibiotics have been administered ≤60 min before incision is made or that antibiotics are not indicated

## Surgical Safety Checklist

**Table 2. Characteristics of Participating Hospitals.**

Site	Location	No. of Beds	No. of Operating Rooms	Type
Prince Hamzah Hospital	Amman, Jordan	500	13	Public, urban
St. Stephen's Hospital	New Delhi, India	733	15	Charity, urban
University of Washington Medical Center	Seattle, Washington	410	24	Public, urban
St. Francis Designated District Hospital	Ifakara, Tanzania	371	3	District, rural
Philippine General Hospital	Manila, Philippines	1800	39	Public, urban
Toronto General Hospital	Toronto, Canada	744	19	Public, urban
St. Mary's Hospital*	London, England	541	16	Public, urban
Auckland City Hospital	Auckland, New Zealand	710	31	Public, urban

## Surgical Safety Checklist

Site No.	No. of Patients Enrolled		Surgical-Site Infection		Prophylactic Antibiotics Given Appropriately (N=6802)		Death		Any Complication	
	Before	After	Before	After	Before	After	Before	After	Before	After
1	524	598	4.0	2.0	98.1	96.9	1.0	0.0	11.6	7.0
2	357	351	2.0	1.7	56.9	76.9	1.1	0.3	7.8	6.3
3	497	486	5.8	4.3	83.8	87.7	0.8	1.4	13.5	9.7
4	520	545	3.1	2.6	80.0	81.8	1.0	0.6	7.5	5.5
5	370	330	20.5	3.6	29.8	96.2	1.4	0.0	21.4	5.5
6	496	476	4.0	4.0	25.4	50.6	3.6	1.7	10.1	9.7
7	525	585	9.5	5.8	42.5	91.7	2.1	1.7	12.4	8.0
8	444	584	4.1	2.4	18.2	77.6	1.4	0.3	6.1	3.6
Total	3733	3955	6.2	3.4	56.1	82.6	1.5	0.8	11.0	7.0
P value			<0.001		<0.001		0.001		<0.001	

## Chlorhexidine Antisepsis



## Chlorhexidine Gluconate

- Damages microbial cytoplasmic membrane; bacteriostatic to bactericidal (concentration-dependent)
- Data to support superiority to povidone-iodine
- Numerous uses in infection control



## CHG Uses in Infection Control

Application	Evidence
<b>Skin antisepsis</b>	
CVC site preparation	50% better than povidone-iodine (catheter colonization)
Surgical hand scrub	86-92% reduction in flora
Source control in ICUs	Reduction in skin flora; reduce risk of CLABSI 6-fold
Preoperative scrub	Superior to other antiseptics in reducing skin flora at surgical site
<b>Impregnated devices</b>	
Vascular catheter dressings	Reduction in catheter colonization (40-50%); decrease rate of CLABSI
Vascular catheters	Reduction in catheter colonization (55%); in BSI (40%) in high-risk groups



Mistone et al. *Clin Infect Dis* 2008; 46:274-81.  
Blessdale et al. *Arch Intern Med* 2007; 167:2073-9.  
Timit et al. *JAMA* 2009; 301:1231-41.



## CHG Uses in Operative Patients

Application	Evidence
<b>Skin antisepsis</b>	
Surgical hand scrub	86-92% reduction in flora
Preoperative scrub	Superior to other antiseptics in reducing skin flora at surgical site

- What about pre-operative bathing with CHG?
- Recent Cochrane review evaluated 7 studies of preoperative bathing or showering with antiseptics for SSI prevention
  - All included 4% CHG
  - CHG v. placebo RR 0.91 (0.8-1.04)
- Why? Error in application?
  - To achieve maximal benefit from CHG, must be allowed to dry



Mistone et al. *Clin Infect Dis* 2008; 46:274-81.  
Webster and Osborne. *Cochrane Database Syst Rev* 2007



## CHG Cloths

- Cloth impregnated with 2% CHG
  - Friction of application likely beneficial
- Cloths reduce bacterial burden on skin
  - To greater extent than 4% CHG topical antiseptic
    - Abdomen - no difference
    - Inguinal fold - CHG cloths led to significantly greater microbial reductions than topical antiseptic at 10 min, 30 min, and 6 hr post-application (p<0.01)
  - Higher concentration of CHG present on skin with cloths compared to showers with CHG soap
- But can it actually prevent SSI?



Edmiston et al. *AJIC* 2007;35:89-96.  
Edmiston et al. *J Am Coll Surg* 2008;



## CHG Cloths: Prevention of SSI

- Quasi-experimental study of 727 consecutive patients undergoing joint replacement
- Protocol:
  - Vigorous scrub with CHG cloths on night before procedure. 3 min x 2. Air dry.
  - Repeated on morning of procedure
- Rate of SSI decreased from 3.19 to 1.59/100 procedures
  - No statistics provided
  - No data on compliance with protocol
  - Rate continued to fall with ongoing monitoring



Eiselt D. *Ortho Nurs* 2009; 28:141-145.



## CHG Cloths: Prevention of SSI

- Other data limited to abstracts
  - Rhee and Harris. 19th Annual National Forum on Quality Improvement in Health Care. 2007
    - Overall rate of SSI decreased from 2.1 to 0.7/100 procedures
  - Rauk et al. Poster at APIC 2008
    - Rate of incisional SSI following CSEC decreased from 2-8 to 0/100 procedures
- Major limitations
  - Single center experiences (often after a problem was identified)
  - Before-after study design
- Bottom line: May be a way to decrease SSI, but would like more data
  - Biologically plausible
  - Seems to be better option than pre-operative CHG showers



## High Inspired O<sub>2</sub> Fraction



## Oxygen and SSI: Basic Science

- O<sub>2</sub> is important for wound healing
- O<sub>2</sub> correlated with collagen deposition
- Tissue hypoxia is a risk factor for wound infection and dehiscence
- Superoxide production by leukocytes proportional to P<sub>O2</sub>
- Many antibiotics require oxygen to exert lethal effects on bacteria



Hunt and Pai. Surg Gynecol Obstet. 1972;136:561-7.  
 Hansen et al. Eur J Surg. 1992;158:521-6.  
 Hopf et al. Arch Surg. 1997;132:997-1004.  
 Allen et al. Arch Surg. 1997;132:997-1005. Kozlowski et al. CMAJ. 2007;176:727-731.

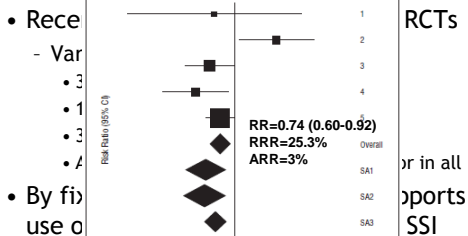


## High Inspired O<sub>2</sub> Fraction

- Several studies have compared FiO<sub>2</sub> of 80% vs. 30%
- 5 RCTs
  - Mayzler (2005; Minerva Anesthesiol)
    - n=38; colorectal procedure for metastatic dz;
  - Pryor (2004; JAMA)
    - n=160; major abd surgery; SSI rate 2-fold higher in intervention group; high rates of obesity; SSI in 14d
  - Belda (2005; JAMA)
    - n=291; elective colorectal; O<sub>2</sub> for 6 hours; SSI in 14d
  - Greif (2000; NEJM)
    - n=500; elective colorectal; SSI in 15d
  - Myles (2007; Anesthesiology)
    - n=2002; non-CT surgery; SSI in 30d



## High Inspired O<sub>2</sub> Fraction



Qadan et al. Arch Surg. 2009;144:359-66.  
 Napolitano L. Arch Surg. 2009;144:366-67.



## Latest Piece of Puzzle

• PROXI Trial  
 - n=1400 patients  
 - Randomized

Adverse Event	80% Oxygen (n = 685)	30% Oxygen (n = 701)
Any	361 (52.7)	369 (52.6)
Wound-related	61 (8.9)	77 (11.0)
Infection		
Urinary tract	23 (3.4)	34 (4.9)
Other	79 (11.5)	83 (11.8)
Charac Postoperative nausea or vomiting	136 (19.9)	135 (19.3)
Surgical procedure, No. (%)		30% Oxygen (n = 701)
Colorectal procedures		
Respiratory	63 (9.2)	57 (8.1)
Gynecological procedures		
Circulatory	57 (8.3)	67 (9.6)
Small-bowel surgery		
Gastrointestinal tract	61 (8.9)	62 (8.8)
Appendectomy		
Other	150 (21.9)	152 (21.7)
Other <sup>b</sup>		
Any serious adverse event	165 (24.1)	154 (22.0)
Receiving adequate antibiotic		
Sepsis	21 (3.1)	15 (2.1)
Receiving timely antibiotic p		
Other infection	29 (4.2)	34 (4.9)
Respiratory	27 (3.9)	25 (3.6)
Circulatory	24 (3.5)	20 (2.9)
Gastrointestinal tract	53 (7.7)	46 (6.5)
Other	47 (6.9)	44 (6.3)

• My opinion: plausible. biologically



Meyers et al. JAMA. 2009;302:1583-9.  
 Hunt and Hopf. JAMA. 2009;302:1588-9.



## Bowel Preparation



## Bowel Preparations in Colorectal Surgery

- Mechanical Bowe Preparation (MBP) typically involves cleansing agent (such as polyethylene glycol) +/- oral antibiotics (such as erythromycin)
  - Traditionally performed in attempt to decrease fecal bacterial burden in the colon to decrease risk for infection
  - Concerns that this practice might increase spillage or offer no real benefit to patient
- Some advocate just oral antibiotic component of MBP



## Does it Work?

- Issue is controversial
  - 100s of articles have looked at it
  - Two recent RCTs have found no clear benefit for MBP
  - One study: higher rates of intra-abdominal abcess in non-MBP arm if anastomatic leak was present
  - Both studies recommended that routine MBP be abandoned for colorectal surgery
- Two recent reviews have tried to make sense of it all



Contant, C, Lancet, 2007  
Jung B, Br J Surg, 2007



### META ANALYSIS

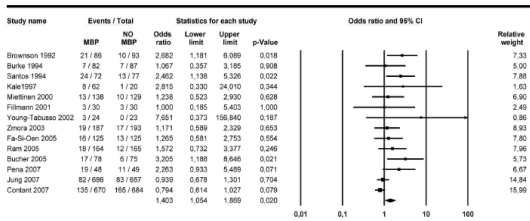
## Updated Systematic Review and Meta-Analysis of Randomized Clinical Trials on the Role of Mechanical Bowel Preparation Before Colorectal Surgery

Karem Slim, MD,\* Eric Vicaut, MD, PhD,† Marie-Véronique Launay-Savary, MD,\* Caroline Contant, MD,‡ and Jacques Chipponi, MD, PhD\*

February, 2009



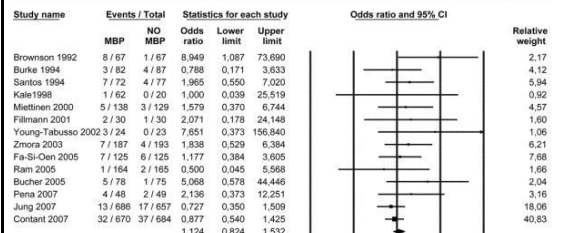
## MBP and SSI



Slim et al. Ann Surg 2009;249:203-9



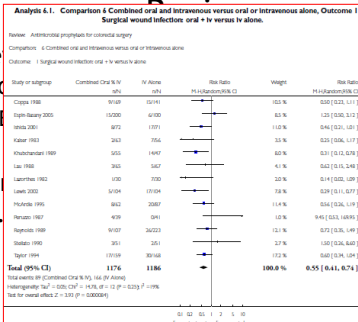
## MBP and Harm? Anastamotic Leak



Slim et al. Ann Surg 2009;249:203-9



## Oral + IV Antibiotics? Cochrane



DukeMedicine Nelson et al. Cochrane Database Syst Rev 2009; 21.CD001181 dicon DUKE INFECTION CONTROL OUTREACH NETWORK

## Bowel Preparation - Summary

- No clear benefit for MBP in published literature
  - This practice continues on a routine basis in many institutions
  - Still considered “standard of care” by many
  - Concerns about medical-legal repercussion if MBP is eliminated
- PO antibiotics may have some added benefit (but controversial)

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## Lots of Other Issues to Consider

- Type of anesthesia
- MRSA screening
- Antibiotic/antiseptic-impregnated \_\_\_\_\_
- Physician-level factors
- Glucose control
- Hypothermia
- Others...

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## Take Home Points

- SCIP is key - appropriate antimicrobial prophylaxis is one of the most important interventions to prevent SSI
  - But there are others!
- Prophylaxis must be adjusted based on size of patient and duration of procedure
- Chlorhexidine emerging as standard
- Some supplemental techniques seem to work (O2) better than others (MBP)

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Questions?

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