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Survey of Surgical Infections Currently Known (SOSICK): A Multicenter Examination of Antimicrobial Use from the Surgical Infection Society Scientific Studies Committee

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Abstract

Purpose: The Scientific Studies Committee of the Surgical Infection Society undertook the present study to examine the prevalence of and indications for antimicrobial use in intensive care units where members of the Society practice.
Methods: Information and data collection sheets were posted on the Internet for download by members interested in participating. All centers were required to obtain approval from their local human subjects research office or equivalent. A one-week time was set during which the center could collect information on any one day, at the center's convenience. Data collection sheets were then sent to the lead author for analysis. Seventeen centers reported data for 371 patients in 22 intensive care units.
Results: Trauma and general surgical patients comprised 224 of the patients (60%). The indications for anti-infective agents were prophylactic (22%), empiric (27%), therapeutic with known pathogen (41%), therapeutic without known pathogen (e.g., cellulitis) (4%), insistence of influential practitioner (4%), or non-anti-infective purposes (e.g., erythromycin for gastric motility) (2%). Only 44%, 29%, and 54% of the orders for prophylactic, empiric, and therapeutic antibiotics, respectively, had date-certain stop dates. The antimicrobial drugs most commonly used were vancomycin, piperacillin-tazobactam, and fluconazole.
Conclusion: Most patients were receiving antimicrobial agents. Polypharmacy was common. Most patients did not have a date-certain stop date. This study sets the benchmark for future study regarding antibiotic prescribing behavior in surgical intensive care units.

The professional and lay press abounds with reports of overuse and inappropriate use of antimicrobial agents. The general public has become aware of the issues of antimicrobial resistance and the potential for a return to the "pre-antibiotic" era. Intensive care units (ICUs) are known for their high antibiotic utilization and as areas of high prevalence of antibiotic resistance [1,2]. The Scientific Studies Committee of the Surgical Infection Society undertook the present study to examine the prevalence of and indications for antimicrobial use in ICUs where members of the Surgical Infection Society practice.

Patients and Methods

A call for participation was made by an e-mail announcement from the central offices of the Surgical Infection Society to the membership. Information and data collection sheets were posted on the Internet for download by members interested in participating (Appendix 1). All centers were required to obtain approval from their local human subjects research office or equivalent. A one-week time was set during which the center could collect information on any one day, at the center's convenience. Data collection sheets were then sent to the lead author for analysis. Seventeen centers reported data for 371 patients in 22 intensive care units. Descriptive statistics are presented.

Results

Table 1 shows the types of ICUs reporting, with the number of patients from each type. Table 2 shows the types of patients enrolled. Trauma and general surgical patients comprised 224 of the 371 patients (60%). Eleven other specialties

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Table 1. Types of ICUs Reporting, with Number of Patients from Each Type

Type of ICU	*Number of units*	*Number of patients*	*Number receiving anti-infective agents*
Burn	2	6	4
Cardiac	1	13	6
Med/surg	6	43	32
Neuro	1	10	4
Neurotrauma	1	10	10
Surgical	11	195	139
Trauma	8	92	69
Not specified	1	2	2
Total	31	371	266

Med/surg = medical surgical; neuro = neurosurgical.

accounted for the remaining 40%, none of which was > 10% of the entire patient population. Forty-five patients (12%) were hospitalized for cancer; 34 of them were receiving at least one anti-infective agent. Twenty-eight (8%) were receiving transplant immune suppression; all 28 were receiving at least one anti-infective agent. Figure 1 shows the distribution of the number of anti-infective agents per patient. Seventy-two percent were on at least one anti-infective drug.

Anti-infective agents and the number of patients receiving them are seen in Table 3. The indications for the agents were prophylactic (22%), empiric (27%), therapeutic with known pathogen (41%), therapeutic without known pathogen (e.g., cellulitis) (4%), insistence of influential practitioner (4%), or non-anti-infective purposes (e.g., erythromycin for gastric motility) (2%). Antibiotics ordered without a clear indication, but at the insistence of an influential practitioner, consisted of 13 drugs. Three of these (imipenem-cilastatin, metronidazole, and piperacillin-tazobactam) made up nine of the 20 (45%) orders for anti-infective agents at the behest of an influential practitioner.

The indications for the antimicrobials most commonly ordered are shown in Table 4. The percentage of antibiotic orders with a certain stop date, stratified by indication, is seen in Figure 2. Non-anti-infective use of anti-infective drugs was uncommon, being limited to five patients receiving erythromycin for gastric motility, all from one center. No patients were receiving fluconazole to increase serum tacrolimus concentrations.

Organisms causing infection can be seen in Figure 3 as a percentage of all organisms. Specific organisms are listed in Table 5.

Table 2. Types of Patients Enrolled, with Number Receiving Anti-infective Agents

Type of patient	*Number*	*Number receiving anti-infective agents*
Burn	9	5
Cardiac/thoracic	32	18
ENT	5	5
General surgical	91	69
Urology	3	3
Gynecology-oncology	1	1
Medical	15	10
Neuro	25	14
Ortho	6	4
Spine	2	2
Transplant	29	28
Trauma	133	96
Vascular	13	6
Not specified	7	5
Total	371	266

ENT = ear, nose, and throat; neuro = neurosurgery; ortho = orthopedic surgery.

Discussion

Antibiotic use has come under scrutiny in recent years as part of the measure of the quality of surgical and medical care [3–5]. Professional societies promulgate guidelines for optimal use of antimicrobial drugs, our Surgical Infection Society included [6–14]. There are no standard guidelines for the use of antimicrobials in the ICU setting, but there are principles, some mutually contradictory, that are commonly accepted. There are no Class 1 data to direct how antimicrobials should be used in the ICU. Differing schools of thought recommend early broad-spectrum empiric antibiotics vs. withholding of antibiotics until infection is proved; restraint in the use of vancomycin vs. liberal use of vancomycin in areas where the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) is high; early empiric antifungal use when risk factors are present vs. withholding of antifungal use until fungal infection is proved, and so on, with various degrees of less-than-Class 1 data in support of the recommended practices. The fact is, we do not know how best to use antibiotics in the ICU. It seemed that a survey of how much, what, and why would be a reasonable place to start to gain a better understanding of what the agenda ought to be in the design of future trials of antimicrobial use in the ICU.

The snapshot study was designed to capture a "day in the life" in the ICUs of members of the Surgical Infection Society. The members of the study group reporting the data did not necessarily direct all, or even any, of the antimicrobial use. We did not collect data regarding who was responsible for the management of antibiotic use, except for the one question that asked if the indication for an antibiotic was the desire of an influential practitioner, as opposed to a rational medical indication. Four percent of antimicrobial use on the study day was attributable to the insistence of an influential practitioner, without a clear medical indication. Although this number seems low, it probably would not seem so to a

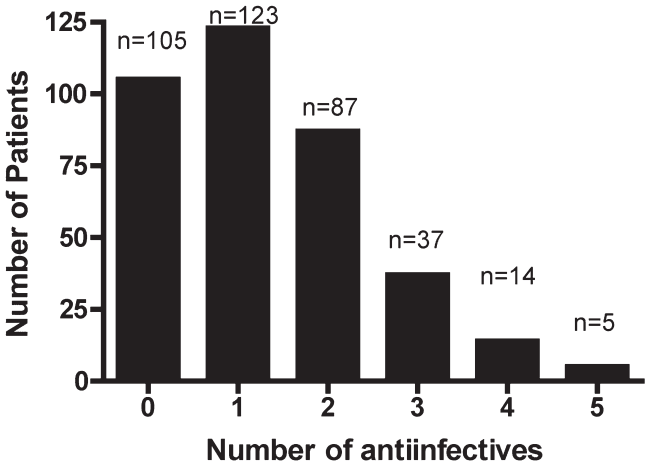

FIG. 1. Distribution of number of anti-infective agents per patient; 71% received at least one.

quality-seeking public. Four percent is too much: We need to approach zero.

Two hundred fifty-three of the 391 patients (65%) were receiving antimicrobial drugs on the study day. Thirty-six percent of these drugs were being given for therapeutic reasons, with a known organism. This use of anti-infective agents probably is justified. By contrast, 32% of the antibiotics were given empirically; it is hard to know if this use is justified. There is intellectual disagreement among the members of the SOSICK Study Group regarding the appropriate indications for empiric antibiotics, and guidelines are needed.

Twenty-three percent of the antibiotics given were for prophylaxis. This number is worrisome. The only indication for which we have data that prophylaxis is effective is in the perioperative surgical situation. These data support a single dose of prophylactic antibiotic prior to operation, and the Surgical Care Improvement Project (SCIP) guidelines allow for as long as 24 to 48 h of postoperative prophylaxis in some cases. If one in five of the patients in the ICUs studied had been in the im-

TABLE 3. ANTI-INFECTIVE DRUGS AND NUMBER OF PATIENTS RECEIVING EACH

Drug	*No. of patients*
Vancomycin	69
Piperacillin-tazobactam	63
Fluconazole	42
Cefazolin	28
Linezolid	25
Metronidazole	24
Ciprofloxacin	22
Imipenem-cilastatin	20
Cefepime	16
Trimethoprim-sulfamethoxazole, levofloxacin, ganciclovir, caspofungin, clindamycin, gentamicin, ceftriaxone	10–15
Ampicillin-sulbactam, erythromycin, tobramycin, valganciclovir, amphotericin B lipid complex, clotrimazole, colistin, meropenem	5–9
Ampicillin, ertapenem, moxifloxacin, piperacillin, aztreonam, cefoxitin, tigecycline, cloxacillin, oxacillin, rifampin, acyclovir, amoxicillin, anidulafungin, azithromycin, cefotaxime, ceftazidime, dapsone, daptomycin, doxycycline, itraconazole, micafungin, minocycline, nystatin, penicillin G, sulbactam, ticarcillin-clavulanic acid, voriconazole	<5

TABLE 4. INDICATIONS FOR ANTIMICROBIALS USED MOST COMMONLY

Drug	*No. of orders*	*Prophylactic use*	*Empiric use*	*Therapeutic use*
Vancomycin	69	4	33	29
Piperacillin-tazobactam	63	2	30	28
Fluconazole	42	16	8	16
Cefazolin	28	22	3	3
Linezolid	25	0	6	18
Metronidazole	24	1	11	8
Ciprofloxacin	22	3	10	8
Imipenem or meropenem	25	10	13	8
Cefepime	16	0	6	9

Number of orders is less than the sum of columns because of antimicrobial use for indications other than prophylctic, empiric, or therapeutic.

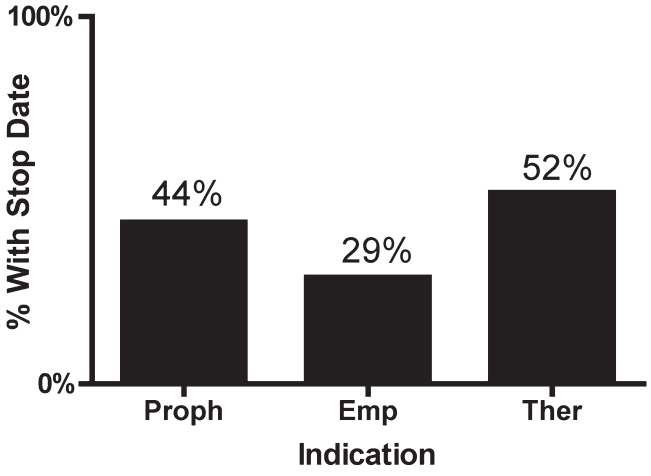

FIG. 2. Percentage of antibiotic orders with certain stop date, stratified by indication. (Proph = prophylactic; Emp = empiric; Ther = therapeutic.)

mediate perioperative period, then having 23% receiving prophylactic antibiotics would be reasonable. However, a large percentage of the orders for prophylactic antibiotics did not have a date-certain stop date, suggesting this use was not perioperative. Further study is needed to understand the use of antibiotics for prophylactic reasons in the ICU.

The subgroups of cancer and transplant patients were analyzed separately because they may reasonably be expected to have a pattern of antimicrobial utilization different from that in the general population. It turned out this was not true for cancer patients, but was true of transplant patients. All transplant patients were receiving at least one antimicrobial agent. Antimicrobial use in transplant patients is a field in desperate need of more research.

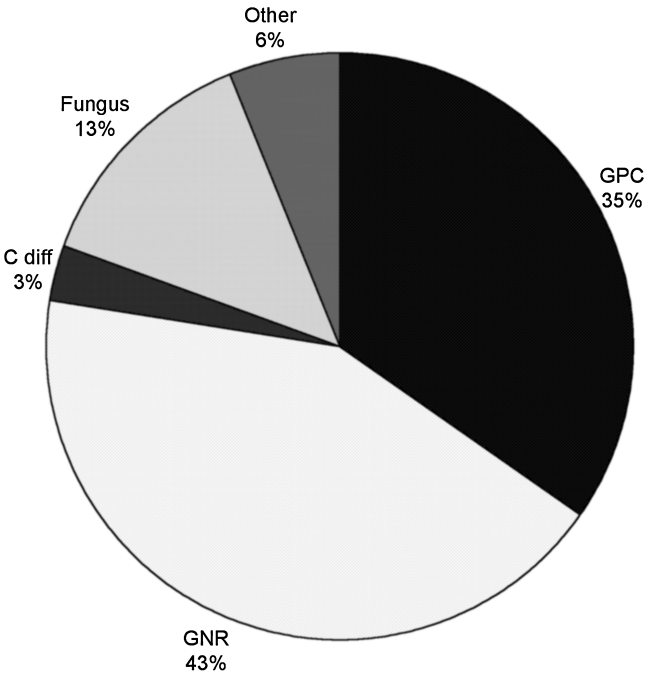

FIG. 3. Organisms causing infection, as percentage of all organisms. (Cdiff = *Clostridium difficile*; GNR = gram-negative bacilli; GPC = gram-positive cocci.)

TABLE 5. ORGANISMS CAUSING INFECTION

Organism	*No.*
Staphylococcus spp.	41
Candida spp.[a]	20
Pseudomonas spp.	14
E. coli	13
Enterococcus spp.	13
Enterobacter spp.	11
Klebsiella spp.	9
Actinobacter spp.	9
Clostridium difficile	5
Proteus spp.	4
Haemophilus spp.	4
GNB NOS[b]	4
Stenotrophomonas maltophilia	4
Serratia spp.	3
Streptococcus spp.	3
Corynebacterium spp.	2
Moraxella spp.	1
Lactobacillus	1
Histoplasma	1
Burkholderia cepacia	1
Bacillus fragilis	1
Bacillus thiuringienesis	1
Citrobacter	1

[a]Ten *C. albicans*, four *Candida* not otherwise specified, two *C. glabrata*, two "yeast," one "fungus," one *C. parapsilosis*.
[b]Gram-negative bacillus, not otherwise specified.

What antimicrobials are we using? The single most-commonly used antimicrobial was vancomycin, a 50-year-old drug long off patent that requires monitoring of the serum concentration. This is consistent with the fact that most of the infections being treated were caused by gram-positive cocci (GPC). Another agent active only against GPC (linezolid) was the fifth most commonly used agent. Daptomycin was used in only one patient (data shown as part of the 0–5 group), and quinupristin-dalfopristin was not in use in any of the study centers on the snapshot day. The respective roles of the various focused anti-gram-positive agents have yet to be defined clearly.

Piperacillin-tazobactam was the second most-commonly used agent. This is logical in light of the fact that the second and third most common groups of organisms isolated were gram-negative bacilli as a group and *Pseudomonas*. Although this finding may be interpreted as overuse of a broad-spectrum agent, it may also be seen as good antibiotic stewardship in that it reflects restraint in the use of carbapenems.

Fluconazole was the third most-commonly used agent, reflecting the changing ecology of ICU infection. The use of amphotericin preparations, echinocandins, and other azole drugs was remarkably low in comparison to the stalwart fluconazole. It is notable that in the ICUs surveyed, of the 16 antibiotics used at least 10 times, 10 are off-patent, generically available drugs. The scrutiny of the effects of marketing on physician prescribing behavior appears to be misguided when applied to surgical critical care populations.

There are substantial limitations to a survey study. Data were self-reported, and therefore subject to bias or misinterpretation of the definitions. We also do not have data

Table 6. Members of the SOSICK Investigators Group

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on the specific diagnoses, the resistance patterns at each institution, or the formulary pressures placed on practitioners at each center. Despite these limitations, we believe this survey provides a baseline understanding of how we are using antibiotics, and can be used for hypothesis generation.

In summary, we have found that (1) most patients in the surveyed ICUs were receiving antimicrobial agents on the snapshot day, with patients receiving more than one antimicrobial outnumbering those on only one; (2) vancomycin, piperacillin-tazobactam, and fluconazole were the agents most commonly used, reflecting the ecology of the organisms infecting our patients; (3) gram-negative bacilli, when *Pseudomonas* spp. are included, and GPC, are most common and similar in frequency; (4) fungi account for a substantial portion of our infections; (5) prophylactic and empiric use of antimicrobials is high, and further study is needed to determine if this use is appropriate; and (6) stop dates are not present in a large number of cases. This study sets a benchmark for future investigation regarding antibiotic prescribing behavior in surgical ICUs.

Acknowledgment

This study would not have been possible without the participation of the SOSICK Investigator's Group (Table 6).

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Appendix 1. Data Collection Sheet

1. What type of ICU is this patient in?

a. Surgical	b. Med/Surg
c. Transplant	d. Trauma
e. Burn	f. Cardiac
g. Neuro	h. Other, please explain

2. Type of patient:

a. General surgical, not listed below	b. Trauma
c. Burn	d. Transplant
e. Neuro	f. Cardiac/thoracic
g. Vascular	h. ENT
i. Medical	j. Other, please explain

3. Is this patient hospitalized for a diagnosis of cancer (Y/N)?
4. Is this patient on immunosuppressant medication for transplantation (Y/N)?
5. Are any systemic (not topical) antibiotics/antifungas/antivirals ordered for today (Y/N)?
6. List anti-infective drugs and organisms below, and choose an indication from the following for each bug/drug combination.
   a. Prophylactic (strictly trying to prevent an infection)
   b. Empiric (high suspicion of infection, may have clinical signs, or Gram stain, or preliminary broad result, e.g., "GNR")
   c. Therapeutic (known pathogen)
   d. Therapeutic (known infection but pathogen not identifiable, as in cellulitis)
   e. Fits none of the above, but influentia practitioner insists, with free text collection of the argument for anti-infectives ("irrational" is an acceptable answer).
   f. Fluconazole to raise tacrolimus levels, or erythromycin for gastric motility, or similar non anti-infective use of anti-infective drug.
7. Is there a *date certain* stop date for this anti-infective? Answer Y/N in DtCert column.

Drug	*Indication*	*Organism (if indication is C)*	*DtCert (Y/N)*