

## National study on the utilization of prophylactic antibiotics in surgery, Belgium, 1986

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### SUMMARY

During the last week of May 1986, a 1-week prospective study on antibiotic utilization in surgical patients was held in 104 (42%) of the 247 Belgian acute care hospitals. All surgical patients with a post-operative stay of at least 3 days were studied, involving 3112 patients. Each patient was observed for 7 days, starting from the day before surgery. Antibiotics were administered to 71·9% of all patients; 21·9% received therapeutic antibiotics and 52·9% prophylactic antibiotics; 2·9% received both. Of the 1285 patients undergoing a surgical procedure with no indication for antimicrobial prophylaxis, 50·7% nevertheless received prophylaxis; 92·8% of patients with a generally recognized indication for prophylaxis received antibiotic prophylaxis. Less than one fifth (17·1%) of all prophylactic courses were stopped on the day of the intervention whilst 26·3% were continued up to the fifth post-operative day or beyond. The most frequently prescribed drugs for this indication included first and second generation cephalosporins and nitroimidazoles. The number of different generic drugs utilized per hospital ranged from 1 to 18 (mean: 7·7).

### INTRODUCTION

The emergence of multi-resistant bacteria remains one of the great challenges in hospital hygiene. Whilst we have a growing number of potent anti-microbial drugs

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at our disposal, new – often transferable – resistance factors develop concomitantly in hospital organisms.

Part of the responsibility for this phenomenon rests upon the irrational use of antibiotics (1–3), and a considerable part of the antibiotics prescribed in the hospital are for prophylaxis (3, 4). Since a large number of hospital-acquired infections occur either in the operation wound or as a direct consequence of a surgical procedure (5), the issue of prophylaxis is particularly sensitive in surgery.

Different timing and administration schedules for prophylaxis have been evaluated and published in the literature (6–8). Surgical procedures can be classified by degree of bacterial contamination and hence risk of post-operative infection (9, 10). Taking into account the infection risk of the surgical procedure and the presence of risk factors in the patient, it is in most instances possible to decide whether or not antibiotic prophylaxis is indicated.

A large number of well-controlled clinical trials determining the effectiveness of specific regimens for specific procedures have been conducted and the subject has been reviewed by several authors (11–16).

Epidemiological data, preferably of local origin, on the colonizing or infecting organisms to be anticipated in a given operation site, procedure and patient should guide the choice to the appropriate product.

The present study describes, on a nationwide basis, the prescribing habits of Belgian surgeons in this field. We have analysed the indication, timing and product choice in view of existing guidelines and the prevailing concepts from the international literature.

## MATERIAL AND METHODS

### *Population*

The target population consisted of all patients undergoing a surgical procedure on one of the study days, in the last week of May 1986, and with a planned post-operative hospital stay of more than 2 days. The definition of a surgical procedure for the purpose of this study was: any technical act performed in the operation theatre requiring general anaesthesia or regional anaesthetic block (rachi, epidural, plexus brachialis...), and fulfilling *at least one* of the following conditions: skin incision of 2 cm or more; tissue resection other than for biopsy alone; implantation of tissue or foreign material (excluding temporary catheterization); performance of a reconstructive or plastic procedure.

All 247 Belgian hospitals with a surgical unit were invited by letter to participate on a voluntary basis, and 121 (49.0%) hospitals responded positively.

### *Data gathering*

In each hospital, a study respondent was designated, who received detailed written instructions as well as instruction sheets for all persons involved in the hospital.

For each eligible patient, an individual form had to be initialized at the operation theatre, so as to obtain relevant clinical and procedure related data directly from the surgeon and the anaesthesiologist. The original front page of the form was subsequently put in the patient's file, for recording all antibiotics

administered during the next 5 days. The duplicate back sheet of the form was kept by the respondent (usually the chief nurse of the operation quarters), in order to ascertain and facilitate complete recovery of all original forms from the wards after the fifth post-operative day.

Besides identification and administrative data, the following data items were collected for each study person: the presence of risk factors (diabetes, malignancy, obesity, steroid or cytostatic drug therapy, radiation therapy, bad general condition or other risk factors), the description and timing of the surgical procedure, the demonstrated or suspected presence of infection before or at the time of the intervention, and the brandname, daily dose and timing schedule of all antibiotics administered from the day before the intervention to the fifth post-operative day included.

Finally, at the fifth post-operative day, or at the patient's discharge, whatever came first, any infection (proven or suspected) was recorded, as well as any other motivation for administering antibiotics.

#### *Data analysis*

All forms were coded and entered into the computer at the Epidemiology Unit of the Brussels Institute of Hygiene and Epidemiology.

Surgical procedures were grouped into 202 intervention groups, according to speciality, body site, type of procedure, procedure-related and site-related infection risk and patient-related infection risk (according to the presence or absence of risk factors, if relevant).

Each intervention group was subsequently classified into one of the following five 'prophylaxis indication classes':

1. No antimicrobial prophylaxis recommended.
2. Indication for antimicrobial prophylaxis debatable or controversial.
3. Prophylaxis generally recommended.
4. Infected procedure: antibiotics administered as therapy.
5. Insufficient data available, either on the survey form or in the literature.

This classification was based on review articles from the literature (11–16) or, if no study was available, on the wound classification (9, 10), and was finalized on a consensus meeting of the National Working Group on Hospital Hygiene.\* The second indication class was purposely kept large, in order to enhance acceptance of the classes 1 and 3.

The administration of antibiotics was considered on a day by day basis; administered antibiotics were considered as prophylactic if no infection was mentioned up to that day. Any antibiotic course starting later than the first post-operative day, however, or following diagnosis of an infection (of any type), was classified as therapeutic.

Hospitals which recorded less than 10 interventions during the study week or for which more than 15% of all form entries were left blank, were excluded from the analysis, as were patients with a postoperative hospital stay of less than 2 days. A systematic check for input errors was performed on each twentieth form; 10 errors were found on the 3222 entries tested (0.3%). Any *P* values mentioned refer to the  $\chi^2$  test, unless otherwise stated.

\* Details are available on request from the first author.

Table 1. *Number of interventions by speciality*

Speciality	Interventions (n)	Percentage
Orthopaedics	872	28.0
General and abdominal surgery	807	25.9
Thoracovascular surgery	380	12.2
Gynaecology	343	11.0
Urology	284	9.1
Ophthalmology	129	4.1
Tumour surgery	102	3.3
ORL (ENT)	96	3.1
Neurosurgery	57	1.8
Plastic surgery	28	0.9
Stomatology	14	0.4
Total	3112	99.8

## RESULTS

*Study population*

One hundred and four hospitals (42.1% of the 247 eligible hospitals in Belgium) effectively participated in the study. After sorting out unsuitable data as stated above, 3112 patient forms from 87 hospitals (35.2%) were eventually included for analysis. These hospitals represent 45.3% of all beds available in acute care hospitals with a surgical unit. Except for very small hospitals (< 100 beds), all sizes of hospitals were homogeneously represented in the study, and they were representatively distributed over the nine provinces.

A total of 50.5% of all interventions performed in these 87 hospitals during the study period were included in the survey. The majority of the interventions not surveyed pertained to patients for whom the postoperative stay was not foreseen as exceeding 2 days. The largest number of patients were in the age classes between 50 and 79 years (64.3%); the median age was 52 years, the mode 62 years.

*The surgical procedures*

Table 1 gives a breakdown of all recorded procedures by speciality. Orthopaedics and general and abdominal surgery account for over 50% of the procedures. Tumour surgery pertains mainly to surgery on the breast, on the thyroid gland and on lymph nodes.

*Risk factors and infections*

Presence of one or more risk factors was mentioned for 28.5% of all patients. Obesity was the most frequently quoted risk factor (336 times), but the definition of this condition was left to the individual clinician. An infection was stated or suspected before or during the intervention in 615 patients (19.8% of all patients). During the 5 post-operative days a total of 108 patients (3.5%) were reported with a new infection. In 76 of those patients no infection had been recorded before or during surgery.

*Antibiotic treatment and prophylaxis – overall results*

A total of 2238 patients (71.9%) received antibiotics on at least 1 of the 7 days they were observed (Table 2); 1645 (52.9%) received antibiotics for prophylaxis, and 682 (21.9%) as treatment. Eighty-nine (2.9%) received both types of regimen. Among the patients without any infection present or suspected before or during the surgical intervention ('M' in the table), as many as 65.9% were given prophylactic antibiotics; in 4.0% the prophylaxis was exclusively administered locally in the wound, while in 61.9% there was oral or parenteral administration. In total, 177 (7.1%) of the initially uninfected patients received local antibiotics in the surgical wound.

*Antibiotic prophylaxis – the indications*

The analysis of prophylaxis utilization has focused on the following three large prophylaxis indication classes:

1. No prophylaxis recommended.
2. Indication for prophylaxis debatable, controversial or unknown.
3. Prophylaxis generally recommended.

Table 2 summarizes the principal results. The majority (92.8%) of patients (without infection before or during intervention) undergoing surgery for which prophylaxis is generally recommended, received antibiotic coverage. On the other hand, among those who underwent clean surgery, and did not suffer from any previous infection, as many as 50.7% received prophylaxis. These figures remained almost unchanged when immunodeficient patients, patients with diabetes or with antecedents of rheumatic fever or patients under corticosteroid therapy were excluded. Table 3 lists the 20 most frequently recorded surgical procedures with their prophylaxis figures.

Among the 76 previously uninfected patients who developed an infection during the first 5 post-operative days, 47 had received peri-operative prophylaxis (62%); after controlling for indication for prophylaxis, this figure appeared to be significantly lower than in all patients uninfected at intervention ( $0.05 > P > 0.01$ ).

*Antibiotic prophylaxis – timing and duration*

Figure 1 summarizes the duration of the prophylactic regimens, classified by the day of onset. Only 17.1% of all oral or parenteral prophylactic courses were not extended beyond the day of the intervention, while 66.1% went on beyond the first post-operative day and 26.3% were still extant on the fifth post-operative day. In 170 patients prophylaxis was initiated before the day of intervention (11.8% of uninfected patients ever receiving prophylaxis, and already hospitalized on the day before their intervention). Forty-two patients were not treated before the first post-operative day (only three of these interventions were completed after 5 p.m.).

Among those patients for whom oral or parenteral prophylaxis was started on the day of the operation, the first dose was generally given close to the start of the intervention (Fig. 2). However, in 25.8% of these patients, therapy was commenced 1 h or more before (11.6%) or after surgery (14.2%).

Table 2. Antibiotic prophylaxis - frequency (in percentage) by prophylaxis indication class

Condition	Use of prophylaxis				Total (n = 3112) % of n	% of M
	Not recommended (n = 1553) % of n	Debatable or unknown (n = 981) % of n	Generally recommended (n = 578) % of n	Total (n = 3112) % of n		
No infection before or during intervention (= M, i.e. patients possibly eligible for prophylaxis)	82.7 (M = 1285)	78.2 (M = 563)	77.0 (M = 445)	80.2 (M = 2497)		
Antibiotics administered	58.5	80.3	93.6	71.9		
Therapeutic antibiotics	17.8	24.9	28.0	21.9*		
Prophylactic antibiotics (all):	41.9	59.2	75.7	52.9	65.9	
Only local antibiotics peri-operatively	3.4	3.8	1.7	3.2	4.0	
Oral or parenteral antibiotics	38.5	55.5	69.7	49.6	61.9	

\* 89 patients (2.9%) had a prophylactic regimen followed by a therapeutic one.

Table 3. Utilization of antibiotic prophylaxis for the 20 most frequent surgical procedures

Procedure (within parentheses: indication class*)	Number of patients (n)	Number without infection before/during intervention (M)	Percentage of uninfected (M) with prophylaxis
Appendectomy (non-perforated) (1)	197	105	37.1
Inguinal/crural hernia repair (1)	137	130	41.5
Abdominal hysterectomy (2)	108	98	79.6
Cholecystectomy (2 and 3)	104	50	72.5
Soft tissue orthopaedics (muscle, tendon, ligament...) (1)	100	94	63.8
Total hip prosthesis (3)	99	92	100.0
Trans-urethral resection of prostate (2)	80	65	84.6
Stripping varicose veins/varicoectomy (1)	80	75	38.7
Large osteosynthesis (other) (2)	71	64	85.9
Coronary bypass (2)	70	69	100.0
Cataract: extraction + implantation (1)	69	63	73.0
Caesarean section (2 and 3)	69	55	69.0
Laminectomy/cure discal hernia (1)	64	61	62.3
Medium size osteosynthesis (2)	55	48	75.0
Fracture of prox. femur (nailing/Moore prosthesis...) (3)	54	52	90.4
Partial colectomy/sigmoidectomy (3)	52	31	100.0
Vaginal hysterectomy (3)	45	42	76.2
Vascular surgery lower limb (except varicose veins) (3)	44	37	100.0
Intramedullary nailing (2)	37	32	78.1
Hallux valgus (1)	34	30	56.7
Total	1569	1293	70.7

\* 1, no antibiotic prophylaxis is recommended; 2, indication for prophylaxis is debatable or controversial; 3, prophylaxis is generally recommended.

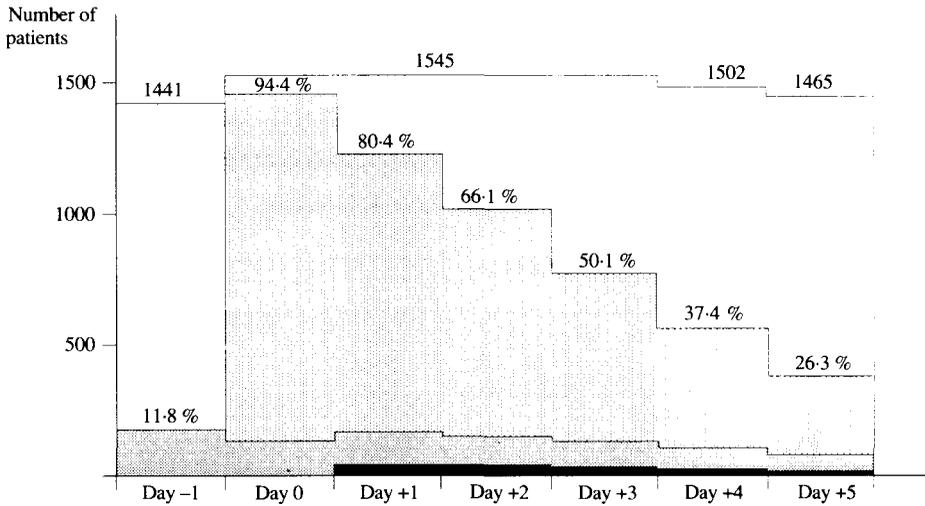


Fig. 1. Timing of prophylactic antibiotics (p.o., i.m., or i.v.). Top line: number of initially non-infected patients ever treated with prophylaxis and (still) present on the day indicated on the x-axis. Number of patients with prophylaxis for whom prophylaxis started on: day 0 (intervention) (▨); day -1 (▩); day +1 (■).

Timing of onset of prophylaxis

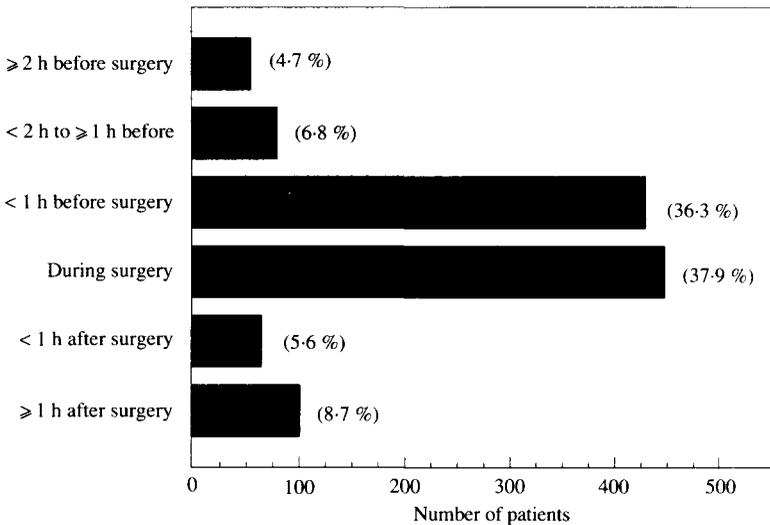


Fig. 2. Prophylaxis (p.o., i.m. or i.v.) started on the day of the intervention, by moment of onset.

*Antibiotic prophylaxis – product choice*

First generation cephalosporins (mainly cefadroxil, cefalexin and cefazolin) and second generation cephalosporins (cefaclor, cefamandole and cefuroxime) together accounted for about 45% of all prescriptions. Ampicillin and the ampicillin-like

products account for 13·1%, and the imidazole antibiotics for 7·2%, as they are frequently associated with either  $\beta$ -lactam antibiotics or aminoglycosides. The latter were used in 6·8% of the cases. Penicillins were rarely utilized in this indication. Overall, two or more antibiotics of different families (17) were combined in one single course in 20·4% of cases.

In 172 cases, antibiotics were locally applied in the wound; the products most frequently utilized were rifamycin (42% of the cases), chloramphenicol (32%) and gentamicin (9%). The number of different generic products utilized for prophylaxis within the same hospital varied from 1 to 18, with a mean of 7·7 different products ( $\pm 3\cdot9$ ), and a median of 7.

#### DISCUSSION

The aim of this study was to analyse the peri-operative and early post-operative usage of antibiotics in Belgian hospitals. The study has obtained a very large participation-rate (42·1% of the eligible hospitals in the country), well distributed over the nine Belgian provinces.

On the other hand, the study only considered the antibiotics given within the hospital, and limited its scope from the day before intervention to the fifth post-operative day. It will more than probably underestimate the real intervention-linked antibiotic consumption for the interventions considered, but outpatient antibiotic utilization is difficult to evaluate in a hospital-based survey, and was intentionally excluded from this study. The study further restricted its scope to patients with a post-operative stay of at least 3 days, which, evidently, has led to the selection of the more complicated surgery. However, this kind of surgery does not necessarily require antibiotic prophylaxis more frequently; the most important factor is the classification of the intervention in terms of contamination class or infection risk.

Even so, the percentage of interventions covered with prophylactic antibiotics is very high: 52·9% overall. Comparable figures on a national scale do not exist for most countries. In the national prevalence survey of hospital-acquired infections in Italy, 39·7% of surgical patients and 31·6% of orthopaedic patients were receiving an antimicrobial treatment on the day of the survey; the corresponding prophylaxis figures were 25·8 and 22·0% (18). Overall, 51·5% of patients undergoing surgery had received antibiotics, and 37·4% had antimicrobial prophylaxis (19). The Spanish prevalence survey recorded an overall prophylaxis prevalence figure of 16·9% in non-infected patients (including non-surgical patients) (20). Other hospital-based studies report prophylaxis rates (incidence) in surgical patients between 5 and 30% (4, 21–25).

In our survey, the majority of patients who really needed antibiotic prophylaxis received it, but as many as half of the patients undergoing surgery for which none was indicated also got prophylaxis (Table 2).

The relative overuse of prophylactic antibiotics is even more pronounced when the timing and duration of the prophylactic courses are considered. The experiments of Miles, Miles & Burke (6, 7), some 30 years ago, and numerous animal studies and work in human patients performed since, have clearly established that the effective period of prophylactic antibiotics is limited to the duration of the intervention.

This study demonstrates that, although most patients receive their prophylaxis immediately before or during surgery, 29% of all prophylactic courses initiated on the day of intervention were either started too soon or too late. Added to this are the 42 patients for whom prophylaxis was only initiated on the first post-operative day.

Of much more concern are the findings related to the duration of prophylaxis: prophylaxis was confined to the day of the intervention (possibly beginning on the day before) in not more than 17.1% of all prophylactic courses and in only 33.9% of the cases was the prophylaxis not extended beyond the first post-operative day. Prolonged prophylaxis not only involves a waste of drugs, material and nursing time, it is also an important factor in the emergence of antimicrobial resistance in hospital organisms (1, 3), which, in turn, could lead to an inflationary demand for more potent drugs in larger quantities. Very short or single-shot antibiotic courses are much less likely to contribute to the induction of resistance (2). Finally, antibiotic overuse represents a source of discomfort for the patient.

When investigating which drugs are most commonly used for prophylaxis, our study indicates a predilection for  $\beta$ -lactam antibiotics, especially for the first generation cephalosporins, and, to a lesser extent, for those of the second generation. At the moment of the study (May–June 1986), no widespread use of the third generation (cefotaxime, cefotetan, ceftazidime and ceftriaxone) was found (2.1% of all prophylactic courses).

When comparing the product choices and their ranking in different European countries, large differences appear (18, 20, 23, 24). This probably reflects both the differences in approach as they are taught in different 'schools' and the marketing policies of the pharmaceutical industry which can be quite different from country to country. We know of antibiotics that are intensively marketed for prophylactic use (only) in a certain country, while they are promoted for therapeutic use or are even not commercialized in neighbouring countries. The clinician is confronted daily with the marketing efforts of the industry. Clinical trials of new compounds, or of new indications (e.g. prophylaxis) for known compounds, are often promotional campaigns in disguise (26). Antibiotic resistance data from teaching hospitals, which are almost inevitably biased towards the more 'problematic' end of the microbial spectrum (1), are easily misused to justify unnecessarily broad-spectrum prophylaxis.

In most of the centres which participated in the study, the variability of product choice is considerable: within the study period, an average of more than seven different generic products per hospital (range 1–18) were used for prophylaxis. We do not have quantitative information on the existence and use of antibiotic policy programmes in the participating centres, but to date no national guidelines are available.

Even so, comprehensive antibiotic utilization policies appear to be needed. In order to be effective, a broad consensus among all concerned hospital staff, including the hospital pharmacist, the microbiologist and the infection-control nurse should be pursued, and threatening or sanctioning interventions should be carefully avoided (27, 30).

Numerous solutions to this problem have been suggested (31), ranging from guidelines and utilization feedback to more restrictive drug formularies, special

drug prescription forms with automatic stop orders or a systematic audit. Antibiotic policies generally bring about considerable reduction in antibiotic costs (32–34), which, in certain reimbursement settings, can be the major incentive towards the implementation of such programmes. In Belgium, the responsibility for the hygiene within each hospital lies in the hands of a pluridisciplinary hospital hygiene committee. If things are to change, much will depend on these committees, and the results of the present study might help them in their efforts.

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