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SURVEY ON ANTIBIOTIC USE IN A SURGICAL INTENSIVE CARE UNIT

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1 Introduction

1.1 Antimicrobials and resistance

Over half of all hospitalized patients are treated with antimicrobial agents which account for 20% to 50% of drug expenditures in hospitals (Schentag, Ballow et al. 1993; Pestotnik, Classen et al. 1996). Although there is no widely accepted consensus concerning the appropriate use of antibiotics in hospitals, it has been estimated that at least 50% of antibiotic use is not appropriate. The determinants of antibiotics use and misuse include factors as diverse as the physician-patient relationship, clinical microbiology, health economics and the most basic definitions of illness and therapy (Avorn and Solomon 2000). Defensive prescribing for medico-legal purposes and lack of continuity of care due to the shortened doctors' shift may also be one of the multifactorial reasons explaining this estimation (Gould 2002). Overuse and misuse of antimicrobials include administration in the absence of a clear indication, administration of a wrong drug, wrong dose, too short or unnecessarily long duration (Pestotnik, Classen et al. 1996; Taylor, Stewart et al. 2001).

Excessive and inappropriate use of antimicrobials has become a global problem (WHO report on infectious diseases 2000), resulting not only in substantial economic burden on health care systems but also in contributing to the selective pressure favoring the emergence of antibiotic-resistant microorganisms (Evans, Pestonik et al. 1998; Yates 1999).

Antimicrobial resistance is a natural phenomenon: in a given microbial population, a small sub-population may show resistance to a given antibiotic. If organisms are left unchallenged, natural resistance provides usually no advantage. However, upon exposure to an antibiotic, selective pressure favors proliferation of the resistant sub-population (Bennett and St Geme 1999; Rubinstein 1999). Resistant organisms naturally pass resistant genes vertically but also horizontally (to other species), further contributing to the spread of resistance.

Shlaes et al. described three mechanisms influenced by antimicrobial usage for resistance development in hospitals: acquisition of resistance, emergence of dormant

resistance and selection of resistant subpopulations (Schlaes, Gerding et al. 1997). Although a clear-cut causal association between antimicrobial consumption at the patient level and antimicrobial resistance is difficult to demonstrate, many observations suggest it (McGowan 1994; Masterton 2000; Monnet 2000; Gould 2002).

For instance, changes in antimicrobial usage are paralleled by changes in the prevalence of resistance. Antimicrobial resistance is more prevalent in nosocomial than in community-acquired infections pathogens. Areas that have the highest rates of antimicrobial resistance also have the highest rates of antimicrobial use (Schlaes, Gerding et al. 1997; Hyatt and Schentag 2000). In other words, the intense selective pressure of antimicrobial use and misuse has been an important factor in the rapid emergence of resistance in many hospitals (Fridkin, Steward et al. 1999; McGowan 2000).

Resistance patterns vary widely among institutions, and make empirical choice of antibiotics increasingly problematic. Many hospitals have developed local guidelines for empiric use of antimicrobials, taking into account microbial and antimicrobial influences in the institution in order to provide patients with the safest and most effective antimicrobial agent (Kaufman, Haas et al. 1998; Rahal, Urban et al. 1998; Monnet 2000). Intensive care units (ICUs) are frequently considered as the epicenters of bacterial resistance, considering the high incidence of nosocomial infections, with infection rates and prevalence of antimicrobial resistance severalfold higher than in the general hospital setting (Jarvis 1996; Livermore 2000; Singh and Yu 2000; Kollef and Fraser 2001). Although ICUs make up only 5% of hospital beds and care for less than 10% of hospitalized patients, infection acquired in these units account for more than 20% of nosocomial infections (Pittet and Harbarth 1998; Gould and Carlet 2000; Singh and Yu 2000).

At least 70% of patients hospitalized in ICU receive antimicrobials, therefore bacteria colonizing patients in an ICU are often a selected population that have been exposed to massive antibiotic pressure (Schentag 1995; Albrich, Angstwurm et al. 1999; Fridkin, Steward et al. 1999; Ibrahim, Gunderson et al. 2001).

The dynamic of acquiring an infection following colonization is complex. Its major contributing factors in ICU patients are:

1. Patients are getting older and more severely ill as advances in cardiovascular, pulmonary, oncological, transplantation and intensive care medicine keep them alive longer.
2. The ability of critically-ill patients to defend themselves against infection is seriously compromised, natural host defense mechanisms might be impaired by underlying diseases or as a result of medical and surgical interventions. Alteration of immune status render them also susceptible to infectious agents, that are usually non-pathogenic.
3. Most ICU patients will have at least one, and often several, vascular accesses and other invasive equipment that break the normal skin and mucous membrane barriers and establish direct access from the external environment to inner body sites, thus increasing the risk of infections.

1.2 Nosocomial infections

Nosocomial infection is a common problem in intensive care medicine (Dettenkofer, Ebner et al. 2001). As explained earlier, it is especially due to the severity of illness of the patients and the high frequency of use of medical devices. Although the cause-effect relationship has never been clearly established, it is well recognized that nosocomial infections are associated with excess morbidity and increase mortality. Therefore, they can be a significant burden on health care resources.

Nowadays, many institutions have initiated surveillance programs to control nosocomial infections. It has been shown that well organized control activities, with systems for reporting infection rates and surveillance involving the systematic collection and analysis of data by trained infection control staff can be effective (Widmer 1994; Pitted, Harbarth et al. 1999; Laupland, Zygun et al. 2002). Indeed, knowledge about the frequency and distribution of nosocomial infections can be important to improve infection control measures.

Two study-design are mainly used to study nosocomial infections: a cross-sectional design (prevalence studies) or a longitudinal design (incidence studies). Prevalence studies

indicate for instance, the number of infected patients among every patient of an hospital at the time-point of study. An incidence study follows up patient risk of infection continuously during a definite period of time. The latter, longitudinal or prospective studies are more accurate than prevalence studies to asses the incidence of nosocomial infections and to determine risk factors. However, they take longer to collect and analyze the data, and are more resource intensive.

In the literature, many studies tend to compare infection rate among different services or hospitals. One of the major problems quoted in these studies is that different techniques of data collection, different types of ward, differences in populations studied and absence of adjustment for risk factors can lead to significant errors of interpretations. Comparisons of incidence of infections adjusted for length of exposure (incidence density) and not only crude incidence rates is one way to diminish the risk of misinterpretations (Legras, Malvy et al. 1998; Pittet and Harbarth 1998).

One major study of nosocomial infection focusing specifically on ICUs has been carried out in Europe (EPIC) in April 1992. This single-day prevalence study was designed to establish the prevalence of nosocomial and other infections in ICUs and to establish the relative importance of risk factors for these infections. The EPIC study provides an estimate of the magnitude of the problem of infections in ICUs. The great variability of rate of ICU-acquired infections among countries (9 to 30%) draw attention to the relative risk of comparing different sites with different case-mix. However, EPIC shows clearly that the most commonly recorded infections among the patients with infections acquired in the ICU were pneumonia (47%), other lower respiratory tract infections (18%), urinary tract infections (18%), bloodstream infections (18%) and wound infections (7%) (Spencer 1994; Vincent, Bihari et al. 1995).

1.3 Antimicrobials and adverse drug reactions

There are accumulating data showing that antibiotic resistance increases mortality and morbidity from nosocomial infections. It also adds substantially to hospital cost by increasing length of stay and other resources utilization (Kollef, G et al. 1999; Kollef, Ward et al. 2000; Niederman 2001). The total costs associated with antibiotics is not only related to resistance but also to multiple sources such as co-medication and adverse drug events (Birmingham, Hassett et al. 1997).

Adverse drug reactions (ADR), according to the WHO definition, is any noxious unintended, and undesired effects of a drug, that occurs at doses used in humans for prophylaxis, diagnosis, or therapy. Both ADR and medication errors are included in the definition of Adverse Drug Events (Bates 1995). The incidence of ADR varies greatly (1,5-30%) depending on the method used to detect them (chart review, computer monitoring or spontaneous reporting) (Bates, Miller et al. 1999; Cullen, Bates et al. 2000).

In a meta-analysis, incidence of adverse drug reactions, including non-serious and serious events was 10.9% (CI 7,9-13,9%) of hospitalized patients. Factors possibly influencing the incidence have been identified: average length of stay, age, gender, renal function, hepatic function and drug exposure (Lazarou, Pomeranz et al. 1998; Leape, Cullen et al. 1999; Cullen, Bates et al. 2000).

Cullen et al., whose study dealt with adverse drug events rather than only drug reactions, found that, although ICU patients had a significantly higher rates of potential ADE than non-ICU patients, after adjusting for the number of drugs administered, the rate was similar in both sectors. No class of drugs was responsible for a disproportionate share of ADE in their study. However, Bordet et al. showed that cardiovascular drugs and contrast media accounted for 36% and 26% of the ADR while drugs affecting blood clotting and antibiotics were the cause of 13% and 14% of adverse drug reactions respectively (Bordet, Gautier et al. 2001). Similarly, in Darchy's report, the drugs implicated in iatrogenic disease remains standard; cardiovascular drugs accounted for 31%, anti-inflammatory and analgesics for 20% and antibiotics for 11% (Darchy, Le Miere et al. 1999).

In his study, Classen states that, although adverse events seem to occur in a small proportion of antibiotic courses, the frequency of antibiotic use makes them account for 23% of all adverse events recorded (Classen, Pestotnik et al. 1997; Avorn and Solomon 2000).

In Switzerland, an epidemiological study of drug exposure and adverse drug reactions reported an incidence rate of clinically relevant ADR for antibiotics of 2,8% (2,0-3.5), in internal medicine units (Fattinger, Roos et al. 2000).

Tracing drug exposure and clinical outcomes are usually the main challenge encountered in drug surveillance study (Grasela, Edwards et al. 1987). In most hospitals, medical records are not computerized and when they are, the co-existence of different databases renders difficult the conduct of pharmacoepidemiology research (Strom 1994).

1.4 Quality improvement

Several interventions for improving antibiotic prescribing are reported in the literature. The aim of most of these interventions is to reduce inappropriate antibiotic use, antibiotic resistance and cost if possible (Gould 2002). Among the strategies frequently employed by institutions in an effort to control both antibacterial use and cost, we find: restrictive or open formularies, stop order systems, dose standardization and antimicrobials order forms.

Restrictive formulary advocates the restriction of antibacterials which are considered unnecessary or problematic (Birmingham, Hassett et al. 1997; Ibrahim, Gunderson et al. 2001). In other words, the pharmacy would not deliver reserved or restricted antibiotics.

On the contrary, **open formularies** allow for the relatively unrestricted availability of most antibacterials. This system reduce the impact of a selective pressure on micro-organisms that could be favored by monopolistic antibacterial use (restrictive formulary) (Rifenburg, Paladino et al. 1996; Birmingham, Hassett et al. 1997; Hyatt and Schentag 2000; Ibrahim, Gunderson et al. 2001).

"Stop orders" are systems that require new orders to be written for continued use of specific antibiotics, at the end of an appropriate period. They are also called automatic stop-

orders since they usually imply an automatical alert system that stops any new orders (Frank, Batteiger et al. 1997).

Antibiotics Order Forms are specific forms that are needed to obtain antibiotics from the pharmacy.

Some groups developed structured educational order forms, addressing specific problems due to antibiotic use, e.g appropriate dosage, or targeting the use of broad-spectrum antibiotics (Avorn and Solomon 2000). In Hammersmith Hospital in London, for instance, strict procedures regarding restricted antimicrobials (3rd generation cephalosporines, aminoglycosides, carbapenem, teicoplanine...) have been introduced. Infectious diseases pharmacists check whether each prescription for reserved antibiotics meets different criteria, such as ID consultation, an authorized prescriber or a satisfactory indication, before processing the order.

Different computer-based system have been implemented to improve antibiotic prescription (Pestotnik, Classen et al. 1996; Evans, Pestonik et al. 1998). They assist the physicians when selecting antibiotics by providing up-to-date antimicrobial susceptibility patterns for nosocomial pathogens recently isolated form the local hospital, by displaying the costs of formulary antimicrobials, by recommending dosages and durations of therapy, by calling attention to drug incompatibilities, and even by creating guidelines for antibiotic use that are locally derived and acceptable to physicians (Burke 1998). These decision support programs are interactive since they usually provide multiple choices depending on the information entered. As such they may be regarded as “Antibiotic consultants”. They rely however on the level of development of the hospital computer system.

“Paper-based” methods (restriction forms, stop orders) and computer-based systems appear effective but one has to keep in mind that antibiotic recommendations based on hospital-wide studies (or on data obtained from another setting) have limited applicability in a given ICU setting since predominant infections, specific populations at risk and offending pathogens are unique to individual ICU (White, Atmar et al. 1997; Yates 1999; Monnet 2000; Schlemmer 2000; Weinstein 2001).

Therefore, on-going ICU-based surveillance of infections, directed at microbial resistance patterns combined with actual antimicrobial influences is of utmost importance

(Emmerson 2000). Firstly, it could direct early empirical therapy whilst awaiting cultures' results and susceptibility testing. Secondly, it would warn about changing patterns of antibiotic susceptibility and enable prompt changes in antibiotic prescribing policy (McGowan 1994; Namias, Harvill et al. 1998). Thus, active antibiotic surveillance can be regarded as a preventive practice, in particular when combined with surveillance of infection and infection control activities (McGowan 1994; Masterton 2000).

At the HUG (University Hospital of Geneva), there is no written policy regarding antibiotic use. The Therapeutic Committee provides some recommendations regarding costly antibiotics. However, strict restriction is rare. Moreover, at the pharmacy level, refusal to dispense a drug following such a policy is not systematic. Furthermore, there is no surveillance of the compliance level to the recommendations.

The Department of Internal Medicine provides written recommendations for use of anti-infective agents, based on local data on microorganisms isolated and susceptibility patterns (annual hospital-wide report of the Central Microbiology Laboratory). However, these recommendations are distributed exclusively in the internal medicine wards and are not used systematically.

In contrast, in a 1996 survey in the USA, 81% of university-affiliated teaching institutions had antibiotic-restriction policies and 56% established official guidance for antibiotic use. In more than three quarters of these institutions, pharmacists contacted physicians overruling policies, and almost half refused to dispense the drug if prescribers did not change the orders (Lesar and Briceland 1996; Dickerson, Mainous et al. 2000). Similarly a 1997 survey effected in 47 American hospitals shows that most institutions had some programs to improve antimicrobial use. However, the latter study observed that only 40% of these institutions reported a system to measure compliance with their programs (Lawton, Fridkin et al. 2000).

1.5 Survey and drug utilization review

Surveillance is defined as "the ongoing, systematic collection, analysis and interpretation of health data essential to the planning, implementation and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know (Gaynes, Richards et al. 2001).

The effective surveillance of antimicrobial susceptibility is important for developing rational empirical therapy guidelines and for directing efforts towards the control and prevention of the spreading of resistant organisms (Masterton 2000). Each institutions needs to conduct its own drug utilisation evaluation to detect areas which need monitoring (Birmingham, Hassett et al. 1997).

Review of clinical records provides greater detail than purchase information and can reflect particular groups of patients and indicate specific problem areas. However, it is more labor and time consuming than other methods, such as pharmacy purchases. The latter are the most easy and economically available estimates of drug usage and trends and they are usually the basis for most hospital drug review and usage studies (nominal systems) (Eckert, Ioannides-Demos et al. 1991).

However, different problems may be encountered while making drug utilization review based on the pharmacy data in a hospital. Drugs may have been obtained through other sources (clinical trial) or, in a hospital where there is no nominal distribution, such as Geneva, the drugs ordered by the wards may not exactly reflect the drugs used for the patients (storage issue). Moreover, with pharmacy data, it is very difficult to approximate time course of actual use. Indeed, most hospitals or wards can easily provide antibiotic purchasing data but they may not be able to provide actual utilization data (Ibrahim, Gunderson et al. 2001).

Whatever the strategy chosen, it can be agreed that it should be accompanied by guidelines for use, policies, protocols or algorithms to be implemented and incorporated into daily activities (Birmingham, Hassett et al. 1997).

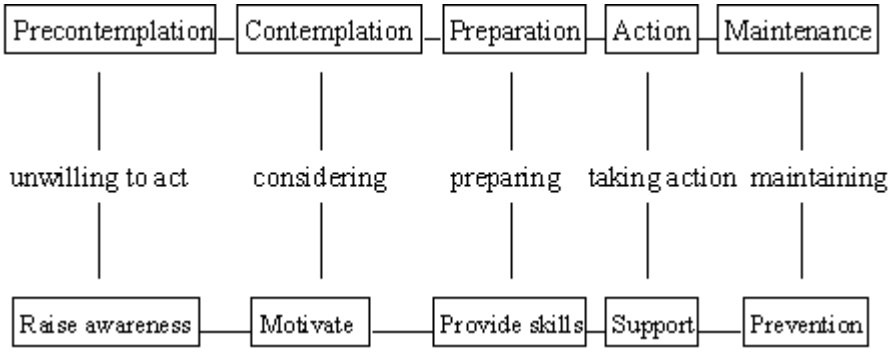
1.6 Behavior change and implementation of changes

1.6.1 Theoretical background

There are different examples of analytical frameworks or health models developed for planning and evaluating health education. Current theories related to behavior changes, involve various models including the Social Cognitive Theory and the Transtheoretical Model (Stages of Change Model) (Protchaska and Di Clemente 1986; Strecher, Champion et al. 1997). The Transtheoretical model identifies five stages of changes through which individuals progress whilst they adopt new behaviors: precontemplation, contemplation, preparation, action and maintenance. It introduces the concept of having different types of intervention depending on the level of readiness to change. In other words, the effectiveness of behavior changing interventions is dependent upon their appropriateness to the stage of change. For example, individuals in a stage of precontemplation require strategies to raise their awareness of the problem and move them onto the stage where they will be ready to contemplate a new behavior. Reinforcement strategies would be useless at that stage (Soumerai, Avorn et al. 1993; Roughead, Gilbert et al. 1999).

Figure 1 : The Stages of Change Model

Different types of intervention depending on the level of readiness to change

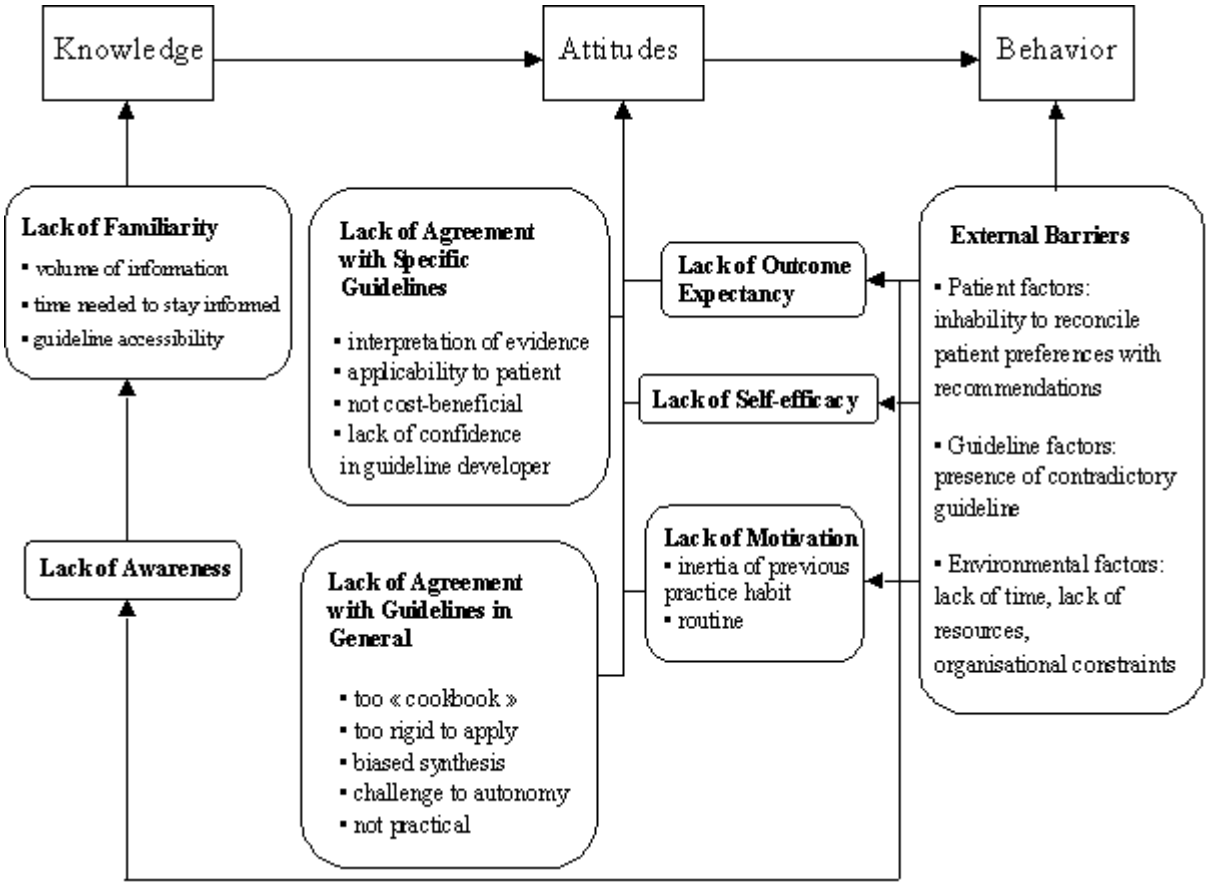


Adapted from Prochaska, DiClemente,
Toward a comprehensive model of change, New York Plenum, 1986

The Social Cognitive Theory and psychological models have been use to describe prescribing intentions and behavior. These models include relationships between beliefs, attitudes, behavior and self-efficacy (the belief that one can actually perform a behavior). So

far, however, these models have not been found to be predictive of actual antibiotic prescribing behavior (Lambert, Salmon et al. 1997; Cabana, Rand et al. 1999). Nevertheless, they allow to detect a variety of barriers to guideline-policies adherence, which include lack of awareness, lack of familiarity, lack of agreement, lack of self-efficacy, lack of outcome expectancy, the inertia of previous practice and external barriers (Cabana, Rand et al. 1999).

Figure 2: Barriers to physician adherence to practice guidelines in relation to behavior change



Adapted from Cabana et al., JAMA 1999, 282, 1459

Even without using complex psychological models, a measure of the attitude towards antibiotic policies may provide an indication of the general predisposition towards compliance with them. It could identify the underlying beliefs that could be targeted to efforts to increase compliance with antibiotic policies (Simpson and Armour 1999).

1.6.2 Practical aspects

One of the important elements that can be drawn from theoretical models is that the attitudinal dimensions of physicians towards antibiotic policies can be useful in the design and implementation of programs intended to improve drug-use processes and outcomes (Simpson and Armour 1999). In other words, when designing an intervention, one should seek the concern and the advice of the prescriber. The use of a "bottom up" consensus seems more beneficial for compliance to policies or restrictions (Frank, Batteiger et al. 1997; McGowan 2000). It is also well-recognized that medical practice is locally driven and that national guidelines are rarely incorporated into everyday practice (Goldmann, Weinstein et al. 1996). Interventions are best accepted when they suit local problems, conditions, and strategic needs (Davis, Thomson et al. 1995; Gross 1997; Roughead, Gilbert et al. 1999; Avorn and Solomon 2000; Richards, Emori et al. 2001; Gould 2002). McGowan stressed the fact that adapting these guidelines to the local situation is a key to their implementation.

The choices of implementations' methods are dependent on various factors including acceptability, applicability, local circumstances, and the prevalence or seriousness of the consequences of irrational drug use, such as drug safety, ever increasing drug purchases or high overall drug costs. For instance, antimicrobial use has microbiological and ecological consequences that go beyond the patient in the bed. Therefore, good antimicrobial stewardship entails more than the immediate benefit to the individual patient being treated (McGowan 2000). Thus, although it might be simple to explain that resistance is important and costly, it is more difficult to convince the prescribers that their individual actions influence resistance (Ibrahim, Gunderson et al. 2001). In this sense, programs affecting drug administration (switch therapy and drug streamlining) have shown success in saving money and decreasing length of hospital stay. But in order to have them accepted by prescribers it is important to insist on the fact that they can also reduce resistance.

The degree of pressure that needs to be exerted for a change can vary. Re-educative strategies are often used to create an awareness of the problem. Multiple strategies, repetition and opportunities for practice are more successful in modifying behavior than single focused initiatives. The addition of persuasive and facilitative strategies may therefore be required.

Practically speaking, these strategies may include the dissemination of written educational materials, didactic educational sessions, local consensus conferences, audit with prescribers feedback, physician prompting, academic detailing. (Dranitsaris, Spizzirri et al. 2001). Academic detailing is a program of one-to-one interactive educational outreach

provided by a clinician, a physician or a pharmacist who have been trained to discuss prescribing decisions with physicians in a manner likely to induce evidence based practice change (Soumerai, Avorn et al. 1993; Avorn and Solomon 2000; Ilet, Johnson et al. 2000; Dranitsaris, Spizzirri et al. 2001). It is usually speculated that a combination of two or more of these methods would have a greater likelihood of success.

1.7 Pharmacoeconomy

Pharmacoeconomics studies allow for the systematic quantification of the value of pharmaceutical products and services (Sanchez 1996). To control drug cost and use, most hospitals use a formulary. The formulary represents a sort of compendium of pharmaceutical products selected by the medical staff (doctors, pharmacists, nurses…) of an institution to reflect current drug preferences of healthcare practitioners and patients. One of the main purpose of a formulary is to optimize therapeutic outcomes and to control the cost of drugs.

Nowadays, most institutions try to pursue pharmacoeconomical analysis of newly marketed drugs to evaluate their inclusion or not in their formulary. These analyses usually extend beyond a simple evaluation of safety and cost of a product. They include an assessment of the efficacy and the "value" of the product or the service. The value includes different outcomes: clinical, economic (direct and indirect costs) and humanistic (consequence of disease or treatment on patient functional status or quality of life) (Walley and Haycox 1997).

1.8 Concluding remarks

Ideally, an antiinfective management program should be designed to make patient-specific and epidemiologic information available at the point of care and at the time when clinical decisions are made, to offer educational information about costs and choices and easy on line feedback, and to be simple to use and to access. Evans adds that any program designed

to measure and improve the quality of care for hospitalised patients must include decisions about the use of antibiotics and the management of infectious disease, given the importance of these issues in inpatient clinical care. No single measure of quality with respect to antibiotic use is likely to be sufficient, bearing in mind that the process of antibiotic use goes far beyond the initial product selected.

Active surveillance can contribute to both measuring and improving quality while optimising patient outcomes (Mann and Wittbrodt 1993; Evans, Pestonik et al. 1998). Routine surveillance of antimicrobial use can aid hospitals in targeting infection-control efforts (Fridkin, Steward et al. 1999), and real-time surveillance can ensure timely, effective therapy (Schentag 1995).

We believe that an active surveillance in the ICUs, involving both the ICU and ward physicians and other sectors including the infection control program (PCI), infectious disease division (DMI), clinical microbiology laboratory (LCB), clinical pharmacology division and the pharmacy can contribute to both measuring and improving quality concerning the use of antiinfective therapy. A data-driven approach will enable defining patient-population at risk of developing infections due to resistant organisms, evaluate the actual use of antimicrobials and their costs and it will eventually enable the development of rational focused recommendations for the use of antimicrobials in our ICUs (Singh and Yu 2000; Kollef and Fraser 2001).

As Burke described, antibiotic prescription includes many elements such as selecting the correct dose, route, and interval of the antibiotic for the specific patient; taking into account the prevention of adverse drug events, the infection control practices and surveillance, decisions to obtain cultures, serum levels and laboratory tests, the need for prophylaxis and the timing of drug administration and the duration of therapy or prophylaxis (Burke 1998). No one discipline is able to grasp this global problem, thus the cooperation of multiple sectors within the hospital will have to be encouraged to optimize antimicrobial use and to face escalating antibiotic resistance.

2 Objectives of the study

There is not much to be found in the literature that would help specific institutions or specific wards to gauge their level of antibiotic utilization over time to establish a baseline from which to start an intervention or to draw comparisons. This study aims to establish appropriate antibiotic monitoring parameters or benchmarks to obtain a precise photograph of antibiotic use in a surgical intensive care unit with the perspective of designing a specific targeted intervention.

The project should provide our surgical ICU (SIC) with an overview of the use of antimicrobial agents, by collecting data in a prospective, standardized, uniform and meaningful manner. Information on both quantitative and qualitative aspects of antibiotic consumption as well as denominators and some potential confounders will be gathered.

The objectives of the study are:

2.1 To describe patterns of antibiotics'use in the ICU

a) What antibiotics are used, for which patients, for how long, how many times treatment is modified during the ICU stay ?
b) What is the proportion of prophylaxis versus therapeutic use ?
c) What are the indications for prophylaxis and therapeutic use ?
d) What is the proportion of empirical versus microbiologically confirmed treatment ?
e) Are antimicrobials adapted to renal function, are drug levels monitored ?

2.2 Analysis of the cost of antimicrobial compared to other drugs

a) Have a precise idea of the antimicrobials' expenditure in the service.
b) Cost relation with other drugs in the service.
c) Determination whether the pharmacy orders data reflect the actual use of antibiotics.
d) Comparisons of costs with the medical intensive care unit (SIM) and with the entire hospital.

2.3 To describe major drug-related adverse reactions in ICU's

a) What is the incidence of major antimicrobial-related adverse reactions ?

b) Is dosaging adapted to renal failure ?

2.4 To improve antibiotic use in ICU

Areas for targeted interventions according to results of the observation periods will be defined. The expected outcomes should be:

A) (a) Development of a continuous quality improvement team for the use of antimicrobials in ICU.

(b) Development of written guidelines adapted to patient population, type of care provided and resistance patterns.

B) (a) Improving use of empirical and therapeutic antimicrobial treatment and duration.

(b) Improving use of prophylaxis treatment and duration.

(c) Improving antimicrobial dosaging (renal failure).

(d) Minimizing the incidence of antimicrobial-related adverse reactions.

3 Methods

3.1 Setting

The follow-up study took place in the surgical ICU (SIC) of the University Hospitals of Geneva (HUG). The SIC covers mainly patients that need post-surgery haemo-dynamic surveillance. Hospitalisation in this service includes organ transplants, cardiac and respiratory failure, polytrauma, septic choc.

Table 1: Definition in few numbers of the SIC

Number of admission	1500 patients/year
Number of beds	20
Mean length of stay	4 days
Occupancy rate	92%
PRN (SIC)	200 points patient/day
PRN (HUG)	90 points patient/day

PRN is a scale defining nursing charges.

3.2 Sample size and Design

3.2.1 Sample

Most patients admitted to the SIC receive an antimicrobial. It was therefore estimated that a two month follow-up including more than 200 patients would be a suitable sample size to obtain a representative "photograph" of antibiotic use in that service.
February the first to March 31st 2002, the files of every patient admitted to the SIC were analyzed.

3.2.2 Team

A physician, a nurse specialized in infection control and a pharmacist constituted the research team. At least two of them collected the data daily. They filled the database "incidence" and its different tables (Figure 3).

3.2.3 Surveillance

The surveillance consisted mainly of a data collection for each patient every day. Actual visits were done 5 days out of 7; week-end data were collected on Mondays. The investigators updated the data daily from admission day to ICU discharge day, after patient's files, charts and lab results. Most information was obtained from the computerized files (Emtec) of the service. This program gather the medical and the nurses' charts for each patient as well as medication, intervention and equipment indications.
The patients were also followed up five days post-discharge. The ones receiving antibiotics at discharge were followed up until the treatment had stopped for more than 24 hours.

3.2.4 Definitions

Nosocomial infections occurring during the study period were categorized by specific infection sites according to standard Centers for Disease Control and Prevention (CDC) definitions that include clinical and laboratory criteria. Infections occurring at more than one site in the same patient were reported as separate infections. To classify an infection as being nosocomial in origin, there must be no evidence that it was present or being incubated at the time of admission to the ICU. Each infection had to be assessed for evidence linking it to hospitalization.
Infections acquired prior to the admission to the SIC were not included in the Data Base but were defined in two groups; community acquired or HUG acquired. "HUG acquired infections" stated for infections acquired in the Hospitals of the University of Geneva in any service except the SIC.

Prophylactic antimicrobial treatment was defined as any antimicrobial agent administered in the peri-operative period (induction included) for the prevention of infection resulting from the surgical procedure. Un-operated patients could also receive prophylactic antibiotics.

Empirical antibiotics included any antibiotic prescribed for an infection without identifying a specific micro-organism.

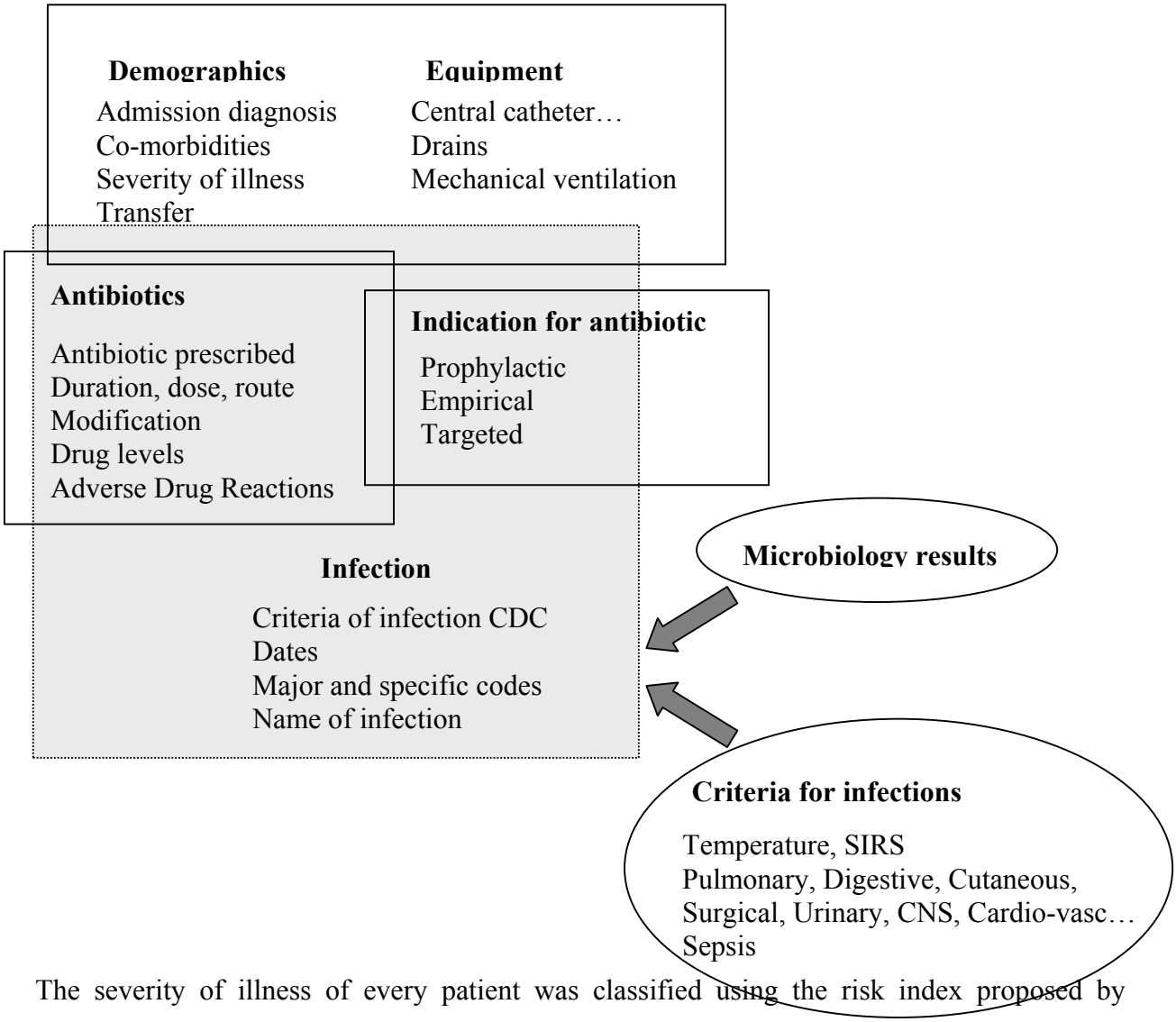
Targeted antibiotics were defined as the antimicrobials administered for a specific clinically localized source of infection, that was documented and confirmed by microbiological results.

3.2.5 Data Base

A pilot period of 10 days prior to the start of the antibiotic survey was used to minimize individual variation in the gathering of the different information necessary to fill the database. Operational definitions were also developed to facilitate the process of data collection (Annexe I).

Collected data included demographic characteristics, admission diagnosis, exposure to invasive devices, antibiotic use and modifications, adverse drug reactions related to antibiotics, indications for antibiotic administration, microbiology results and nosocomial infections according to CDC criteria.

Figure 3: Framework of the Access® database



The severity of illness of every patient was classified using the risk index proposed by McCabe (non-fatal, fatal < 5 years, fatal < 6 months) (McCabe and Jackson 1962). Patient's comorbidities were recorded according to the Charlson's score. This Index contains 19

categories of comorbidity, which are primarily defined using ICD-9 diagnoses codes. Each category has an associated weight, which is based on the adjusted risk of one-year mortality. The overall comorbidity score reflects the cumulative increased likelihood of one-year mortality; the higher the score, the more severe the burden of comorbidity (Charlson, Pompei et al. 1987). No co-morbidities corresponded to a zero score.

Precise definitions can also be found in "Le guide de l'enquêteur", Version 2002-2.-F 24.4.02, Snip 02, by Swiss Noso.

3.2.6 Ecomomics

Different data concerning costs and amount of drugs ordered to the pharmacy of the HUG were obtained via a BusinessObject® computer interface. This program allowed different request on the main server of the HUG (*Diogene*).
In *Diogene*, drugs are classified according to the Galenica Codex coding system. Under "Antimicrobials", one finds 6 sub-classes of medications: antibiotics, antifungals, anti-tuberculoses, antiviral, vaccines and immunoglobulines.
We separated Antimicrobials in two groups: "Antibiotics" gathering antibacterial and antifungal treatments and the "Antimicrobials +vaccine + antiviral" with the 4 others sub-classes.

4 Results

All patients admitted to the SIC for more than 24 hours from February the first to the 31st of March 2002 were included in the study.

4.1 Demographics

Table 2: Number of patients included

Number of patients included	**226**
Percentage of men	62%
Percentage of women	38%
Number of patient-days of follow up (SIC)	**1137**
Number of patient-days of follow up (other wards only)	**1470**
Total number of patient-days of follow up	**2607**

Table 3 : Mean Age (years)

All patients		54.6 ± 18	
Non-infected patients	54 ± 19	Infected patients	55 ± 17
Non-infected men	54 ± 19	Infected men	53 ± 17
Non-infected women	55 ± 19	Infected women	60 ± 18

Table 4: Mean length of stay (days) calculated over the two months

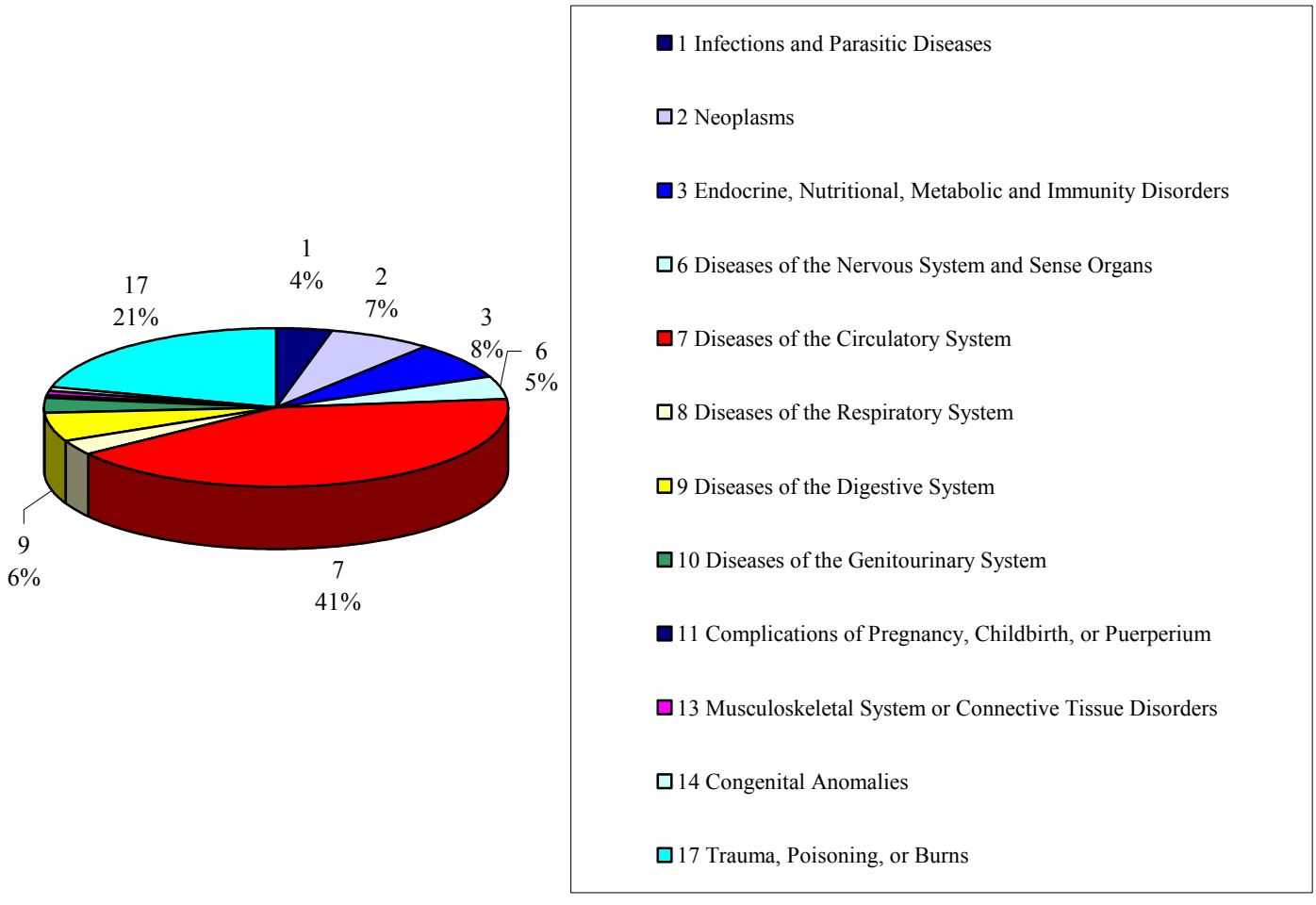
	All patients	Non-infected	Infected patients
Mean length of stay	5.0 ± 7.0	3.3 ± 3.2	10.5 ± 9.8
Median length of stay (min-max)	3 (1-56)	2 (1-34)	7 (1-56)

Age and average length of stay obtained during our two months survey were comparable to the numbers obtained from the service on a yearly basis.

Table 5: Number of patients per detailed length of stay

	nb of patients	% patients	nb of Infected-patients	% Infected-patients
Stays ≤ 72 h	94	41 %	2	4 %
> 72 h	132	59 %	46	96 %
> 7 days	38	17 %	25	52 %
Patients with hospital stays (>48h) prior to admission to the SIC	75	33 %	15	31 %

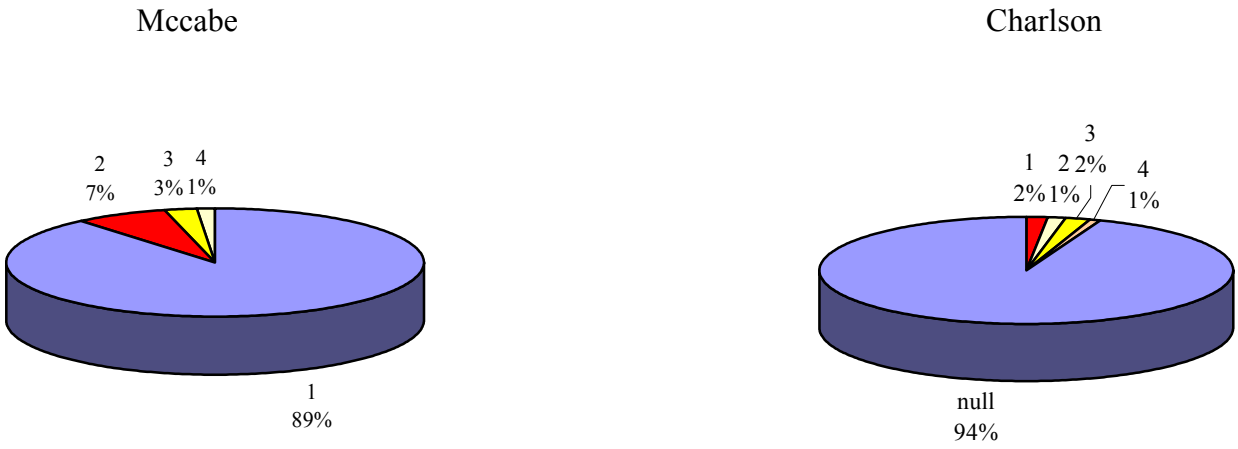
Figure 4: Reasons of admission to the SIC



The severity of illness of every patient was classified using the risk index proposed by McCabe (1 = non-fatal, 2 = fatal < 5 years, 3 = fatal < 6 months) (McCabe and Jackson 1962).

Patient's comorbidities were recorded according to the Charlson's score (Charlson, Pompei et al. 1987).

Figure 5: Co-morbidities, McCabe and Charlson scores



From the McCabe and the Charlson scores, one could assume that we are dealing with a surgical intensive care unit rather than a medical service. Indeed, the risk indices are very low (majority of "1 = non-fatal" for McCabe and zero score for Charlson) which means that most patients had no comorbidities at admission to the service.

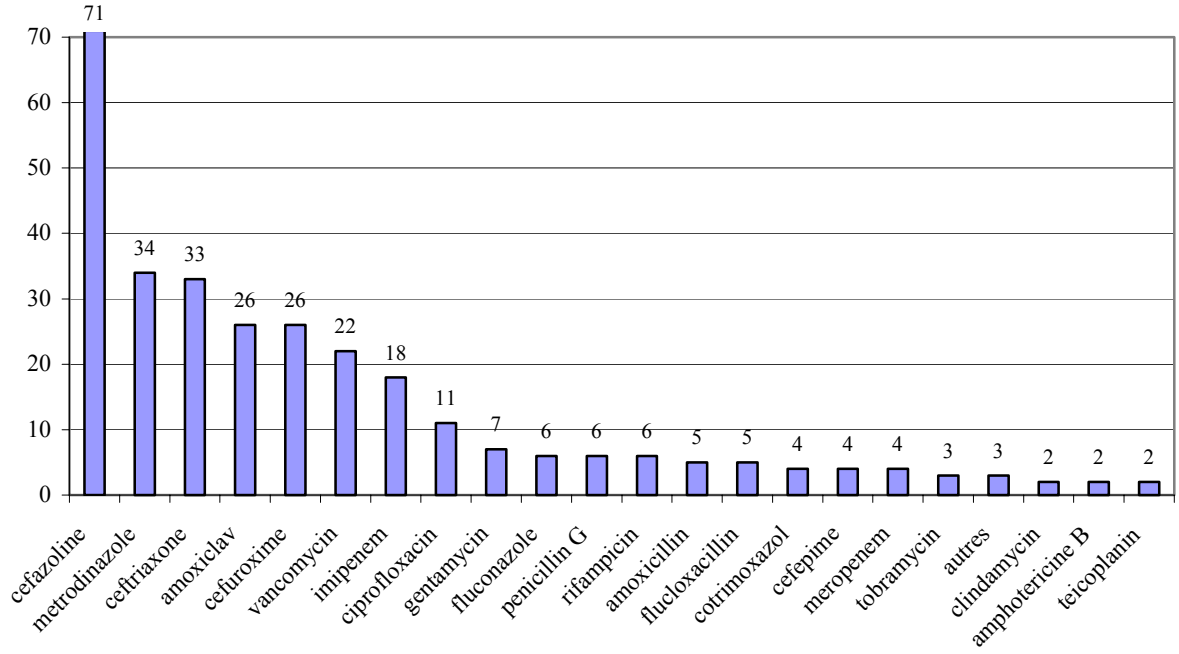
Table 6: Distribution of surgical interventions (n= 226 patients)

Intervention	nb of patients	% of patients
no intervention	60	26.5 %
cardio-vascular surgery	54	24 %
neurosurgery	45	20 %
abdominal surgery	31	14 %
transplant	11	5 %
orthopedic surgery	8	3.5 %
ear-nose-throat	5	2 %
thoracic	5	2 %
others	4	2 %
genito-urinary	3	1 %
total	226	100 %

4.2 Antibiotics

38 different antibiotics were used during the two-month period. They were separated in three groups of indication; prophylactic, empirical and targeted as defined in the Methods section.

Figure 6: Main antibiotics used



The following antibiotics are not on the graphic since they were given only once; Amikacin, ceftazidime (Fortam®), clarithromycin (Klacid®), cefoxitime (Mefoxitin®), norfloxacin (Noroxin®), piperacillin (Pipril®), itraconazole (Sporanox®), thiamphenicol (Urfamycin®) and other cephalosporins.

4.2.1 Prophylaxis

226 patients

172 patients received at least one antibiotic (77%)

142 patients with prophylactic antibiotics

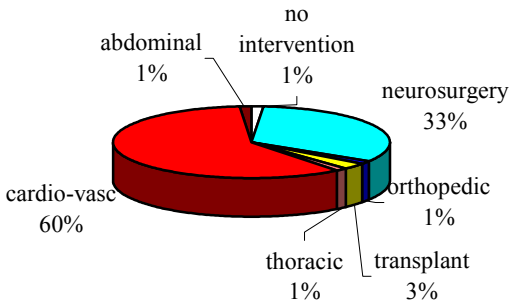
As expected in a surgical intensive care unit, most patients received prophylactic antibiotics.

The choice of antibiotic regimens for surgical prophylaxis is usually made on the recommendation of the Medical Letter 1995, 17, 89-92. Some local guidelines are also used in specific situations (epidemic). At the time of the study, no local guidelines were used.

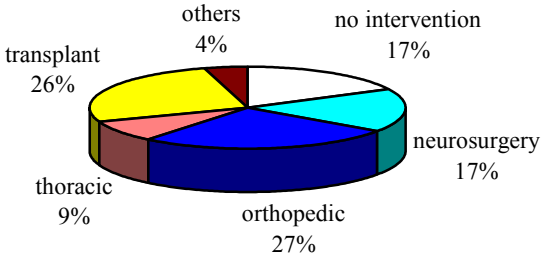
We collected information (name and dose of antimicrobials) on prophylaxis used at the time of surgery and in the following hours or days. We did not check the time, in relation to the skin incision, of administration of the antibiotics.

Figure 7-11: Prophylaxis depending on the interventions

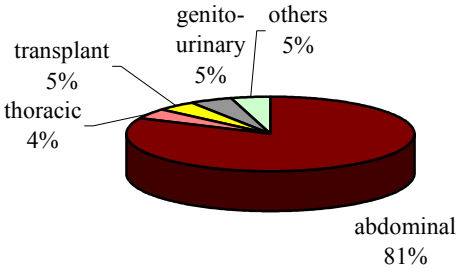
cefazoline (Kefzol) n=71



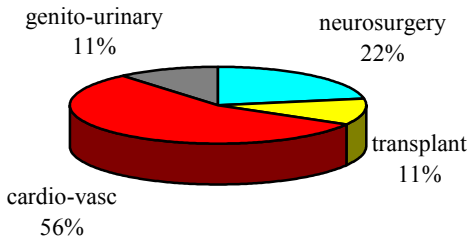
cefuroxime (Zinacef) n= 23



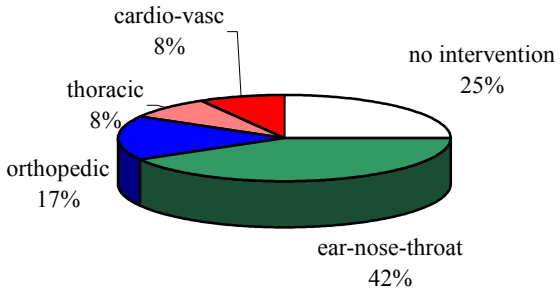
ceftriaxone/metronidazole (Rocephine/Flagyl) n= 22



vancomycin (Vancocin) n = 9



amoxiclav (Augmentin) n=12



Besides the choice of antibiotic in the peri-operative period, the duration of treatment is also interesting to observe. We collected information on the length of treatment for every prophylaxis administered. We computed means and medians, relatively to days and doses, for the antibiotics that were the most frequently used.

On table 7, the "induction" column states for the number of patients that received the antibiotic only before or during the surgery.

Table 7: Mean and median durations of prophylaxis per antibiotic (days)

DCI/Antibiotic	n= nb patients	mean (day)	median (day)	min (day)	max (day)	Only at induction (nb patients)
cefazoline (Kefzol®)	45	**2.7**	**2**	1	14	26
cefuroxime (Zinacef®)	21	**4.9**	**3**	1	13	2
amoxi-clav (Augmentin®)	12	**5.3**	**2**	1	19	0
ceftriaxone/metronidazole (Roceophine/Flagyl®)	9	**6.2**	**3**	1	14	13
vancomycin (Vancocin®)	7	**1.7**	**1.5**	1	3	2

Table 8: Mean and median number of doses

DCI/Antibiotic	n= nb patients	mean (dose)	median (dose)	min (dose)	max (dose)
cefazoline (Kefzol®)	45	**6.5**	**4**	1	54
cefuroxime (Zinacef®)	21	**11.2**	**5.0**	2	36
amoxi-clav (Augmentin®)	12	**13.6**	**3.5**	1	39
ceftriaxone/ metronidazole (Roc/Flagyl®)	9	**5.1**	**3**	1	14
vancomycin (Vancomycin®)	7	**1.9**	**1**	1	5

The length of stay in the SIC can be relatively short, therefore it is quite common for patients to leave the SIC unit with a prophylaxis to be continued or stopped while admitted in a ward. We wanted to observe whether they were some disruptions in treatment in one or the other direction.

Table 9: Number of doses of prophylaxis, SIC / other wards

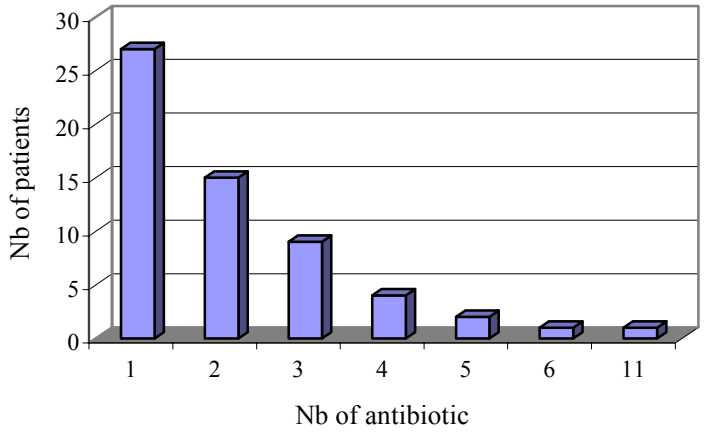
DCI/Antibiotic		n= nb patients	mean	median	min	max
cefuroxime (Zinacef®)	**SIC**	21	**6.1**	**4**	2	36
	others	8	**13.4**	**16.5**	2	22
amoxi-clav (Augmentin®)	**SIC**	8	**7.2**	**5**	1	24
	others	7	**13**	**4**	1	31

Cefazoline does not figure on table 9 since we observed only 3 cases where patients received long prophylactic treatment (confirmed as such), respectively 44, 22 and 8 doses while in the wards.

4.2.2 Empirical or targeted treatment

We illustrated (Figure 12) the number of different antibiotics received per patient during their stay in the ICU and the couple of days post discharge. Patients could receive different antibiotics at different times during their stay, the graphic does not illustrate the number of bi- or tri-therapies. Patients receiving only prophylactic antibiotics were not included.

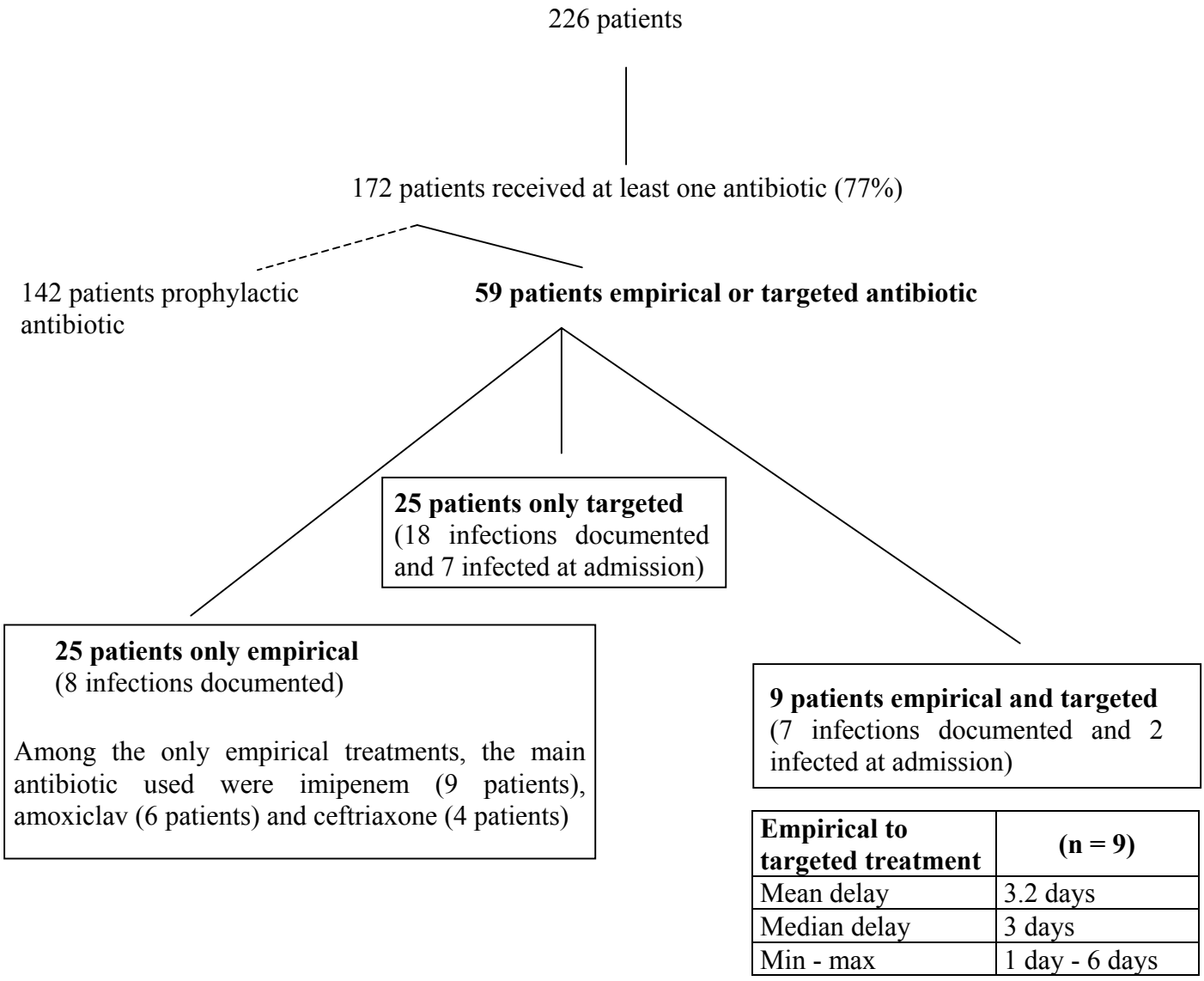
Figure 12: Number of different empirical or targeted antibiotics per patient (n=59)



In our survey, antibiotherapies were segregated in three defined groups; prophylaxis, empirical and targeted treatment.

To get a panoramic view of the distribution of these indications, we drew the following scheme (Figure 13). The view is macroscopic since specific clinical and microbiological indications for antibiotherapy were not strictly evaluated.

Figure 13: Scheme of antibiotics' indications



Empirical to targeted treatment	(n = 9)
Mean delay	3.2 days
Median delay	3 days
Min - max	1 day - 6 days

4.3 Infections

Prior to their admission to the SIC, 29 patients were infected; there were 17 community acquired, 11 HUG acquired and 1 other hospital acquired infections.

As shown on the data-base framework (Figure 2), different tables were used in the survey data base. One table consisted of a follow-up of nosocomial infections. The clinicians' diagnosis of infections were based on the different clinical signs of infection collected during the daily follow-up and the microbiological results obtained from the laboratory. Most cases were also discussed with an infectious disease specialist. The infections acquired prior to the admission to the SIC were not included in our "nosocomial infection table" and therefore were not entered in our data base.

Number of nosocomial infections	71
Number of infected patients	48

We calculated the percentages of infections depending on surgical interventions. We grouped same types of interventions when the percentages of infections were similar. You can find the numbers for detailed interventions in the Annexe II.

Table 10 : Nosocomial infections acquired in the SIC depending on the type of surgical interventions

Intervention (226 patients)	nb infections	nb infected	% infections	% infected
no intervention (n =60)	14	12	23 %	20 %
cardio-vascular surgery (n=54)	18	13	33 %	24 %
neurosurgery (n=45)	10	8	22 %	18 %
abdominal surgery (n=31)	13	6	42 %	19 %
transplant (n=11)	7	3	64 %	27 %
orthopedic surgery (n=8)	3	3	37.5 %	37.5 %
ear-nose-throat (n=5)	0	0	0 %	0 %
thoracic(n=5)	1	1	20 %	20 %
others (n=4)	3	1	75 %	25 %
genito-urinary (n=3)	2	1	67 %	33 %
total (n = 226)	71	48	31 %	21 %

During the two months survey, 71 infections were detected. 60 of them were detected in the SIC service (41 patients).

Table 11: Incidence of nosocomial infections acquired in the SIC (01.02.2002 to 31.03.2002)

Nb of infections	**71**
Nb of infected patients	**48**
Total nb of patients	**226**
Total nb of follow up days (SIC)	**1137**
Nosocomial infections incidence rate	**31.4 %**
Infected incidence rate	**21.2 %**

$$\text{Incidence density} = \frac{\text{nb of infections}}{\text{total of follow up days (SIC)}} x\,1000 = \text{nb of infections per 1000 patient days}$$

Incidence density (SIC)	**62.4 per 1000 patient days**

Table 12: Distribution of nosocomial infections acquired in the SIC

Infection site	nb of infections (%) n= 71	during ICU stay n=60	post-discharge n=11
PNEU	30 (**43%**)	27 (45%)	3 (27%)
LRI	6 (8%)	6 (10%)	-
SSI	11 (**16%**)	7 (12%)	4 (37%)
BSI	5 (7%)	5 (8%)	-
CVS	5 (7%)	5 (8%)	-
UTI	5 (7%)	5 (8%)	-
GI	6 (8%)	3 (5%)	3 (27%)
CNS	1 (1%)	1 (2%)	-
EENT	2 (3%)	1 (2%)	1 (9 %)

Of the 71 infections documented, 11 (15.5%) were detected during the 5 days post-discharge surveillance.

PNEU	Pneumonia	**BSI**	Bloodstream infection	**GI**	Gastro intestinal infection
LRI	Lower respiratory tract infection	**CVS**	Central venous system	**UTI**	Urinary tract infection
CNS	Central nervous system	**SSI**	Surgical site infection	**EENT**	Ear-Eyes-Nose-Throat infections

Pneumoniae (PNEU) were the main infections observed during the survey with 30 episodes and 36 once combined with lower respiratory tract infections (LRI).

Table 13: Pneumoniae depending on the surgical interventions (n =36 infections PNEU-LRI)

Intervention	nb of pneumonia	% of pneumonia
no intervention (n=60)	9	15 %
cardio-vascular surgery (n=54)	12	22 %
neurosurgery (n=45)	6	13 %
abdominal surgery (n=31)	4	13 %
transplant (n=11)	3	27 %
orthopedic surgery (n=8)	1	12 %
thoracic (n=5)	1	20 %
ear-nose-throat (n=5)	0	0 %
others (n=4)	0	0 %
genito-urinary (n=3)	0	0 %

Table 14: Detailed surgical interventions (n =36 infections PNEU-LRI)

Intervention	nb of pneumonia	% of pneumonia
no intervention (n= 60)	9	15 %
heart by-pass (n=22)	8	36 %
heart (n=13)	2	15 %
vascular (n=19)	2	11 %
thoracic (n=5)	1	20 %
neurosurgery (n=45)	6	13 %
abdominal surgery	4	13 %
orthopedic surgery (n=8)	1	12 %
transplant (n=11)	3	27 %
heart transplant (n=1)	1	100 %
lung transplant (n=3)	2	66 %

As mentioned in the Methods section, we collected data on patient's equipment. We compared the number of days with the tube and the incidence of pneumoniae.

Table 15: Number of days of intubation and pneumonia (n = 36)

days with tube	nb patients with pneumonia
no tube	9
1 to 2 days	10
3 days	7
4 to 6 days	4
7 day and more	6

Table16: Number of days of intubation depending on the surgical interventions

			nb of days of intubation				
Intervention	nb patients with tube	% tube	mean	median	min	max	% PNEU-LRI
cardio-vasc (n=54)	52	96 %	2.9 ± 4.8	1	1	29	22 %
no intervention (n=60)	26	43 %	3.6 ± 5.0	2	1	22	15 %
abdominal (n=31)	14	45 %	4.7 ± 7.2	2	1	28	13 %
craniotomy (n=28)	12	43 %	3.1 ± 3.0	3	1	11	14 %
shunt (n=8)	7	88 %	1.6 ± 0.5	2	1	2	12 %
laminectomy (n=9)	2	22 %	3.0 ± 1.4	3	2	6	11 %
ear-nose-throat (n=5)	5	100 %	8.4 ± 4.3	10	2	12	0 %
orthopedic (n=8)	5	63 %	2.8 ± 2.9	2	2	8	12 %
thoracic (n=5)	3	60 %	2.0 ± 1.0	2	1	3	20 %
genito-urinary (n=3)	2	67 %	2.5 ± 2.1	2,5	1	4	0 %
lung transplant (n=3)	3	100 %	7.0 ± 4.9	10	2	11	100 %
heart transplant (n=1)	1	100 %	2.0 ± 2.0	2	2	2	66 %
others	3	75 %	6.0 ± 5.3	4	2	12	0 %

In Table 16, we showed the detailed results for neurosurgery (craniotomy, laminectomy and shunt) since the results were too different to be grouped.

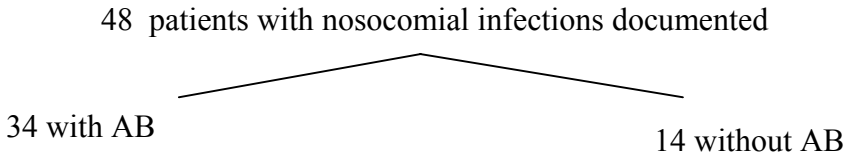
We also checked if patient received anti-acids treatment, knowing that it may also be a risk-factor for developing infections.

Table 17: Patients receiving anti-acids in the SIC, numbers of days of treatment

		Non-infected	Infected
Nb patients with anti-acids		141	46
% of patients		79 %	96 %
Nb of days of treatment with an anti-acid	mean	2.4	5.6
	variance	2.1	33.5
	median	2	4
	min	1	1
	max	13	36
	Wilcoxon Rank-sum test	P< 0.05	

Annexe III : table with anti-acids during the whole follow up (SIC and other wards).

4.3.1 Infections and antibiotics



We measured the delay (day) between the diagnosis of infection and the first therapeutical antibiotic (empirical or targeted). The sample consisted of 46 episodes of infection. 32 episodes (not patient) were treated in the SIC and 14 in the other wards.

Table 18: Delay between the first antibiotic and our diagnosis of nosocomial infection

	Mean (day)	Median (day)	Min (day)	Max (day)	nb infections
SIC	3.3	1	0	12	32
Others	3.9 (2 post transfer)	3 (1 post transfer)	0	12	14
Overall	3.7	2.5	0	12	46

4.4 Side effects and complications related to antibiotic use

4.4.1 Adverse reactions

Besides the elements described earlier, we also followed up side effects and complications with antimicrobial treatments. We checked every patient receiving antibiotics, also the ones getting only prophylactic drugs (142 of them). Their files (computerised in the SIC or on paper on the other wards) were analysed in relation to adverse reactions, but no patients were visited. It is important to note this point since complications or drugs' side effects are not always mentioned in the files, if ever detected. However, we could ask assistant doctors or nurses when we had suspicions of complications while reading the files.

One patient presented central nervous system disturbance possibly associated with meropenem. That patient received many treatments, including ciclosporine, omeprazole, mycophenolate mofetil and ganciclovir, that could also be neurotoxic. We also observed a drug-drug interaction for that patient, involving itraconazole and ciclosporine.
One patient presented a cutaneous rash during his amoxiclav treatment. The reaction resumed when his treatment was changed to clindamycin (Dalacin®) (positive de-challenge).

4.4.2 Renal function and drug monitoring

Most antibiotics are eliminated by renal tubular excretion or glomerular filtration. Therefore many treatments need to be adapted in case of renal failure, with doses or time intervals varying depending on the levels of creatinine clearance. When the data was available (weight and serum creatinine), glomerular filtration was calculated using the Cockroft formula.

Table 19: Creatinine clearance < 100 ml/min (n = 78)

glomerular filtration ml/min	nb of patients
50-100	53 patients
20-50	18 patients
10-20	7 patients

Out of these 78 patients with a calculated creatinine clearance lower than 100 ml/min, 32 had antibiotics that might have needed adjustment in renal failure.
The antibiotics involved were: vancomycin, gentamycin, tobramycin, cefuroxime, cefepime and cefazolin. Dosages of these antibiotics were checked using the Sanford Guide to Antimicrobial Therapy (Sanford, Gilbert et al. 2002), and a review paper on antibiotics used in ICU patients (Garbino, Romand et al. 1998). Dosages of antibiotics had been adapted to the renal function in all cases.

To achieve efficient antimicrobial levels and avoid adverse effects, drug monitoring (TDM) can be used. During the survey, antimicrobials serum concentrations were monitored for 9 patients out of the 59 receiving an empirical or targeted treatment.

Table 20: Dosage monitoring of antibiotics (n = 9)

vancomycin	4 patients
vancomycin and tobramycin	2 patients
vancomycin and gentamycin	1 patient
teicoplanin	1 patient
gentamycin	1 patient

4.4.2.1 Once-Daily Aminoglycoside (ODA) program

In the last 10 years, many randomised trials have compared a single daily dose with multiple doses of aminoglycosides (Nicolau, Freeman et al. 1995; Barletta, Johnson et al. 2000; Buijk, Mouton et al. 2002). We wanted to observe if the ODA was used in the SIC.
During the survey, 10 patients received aminoglycosides (7 patients gentamycin and 3 tobramycin). Only two of them received a single daily dose of aminoglycosides (1 gentamycin and 1 tobramycin) and all the others received twice or three doses daily.

4.5 Economy and costs

4.5.1 Antimicrobials and drug costs

On the basis of total drugs purchases to the pharmacy, expenditure for antimicrobials was evaluated. The computer program *BusinessObject*, was used to collect this data for the SIC (surgical intensive care), the SIM (medical intensive care) and the whole hospital (HUG).
Diogene, the HUG server program groups antimicrobials with vaccine, immunoglobuline and antiviral drugs. In order to obtain representative figures of antibiotic use in both our intensive care units and in the entire hospital, we selected a cost-lists including only antimicrobials without immunoglobuline, antiviral or vaccine.

Table 21: Drug costs for a year (01.10.01 to 30.09.02)

	Antibiotics (SFr)	**Antimicrobials** +antiviral +vaccine **(SFr)**	**All drugs (SFr)**	**Antibiotics % of costs**	**Antimicrobials** +antiviral +vaccine **% of costs**
SIC	196'301	261'166	1'064'929	**18.4 %**	24.5 %
SIM	241'468	292'160	1'053'249	**22.9 %**	27.7 %
HUG	4'868'165	12'005'488	44'675'265	**10.79%**	26.9 %

In the intensive care units and in the whole of the University Hospitals of Geneva (HUG) antimicrobials account for around 10 to 23 % of total drugs costs.

4.5.2 "Just in time" system and Drug Utilization Evaluation (DUE)

During the two months period, we followed antibiotic administration (each dose) for every patient admitted to the SIC. In the HUG there is no tool to evaluate the numbers or the costs of administered drugs, to estimate an "effective" total costs. Indeed, the hospital deals with a non-nominal distribution system, which means that drugs are distributed to a service and not to specific patients. It is also impossible to make an estimation of drug use via prescriptions since the system is not yet computerised.

We therefore added up the costs of each dose of antimicrobials administered in the SIC from the 1st of February to the 31st of March 2002. We obtained a sum of around 30'000 SFr, from which about 10'000 SFr is constituted by prophylactic antibiotics (33%).
The amount obtained from *BusinessObject* (pharmacy purchase) for the SIC during the two months period is 34'530 SFr for antimicrobials and 176'823 SFr for all drugs.
It is important to note that we dealt with purchase cost of antimicrobials and not global cost throughout the survey. We did not include the cost of assays and preparation of the antibiotics or time dedicated by the medical and nursing staff, we only used the net drug prices as invoiced by the pharmacy.

4.5.3 Top Drug lists

One of the commonly used methods to analyze costs is to make ranking of most costly and/or most frequently ordered drugs, and constitute a "Top drugs list". Although pharmaceutical companies are very anxious to obtain an institution's top list, in order to "place" their newcomers at a good rank, these lists are principally made for the institution itself.
In Table 22 we compare the "Top 12" antibiotics for costs or quantities for the SIC during the year period during which the survey was made (01.10.01 to 31.09.02). The antibiotics-list for the SIC that year had 77 items (42 DCI). The same drug with different dosages or galenic forms constituted different items.

Table 22: "Top 12" of antibiotics depending on costs or quantities for the SIC

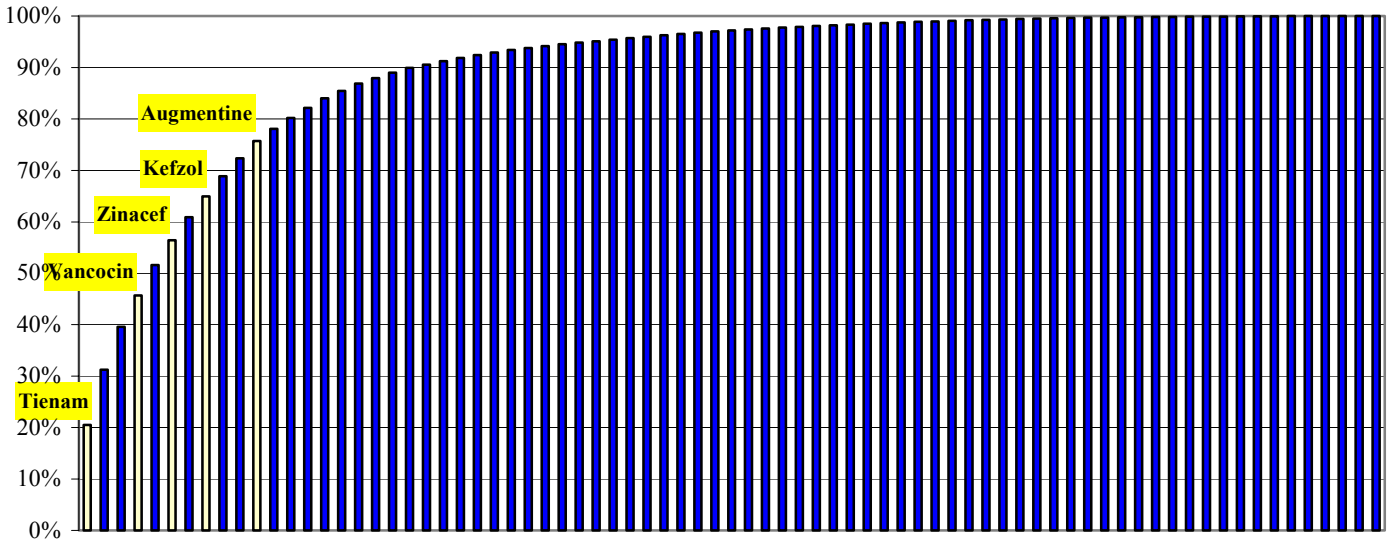
cost			**amount**		
Drug names		(Sfr)	Drug names		(box)
Tienam 500mg	imipenem	40'216	Kefzol 1 g	cefazoline	1'610
Cancidas 50mg	caspofungin	21'125	Vancocin 500 mg	vancomycin	961
Diflucan 200 mg	fluconazole	16'366	**Metronidazole 500mg**	metronidazole	878
Vancocin 500 mg	vancomycin	11'980	Zinacef 1,5 g	cefuroxime	818
Rocephine 2 g	ceftriaxone	11'597	Tienam 500mg	imipenem	383
Zinacef amp 1,5 g	cefuroxime	9'492	Diflucan 200 mg	fluconazole	308
Maxipime 2 g	cefepime	9'132	Rocephine 2 g	ceftriaxone	281
Kefzol 1 g	cefazoline	8'744	Ciproxin 200 mg	ciprofloxacin	247
Ciproxin 200 mg	ciprofloxacin	7'917	Augmentine1,2 g	amoxiclav	217
Floxapen 1 g	flucloxacillin	7'771	**Pipril 4 g**	pip-tazo	105
Augmentine 1,2 g	amoxiclav	6'802	**Klacid 500 mg**	clarithromycin	95
Meronem 1 g	meropenem	6'578	Maxipime 2 g	cefepime	93

From the Table 22, we can see that many drugs are found on both "top 12": under cost and amount. Very costly and rarely ordered drugs (bold on the left chart) figure only on the cost side of the chart. On the contrary, the bold items figuring only on the amount side of the chart, are relatively cheap drugs often ordered to the pharmacy.

With ranking lists, the Pareto bar graphs are also frequently used to illustrate costs distribution.

Pareto's graphs allow to arrange information in a way that priorities for process improvement to be established. It helps to demonstrate that the first few contributing causes to a problem usually account for the majority of the result. In our case, the first few antibiotics used in the service contribute to the major costs.

Figure 14: Pareto diagram with cumulative percentages of costs
SIC for a year (01.10.01 to 31.09.02)



On figure 14, we can see that the first five antimicrobials account for 50% of the costs or the first 12 of Table 22 (15.5% of the antibiotic-list) for 80% of the costs.

We also compared the "Top 12" antibiotics of the SIC, the SIM and the entire hospital (HUG) during the same period (01.10.01-30.09.02).

Table 23: Comparison of the "Top 12" for antibiotics SIC, SIM and HUG

SIC			**SIM**		
Drug names		cost (Sfr)	Drug names		cost (Sfr)
Tienam 500mg	imipenem	40'216	Tienam 500mg	imipenem	46'370
Cancidas 50mg	caspofungin	21'125	**Ambisome 50 mg**	amphotericin B	38'728
Diflucan 200 mg	fluconazole	16'366	Meronem 1 g	meropenem	19'991
Vancocin 500 mg	vancomycin	11'980	Rocephine 2 g	ceftriaxone	17'880
Rocephine 2 g	ceftriaxone	11'597	**Tazobac 4 g + 0,5 g**	pip-tazo	15'819
Zinacef amp 1,5 g	cefuroxime	9'492	Vancocin 500 mg	vancomycin	10'163
Maxipime 2 g	cefepime	9'132	**Klacid 500 mg**	clarithromycin	9'734
Kefzol 1 g	cefazoline	8'744	**Tavanic 500mg**	levofloxacin	9'585
Ciproxin 200 mg	ciprofloxacin	7'917	Augmentine 1,2 g	amoxiclav	7'750
Floxapen 1 g	flucloxacillin	7'771	Cancidas 50mg	caspofungin	7'545
Augmentine 1,2 g	amoxiclav	6'802	Maxipime 2 g	cefepime	7'334
Meronem 1 g	meropenem	6'578	Ciproxin 200 mg	ciprofloxacin	7'152

The bold items are the one that are not in the "Top 12" of both ICU services. Kefzol® and Zinacef® are antibiotics mainly used in prophylaxis, it is therefore logical that they figure only on the surgical ICU (SIC) side of the chart.

HUG		
Drug names		cost (Sfr)
Tienam 500mg	imipenem	673'300
Rocephine 2 g	ceftriaxone	607'719
Ambisome 50 mg	amphotericin B	422'761
Targocid 400 mg	teicoplanin	214'606
Maxipime 2 g	cefepime	200'328
Augmentine 1,2 g	amoxiclav	193'930
Vancocin 500 mg	vancomycin	183'907
Zinacef 1,5 g	cefuroxime	134'064
Diflucan 200 mg	fluconazole	117'508
Rocephine 1 g	ceftriaxone	109'005
Cancidas 50mg	caspofugin	106'382
Meronem 1 g	meropenem	105'047

5 Discussion

5.1.1 Prophylaxis

The different pie charts (Figures 7-11) illustrate that for certain type of surgery, only a few different antibiotics are used. The choice of antibiotics for surgical prophylaxis seems to be made in most case on the specific recommendations of the hospital. One may be surprised to see that vancomycin figures among the prophylactic regimens for 9 patients. Its use has been recently encouraged in the HUG for patients at risk of being MRSA (methicillin resistant staphylococcus aureus) carriers.

Although the length of therapeutical antimicrobial treatment may be somehow controversial, it is not the case with prophylaxis. Indeed, prophylaxis is not meant to last and crosses the line to become therapeutical treatments. In our survey of length of prophylaxis, we noticed some critical areas.

Some prophylactic treatments with amoxi-clav or cefuroxime lasted relatively long once the patients were in the wards. In every case, we checked if the treatment was still considered as prophylactic and most of the time we had confirmation by the physician in charge. At the time, we simply collected the information without arguing that with Kefzol® and Augmentin®, respectively 54 and 39 doses would not be considered as a prophylactic treatment at all.

Although the numbers of such events, compared to studies on the subject, are quite small to come to a conclusion, it could illustrate some directions where recommendations for prophylaxis could be made (Kern, Rose et al. 2001).

5.1.2 Empirical and targeted antimicrobials

On the “tree-graph” (Figure 13), we can see on the right side branches, that most patients receiving a targeted treatment did so right away (25 patients out of the 34 who received at least one targeted antimicrobial). In other words, the group receiving empirical treatment that was then streamlined to a targeted treatment is relatively small (9 patients)

compared to the two other groups receiving uniquely either empirical or therapeutic antimicrobials.

In their study, Kollef et al. demonstrated a statistically significant association between the initial administration of inadequate antimicrobial treatment of infections and hospital mortality for adult patients requiring ICU admission. They concluded that the choice of initial empirical treatment is therefore crucial, while observing that antimicrobial treatment should be administered early in the course of infection to be most effective (Kollef, Ward et al. 2000). In our case, although we did not evaluate appropriateness of treatment, we analysed if the latter was empirical or targeted (confirmed microbiologically). We noticed that most treatment are confirmed when initiated. This may illustrate a trend that treatments are regularly started only when microbiological confirmation is obtained. The delay of treatment detailed in Table 18 may be on more aspect that describe such a trend.

5.1.3 Infections

Many papers illustrate that nosocomial infections vary in incidence and type between different ICUs (Spencer 1994). The infection rates obtained in our study are difficult to extrapolate to or compare with other ICUs that may be combined (medical and surgical) or different in their settings. However, awareness of infection rates has been shown to be an important factor in successful implementation of various policies, therefore the different rates obtained in our study may be used as a baseline for quality improvement (Harbarth, Ruef et al. 1999; Vincent 2000).

We collected prospective data, and infectious status of all patients were carefully analysed during the two months. With such a procedure one could have expected a relatively high rate of infections compare to studies using a 1-day point prevalence approach or studies based on questionnaires where infections are probably underscored.

We obtained an incidence density of 62.4 per 1000 patient-days. As previously said, it is difficult to compare that number with any data in the literature, where settings and surveillance approaches vary greatly. In the medical ICU of our hospital, however, in a similar study including more patients, they obtained 70.7 per 1000 patient-days (Hugonnet, Eggiman et al. 2002).

Patterns of nosocomial infections are of more value than rates of infections in the adoption of appropriate policies for the control of infection within an ICU. The main source of infection in our study are respiratory tract (51%), surgical wounds (16%) and bloodstream (14%) which are very similar to published results (Spencer 1994; Vincent 2000). These numbers could provide baseline data for rational priorities in allocation of resources for infection control activities.

In a recent study evaluating the usefulness of post-discharge surveillance of infections in a medical intensive care service, 5.6 % of infections were detected after discharge (Hugonnet, Eggiman et al. 2002). The authors concluded that at a time of cutbacks in resources, surveillance strategies needed to be rationalized and that the effort needed to perform post-discharge surveillance added insufficient benefit to be recommended. Although the sample size is much smaller, the 15.5 % of nosocomial infections detected post-discharge in our study indicates that it may be otherwise in a surgical intensive care unit. Indeed, many infections acquired in surgical units may not be clinically apparent at the time of discharge. For instance, surgical site infections can occur up to 30 days after surgery. With our mainly 5 days post-discharge surveillance, we probably missed a number of these infections, which implies that, with a longer surveillance, we may obtained an even higher percentage.

5.1.4 Adverse reactions

As mentioned in the literature review, incidence for antibiotic related adverse reactions (clinically relevant) was not very high (2,8% patients in Fattinger's study). We followed 226 patients; 172 of them received at least one antibiotic. We could therefore have expected to find a maximum of 4-5 patients with clinically relevant complications related to antibiotics. Only two patients presented side effects during our study.

This can be explained by different reasons:

- Among the 172 patients, 142 received only prophylactic drugs. They therefore had relatively short treatments and had less chance to develop complications.
- We only analysed patients files; complications or drugs' side effects are not always mentioned, if ever detected, in the files.
- We did not use a "tracking" method to detect adverse drug reactions and we undoubtedly missed some of these events. "Tracking" would have involved an analysis of each patient's total medication and also a search for reactions that are commonly related to antibiotic use (Foxworth 1997).
- Sample sizes in studies on incidence of adverse drug reactions are usually much larger than our 226 patients. In Cullen's study for instance, they gathered more than 4000 ICU patients (Cullen, Sweitzer et al. 1997)

For the patient presenting central nervous disturbance, the consultant from the Clinical Pharmacology Department eventually concluded that the imputability of the meropenem was improbable. However, ciclosporine, ganciclovir, mycophenolate mofetil and omeprazole were equally and possibly (21-60%) responsible for the reaction.

5.1.5 Drug monitoring

A couple of studies in the literature try to describe the effectiveness of antibacterials using pharmacokinetic/pharmacodynamic relationships. They show for instance that the ratio of peak serum concentrations to minimum inhibitory concentration (MIC) and the area under the serum concentration-time curve to MIC are important predictors of successful outcomes for quinolone and aminoglycoside (Schentag, Strenkoski-Nix et al. 1998; Rubinstein 1999; Schentag, Gilliland et al. 2001).

In our survey, no quinolones were used and only a couple of patients receiving aminoglycosides had drug serum monitoring.

Targeting antimicrobials doses to MIC and renal function, using shorter courses of therapy and streamlining drug regimens is becoming frequent in certain centers. It usually implicates a lot of human resources, having pharmacokinetics specialists discussing laboratory results before proposing an optimal drug dose. In our hospital, knowing that such investment on human resources would be unthinkable, we believe that giving preference to dose targeting in the process of antimicrobial use would mainly increase the number of requests for laboratory results without influencing practice.

5.1.6 Once-Daily Aminoglycosides program

In a meta-analysis, Barza et al stated that without pre-existing renal impairment, once daily administration of aminoglycosides is as effective as multiple daily dosing and has a lower risk of nephrotoxicity with no greater risk of ototoxicity (Barza, Ioannidis et al. 1996). Although the ten patients receiving aminoglycosides in our survey do not constitute a sample that would enable to draw any conclusion, the actual practice of treating patients intermittently with larger doses rather than with several smaller doses does not seem to be current yet in the SIC.

5.1.7 Economics and costs

It may be relatively risky to draw comparisons of drug costs (even if calculated per admission or per patient-day) between hospitals or between different services without being misled. Indeed, percentages may reflect differing patient-mixes rather than true differences.

In order to put the numbers into some context, we compared the pharmacy purchasing costs during a whole year for the SIC, the SIM and the whole hospital, having previously mentioned risk of misinterpretation.

No adjustment for case-mix could be done, since no survey was conducted in the SIM, or in the rest of the hospital. In table 21, we can see that in both our intensive care units, antibiotics account for 20% of the total drugs costs. Similarly, in the literature, antibiotics account for about 10-30 % of the total drug budget of an institution (Blanc, Von Elm et al. 1999; Gauzit, Icare et al. 2000). In Rifenburg et al. study, in 1994 antimicrobials account up to 41% of the medication budget (Rifenburg, Paladino et al. 1996)!

From table 21, we can also see that the total drug budget of both intensive care services represents 5 % of the total drug cost for the entire hospital.

5.1.8 Drug use evaluation (DUE)

Our laborious estimation of effective drug costs in the SIC indicates that the SIC drug order procedure to the pharmacy is a "just in time" system. In other words the costs of the daily orders to the pharmacy and the actual cost of the drugs given to the patient are similar. Thus, we could consider that those drugs ordered were usually the drugs used. This is a valuable information in a non-nominal distribution system, if we want to do "drug use evaluation" (DUE) or if we want to elaborate lists of indicators on the use of certain drugs. Moreover, from the comparisons of the percentages for antimicrobials over the year and during the two months we can see that the two-month purchases are representative of the round the year pharmacy purchases. There are in that sense no seasonal effect on SIC's drug orders to the pharmacy.

5.1.9 Pareto and ranking

Pareto diagrams were first used to illustrate the critical point that needed changes in manufacturing processes. In our context (Figure 14), it shows which are the drugs that constitute the heaviest economical burden. Or, on the other hand, it shows which antimicrobials should be targeted for the bigger economical impact.

We all agree that savings on drug costs are by far outweighted by savings on overall outcomes such as a reduction of the length of stay. Nevertheless Pareto diagrams, dealing uniquely with net costs, can still be interesting. Indeed, they illustrate that where it is difficult to act on drug consumption it may be possible to act on the prices and vice and versa. Where the prices are very high it may be important to precisely define the field of use of these products. In other words, ranking charts or Pareto diagrams could motivate the development of guidelines for some drugs and the gathering of persons able to negotiate good prices for other drugs.

5.1.10 Limitations

The drawback of multidisciplinary or wide approaches in a study is firstly the relative heaviness of the analytical tool. In our survey we attached different tables related to antibiotic use to an existing infection incidence database. This involved a high quantity of links between data and some redundancy in the information collected. For future studies a streamlined version of the Access® database would save a lot of time during the different requests made for the analysis of the results.

A streamlined version would also reduce the time of daily data collection and allow for a longer period of follow-up. Eventually the sample sizes obtained would be bigger and the statistical analysis would be more powerful.

6 Conclusion

If there are no clear cut judgement and no real evaluation of adequation of treatment in our study, it is intentional. In fact, the main idea of this small study was to conduct a general utilization review of antibiotic use to document the problem areas in our surgical intensive care unit. We tried to influence actual practice as less as possible and although we somehow checked practice with antibiotics during the two month survey we tried not to place ourselves in a policing role.

Monitoring of antimicrobial use in the SIC helped us distinguish problem areas. Indeed, we believe that the "photographic" system of our pilot study allowed evaluation of different parameters of importance as well as trends associated with the use of antimicrobial drugs. Length of prophylaxis is one of them.

Intensive care units are very busy areas where the struggle between life and death can be confronted many times in the same day. In these units, the emergency of most acts accomplished by the different doctors makes it difficult for them to have a perspective overview of the situation. As mentioned in the literature review, antibiotic use has microbiological and ecological consequences that go beyond the patient in the bed. In this sense, we believe that a survey of practice accomplished by outsiders from the unit helped to obtain a perspective snap shot of the situation of antibiotic use; a picture that would have been difficult to obtain from insiders. Moreover, the different professional origins of the research team helped to lighten various shadowed areas of antibiotic use in the service.

In relation to behavioural aspects, we think that our original work will help raise awareness of the complexity and the multi-dimensional aspects of antibiotic use. In a near future, we hope that the collection of diverse information in relation to antibiotic use could be a strong motivating factor for achieving effective implementation of infection control policies including those for antibiotic use.

The economical aspects presented in this study showed, for instance, that the restriction of imipenem would probably reduce antimicrobial costs. However, we all know that such restriction would end up with the use of another antibiotic (4th generation cephalosporins or simply meropenem) becoming the leader. Single strategies involving only cost reduction would just displace the problem from one antibiotic to another.

In that sense, we hope that this study illustrates the need for connecting different actors in order to obtain a global impact on the global problem of antibiotic use.

7 Future prospects

Possible targeted interventions should be designed in the areas detected during our study. Optimal setting up methods should be discussed to increase the likelihood of the acceptance of more rational attitudes toward antibiotic use by prescribers. Eventually, it would also be interesting to promote further evaluation regarding the impact of policies on outcome in the critically ill.

Because of the relatively small sample sizes, we did not discuss all the information collected during our survey. In the near future, diverse data such as the incidence of pneumonia (ventilated or not) or the use of anti-acids, could be studied in more detailed.

A validation of the consumption measures should be carried out in order to use them as an additional assessment tool for reviewing drug utilization. For instance, a follow-up of anti-acids as well as antibiotics could be established.

We believe that drug utilization reviews will become necessary in important institutions during a cutback period.

For the various reasons illustrated in our study, antibiotics are clearly the first drug category where a multi-disciplinary approach is essential. In that sense, discussions should be started to determine the possibility of involving a pharmacist in the infection prevention team.

Pharmacists can play a significant role towards the rational use of antibiotic treatments. Indeed, in a multi-system approach to cost control, they can help tackling at the same time the demand, price, misuse as well as providing incentives for changes.

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Annexe I

Définitions opérationnelles de la base de donnée d'incidence des infections aux SIC

Données principales

N° : Numéro de saisie. Numéro d'allocation du patient dans la base de donnée. Il permet de retrouver rapidement le patient correspondant en inscrivant le numéro dans la case inférieur gauche de la table, il doit être inscrit pour chaque nouveau patient.
Nom Prénom Date de naissance : *JJ ;MM ;AAAA* Sexe *menu déroulant*
Date d'entrée HUG : *JJ MM AA* Date entrée SIC : *JJ MM AA*
N° de dossier : numéro unique attribué au patient dès son admission, valable uniquement pour la période d'hospitalisation en cours (si un patient est réadmis au HUG il reçoit un nouveau numéro).
Boxe : localisation du patient dans le service des SIC. En cas de transfert (boxe suivant) pour mouvement interne du patient.
Motif d'admission aux SIC:
Urgence : menu déroulant (oui/non = entrée elective)
Motif d'admission SIC : diagnostique médical selon ICD-9.
Texte : identification de l'intervention ou de la pathologie si pas d'intervention chirurgicale (définitions du menu déroulant).
Provenance : Service, autre hôpital, domicile, inconnu
Provenance Unité : A remplir si patient dans l'HC.
ASA : classe de risque d'anesthésie inscrite sur la feuille d'anesthésie (1-5)
Classe de contamination : Propre, Propre-Contaminé, Contaminé, Sale Infectés (Annexe)
Durée d'intervention : voir le temps d'intervention en minutes sur la feuille d'anesthésie (le début correspond au coup de bistouri)

Diagnostique

Infecté à l'entrée : oui, non, inconnu
McCabe : inconnu, non-fatal, fatal dans les 5 ans, fatal dans les 6 mois (voir annexe)
Diagnostique : Si le patient est admis en post-op, le diagnostique correspond à l'intervention chirurgicale (menu déroulant) si pas d'opération, mettre l'ICD 9.
Les autres diagnostiques correspondent à la ou les pathologies sous-jacentes responsables de l'admission aux SIC (définition menu déroulant).

Comorbidités : Charlson (annexe) les comorbidités n'incluent pas ni ne reprennent les diagnostiques mentionnés dans les motifs d'admission ou les diagnostiques secondaires.
Cliquer sur les cases correspondantes aux comorbidités présentées par le patient.

Autres :

Corticoïde, immunosuppresseur : cocher la case dès qu'ils sont présents à l'admission.
Transplantation : à remplir si le patient est un transplanté (moelle, organe solide).
Délai : correspond au délai de la transplantation (inférieur à 3 mois, supérieur à 3 mois)
NO : à remplir s'il y a utilisation d'oxyde nitrique

Sortie / Transfert :

Date de transfert *JJ MM AA* Unité : lieu de transfert
Motif de sortie : DCD, domicile, transfert

Encadré : Cliquer sur la colonne nom ou N° doss. et ensuite sur l'icône « jumelle », et inscrire dans la boite de dialogue l'élément recherché et cliquer « enter » afin de trouver le numéro de saisie d'un patient par exemple (réadmission au SIC par exemple). Afin d'afficher la page d'un patient, il faut inscrire son numéro de saisie retrouvé dans la case la plus inférieure gauche de la page.

Table d'équipement :

N°doss : numéro d'admission qui s'inscrit automatiquement
Date *JJ MM AA*
PRN : Projet de recherche en nursing correspondant à un chiffre calculé 3 fois par jour par l'équipe infirmière. La valeur la plus élevée est sélectionnée.
Intervention 1, 2 : intervention ou acte technique réalisé pendant le séjour aux SIC (annexe définitions) Si plus de 3 interventions durant une journée, remplir une nouvelle ligne à la même date.

CVC : nombre de catheter veineux central
CVP : nombre de catheter veineux périphérique
CAP : nombre de catheter artériel périphérique
Swan : Swan-Ganz
CAC : catheter artériel central incluant les cathéter artériels fémoraux.
PAC : port-a-cath
SNG : sonde naso-gastrique
SU : sonde urinaire (sonde à demeure)
Tube : tube endotrachéal ou canule de trachéotomie
VNI : ventilation non invasive incluant la CPAP
Drain : nombre de drains incluant les lames, les stomies, le catether péridural, le drainage ventriculaire externe, PIC (pression intracranienne).
Antiac : nombre d'antiacide incluant l'Ulcogant
Ther : nombre d'antibiotiques thérapeutiques
Prop : nombre d'antibiotiques prophylactiques
Loc : nombre d'antibiotiques locaux incluant la décontamination digestive et la désinfection nasale.
Immuno : nombre d'immunosuppresseur incluant les corticoïdes.
Lipide : alimentation parentérale contenant des lipides et l'utilisation de propophol (Disoprivan®).

Retour SIC :

A remplir pour un patient re-admit aux SIC pendant la même hospitalisation (même numéro de dossier). Case à choix multiples à remplir (oui). Cliquer sur Retour SIC et mettre le numéro de saisie du patient dans la boite de dialogue. Introduire la date de retour aux SIC, le code de réadmission (menu déroulant) ainsi que le motif de réadmission.

Infection :

Cliquer sur Infection et mettre le numéro de saisie du patient dans la boite de dialogue.
Numérotation de l'infection
Définition : critères des infections définis selon l'organisme : CDC, UPCI,UPCI modifié
Date de l'infection correspond à la date de début des signes cliniques (*JJ MM AA*)
Major Code et Specific Code : codes utilisés pour la classification des infections
Nom de l'infection
GE unit : unité à laquelle l'infection est attribuée (menu déroulant)
Communautaire : à cocher si infection communautaire (oui)
Equipement : Equipement à risque pour l'infection incriminée (Tube, cathéter, sonde urinaire, drains…)
Jours-équipement : Nombre de jour où l'équipement sus-mentionnée était présent jusqu'à la date de l'infection. Pour les bacteriémies sur catheter, le nombre de jour d'équipement correspond au nombre de jour cathéter (multiplier le nb de jour par le nombre de voie)
MRSA, BLSE, VRE : à cocher si ces germes sont en cause.
Critères (1 à 7) et sous-critère (a-h) à cocher en fonction des critères présents dans les définitions (CDC, UPCI).
Germes (1,2,3) : menu déroulant pour le germe responsable de l'infection
Case infection : Endogène/Exogène
Case Contamination : oui/non
Case Bactériémie secondaire : à cocher si bactérie secondaire associé à l'infection décrite.
Case source : organe source de la bactériémie.

Antibiotique :

Cliquer sur Antibiotique et mettre le numéro de saisie du patient dans la boite de dialogue.
Date : *JJ MM AA*
Induction : inscrire le chiffre 1 si l'antibiotique a été administré lors de l'induction de l'anesthésie.
Poids et Age
Antibio (menu déroulant), Dose (mg), nb de dose /24h
Indication : 1= prophylaxie, 2 = traitement empirique, 3 = traitement confirmé microbiol.
Modification antibio (oui/non)
Raison de la modifiaction (menu déroulant)
1 = réduction du spectre, infection confirmée
2 = germe résistant, infection confirmée
3 = ajout d'un antibiotique, infection confirmée
4 = suppression
Valeurs de TDM : Pic et vallée
Créatinine plasmatique
Calcul de la clearance (Cockroft)
Effet secondaire oui/non (fiches papier pour imputabilité)

Annexe II

Percentages of infections and infected patients per detailed interventions

Neurosurgery:	nb patient	nb infections	nb infected	% infected
craniotomy	28	6	4	14.3 %
laminectomy	9	1	1	11.1 %
shunt	8	3	3	37.5 %

Cardio-vascular	nb patient	nb infections	nb infected	% infected
heart by-pass	22	11	7	31.8 %
heart	13	5	4	30.8 %
vascular	19	2	2	10.5 %

Abdominal	nb patient	nb infections	nb infected	% infected
gastric	17	2	2	11.8 %
colon	3	7	1	33.3 %
spleen	3	1	1	33.3 %
gall	1	2	1	100.0 %
laparotomy	4	1	1	25.0 %
cholecystectomy	1	0	0	0.0 %
small intestine	1	0	0	0.0 %
hernia	1	0	0	0.0 %

others	nb patient	nb infections	nb infected	% infected
endocrine	1	0	0	0.0 %
arteriography	3	3	1	33.3 %

transplant	11	7	3	27.3%
lung	3	4	1	33 %
heart	1	2	1	100 %
liver	3	1	1	33 %
kidney	4	0	0	0 %

Annexe III

Patients receiving anti-acids during the survey (SIC and other wards)
numbers of days of treatment

		Non-infected	Infected
Nb patients with anti-acids		152	46
% of patients		85.4 %	95.8 %
Nb of days of treatment with an anti-acid	mean	5	8,1
	variance	12.41	51.12
	median	5	6
	min	1	1
	max	29	36
	Wilkoxon Rank sum test	P< 0.05	