SURVEILLANCE AND CONTROL OF HOSPITAL-ACQUIRED INFECTIONS IN THE NETHERLANDS: TEN-YEAR EXPERIENCE IN AN ACUTE CARE HOSPITAL

SURVEILLANCE EN PREVENTIE VAN
ZIEKENHUISINFEKTIES IN NEDERLAND:
TIEN JAAR ERVARING IN EEN ALGEMEEN ZIEKENHUIS

PROEFSCHRIFT

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"GOOD SURVEILLANCE
DOES NOT NECESSARILY ENSURE
THE MAKING OF THE RIGHT DECISIONS,
BUT IT REDUCES THE CHANCES OF WRONG ONES".

ALEXANDER D. LANGMUIR

SCIENTIA SERVIAT CARITATI

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LIST OF ABBREVIATIONS

APO	Adverse Patient Outcome
BSI	Blood Stream Infection
CDC	Centers for Disease Control, Atlanta, GA, USA
CI_{95}	Confidence Interval 95%
CIE	Center of Infectious Disease Epidemiology of the RIVM
HAI	Hospital-Acquired Infection
ICP	Infection Control Practitioner
LRES	Lower RESpiratory infection
NNIS	National Nosocomial Infections Surveillance system
PSZU	Project Surveillance of hospital-acquired infections in the Utrecht region.
RIVM	National Institute of Public Health and Environmental Protection
SENIC	Study on the efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals
SIG	National Medical Registry
SRWD	Surgical Wound Infection
SSI	Surgical Site Infection
USA	United States of America
UTI	Urinary Tract Infection
WHO	World Health Organization
WIP	Working party Infection Prevention

INTRODUCTION

Preface

When a patient is admitted to a hospital a complication, an Adverse Patient Occurrence (APO), may occur. A special type of such a complication is an infection. Hospital-acquired infections (HAI) affect the population admitted to hospitals worldwide. HAI, also called nosocomial infections, are a threat to the health of the patients and, therefore, a threat to the quality of care; they should be prevented.

With the goal to prevent HAI a system of continuous surveillance and control of HAI was started in 1984 in Oudenrijn Hospital, a 270-bed general hospital in the city of Utrecht, the Netherlands. After the system has been applied for 10 years, the question can be raised: does it really work? Is continuous surveillance of HAI feasible, does continuous surveillance produce targets for intervention and has any impact been noticed on the rate of HAI? The aim of this thesis is to answer these questions using the experience of 10 years continuous surveillance and control of hospital-acquired infections in the Oudenrijn Hospital, Utrecht.

The lay out will be as follows. The introductory Part One gives a historical, global, overview of the emergence of surveillance of HAI. Part Two describes the methods used in Oudenrijn hospital to identify HAI. Part Three describes the way the problem of HAI was addressed by identifying targets for preventive actions, and the results of such actions. Four surveillance-triggered studies are included. Of these, three studies are on the prevention of catheter-associated urinary tract infections and one study is on the costs of HAI in the Oudenrijn Hospital. Part Four describes the developments towards a national network of standardised surveillance of HAI in the Netherlands. The feasibility of continuous surveillance, the ability to identify targets for interventions, and the impact of such prevention on infection control are discussed. Recommendations are made for future research and development.

Chapter 1. Historical overview

Data collections on hospital-acquired infections (HAI) are known from the eighteenth century onwards. The interest for these data subsided when the occurrence of HAI decreased with the introduction of antisepsis, asepsis and antibiotics. The importance of data on HAI was felt again in the 1950s because of the staphylococcal epidemics in hospitals. In the '80s and '90s new diseases, the rapid emergence of multiple resistance to antibiotics, and increasing numbers of immunocompromised patients renewed the interest in infections in general and in hospital acquired infections in particular. Insight in the magnitude of the problem was obtained in incidence and prevalence studies. Surveillance of HAI emerged and definitions of HAI were developed.

Data on infections and deaths due to hospitalization are known for over two centuries [1]. From 1784-1822 mortality rates in the Vienna Lying-in hospital were 1.2 per 100 deliveries, this rate rose to 5.3 per 100 deliveries in the period from 1823-1846. It was Ignaz Semmelweiss who hypothised that the contamination of the wounds by cadaveric material via the hands of the medical students was the cause of puerperal fever and maternal death in Division I of the hospital. The intervention consisted of desinfection of hands after the contact with the cadavers, which resulted in a decrease in maternal deaths from almost 10 % to 1.3 %. In England in 1863 William Farr's data on mortality in hospitals of England were published by Florence Nightingale. She concluded that hospitals are unhealthy places, identifying hospitalization as a risk factor for death [2].

Simpson presented in 1869 data on mortality after amputation and identified surgery in a large metropolitan hospital as a risk factor for mortality. It was Lister who developed preventive measures based on the hypothesis that wounds became infected by micro-organisms. He introduced "the antiseptic system of treatment" using carbolic acid as antisepsis[3]. Only one table from his collected

papers is known with a summary of his early results:[4]

Table 1. Mortality after amputation in the years before and after the antiseptic period 1864 - 1969 (Joseph Lister).

Before the Antiseptic Period.

1864.

Seat of Amputation	*No.of Amputations*	*Recoveries*	*Deaths*
Shoulder	*1*	*0*	*1*
Arm	*3*	*1*	*2*
Forearm 3	*2*	*1*	
Thigh	*1*	*1*	*0*
Leg	*4*	*3*	*1*
Knee	*2*	*1*	*1*
Ankle	*3*	*2*	*1*
Totals	*17*	*10*	*7*

1866.

Arm	*2*	*1*	*1*
Elbow	*1*	*0*	*1*
Forearm 2	*2*	*0*	
Thigh	*4*	*0*	*4*
Knee	*6*	*4*	*2*
Leg	*1*	*1*	*0*
Ankle	*2*	*1*	*1*
Totals	*18*	*9*	*9*

On the other hand, we have·

During the Antiseptic Period.

1867.

Seat of Amputation	*No.of Amputations*	*Recoveries*	*Deaths*
Arm	*1*	*1*	*0*
Forearm 2	*2*	*0*	
Knee	*2*	*2*	*0*
Leg	*1*	*1*	*0*
Ankle	*1*	*1*	*0*
Totals	*7*	*7*	*0*

1868.

Shoulder	*1*	*1*	*0*
Forearm 2	*2*	*0*	
Thigh	*1*	*1*	*0*
Knee	*8*	*5*	*3*
Ankle	*5*	*5*	*0*
Totals	*17*	*14*	*3*

1869.

Shoulder	*2*	*2*	*0*
Arm	*2*	*2*	*0*
Forearm 2	*1*	*1*	
Thigh	*1*	*0*	*1*
Knee	*3*	*2*	*1*
Leg	*3*	*3*	*0*
Ankle	*3*	*3*	*0*
Totals	*16*	*13*	*3*

From reference 4.

" The hospital records are unfortunately imperfect for one of the three years immediately preceeding the antiseptic period", Lister comments. He admits that these numbers are too small for a satisfactory statistical comparison, but " when the details are considered, they are highly valuable with reference to the question we are considering"[4].

Antisepsis developed into asepsis and with the introduction of antibiotics (sulfonamides in 1935 and penicillin in 1945) the rates of wound infections decreased, as did the interest in data on hospital acquired infections.

In the 1950s penicillin-resistant staphylococcal epidemics began to plague the hospitals in the USA and Europe and the interest in infection surveillance and control was renewed [5].

In the USA Williams published his book on "Hospital Infections" in 1960 and in 1963 Langmuir provided the basic framework for the way to approach the problems of nosocomial infections at the Centers for Disease Control and Hospital Epidemiology, Atlanta USA [6] [7]. Langmuir is called "the father of the shoe leather epidemiology", stressing the need for surveillance [8]. He defined surveillance (of hospital acquired infections) as the continuous collection, collation and analysis of data required for the planning, execution and evaluation of (infection control) policies, with dissemmination of the information generated to those who need to know [7].

In England Colebrook suggested in 1955 that a Medical Doctor should be appointed as infection control officer in every hospital. He also wanted, at least in some hospitals, a systematic check, year by year, on all the infections acquired in hospital. And these should be published [9]. Moore appointed the first infection control nurse in 1959 [10]. This served as an example for similar positions in the hospitals in the United States [11] [12] [13]. Moore suggested at the International Conference on Nosocomial Infections in 1970 that incidence rates could not be used for determining changes in a hospital or for comparisons between hospitals

[14]. So, in England prevalence surveys rather than incidence studies have been carried out between 1968 and 1970, and were repeated in the '80s and '90s, and the collection of incidence data remained of little interest there [15 16 17 18].

In the Netherlands a national symposium was held in 1959 on the subject "Crossinfections in Hospitals" where the problems of staphylococcal infections were discussed along with hygienic problems in hospitals. Following this symposium professor K.C.Winkler from the University of Utrecht suggested to the governement to pay special attention to this problem, which finally resulted in the installation of a committee of the national Health Council. The task of the committee was to prepare guidelines, based upon known results from research, for prevention and control of hospital-acquired infections. In 1976 the committee finished the task and presented its "Advice on revised guidelines for prevention and control of nosocomial infections" to the Minister of Public Health and Environmental Hygiene [19]. This document stated that assessment of the frequency of hospital-acquired infections is a prerequisite for judging if infection control measures have been succesful or need to be adjusted. It was advised to maintain a continuous and prospective registration of nosocomial infections, with emphasis on certain risk factors and services (pp 22-23 of reference 19).

In 1970 the Centers for Disease Control (CDC) in Atlanta, USA, cosponsored the 1st International Conference on Nosocomial Infections and at this conference the initial description of what later became known as the National Nosocomial Infection Surveillance system (NNIS) was presented [20 21].

The CDC invited selected hospitals to routinely report their data on nosocomial infections, using the surveillance method and infection definitions developed by CDC in pilot studies. This system entailed hospital wide surveillance of all sites and services. In October 1986 the system was changed. More precise measurements of nosocomial infections risks and outcomes in specific patients groups were sought. Therefore, NNIS surveillance components were introduced in addition to the hospital wide surveillance [22 23].

However, the goals of NNIS did not change much over the years, and included:

1. Collect surveillance data from a sample of acute-care hospitals in the United States to permit valid estimation of the magnitude of nosocomial infections in hospitalized patients.
2. Analyze and report nosocomial infection surveillance data to permit recognition of trends in infection rates, antimicrobial resistance, and nosocomial pathogens.
3. Provide hospitals with risk-adjusted nosocomial infection data that can be used for comparison.
4. Assist hospitals in developing surveillance and analysis methods that permit timely recognition of nosocomial infection problems and prompt intervention with appropriate infection control measures.
5. To conduct collaborative research studies with NNIS hospitals (e.g. describe the epidemiology of emerging infections and pathogens, assess the importance of potential risk factors, further characterize nosocomial pathogens and mechanisms of resistance, and evaluate alternative surveillance and prevention strategies) [24].

Thus, the basis for todays surveillance of HAI was prepared and the technique of continuous surveillance and the use of standardised definitions of nosocomial infections were introduced [25]. A number of USA-hospitals adopted such surveillance and control programs in the 1960s and 1970s in response to an urgent call from the American Hospital Association and CDC, which was supported by the Joint Commission on Accreditation of Hospitals [8 26]. Since no one was able to define what was important in infection control and no one could answer the question whether a surveillance and control program would be efficacious, the Study on Efficacy of Nosocomial Infection Control (SENIC Project) was undertaken in 1974 [27]. The project employed a study design and methodology constructed such that any effect of investigator bias could be ruled out [28]. The central hypothesis tested in the SENIC study was that *"in hospitals conducting ongoing sur-*

veillance of infections and using the resulting information along with studies in the literature and guidelines from other sources to direct active infection control programs to overcome the inertia of ward routine and change high-risk patient care practices to preventive ones, the incidence rate will drop and thereafter remain at some irreducible minimum rate.

The primary objectives of the study were threefold "*1) to determine if (and, if so, to what degree) the implementation of surveillance and control programs (ISCPs) has lowered the rate of nosocomial infection, 2) to describe the current status of ISCPs and infection rates, and 3) to demonstrate the relationships among characteristics of hospitals and patients, components of ISCPs, and changes in infection rates* [29]."

Data were collected in three phases. In phase I a questionnaire was sent to 6,586 US hospitals to obtain information needed to calculate an initial surveillance index and a control index. The surveillance index measured the extent to which each hospital conducted active surveillance of nosocomial infections, the control index measured the intensity of efforts to intervene in the care of patients to reduce the infection risk. From these a random sample of 338 hospitals was subsequently selected. In phase II trained interviewers were sent to these hospitals to interview 12 hospital personnel most likely to have important duties on infection surveillance and control. Also, a random sample of staff nurses were interviewed. In phase III infection rates in 1970, before establishing surveillance and control programs, were compared to the rates in 1976, the time of the phase I survey. The two study populations each yielded 169,000 patients. Every patient's entire medical record was reviewed.

Parallel analyses were performed for each site of infection. Stepwise multiple lineair regression was used as the principal model-building technique. The pool of potential predictor variables used in developing these models included the following classes of variables: 1) the 1970 infection rate, 2) the five-year change in medical practice variables, 2) the five-year change in average patient risk, 4)

the five year change in dynamic hospital characteristics, 5) the 1976 measurement of hospital characteristics, characteristics of the infection surveillance and control program adopted between 1970 and 1975-1976 [27].

The results from SENIC indicated that "*establishment of an intensive surveillance and control program was strongly associated with reduction in rates of nososcomial urinary tract infection, surgical wound infection, pneumonia and bacteremia between 1970 and 1975-76, after controlling for other characteristics of the hospitals and their patients. Essential components of effective programs included conducting organized surveillance and control activities and having a trained, effectual infection control physician, an infection control nurse per 250 beds, and a system for reporting infection rates to practicing surgeons. Programs with these components reduced their hospitals' infection rates by 32%. Since relatively few hospitals had very effective programs, however, only 6 % of the nation's approximately 2 million nosocomial infections were being prevented in the mid-1970s, leaving another 26 % to be prevented by universal adoption of these programs. Among hospitals without effective programs, the overall infection rate increased by 18% from 1970 to 1976* [30]."

While in the 1980s in the USA ongoing surveillance was practised, Europe conducted prevalence studies. In the 1980s national surveys were carried out in the United Kingdom [17], in Norway [31], Italy [32], and in Belgium [33] that estimated the magnitude of the problem. Internationally, the World Health Organization (WHO) took the initiative in 1983- 1984 and conducted a prevalence survey in 55 hospitals in 14 countries throughout the world to determine the extent of the occurrence of HAI. This survey was meant to prepare the way for the development of a surveillance system for nosocomial infections and antibiotic resistance, being one of components of the WHO Global Medium Term Programme for 1984-1989 [34].

In the eighties and early nineties the renewed interest in infectious diseases in

general, and nosocomial infections in particular, was generated by the emergence of several new diseases (e.g AIDS caused by HIV), the discovery of the infectious etiology of "old" diseases (e.g peptic ulcer disease caused by *Helicobacter pylori*[35]) and the rapid spread of antimicrobial resistance among the major bacterial species pathogenic to man (e.g. methicillin-resistance among *Staphylococcus aureus* and penicillin-resistance among pneumococci [36 37 38]). In hospitals these challenges to man were further compounded by the ever increasing numbers of patients that by age (premature neonates, elderly) underlying disease and/or treatment are severely immunocompromised, and, thus, extremely susceptible to the development of nosocomial infections [39 40 41].

The magnitude of the problem of nosocomial infections can be studied in incidence or prevalence studies and, consequently, is commonly expressed in two measures of disease frequency: incidence rates and prevalence rates. Incidence rates are a measure of events, prevalence rates are a measure of what prevails at a certain moment. The incidence of a disease is the number of new cases in a certain period of time. The incidence rate (incidence density) is the number of new cases per specified unit of population and time [42]. The rate of nosocomial infections is often expressed as the number of infections (numerator data), collected on the hospital population which is expressed in the number of patients admitted or discharged (denominator data) [43]. The number of nosocomial infections per number of admissions or discharges from hospital is neither an incidence rate nor a cumulative incidence, cumulative incidence being the incidence per number of persons present at the start of the period under investigation [44]. In search of adequate denominators alternatives have been offered to calculate the rates per patient days or patients at risk [45]. Incidence measured as early as possible after onset of the infection is most useful when studying causal factors, since causal factors occur prior to the onset of the nosocomial infection.

The prevalence of a disease is the frequency of the disease, measured at a designated point in time. The prevalence rate is the proportion of the population

with the disease in the numerator and the total population (affected and unaffected) in the denominator [45]. Prevalence measures are considered to be somewhat inferior to incidence, because prevalence rates are influenced not only by the causal factor(s) but also by the duration of the infection.

Data collection on infections requires well standardised definitions in order to obtain reproducible information. MacMahon uses two distinct types of criteria to categorize ill persons into groups: manifestational criteria and causal criteria [42]. Manifestational criteria are used to group ill persons according to the "manifestations", i.e. signs and symptoms, behavior, physiology, of the disease. Examples are diabetes mellitus, cancer, collumfractures, and urinary tract infections. Causal criteria make grouping dependent on the similarity of persons with the same "event" believed to be the cause of their illness. Examples are birth trauma, burns, lead poisoning, and catheter-induced infections.

The Centers for Disease Control published several sets of definitions for nosocomial infections, using both manifestational and causal criteria. The first set from 1969 was expanded upon in 1974 for the hospitals participating in NNIS. However, these criteria remained unpublished [21 46]. In 1988 the criteria which are used until today were published. A minor modification concerning the definitions of surgical wound infections was published in 1992 [47 48]. (See Appendix A for the full published set of definitions).

The CDC definitions are based on a few major principles. Information used to determine the presence and classification of an infection involves various combinations of clinical findings and results of laboratory and other diagnostic tests. A physician's or surgeon's diagnosis of infection is acceptible, when derived from direct observation during surgery, endoscopic examination or other diagnostic study or based on clinical judgement, unless there is compelling evidence to the contrary. For an infection to be defined as nosocomial there must be no evidence that the infection was present, or incubating, at the time of hospital

admission. An infection that is associated with a complication or extension of infection(s) already present on admission is not a nosocomial infection, unless a change in pathogens or symptoms strongly suggest a new infection. An infection in an infant that is known or proved to have been acquired transplacentally and becomes evident shortly after birth is not a nosocomial infection (unless the infection was nosocomially acquired by the mother). No specific time during or after hospitalization is given to determine whether an infection is nosocomial or community-acquired, except for a few situations that are referred to in the definitions. Each infection must, thus, be assessed for evidence that links it to hospitalization. These definitions have also been accepted in the Netherlands where the Working Party on Infection Prevention (WIP) provided the translation in Dutch [49].

The above described developments had their impact on individual hospitals in the Netherlands [50 51 52].

When, in 1983, the Oudenrijn Hospital was confronted with the choice of a method to identify hospital-acquired infections, the method of continuous hospital-wide surveillance was chosen, since this method was considered to be superior over prevalence surveys. (Please note that the more detailed NNIS components had not yet been developed at that time).

The program of hospital-wide surveillance and control, which has now been in operation for over 10 years, is evaluated in this thesis. This thesis will address the following questions:

1) Is a system of continuous hospital-wide surveillance of hospital-acquired infections feasible in an acute-care facility in the Netherlands?

2) Does such a system of continuous surveillance of hospital-acquired infections produce relevant targets for intervention?

3) Did this system of continuous surveillance of hospital-acquired infections have a significant impact on the prevention and control of hospital-acquired infections in this hospital?

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PART TWO

INDENTIFICATION OF THE PROBLEM

Introduction

In 1984 an infection control program was started in the 270-bed OudenrijnHospital with the ultimate goal to reduce the risk of nosocomial infections for the patients. To get an idea of the magnitude of the problem of nosocomial infections in the hospital two actions were initiated. First, a retrospective chart review of all episodes of bacteremia was performed, since bacteremia is recognized as an infection which increases morbididty and mortality in hospitalized patients [1 2]. Secondly, a hospital-wide surveillance of all types of nosocomial infections was started in order to know the endemic rate of nosocomial infections in this hospital, to select targets for interventions, to evaluate the efficacy of such preventive measures, and to recognize trends over time.

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Chapter 2.

Bacteremia in two general hospitals: the tip of the iceberg of nosocomial infections

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Summary

Bacteremia in two general hospitals; the tip of the iceberg

In one year, 197 episodes of bacteremia occurred in 174 patients admitted to two general hospitals. The sources of infection and the moments of occurrence were studied. The incidence of bacteremia was 1.15 per 100 admissions in the larger university-affiliated hospital and 0.84 in the smaller non-teaching hospital. 43% of these bacteremias were due to urogenital tract infections, virtually always caused by *Escherichia coli* and other Gram-negative bacteria of the family of Enterobacteriaceae. In 20% of the bacteremias the source of infection was an infected wound, a decubitus ulcer or an intravascular catheter. The predominant causative agents isolated in these cases were *Staphylococcus aureus* and *Staphylococcus epidermidis*. 29 of the 174 (17%) patients died, 23 (13%) of them as a

consequence of sepsis. 68 % of the bacteremias could be classified as nosocomial. A system of active surveillance of nosocomial infections revealed an infection rate of 7.1 per 100 admissions in 1984 in the smaller hospital; 57 % of these involved the urinary tract. Future efforts to curb hospital-acquired infection should focus on urinary tract infections and infections of intravascular catheters, wounds and other skin defects. A continuous active surveillance system for hospital acquired-infections is of prime importance.

Introduction

Bacteremia is a growing threat to infected patients. Morbidity and mortality are increased by it; mortality may rise up to 50 % [1,2]. A Dutch study in the period of 1972-1977 showed that three quarters of the cases of bacteremia occurred during hospital admission and are, therefore, nosocomial infections [2]. Mortality is higher when the infection occurs during admission than when bacteremia is present at admission [1,2]. The type and severity of the underlying disease determines to a large extent the risk of nosocomial bacteremia, that means the level of the patient's immune status, and the number and type of invasive diagnostic and therapeutic procedures which the patient undergoes during admission (iatrogenic breaches of the immune status). In this respect university hospitals and non-university hospitals will differ; therefore, the results and conclusions in relation to the cause of bacteremias in a university hospital cannot be considered to be valid for a non-university hospital.

We studied all bacteremic cases that occurred during one year (1984) in patients admitted to a medium-size 525-bed hospital in the centre of the city (Diakonessenhuis, Utrecht) and to a smaller 270-bed general hospital (Oudenrijn hospital, Utrecht). Also in the smaller hospital an infection surveillance and control program was developed and put into practice for the same year.

Patients and methods

All patients admitted to one of both hospitals were included in the study. Bloodcultures were taken by adding 5 ml venous blood to a culture-bottle with 50 ml BHI bouillon and to 50 ml medium (Schaedler-bouillon) for isolation of obligate anaerobes. Isolated micro-organisms were identified by standard methods[3]. The number of cultures taken per patient varied from one to seven; in general, the sicker the patient, the more cultures were taken. Single positive cultures which after three days culturing were positive with only nonpathogen skinflora, such as species of Corynebacteria (diphteroids), Propionibacterium, Bacillus or coagulase-negative Staphylococci, were considered contaminants and were excluded from the study; these were mostly cultures taken from patients with clinically nonsignificant episodes of fever. Patients were included in the study as soon as their bloodculture showed growth and they stayed in the study until the moment of discharge or death. From every patient the dates of admission and discharge were recorded, together with the (probable) diagnosis and the hematological, biochemical and microbiological findings from the bacteremic episode. Also, the course of temperature, the bloodpressure, the heartrate and the urine production were recorded. The source or port of entry into the bloodstream was assessed for every bacteremic episode whenever possible. A source of infection was accepted as such when the same micro-organism (the same species with identical resistance pattern) could be isolated in a culture from material from the source of infection or port of entry; in a number of cases the presumed source of infection could only be identified on clinical grounds, for example by echography of an organ with no means of access to take cultures. A bacteremic episode was considered clinically significant if at least three criteria were met: (1) temperature > 38° C, (2) heartrate > 100 /min., (3) chills, (4) decrease in systolic bloodpressure > 30 mm Hg, (5) leukocytosis > 10 x 10^9 cells/l, and (6) oliguria < 600

ml/day. Every bacteremic episode that was evident clinically or microbiologically after 72 hours after admission was considered nosocomial, unless there was evidence to the contrary. Hospital-acquired infections were detected by weekly ward-visits by an infection control practitioner. During these "infection visits" the medical records, the temperature chart and nursing cardex of all patients present in the ward were reviewed; to try to determine whether nosocomial infections had occurred in the week prior to the "infection visit". Infections were considered nosocomial when these infections occurred after hospital admission and were neither present nor incubating at the time of admission; in case of doubt, infections were considered nosocomial if they had occurred at least 72 hours after admission [4]. Criteria for the different types of infection (urinary tract, respiratory tract, skin etc.) were those of the Centers for Disease Control (CDC, Atlanta, Georgia, USA)4. The results of the cultures from the medical microbiologic laboratory were merely supportive to this active data collection system.

Results

In both hospitals together 2,375 bloodcultures were taken in one year, 291 (12,3%) of these were positive. These positive cultures were found in 197 bacteremic episodes in 174 patients; 29 (17%) patients died, of whom 23 (13%) directly or indirectly from septicemia. 107/197 (54%) bacteremic episodes fulfilled the criteria of clinically significant bacteremia. This happened more often in patients with a bacteremia caused by Gram-negative bacteria (71 % of such cases) than in patients with cultures with Gram-positive micro-organisms (46%; difference is significant, chi-square = 8,4, $p < 0,01$). The types of causative micro-organisms with their port of entry are presented in table 1.

Table 1. Isolated micro-organisms with porte d'entree in the bloodstream

	number of isolates with porte d' entree in the bloodstream							
Micro-organism	*urinary tract*	*intra-vasc cath*	*skin wound*	*resp tract*	*intra abdom*	*other*	*un-known*	*total (%)*
Escherichia coli	43	0	2	0	8	0	4	57(27)
other *Entero-bacteriaceae*	25	1	3	3	7	1	1	41(19)
Staphylococcus epidermidis	7	10	3	0	2	0	6	28(13)
Staphylococcus aureus	3	3	9	0	1	0	2	20(9)
anaerobes	1	0	5	0	7	2	2	17(8)
Streptococcus pneumoniae	0	0	0	8	1	1	1	11(5)
Gram-negative rods, glucose nonfermen-ting***	3	2	1	1	0	0	3	10(5)
Candida albicans	1	2	0	0	1	0	1	5(2)
other	6	2	1	1	2	8	6	26(12)
total								215(100)

* prostate included
** surgical wounds included
*** Pseudomonas etc.

Facultative anaerobic micro-organisms from the Enterobacteriacae family were most frequently isolated (27% *Escherichia coli* plus 19% others) from the positive bloodcultures: these were mostly isolated from sources of infection in the urinary tract, sometimes from intra-abdominal infections. Staphylococci were the most frequently isolated causative micro-organisms, coming from infected intravascular catheters and subcutis; 10 cases of urosepsis and 10 infections from unknown sources were caused by these organisms. Strict anaerobe micro-organisms

(especially types of Bacteroïdes and Clostridium) were mostly isolated from intra-abdominal sources of infections or from skin lesions (decubitus!). Most of the time pneumococcal-bacteremia was correlated with infections in the lower respiratory tract. The other micro-organisms did not show any special preference to the location of their porte d'entree in the bloodstream. From all the bacteremias 134/197 (68%) were nosocomial according to our definition; they occurred during hospital admission and were not present or incubating at the time of admission (table 2).

Table 2. Community- and hospital-acquired bacteremias and source of infection

source of infection	*bacteremias total number (%)*	*bacteremias number nosocomial (%)*
urinary tract	85 (43)	57 (67)
intra abdominal	25 (13)	14 (56)
intravascular line	22 (11)	22 (100)
skin and wounds	17 (9)	15 (88)
respiratory tract	12 (6)	6 (50)
other	12 (6)	3 (25)
unknown	24 (12)	17 (71)
total	197 (100)	134 (68)

This included all bacteremias related to infected intravasal catheters, almost 90% of all bacteremias occur in infected skin lesions (surgical wound infections included) and 67% of all cases of urosepsis. 94 (50%) of all bacteremic cases originated from these three types of nosocomial infections. In both hospitals the sources of bacteremias were about equally divided. In both hospitals 43 % of the bacteremias were caused by urinary tract infections, 10-14 % by intra-abdominal sepsis, 7-12 % by infected skin lesions, and 12% by unknown sources. The percentage of bacteremias caused by infected intravascular catheters was higher in the medium-size hospital (14%) than in the smaller hospital (5%), but this difference was statistically not significant (chi-square = 2,99; $0,05 < p < 0,1$). A

closer look at the cases of nosocomial urosepsis revealed that these were related to the use of urinary catheters or instrumentation at this site. 43/57 (75%) episodes of hospital-acquired urosepsis were preceded by interventions in the urinary tract, a statistically significant difference with 7/28 (25%) bacteremias originating from the urinary tract that were already present at the time of admission of the patient (chi-square = 19,7; $p < 0,001$). A one-day prevalence study showed that 56/686 (8%) of the patients in the hospital had a urinary catheter in place, in 32 patients for longer than one week (indwelling catheter); in 35 (63%) of these catheterised patients the urine contained significant numbers of micro-organisms.

Further study of bacteremic infections originating from intravascular catheters showed that these developed 5-22 days after insertion of the catheter; half of these cases occurred between the 5th and 10th day of infusion therapy. A prevalence survey in one of the hospitals showed that on one day in 16% of the admitted patients one or more intravascular catheters were present, 16% of which in the same insertion site for over one week.

In order to obtain better insight in the incidence of all types of hospital-acquired infections, an active surveillance system was implemented in the smaller hospital. This meant that the infection-control practitioner visited every ward weekly and decided whether nosocomial infections had occurred in the preceding week. In 5775 admissions 413 infections were found, a frequency of 7.1 infections per 100 admissions. The largest category was urinary tract infections (57%).

Discussion

In our study in two general hospitals more than 65 % of all bacteremias occurred during admission of the patients to hospital. These bacteremias are a large part

of all the nosocomial infections occurring annually in hospitals. Nosocomial bacteremia is caused by infections following instrumentation in the urinary tract, by infected intravascular catheters, postoperative surgical wound infections and infected skin lesions. The incidence of bacteremia in hospitals in the Netherlands is not well known. Michel and Priem found a mean incidence of 1.32 bacteremias per 100 admissions in the University Hospital in Rotterdam in the period of 1972-1977 [2]. In the two general hospitals in our study the incidences were 1.15% in the medium-size hospital and 0.84% in the smaller hospital. Comparative American figures showed incidences of 1.65% for the Colorado University Hospital and 0.75% for the Denver Veteran Administration Hospital [5]. The estimate for the total of the United States is 1 bacteremia per 100 patients admitted [6]. The difference in incidence would mainly depend on the type of hospital; high incidences in university centers and other large institutions, low incidences in smaller hospitals [1 6 7 8].

The great contribution of nosocomial infections to the occurrence of bacteremias in both general hospitals is, at first glance, surprising (68% of the bacteremias occurred during admission). Although the growing importance of the occurrence of bacteremias due to nosocomial infections was noticed earlier [1], one could have expected lower incidences for general hospitals, especially for the smaller hospital [7 9]. The nosocomial bacteremia rate in the medium-size hospital was 71 and in the smaller hospital was 62: the difference was not statistically significant. It is supposed that this rate depends very much on the type of patient in the hospitals; large, mostly university affiliated centers have the highest rates [1 5]. Michel and Priem concluded that 75% of the bacteremias included in their study in the University Hospital in Rotterdam, occurred during admission [2]. In our study, the urogenital tract (43%) was the most important port of entry for bacteremic infections. Other important sources were intra-abdominal infections (13%), infected vascular catheters (11%), skin lesions (9%), and respiratory infections (6%); 12% of the bacteremias had unknown sources. This

relative percentage is unlike what was found in other studies because of the high number of urosepsis [2 5 7]. These differences cannot be easily explained, but are probably influenced by the types of patients and the definitions of the sources of infection. We applied the definitions of the National Nosocomial Infections Study of the CDC as our guideline [4].

There was a clear relationship between the isolated micro-organism and the different sources of infection. *Escherichia coli* and other types of Enterobacteriaceae were isolated from 46% of all the positive bloodculturs and originated mostly from the urinary tract. Staphylococci were isolated in 22% of the cases and originated from intravascular catheters, skin lesions and surgical wound infections; pneumococci originated almost always from the lower respiratory tract. On the whole, these findings agree with Weinstein et al[5].

To get a better insight in the incidence of nosocomial infections, we developed a surveillance system following Wenzel et al.[10], who also used the definitions of the National Nosocomial Infections Study [4 11]. It is an active surveillance system by which all the wards are visited at least once weekly by the infection control-practitioner. An active surveillance system gives a complete and valid picture of the incidence of hospital-acquired infections and is in this respect superior to passive surveillance systems, including those which depend only on results of cultures [10 12]. The bacteriological laboratory results can have an important supportive role in an active surveillance system, especially when they are preselected for this goal using a computerprogram [13].

Additional benefits of an active and continuous surveillance system are the frequent contact between the wards and the infection control practitioner ("education permanente"), early recognition of (mini-)epidemics and other infection control problems on the wards, and the evaluation of the effects of preventive measures and guidelines. For data management and analysis of nosocomial infection surveillance data, several computerprograms are available.

We found 7.1 hospital acquired infections per 100 admissions in a 270-bed

general hospital. Comparable figures in the Netherlands are not available. In the National Nosocomial Infections Study the mean frequency in 1983 in 54 participating hospitals in the United States was 3.3 per 100 discharges, in the category comparable to the smaller hospital 2.4 per 100, and in the larger hospitals, university or university-affiliated hospitals, up to 4.1 per 100 patients [14]. This may be an underestimation of the true incidences between 5 and 6% [15]. Wenzel et al. found 6 hospital acquired-infections per 100 admissions in the University of Virginia Hospital in the period 1972-1975 [16]. Although comparing these results with American figures is scientifically incorrect, our study shows more or less the same incidence of nosocomial infections in the smaller general hospital in the Netherlands. If our results are extrapolated to all general and university hospitals in our country, then 110,547 nosocomial infections occur in 1,557,000 admissions annually[17], among them, 7,783 cases of bacteremia, from which more than 1,000 patients die. Bacteremia can be justly called the visible tip of the iceberg. As a consequence of our study the prevention of nosocomial infections should be directed at urinary tract infections (catheters), infections due to intravascular infusionsystems and infections in surgical wounds and decubitus ulcera.

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Chapter 3.

Surveillance and control of hospital-acquired infections in the Oudenrijn Hospital 1984-1993

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Introduction

Hospital-acquired infections (HAI) are infections that develop in patients during their stay in hospital. The infections are not present nor incubating at the time of admission and may be of iatrogenous, endogenous or exogenous origin.
HAI add to morbidity, mortality and costs[1]. Infection rates may vary from less than one percent to 15 percent of the patients admitted to a given hospital, depending primarily on the type of services provided [2]. It has been shown that an active surveillance and control system of HAI may result in a significant decrease in infection rates [3]. In the Oudenrijn Hospital, Utrecht, the Netherlands, a hospital-wide surveillance and control system was introduced in 1984 and maintained for over 10 years. Preventive actions were based upon the findings from the surveillance.

Patients and methods

The Oudenrijn Hospital is a 270 - bed general hospital in the city of Utrecht, the Netherlands, providing 18 medical services distributed over eight nursing units. Surveillance of hospital acquired infections, based upon Wenzel et al., was performed hospital-wide for at least nine months of the year[4].

The infection control practitioner responsible for the surveillance routinely visited each ward on a weekly time schedule, reviewing patient charts for data to assess nosocomial infections. These charts contain information on clinical signs and symptoms of the patient; microbiology and other laboratory reports; reports of radiology and pharmacy; reports on operations and other diagnostic and therapeutic interventions. When pertinent information was lacking the attending nurse or physician was consulted. HAI occurring after the patient's discharge were not included unless the patient was readmitted because of his HAI. HAI were categorized using CDC definitions and modified CDC criteria which are based upon clinical and laboratory findings [5] (See Appendix 1).

The data collected consisted of demographic data, data on the HAI itself, patient- and treatment-related riskfactors, and the microbial pathogens involved. Equivocal cases of nosocomial infections were discussed with the medical microbiologist until consensus was reached. Denominator data included the number of admissions and patient days for each medical service and nursing unit, and were obtained from the hospital administration service. Data were stored and analysed with dNOSO [tm] and, subsequently, BAS-IC (Epi-systematics [tm]) software. Monthly two-way tabulations and incidences per 100 admissions and per 1,000 patient days were routinely discussed in the infection control committee. Postoperative wound infections were analysed per type of operative procedure as classified in the National Medical Registry of the Netherlands [6]. Wound infection rates were routinely reported back to the surgeons. Annual reports, containing infection rates per unit and per service, relative frequency per type of infection, and wound infection rates were sent to all

members of the infection control committee (including the medical director), physicians and nursing managers. These annual reports were also included in a yearly update of the Infection Control Handbook containing the infection prevention guidelines, which was kept in every nursing unit.
Targets for in-depth evaluation and preventive action were formulated upon the outcomes of the analysis of surveillance data. Ongoing educational activities, implementation of control measures and evaluation of these measures as evidenced by the surveillance reports, took place throughout the year.
The data shown are restricted to these months of surveillance.

Results

From 1984-1993 a total number of 2,772 HAI were found among 56,410 patients admitted who generated 611,310 patient days in the 92 months of hospital-wide surveillance. The overall incidence of HAI over these 10 years was 4.9 per 100 (CI_{95} 4.7-5.0) admissions and 4.5 (CI_{95} 4.4-4.7) per 1,000 patient days.
In the following both incidences per 100 admissions and per 1,000 patient days will be mentioned as much as possible.
From the infected patients 66 % were female and 34 % were male, which closely reflected the sex ratio of all patients admitted (66 % female and 34 % male). The incidence of HAI increased with the age of the patients. The lowest incidence was found in the age category 1-14 years: 1.1 % (CI_{95} 0.8-1.6) and the highest incidences were in patients from 65-74 years, 7.0 % (CI_{95} 5.4- 8.8), and in patients above 75 years, 10.7 % (CI_{95} 8.5-13.6), (Figure 1).

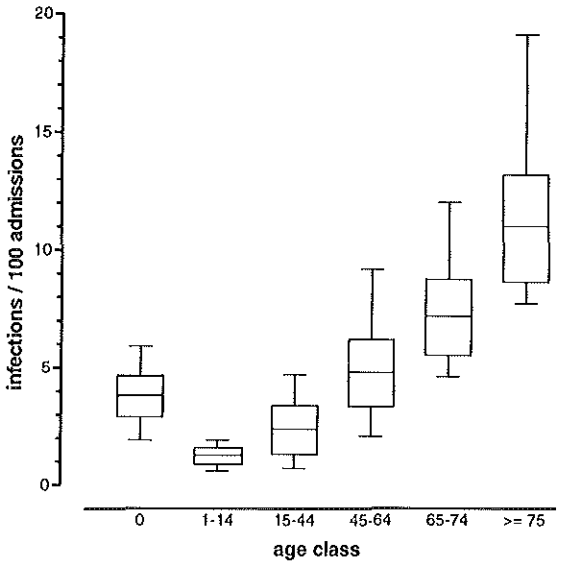

Figure 1. Average yearly incidence of nosocomial infections per 100 admissions by age class, 1984-1993. Data for each age class are presented as a box-plot representing the means and the 95% confidence interval. The brackets indicate the extreme values observed over the 10-year period.

Thus, infection rates within the 1-14 year cohort of patients were significantly lower than those of all other age class except for those 15-44 years old. And on the other hand rates of HAI within the 75 years-and-older cohort of patients were significantly higher than those of all other age classes except the 65-74 year olds. There was an almost ten-fold difference between the lowest (1-14 year) and highest (75 years and older) HAI incidences observed.

Infections most frequently found were urinary tract infections (43%), followed by surgical wound infections (19%), lower respiratory infections (11%), skin and soft tissue infections (11%) and bacteremias (10%). Postoperative lower respiratory infections were uncommon with an incidence of 1 per 1,000 patients given general anesthesia. The frequency of types of infection changed over time (Table 1).

Table 1A. Yearly incidence of hospital-acquired infections by type of infection.

incidence per 100 admissions								
year	*uti*	*swi*	*lres*	*bsi*	*cut*	*oth*	*all HAI*	*admissons*
1984	4.4	0.9	1.2	0.6	0.4	0.1	7.6	5,141
1985	3.7	0.8	0.6	0.4	0.5	0.1	6.1	5,107
1986	2.6	1.1	0.6	0.4	0.4	0.1	5.2	5,177
1987	2.7	1.2	0.7	0.6	0.4	0.3	5.9	5,236
1988	1.8	1.3	0.4	0.4	0.7	0.3	4.9	5,418
1989	1.6	0.8	0.5	0.5	0.7	0.5	4.6	6,665
1990	1.3	1.1	0.3	0.5	0.6	0.6	4.4	5,638
1991	1.1	1.0	0.5	0.5	0.6	0.4	4.1	5,888
1992	1.2	0.6	0.4	0.5	0.5	0.4	3.6	5,876
1993	1.4	0.5	0.5	0.3	0.6	0.3	3.6	6,264

uti = urinary tract infection; swi = surgical wound infection; lres = lower respiratory infection; bsi = bloodstream infection; cut = cutaneous infection; oth = other infections HAI = hospital-acquired infections.

Tabel 1B. Yearly incidence of hospital-aquired infections by type of infection.

incidence per 1,000 patientdays								
year	*uti*	*swi*	*lres*	*bsi*	*cut*	*oth*	*total*	*patient days*
1984	3.5	0.8	0.9	0.5	0.3	0.1	6.1	63,728
1985	3.1	0.7	0.5	0.3	0.4	0.1	5.1	61,285
1986	2.2	1.0	0.5	0.3	0.3	0.1	4.4	60,907
1987	2.4	1.0	0.6	0.6	0.4	0.2	5.2	59,742
1988	1.6	1.2	0.4	0.4	0.6	0.3	4.5	59,414
1989	1.5	0.8	0.4	0.5	0.7	0.5	4.4	70,771
1990	1.3	1.0	0.3	0.5	0.6	0.5	4.2	57,840
1991	1.1	1.0	0.5	0.6	0.5	0.4	4.1	57,832
1992	1.2	0.6	0.4	0.5	0.5	0.4	3.6	58,436
1993	1.4	0.5	0.5	0.4	0.6	0.3	3.7	61,355

uti = urinary tract infection; swi = surgical wound infection; lres = lower respiratory infection; bsi = bloodstream infection; cut = cutaneous infection; oth = other infections HAI = hospital-acquired infections.

Bloodstream infections included those originating from an intravenous cathetersite. Infections in the gastrointestinal tract, upper respiratory tract and cardiovascular system were less commonly found and are classified under "other" in the figures and tables.

The incidence decreased from 7.6 per 100 admissions in 1984 to 3.6 per 100 admissions in 1993, a 53% decrease. The incidence per 1,000 patient days (days at risk) decreased from 6.1 per 1,000 patient days in 1984 to 3.7 in 1993, a 39% decrease. The decrease in incidence of urinary tract infection per 100 admissions was 68% and per 1,000 patient days 60% . These differences in the extent of the decrease in the two incidence rates is primarily due to a concurrent decrease in the average length of hospital stay observed in this same decade (Figure 2). The average length of stay decreased by 20% and, in contrast, the number of admissions increased by 18 %. However, significant differences in trends by service were found; the combined service of Gynecology/Obstetrics showed a decrease in both average length of stay and in the number of admissions; in contrast, orthopedic service showed relative stability in their average length of stay as well as a temporary decrease in the number of admissions to this service. More dramatically, the number of patients admitted to the pediatric service increased > 100% within a two-year period ('88-'90) which was related to expansion of its medical staff.

Infection rates were highest in Medical service, General surgery, Gynecology, Pediatrics and Orthopedics (Table 2). These five services changed ranks when the HAI incidences were calculated per 1,000 patient days versus per 100 admissions. The Medical service is ranked first when incidence was calculated per 100 admissions (Table 2B). However, Gynecology ranked first if the HAI incidence per 1,000 patient days was calculated, and in this manner Medicine is ranked fifth (Table 2A). The infection rates were lowest in Obstetrics, Cardiology, Ophtalmology and in the Ear-Nose-Throat service. The middle ground was occupied by Urology, Neurology and Pulmonology, whether the incidences were expressed per 100 admissions or per 1,000 patient days.

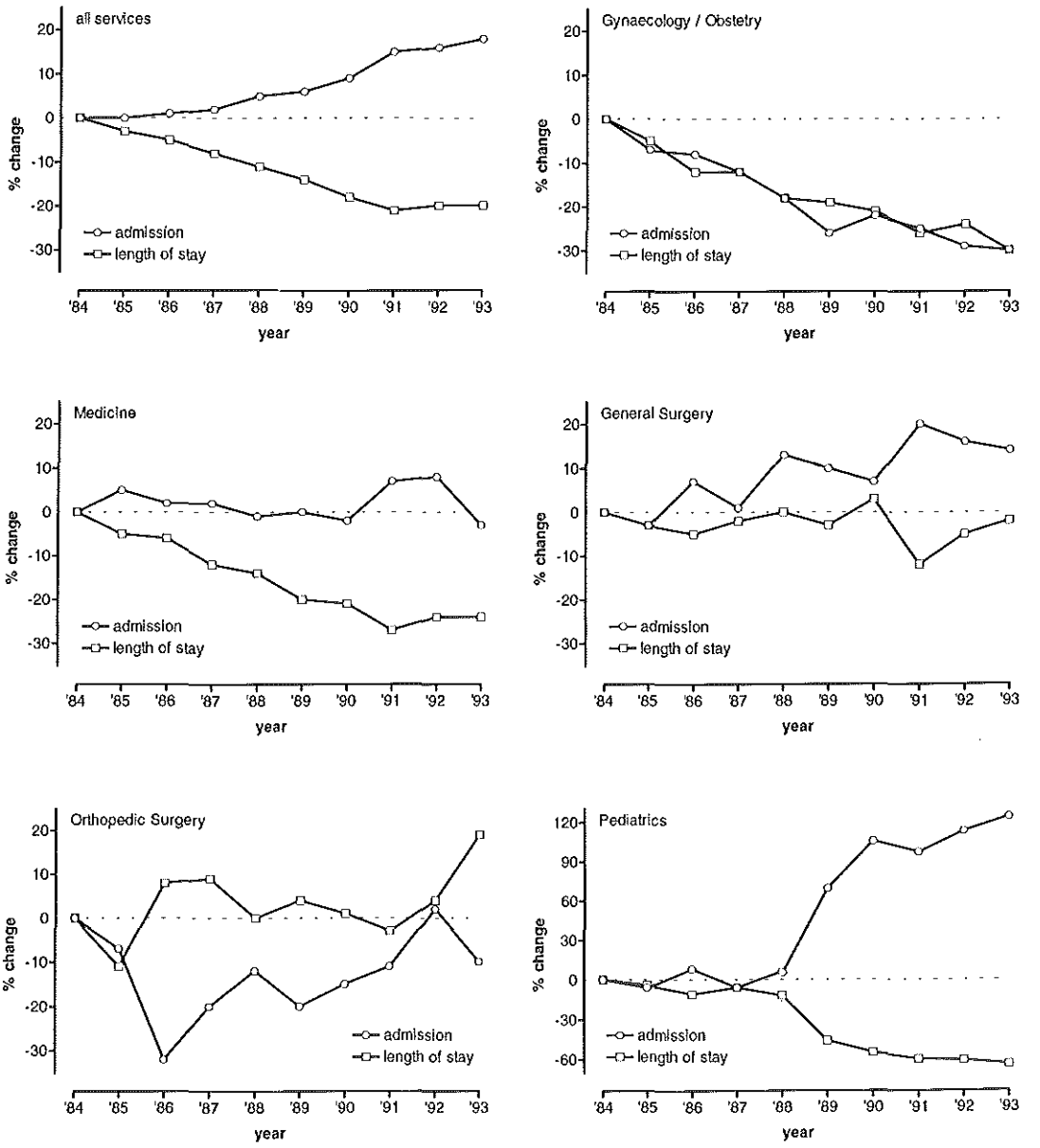

Figure 2. Trends in average lenght of stay and number of admissions for all patients compared to trends in the services of gynecology/obstetrics, medicine, general surgery, orthopedics and pediatrics. Please note that the range of % change on the y-axis are the same for all panels exept for pediatrics (lower right panel).

Table 2A. Infection rate per 1,000 patient days by service, 1984-1993.

year	*medicine*	*general surgery*	*gyne-cology*	*obste-trics*	*urology*	*pulmo-nology*	*pedia-trics*	*neuro-logy*	*ortho-pedics*	*cardio-logy*	*ear-nose-throat*	*ophtal-mology*	*derma-tology*
1984	4.3	8.8	19.4	3.9	7.6	5.1	2.7	5.2	3.5	2.0	0	0	0
1985	4.9	5.8	16.8	3.0	1.8	2.4	3.2	2.3	3.2	1.0	0	0	0
1986	4.4	6.0	13.2	2.7	4.6	1.7	3.4	0.8	5.6	0.7	0	0	0
1987	5.6	8.9	10.1	2.7	3.9	2.3	3.7	3.1	8.8	1.1	0	0	0
1988	4.0	7.0	6.1	3.5	5.0	2.8	5.5	3.2	6.9	2.0	0	0	0
1989	3.4	7.1	7.1	3.5	3.9	4.5	5.9	5.0	4.7	1.5	0.5	1.1	0
1990	4.1	4.4	6.9	1.2	5.3	2.3	6.7	2.2	10.0	2.8	0	4.1	4.3
1991	3.0	5.5	5.8	3.0	4.4	6.6	4.6	4.2	2.9	3.6	0.9	1.6	0
1992	4.4	5.1	2.5	1.2	3.2	1.4	5.4	3.0	2.9	2.0	0	0	0
1993	4.5	3.6	2.7	0	1.7	2.6	5.1	4.5	5.0	3.1	0.9	1.2	0
10-yr mean	4.3	6.2	9.1	2.5	4.1	3.2	4.6	3.4	5.4	2.0	0.2	0.8	0.4
CI_{95}	3.7-4.8	5.0-7.5	5.0-13.2	1.6-3.4	3.0-5.7	2.0-4.4	3.7-5.6	2.4-4.4	3.6-7.1	1.3-2.7	ND*	ND	ND
SEM	0.23	0.55	1.8	0.39	0.54	0.528	0.42	0.44	0.79	0.95	ND	ND	ND

ND = Not Done

Table 2B. Infection rate per 100 admissions by service, 1984-1993.

year	*medicine*	*general surgery*	*gyne-cology*	*obste-trics*	*urology*	*pulmo-nology*	*pedia-trics*	*neuro-logy*	*ortho-pedics*	*cardio-logy*	*ear-nose-throat*	*ophtal-mology*	*derma-tology*
1984	9.4	9.7	16.5	2.3	8.7	8.1	5.8	5.6	4.7	3.1	0	0	0
1985	10.2	6.1	14.4	1.6	1.9	3.6	6.6	3.1	3.8	1.1	0	0	0
1986	9.1	6.2	12.0	1.3	4.9	2.6	6.5	1.3	8.1	0.8	0	0	0
1987	10.7	9.4	8.5	1.3	3.8	3.3	7.5	4.6	12.9	1.3	0	0	0
1988	7.5	7.6	5.7	1.4	4.4	3.9	10.0	3.7	8.5	2.5	0	0	0
1989	6.0	7.5	4.2	2.1	3.1	7.9	6.8	6.3	6.5	1.7	0.2	0.5	0
1990	7.3	4.9	4.0	0.7	4.3	3.0	6.3	2.2	14.0	3.4	0	1.5	16.7
1991	4.9	5.3	5.0	1.6	3.4	9.3	4.0	4.4	3.9	4.5	0.3	0.5	0
1992	7.4	5.4	1.8	0.6	2.3	1.8	4.4	3.0	4.4	2.2	0	0	0
1993	7.0	3.3	2.2	0	1.2	3.7	3.9	5.0	7.6	3.3	0.3	0.4	0
10-yr mean	8.0	6.5	7.4	1.3	3.8	4.7	6.2	3.9	7.4	2.4	0.08	0.3	1.7
CI_{95}	6.6-9.3	5.1-8.0	3.7-11.1	0.7-1.7	2.3-5.3	2.8-6.6	4.9-7.5	2.8-5.0	4.8-10	1.5-3.2	ND*	ND	ND
SEM	0.59	0.64	1.64	0.22	0.66	0.84	0.58	0.49	1.14	0.37	ND	ND	ND

ND = Not Done

The incidences in nosocomial infections in Gynecology decreased over the years from 16.5 (CI_{95} 13.9-19.2) per 100 admissions (19.4 [CI_{95} 16.3-22.9] per 1,000 patient days) in 1984 to 2.2 (CI_{95} 1.1-3.8) per 100 admissions (2.7 [CI_{95} 1.4-4.9] per 1,000 patient days) in 1993 (Table 2). This decrease was primarily due to an active intervention-program directed at preventing urinary tract infections in these patients (*vide infra*). The incidences in Pulmonology and Neurology fluctuated. Lower incidences were found in Urology and Cardiology. Hardly any infections were found among patients admitted to Ear-Nose-Throat, Ophtalmology and Dermatology, these figures being too low (frequently zero) to calculate the 95% confidence intervals and standard errors of the mean. The high incidence in Dermatology in 1990 was due to one infection among six patients.

The predominant types of infection clearly differed among the services (Table 3).

Table 3. Hospital-acquired infections by service and by type of infection, 1984-1993.

service	uti	swi	lres	cut	bsi	oth	total
medicine	*3.9**	0.2	*1.4*	*0.7*	*1.3*	*0.5*	8.0
surgery	1.7	*2.6*	0.9	0.3	*0.7*	*0.3*	6.5
gynaecology	*5.2*	*2.2*	0.1	0.0	0.1	0.0	7.6
obstetrics	0.4	0.4	0.0	*0.4*	0.1	0.0	1.3
urology	2.1	0.4	0.3	0.2	*0.7*	0.2	3.9
pulmonology	1.1	0.0	*2.2*	0.3	*0.9*	0.1	4.6
pediatrics	0.4	0.3	0.8	*3.3*	0.3	*0.6*	5.7
neurology	2.6	0.3	0.4	0.3	0.1	0.2	3.9
orthopedics	*3.5*	*2.3*	0.5	*0.4*	0.2	*0.3*	7.2
cardiology	1.3	0.1	0.4	0.1	0.3	0.2	2.4
ear-nose-throat	0.0	0.1	0.0	0.0	0.0	0.0	0.1
ophtalmology	0.0	0.3	0.0	0.0	0.0	0.0	0.3
dermatology	0.0	0.0	2.2	0.0	0.0	0.0	2.2
all	2.1	0.9	0.6	0.5	0.5	0.3	4.9

* Incidence per 100 admissions.

UTI=urinary tract infection, SWI= surgical wound infection, LRES=lower respiratory infection, BSI= bloodstream infection, CUT= cutaneous infection, OTH= other infections.

In italics: per type of infection the services with the highest incidences are indicated

In the medical service urinary tract infections, lower respiratory tract infections and bloodstream infections were found most frequently. In surgical patients, however, the infections most frequently found were surgical wound infections and urinary tract infections. The cutaneous infections detected in pediatric patients were mostly pustulae in newborns or babies, neonatal conjunctivitis and few umbilical stump infections.

The high incidence of infections in Gynecology was primarily due to catheter-related urinary tract infections in the first years of surveillance. Hospital-acquired bloodstream infections were predominantly seen among patients admitted to the Medical service, General surgery, Pulmonology and Urology.

The overall surgical woundinfection rate changed slightly over the years and varied from 2.4 % (CI_{95} 1.9-3.1) in 1988 to 1.1 (CI_{95} 0.7-1.5) in 1993 (Table 4).

Table 4. Yearly incidence of surgical wound infections.

year	*number of surgical procedures**	*number of infections*	*%*	CI_{95}
1984	3,060	48	1.6	1.2 - 2.1
1985	2,785	40	1.4	1.0 - 2.0
1986	2,931	56	1.9	1.5 - 2.5
1987	2,676	61	2.3	1.8 - 2.9
1988	2,854	69	2.4	1.9 - 3.1
1989	2,949	53	1.8	1.4 - 2.4
1990	2,670	59	2.2	1.7 - 2.8
1991	2,923	58	2.0	1.5 - 2.6
1992	2,883	38	1.3	0.9 - 1.8
1993	3,116	33	1.1	0.7 - 1.5
total	28,847	515	1.8	1.6 - 1.9

* Only procedures performed in the operating theatres were included.

No trend could be discerned in this rate. However, the incidence of surgical wound infections differed per type of procedure as classified by the National Medical

Registry of the Netherlands (Table 5).

Table 5. Incidence of surgical woundinfections by group of surgical procedure, 1984-1993.

SIG code	*description of groups of surgical procedures included*	*number of infections / number of operations*	*rate*
01	laminectomy, group 33 included	13/ 578	2.3
02	peripheral nervous system	1/ 277	0.4
03	thyroid	1/ 154	0.6
05	eye	6/1,972	0.3
06	ear	1/ 488	0.2
07	nose	1/1,114	0.1
08	tonsills/adenoid	1/2,139	0.0
12	varicose veins	4/360	1.1
13	vascular other (no thoracic)	5/ 55	*9.1*
14	blood & lymphatics	3/ 149	2.0
15	mammae	21/1,585	1.3
17	oesophagus/ stomach	18/ 248	*7.3*
18	colon	51/ 775	*6.6*
19	appendectomy	52/1,109	*4.7*
20	rectum / anus	14/ 877	1.6
22	choledochus & gallbladder	19/ 976	1.9
23	abdomen & peritoneum	11/ 448	2.5
24	inguinal hernia	17/1,632	1.0
25	nephro-urinary tract	6/1,341	0.4
26	male reproductive organs	7/1,592	0.4
27	hysterectomy	94/1,612	*5.8*
28	curettage	5/1,127	0.4
29	female reproductive organs	29/1,258	2.3
30	Cesarean section	31/ 934	*3.3*
33	musculoskeletal	84/3,589	2.3
34	skin & soft tissue	17/ 624	2.7

Groups in which no infections were found are not included in the table.

Codes are derived from the National Medical Registraty (SIG, Utrecht)

In italics: type of procedures with highest incidence of postoperative woundinfection

The major classes of surgical procedures could be broken down into subgroups if further analyses were required. Decreasing infection rates could, thus, be highlighted for appendectomy and hysterectomy following the institution of antimicrobial pre-operative prophylaxis (*vide infra*).

A total number of 2,176 cultures were taken from 2,772 infections, this means that no cultures were taken in 22 % of the cases of hospital acquired infections. The number of pathogens cultured was 3,318; 19 % were *Escherichia coli*, 13 % were *Staphylococcus aureus* and 11 % were coagulase-negative staphylococci frequently from skin and soft tissue infections and from bloodstream infections (Table 6).
Multiple resistance in Gram-negative pathogens did occur only sporadically, especially in the first years of surveillance.
No large shifts in the distribution of nosocomial pathogens did occur over the years. Trendanalyses of pathogens isolated from nosocomial urinary tract infections showed a decrease in Enterococci and an increase in *Staphylococcus aureus* and Candida species.
In surgical wound infections a decrease in isolation of *Staphylococcus aureus*, *Escherichia coli* and Enterococci was noticed versus an increase in coagulase-negative Staphylococci. In lower respiratory tract infections the isolation of *Escherichia coli* decreased, in cutaneous infections no significant trends could be noticed. Trends in pathogens isolated from bloodstream infections showed a decrease in *Escherichia coli*, Proteus and Enterococci species, while a slight increase was found in isolation of *Staphylococcus aureus* and coagulase-negative Staphylococci (data not shown). In summary, the overall trend was one of a decrease in isolation of *Escherichia coli* and Enterococcal species, and an increase in the isolation of *Staphylococcus aureus* and coagulase-negative Staphylococci .

Table 6. Pathogens most frequently isolated in hospital acquired infections, per site of infection, in 1984-1993.

	frequency of isolates (%) from							
microorganism species	*uti*	*swi*	*lres*	*cut*	*bsi*	*oth*	*all sites*	*%*
Escherichia coli	*31.5*	*11.8*	9.8	6.8	*18.7*	2.9	619	18.7
Staphylococcus aureus	4.4	*19.5*	9.8	*30.0*	*13.4*	*12.9*	429	12.9
coagulase negative Staphylococci	7.9	*11.2*	0.7	18.0	*23.0*	11.7	354	10.7
Enterococcus species	*12.5*	4.4	0.7	3.8	3.6	1.2	224	6.8
Proteus species	9.8	3.3	1.3	2.6	3.6	0.6	178	5.4
Klebsiella species	7.0	3.7	7.3	2.1	4.6	2.9	174	5.2
Candida species	4.2	1.3	6.0	3.1	1.6	25.2	149	4.5
Enterobacter species	4.7	1.7	4.5	0.5	2.0	1.8	102	3.1
Pseudomonas species	3.7	2.0	5.8	1.7	3.0	0.6	102	3.1
hemolytic streptococci	2.8	5.6	1.5	4.3	2.6	4.1	117	3.5
Streptococcus pneumoniae	0.2	0.4	*18.1*	0.7	3.3	1.2	93	2.8
Bacteroides species	0.2	8.4	0	1.9	4.6	1.2	89	2.7
Moraxella catarrhalis	0	0	*12.6*	0.7	0	0.6	54	1.5
Haemophilus influenzae	0	0.3	11.1	0.9	0.3	1.2	53	1.5
Anaerobes	0.6	3.2	0.5	1.4	1.0	0.6	37	1.2
other	*11.0*	*23.0*	*10.1*	*22.0*	*14.8*	*31.6*	544	16.4
total number of isolates	1,274	748	397	423	305	171	3,318	100

In italics: frequency of isolation > 10 %

Interventions

Based on the data gathered in 1984 the first target for intervention was chosen to be the reduction of catheter-associated urinary-tract infections in gynecological

patients. Potential value of prophylactic norfloxacin given to the patients, while having a bladder catheter, was investigated in a pilot study. It was concluded that once daily doses of 200 mg oral norfloxacin would, at least in part, be effective in preventing catheter-associated bacteruria and pyuria following reconstructive gynaecologic surgery [7] (for details see Chapter 4). This resulted in a significant decreased rate of nosocomial urinary tract infections in these patients (Figure 3).

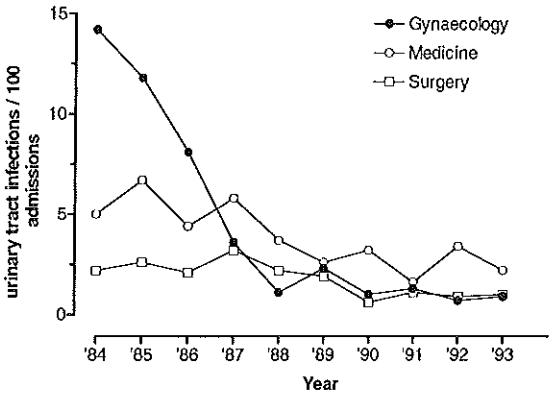

Figure 3. The effect of norfloxacin (200 mg O.D.) prophylaxis for catheter-associated urinary tract infections in gynecologic patients. No prophylaxis was given to surgical and medical patients.

The impact of concurrent antimicrobial therapy on catheter-associated urinary tract infection was then studied further[8] (see Chapter 4). Additional patient groups were subsequently identified who could benefit from antimicrobial prophylaxis for prevention of catheter-associated urinary tract infection and this was further tested in a prospective trial [9] (see Chapter 4).

Subsequently, efforts were directed at reducing surgical wound infections, since they were prevalent and were well known to be associated with high morbidity and costs [10] (see Chapter 4). Wound infection rates were reviewed in search of priorities and options for preventive measures. The infection rate in appendectomy seemed irreducible, until a Danish multicenter study provided evidence for the efficacy of antibiotic prohylaxis in reducing surgical wound infections following appendectomy [11]. In consultation with the surgeons and the hospital pharmacist a

single pre-operative 2 g dose of cefotetan became the prophylaxis of choice to reduce infections following appendectomy in 1990[12]. Thereafter, a significantly lower infection rate was noted from 1990 onwards (Figure 4).

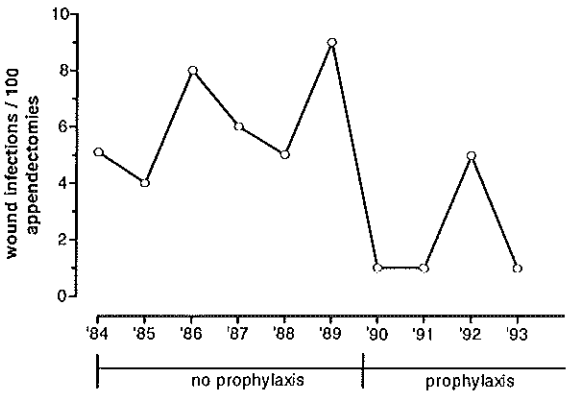

Figure 4. Incidence in surgical wound infections following appendectomy in Oudenrijn hospital, 1984-1993. The average infection rate was 6.2% (CI_{95} 4.6-8.3) prior to the start of antibiotic prophylaxis in 1990, in the 1990-1993 period the average infection rate was 2.2% (CI_{95} 0.9-4.2) using prophylaxis. Prophylaxis consisted of a single infusion of 2g cefotetan just prior to surgery.

Prior to prophylaxis the average yearly rate was 6% (CI_{95} 4.6-8.3), but it became 2% (CI_{95} 0.9-4.2) after prophylaxis was realised.

A study on the efficacy of antibiotic prophylaxis in gynaecologic surgery provided a tool for reducing surgical wound infections in gynecologic patients [13]. Patients with non-elective Cesarean sections and patients with hysterectomy were given 2.2 g amoxycillin/ clavulanic acid (Augmentin^r) prophylaxis intravenously[12]. The protocol was implemented in 1992 and resulted in a significantly lower wound infection rate in Cesarean section and hysterectomy from 1992 onwards (Figure 5). Prior to prophylaxis the average yearly infection rate was 7% (CI_{95} 6.0-9.0), and it became 1% (CI_{95} 0.3-3.5) following the institution of prophylaxis.

Another target for prevention became primary bloodstream infections in patients with central lines, since this rate was considered too high and options for interventions seemed available. Prevention was focused on central lines used for total parenteral nutrition. In 1990 a guideline was developed in cooperation with the nursing department and anaesthesiologists, concerning the daily care and frequency of change of lines and dressings. Two years after the introduction of this

guideline additional interventions were indicated since infection rates were rising again.

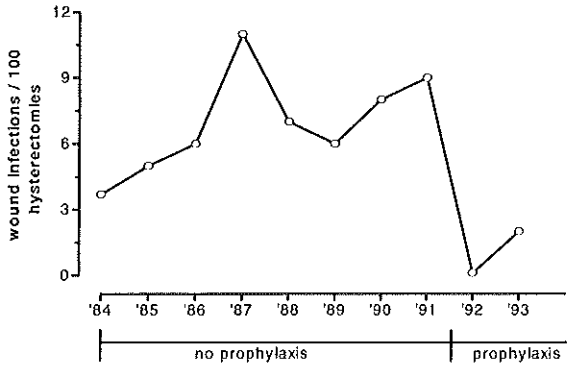

Figure 5. Incidence of wound infections following hysterectomy in Oudenrijn hospital, 1984-1993. The average infection rate was 7.4% (CI_{95} 6.0-9.0) prior to the institution of prophylaxis at the start of 1992, thereafter the rate was 1.2% (CI_{95} 0.3-3.5). Prophylaxis consisted of a single infusion of 2.2 g amoxicillin-/clavulanic acid just prior to surgery.

Higher infection rates were associated with prolonged duration of catheter-in-situ and a jugular insertion site [14] (Table 7). In 1993 it was agreed with the anesthesiologists to insert only subclavian vein catheters rather than jugularis catheters unless contraindicated.

Table 7. Incidence of bloodstream infections in relation to type of central-line and duration of catheter in situ 1989-1992.

number of days in situ	*bacteremias/ number of central lines (%) placed in the*	
	jugular vein	*subclavian vein*
1 - 7	2 / 20(10)	0 / 0(0)
8 - 14	6 / 19(32)	0 / 5(0)
> 14	6 / 14(43)	0 / 9(0)
total	14/ 53(26)	0 /14(0)
mean number of days in situ	13	11

These interventions resulted in a relative reduction in the use of jugular catheters in preference to the use of subclavian catheters from 1994 onwards (Table 8). However, in this year central venous-line associated bacteremia remained at 10-

20% incidence rate and was now also seen in patients with subclavian vein catheters.

Table 8. Number of infections associated with type of central-line for total parenteral nutrition, 1989-1994.

	incidence sepsis/ site of central line (%)				
year	*subclavian vein*	*jugular vein*	*unknown**	*all types*	CI_{95}
1989	0 / 1 (0)	2 / 6 (33)	3 /12 (25)	5 /19 (26)	9.2-51.2
1990**	0 / 0 (0)	1 / 8 (13)	0 / 5 (0)	1 /13 (8)	0.2-36.0
1991	0 / 5 (0)	5 /19 (26)	0 / 3 (0)	5 / 7 (19)	6.3-38.1
1992	0 / 8 (0)	6 /20 (30)	1 /14 (7)	7 /42 (17)	7.0-31.4
1993**	0 / 9 (0)	2 /10 (20)	0 / 7 (0)	2 /26 (7)	0.9-25.0
1994**	2 /19 (11)	3 /14 (21)	0 / 5 (0)	5 /38 (13)	4.4-28.1
total	2 /42 (5)	19/77 (25)	4/ 46 (9)	25/165(15)	9.7-20.6

* Site of central venous line not recorded

** Interventions introduced at start of indicated year, see results

Discussion

A system of active, continuous hospital-wide surveillance and control of nosocomial infections in the Oudenrijn hospital was introduced in 1984 and maintained throughout 1995. The first ten years, 1984-1993, were evaluated.

The ultimate goal was to reduce the incidence of the adverse patient outcome of nosocomial infections. To evaluate the surveillance system several factors must be reviewed[15].

The first subjects under consideration are the nosocomial infections (numerator data) and the population at risk (denominator data).

The incidence of nosocomial infections varies by body site and is mainly determined by intrinsic and extrinsic riskfactors including underlying disease

conditions and exposure to invasive medical interventions. The distribution of the major infection sites in Oudenrijn Hospital showed that urinary tract infections were the main problem, followed by surgical wound infections, lower respiratory infections, skin and soft tissue infections and bacteremias. Slightly different rankorders were reported in the hospital-wide surveillance data of non-teaching hospitals > 200 beds by the NNIS system, although urinary tract infections remained the major problem [16]. Pathogens most frequenly found were *Escherichia coli* especially isolated in urinary tract infections and bloodstream infections, and *Staphylococcus aureus* in skin and soft tissue infections and surgical site infections. These were the nosocomial pathogens most frequently found in hospital-wide surveillance in NNIS hospitals as well, albeit that the major sites in which the pathogens were isolated, differed somewhat: *Escherichia coli* from urinary tract infections and surgical site infections, and *Staphylococcus aureus* from pneumonia and surgical site infections [16]. These differences might partly be due to differences in casemix, riskfactors and diagnostic protocols.

Heterogeneity in these factors is too great such that the crude overall infection rate cannot be used for intra- and interhospital comparisons across time [2]. Therefore, comparisons over the years were made at more refined levels of riskfactors and of site-specific infection rates within services.

Advanced age is a recognised risk for nosocomial infections [17] [18] [19]. We observed an almost ten-fold difference in infection rate between the lowest (1-14 years) and the highest (75 years and over) incidences by age group. Over the years an increase in the overall infection rate was expected since the proportion of admissions of patients aged 75 years and over, i.e. those with the highest infection rate, increased from 11,3 % in 1984 to 19,4 % in 1993 (Figure 6). If the age-class specific incidences of hospital-acquired infections had remained at the 1984 level during the 10 years of surveillance until 1993, then many more infections would have occurred in all age groups except those up to 14 years; thus, many more infections would have been seen in the other age groups than were actually

observed. The data show that especially in the higher age groups, i.e. those that have the highest infection rates, the greatest deficit in the number of infections was observed (Figure 7).

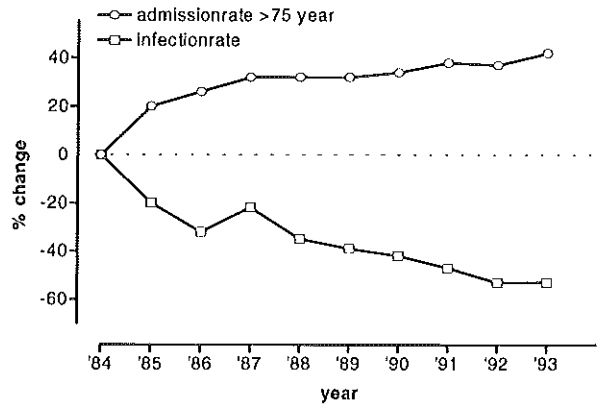

Figure 6. Observed changes in the proportion of admissions by patients aged 75 years and over and in the incidence of hospital-acquired infections in the Oudenrijn hospital, 1984-1993.

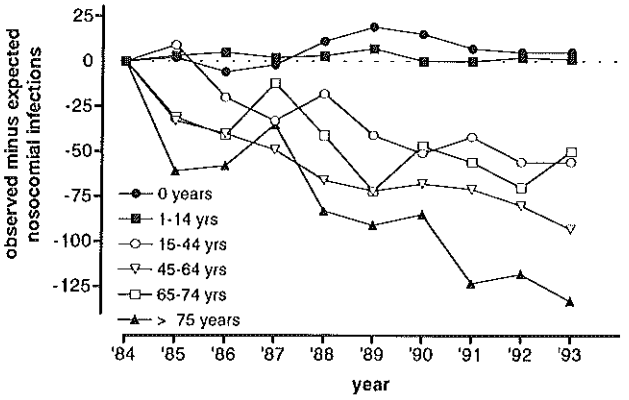

Figure 7. Observed minus expected numbers of nosocomial infections per age group, 1984-1993. The expected numbers of hospital-acquired infections were calculated on the basis of the incidence per age group found in 1984.

If the 1984 incidences had not changed over the years then a total number of 2,008 extra nosocomial infections would have been observed than were actually recorded in this decade. Also, the extra morbidity in these patients would have generated additional costs, estimated to run up to one million guilders, to require 22,088 extra nursing procedures and 6,024 extra patient days in hospital (see Chapter 4).

Following in-depth evaluation of infection rates by service targets for intervention

in subgroups with specific risks were identified.

In a selected group of gynecologic patients measures were applied to prevent indwelling catheter-related urinary tract infections. The efficacy of this intervention in this subgroup of patients was shown in clinical trials [7 9] (see Chapter 4). Following the introduction of this preventive measure in routine practice the incidence of urinary tract infections per 100 admissions in this service dropped from 14.2% in 1984 to 0.9% in 1993 (Figure 3).

The other target in the gynecologic service was the reduction of surgical site infections following hysterectomy (Figure 5). The wound infection rate before the use of antimicrobial prophylaxis was 7.4 (CI_{95} 6.0-9.0) and following the introduction of the use antimicrobial prophylaxis 1.2 (CI_{95} 0.3-3.5). Thus a clear breach in the rate of wound infection following hysterectomy was obtained. These interventions contributed to a decrease in the overall service-specific infection rate and in the overall wound infection rate (Table 2 and 4).

In General Surgery preventive action was targeted at reducing the rate of surgical wound infections. The rate of surgical site infections was monitored and analysed by type of surgical procedure (Table 5). The surgical procedures were not stratified by measures of patient susceptibility to infection such as surgical wound class or duration of surgery[20]. Such stratification would have resulted in numbers of infections and surgical procedures too small for meaningful comparisons. Information on superficial or deep surgical site infection was recorded only during the last two years. The general preventive measure of feed back of wound infection rates to the surgeons was introduced as early as in 1984. However, this did not have a noticeable impact on the wound infection rate. Specific intervention in this service was the prevention of surgical wound infections following appendectomy by using preoperative antimicrobial prophylaxis. Such prophylaxis resulted in a significant reduction in the rate of wound infections. The infection rate before the introduction of the use of prophylaxis (6.2% [CI_{95} 4.6-8.3]) differed significantly from the rate (2.2 % [CI_{95} 0.9-4.2]) after this intervention (Figure 4). These rates did not differ

significantly from the crude infection rate following appendectomy reported in a recent multicenter study in the Netherlands [21]. However, interhospital comparisons of surgical wound infection rates by type of procedure is of limited value when corrections are omitted for variations in patient's risk factors, stratification by wound class or other patient risk index and, last but not least, the use of antimicrobial prophylaxis [22]. Our surveillance of surgical wound infections encompassed only clinical patients since a suitable protocol for postdischarge surveillance was not yet developed. Proportions of 12% to 50% of surgical wound infections found in postdischarge surveillance have been reported [23 24 25], suggesting underreporting of wound infections in our system.

Surveillance proved to be a tool for the recognition of surgical wound infections and subsequent to indicate options for interventions. This is in accordance with other reports on surveillance of wound infections, be it carried out in single- or multicenter studies [24 26 27 28 29].

Intravascular infusion lines accounted for 11% of all possible sources of bloodstream infections (BSI) as was shown in a previous study in Oudenrijn Hospital (see chapter 2) [30]. Following the recommendation of that study prevention of BSI was directed at reducing infections associated with intravascular catheters (primary BSI), although the incidence of 4.3 primary BSI per 1,000 admissions compared favourably to incidences of 3.8 primary BSI per 1,000 discharges reported in acute care hospitals of comparative size [31]. In 1989 appropriate denominator data were retrieved from the pharmacy department and from then on device-specific surveillance was continued throughout 1994 (table 8). The reduction of the infection rate observed in 1990 failed to hold in spite of adherence to the infection control guidelines. Thus, new preventive measures were proposed. In 1994 a preferential insertion of catheters in the subclavian vein rather than in the jugular vein was agreed upon. Lower infection rates may be realised when other risk factors including the duration of catheterization and the type of insertion-site dressing are brought under control [14 32].

The sensitivity, specificity and accuracy of the method of data collection in our surveillance system should be considered. A single trained Infection Control Practitioner collected data on patients with HAI (numerator data) prospectively by weekly ward visits over a nine months period each year. The appropriate denominator data were retrieved from the hospital administration and other data sources in the hospital. Written CDC definitions of HAI were always at hand and were consulted frequently to assure the reproducibility of the surveillance system. In this way the surveillance method remained the same over the 10 years. Occasionally, two Infection Control Practioners reviewed the same population on the same day to determine the interrater reliability. The agreement at those times was 100% (data not shown). We recommend that such checks should be repeated regularly.

Completeness of data was assured by routinely checking the monthly linelistings output from the computer at least for correctness of type of infection, service and pathogen. Another check was to assure the sensitivity with regard to patient finding. When a patient, from which a positive culture was included in the daily microbiology laboratory output, had been missed during the ICP's ward visit, then the patient's chart was retrieved from wherever in the hospital. Still patients were missed: 8% of the admitted patients were not seen by the Infection Control Practitioner, as was shown in a recent interhospital study in which the Oudenrijn Hospital participated [19]. Across time probably more infections may have been missed due to a 18% decrease in average length of stay (figure 2). On the other hand a 20% increase in admissions was observed, thus more people were at risk of a HAI for a shorter period of time. Of these people an increasing proportion was at higher risk of infection due to old age (figures 1 and 6) and, consequently, a higher incidence in infections was to be expected.

Finally, the feasibility of hospital-wide data collection was weighed carefully against the benefit of the use of the surveillance data. By analyzing these data infection control problems were recognized, timely appropriate intervention

measures were instituted and their efficacy was evaluated. The information generated by surveillance was also used to set priorities in educational activities and in development and implementation of protocols. The site-specific rates by service and nursing unit and the proportions of infection sites were added to in the Infection Control Handbook in a yearly update, suggesting the association between the process and outcome of infection control practices. Sometimes the analysis of data did result in abstaining from rather than instigating further action: for example on the basis of analysis of surveillance data it was decided not to act upon the advice of the Dutch Working Party Infection Prevention (WIP) to use bacterial filters in the ventilator circuit of every patient undergoing general anesthesia [33].
The surveillance activities were interwoven into "education permanente". Conducting surveillance in weekly ward visits did increase the visibility and accessibility of the Infection Control Practioner, leading to consultations in an informal manner on the "shop-floor". On average the Infection Control Practitioner spend 10 hours weekly on surveillance activities, which amounts to 31 % of the available time (50% was mentioned elsewhere[34]). The size and type of the Oudenrijn Hospital, the quality of medical and nursing records, and the absence of an intensive care unit and patients on long-term ventilatory support in the first years of surveillance might have influenced the feasibility of hospital-wide surveillance favourably. Once the routine was established the infection control committee and the Infection Control Practitioner preferred to continue in the same way, even after an intensive care unit was built.
To facilitate data collection optimal use of denominator data collected by other departments for other reasons was aimed for: data on admissions and patient days by service and nursing unit were derived from the hospital administration department, data on surgical procedures were derived from the medical registration, data on general anesthesia from the anesthesiologists, data on central lines for total parenteral nutrition from the hospital pharmacy, and data on cultures and multiresistant microorganisms were derived from the microbiology laboratory.

As soon as the denominator data on the use of indwelling urinary-tract catheters will become available from other sources in the hospital, the rates of indwelling catheter-associated urinary-tract infections will be included in the routine reports. The feasibility and ease of data collection was enhanced with the access to demographic patient data in the hospital's computersystem. The use of electronic data bases will further increase the efficiency of surveillance [17 35 36].

Hospital-wide surveillance was adopted in the United States in the 1970s. However, in the 1980s this comprehensive surveillance was considered too time-consuming and its results not valid for interhospital comparisons. Thus, other surveillance options were introduced. From 1986 onwards all NNIS data were collected using one of four standardized surveillance components: the existing hospital-wide surveillance option, and adult and pediatric intensive care unit surveillance, high-risk nursery surveillance, and surveillance of the surgical patients [2 37]. In a hospital the type of surveillance should be conducted that best meets its explicit goals within the limits of available resources of personnel and material. As stated by Brachman: "a logical endpoint to surveillance is formulating control and prevention measures from interpretation of the analyzed data. Whithout a specific action, surveillance is purely archival; that is the data increases use of shelf space, but does not decrease the occurrence of disease"[38].

The experience in the Oudenrijn Hospital showed that it is feasible to conduct hospital-wide surveillance over prolonged periods of time and that a decrease in the occurrence of nosocomial infections can be achieved through it. The results of the SENIC study suggested that by adopting a hospital-wide surveillance and control program approximately 1/3 of the nosocomial infections can be prevented [3]. In our study a 53% decrease was observed in the incidence of HAI across the years following the adoption of a hospital-wide surveillance and control program. All in all approximately 2,000 nosocomial infections may have been prevented since the inception of this program in 1984.

For further discussion see Part four.

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Chapter 4.

Supporting studies

Introduction

On the basis of the analysis of the data from the first year of surveillance (1984) an initial target was set to reduce nosocomial urinary tract infections in gynaecologic patients. This required further study on the prevention of catheter-associated urinary tract infections. It was found that patients requiring 5 to 10 days bladder catheterisation following reconstructive gynaecologic surgery were routinely given a therapeutic course of nitrofurantoin at the time of catheter removal to prevent asymptomatic bacteremia to become symptomatic once the catheter was removed. We elected to attempt to prevent asymptomatic bacteremia from arising during bladder catheterisation and therefore studied the effect of norfloxacin prophylaxis on the incidence of bacteruria and pyuria at the time of catheter-removal in these patients in a pilot project. In the course of these studies we also evaluated the impact of concurrent antimicrobial therapy (i.e. antibiotics given for other reasons during the catheterisation period) on the incidence of catheter-associated urinary tract infections and found this impact to be highly significant. Finally, we selected groups of patients requiring 3-14 days of bladder catheterisation who could benefit from antimicrobial prophylaxis in the prevention of catheter-associated urinary tract infections, and this was studied in a double blind randomised clinical trial. These three studies have been published.

Last but not least it was felt that proper information on the costs of hospital-acquired infections in the Netherlands in general and in Oudenrijn Hospital in particular was lacking. Consequently, decisions regarding the intro-

duction of infection control measures could not be supported by proper studies of the costs and consequences that could be saved by them. We, therefore, performed an analysis of the costs and extra nursing effort spent for nosocomial infections in the Oudenrijn Hospital.

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Postoperative Prophylaxis with Norfloxacin in Patients Requiring Bladder Catheters

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The effect of once daily doses of 200 mg oral norfloxacin on the occurrence of catheter-associated bacteriuria (> 1000 CFU/ml) and pyuria was studied in 105 post-operative gynaecologic patients. Norfloxacin was given from the second day after surgery until catheter removal. Bacteriuria developed in 32 of 51 (63%) control patients compared to 8 of 54 (15%) patients receiving norfloxacin ($p < 0.001$). Pyuria was present in 22 of 51 (43%) control subjects versus only 3 of 54 (5%) patients treated with norfloxacin ($p < 0.001$). Bacteria isolated from control patients comprised species of *Enterobacteriaceae* (40%), *Staphylococcus* (35%), and *Streptococcus* (17%); seven isolates were resistant to multiple antibiotics reflecting their nosocomial origin. In contrast, strains isolated from norfloxacin-treated patients comprised non-fermenting gram-negative rods (79%, usually *Alcaligenes* or *Acinetobacter* spp.) and faecal streptococci (12%). It is concluded that once daily doses of 200 mg oral norfloxacin are effective in reducing the rate of catheter-associated bacteriuria and pyuria following reconstructive gynaecologic surgery.

Catheter-associated urinary tract infections comprise the largest group of all infections acquired during hospitalisation (1, 2). Except for the sterile closed drainage system, measures proposed to reduce the incidence of catheter-associated urinary tract infection have yet to gain wide acceptance (3). The value of antibiotic therapy in prevention of infections during catherisation has been neither definitively confirmed nor refuted by controlled trials. Several large studies in various categories of patients have shown that if catheterised patients are given systemic antibiotic therapy for other reasons, the incidence of urinary tract infection is much reduced (4–9). Controlled studies of antibiotic prophylaxis in selected groups of patients have also shown a beneficial effect (10–13). Opponents of antibiotic prophylaxis argue, however, that it may lead to widespread use of antimicrobial agents with inevitable emergence of resistant microflora in hospitals and a higher incidence of drug-related toxicity in patients (2, 4, 5, 9, 13). In addition, studies showing a protective effect of antibiotics indicate that the effect is lost if the period of catheterisation exceeds 7 to 14 days (4, 5, 8). Finally, not all antibiotics are equally effective in protecting the urinary tract during catherisation (11, 14–16). Thus, antibiotic prophylaxis with well-chosen regimens may only be beneficial in groups of patients at risk of acquiring urinary tract infection during bladder catheterisation periods of less than two weeks. The little studied group of female patients requiring 5 to 10 days of catheterisation following reconstructive gynaecologic surgery has a high rate of urinary tract infection at the time of catheter removal. In our hospital such patients are routinely given a subsequent therapeutic course of nitrofurantoin to prevent symptomatic infection. The primary goal of this study was to determine the effect of norfloxacin given prophylactically on the incidence of bacteriuria and pyuria at the time of catheter removal in these patients.

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Materials and Methods

Patients and Prophylaxis. One hundred and five patients admitted consecutively to the department of gynaecology of the Oudenrijn hospital were entered into a sequential trial consisting of no prophylactic therapy (n = 23), prophylactic therapy with norfloxacin (n = 54) and, again, no prophylactic therapy (n = 28) in a study of occurrence of catheter-associated urinary tract infection following gynaecologic surgery. No perioperative prophylactic therapy was given. Patients who had undergone antibiotic therapy within the last week or were still undergoing such therapy were excluded from the study. The patient groups were comparable with respect to age distribution, main gynaecological disorder requiring surgery, type of operation performed, and type of post-

operative bladder drainage (Table 1). None of the patients suffered from severe underlying illness associated with compromised host defenses. No significant differences were found between the first and second control group, with respect to patient characteristics or the rate of bacteriuria or pyuria, so that the results of these groups are presented combined as one control group. All catheters were inserted just prior to surgery in the operating theatre by qualified personnel using aseptic techniques. No disinfectants were used subsequently during daily meatal care in the wards, and catheters were removed by trained nursing staff.

Prophylaxis patients were given 200 mg norfloxacin p.o. once a day from the second postoperative day until catheter removal. Upon catheter removal the first group of control patients were given the routine course of nitrofurantoin (4 x 50 mg p.o. daily for 7 to 10 days) the second group received a course of norfloxacin (400 mg bid). Patients were followed up by interview six weeks after discharge from hospital. All patients given prophylactic norfloxacin were informed about the goals and design of the study and consented to participate.

Bacteriological Investigations. A specimen of catheter urine was collected from each patient just before removal of the catheter, and, in 15 prophylaxis patients with culture-positive urine, again on the day of discharge from hospital. Urine was distributed over a dipslide (Urotube, Hoffman-La Roche, FRG) for culture and colony counting. A sediment spun from 5 ml urine was used for Gram staining and for inoculation of blood and McConkey agar. Bacteriuria was scored as "sterile" (no growth), $< 10^2$ CFU/ml (growth from sediment only), 10^2-10^3 CFU/ml, 10^4-10^5 CFU/ml, and $> 10^5$ CFU/ml. Significant bacteriuria was defined as $> 10^3$ CFU/ml. All micro-organisms were identified to at least the genus level, and the antimicrobial sensitivity tested using Microscan microdilution panels (Baxter, the Netherlands) that permitted MIC determinations for ampicillin, carbenicillin, piperacillin, tetracycline, cefamandole, cecotaxime, cotrimoxazole, gentamicin, tobramycin and amikacin. Sensitivity to norfloxacin was tested by agar diffusion using tablets (Rosco, Denmark). Multiple resistance was defined as resistance to at least ampicillin, cefamandole and one of the aminoglycoside antibiotics. The presence of leukocytes in the urine sediment was scored as "not detected", < 5 leukocytes/HPF, 5–9 leukocytes/HPF, 10–20 leukocytes/HPF or > 20 leukocytes/HPF.

Surveillance of Nosocomial Infections. The incidence of hospital-acquired infections in this hospital has been under constant hospital-wide surveillance since January 1984 (17). Surveillance is carried out through weekly visits by the infection control nurse of each ward using methods modified from those of Wenzel et al. (18).

Statistical Analysis. The differences in the rates of bacteriuria and pyuria between control and prophylaxis patients were analyzed by the chi-square method.

Table 1: Diagnosis, procedures and type of bladder drainage in prophylaxis group versus control group.

	Norfloxacin-treated group n = 54	Control group n = 51
Age (years)		
Median	46	47
Range	27–80	30–87
Diagnosis		
Prolapse	46 (85%)	42 (82%)
Uterus myomatosis	8 (15%)	9 (18%)
Operation		
Colporrhaphy + abdominal hysterectomy	35 (65%)	28 (55%)
Colporrhaphy + vaginal hysterectomy	10 (18%)	6 (12%)
Colporrhaphy	9 (17%)	15 (29%)[a]
Other	0 (0%)	2 (4%)
Bladder drainage		
Suprapubic catheter	28 (52%)	31 (61%)
Urethral catheter	26 (48%)	20 (39%)

[a] $x^2 = 2.42$, $p > 0.1$ compared to norfloxacin group.

Results

The overall incidence of hospital-acquired infections in 1984 before beginning this study was 7.1 cases of infection per 100 admissions. Nosocomial urinary tract infections accounted for 57% of the total number of infections, and 40% of all nosocomial urinary tract infections occurred in female patients admitted for gynaecologic surgery. In this trial the 51 control patients and 54 prophylaxis patients had an average postoperative duration of bladder catheterisation of 6.9 days and 7.4 days respectively; the duration of catheterisation varied from 5 to 12 days.

The use of prophylactic low-dose norfloxacin significantly reduced the prevalence of both bacteriuria and pyuria at the time of catheter removal (Figure 1). Significant bacteriuria was present in 32 of 51 (63%) control patients compared to 8 of 54 (15%) patients who had received norfloxacin ($p < 0.001$). Apyuria score of $\geq$ 5–9 leukocytes/HPF or more was found in 22 of 51 (43%) control patients in contrast to a low rate of only 3 of 54 (5%) patients receiving norfloxacin ($p < 0.001$). In prophylaxis patients bacteriuria never exceeded 10^5 CFU/ml and if leukocytes

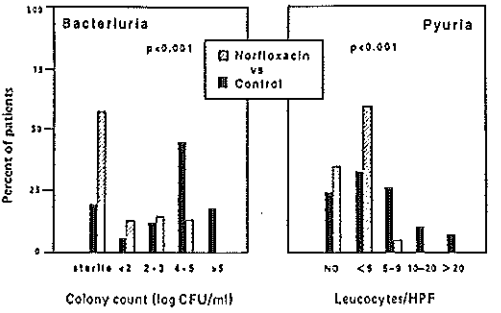

Figure 1: Effect of norfloxacin, 200 mg p.o. once a day, on the level of bacteriuria (left panel) and pyuria (right panel) at the time of catheter removal. ND = not detected.

were present in urine sediment the count was less than 10/HPF (Figure 1). The type of bladder drainage (urethral versus suprapubic) had no significant effect on the rates of bacteriuria and pyuria in either control or norfloxacin-treated patients (data not shown). Prophylactic norfloxacin therapy not only reduced the prevalence and level of bacteriuria, it also strikingly changed the species distribution of the bacteria isolated. The predominant species of bacteria found in urine samples from control patients were, as expected, *Escherichia coli* and other *Enterobacteriaceae* (40% of all isolates), staphylococci (35%) and streptococci (17%) (Table 2). In contrast, positive urine cultures in prophylaxis patients yielded species of glucose-non-fermenting bacteria in 79% of the cases. The high proportion of non-fermenting *Alcaligenes* spp. (40%) among the isolates was especially striking (Table 2). When only urine samples with significant bacteriuria ($> 10^3$ CFU/ml) were considered, this striking difference in species distribution remained (Table 2).

Nine strains of bacteria isolated were resistant to multiple antibiotics. Seven strains were isolated from urine samples of control patients and included *Citrobacter freundii* (n = 4, resistant to cotrimoxazole, gentamicin, tobramycin, ampicillin, carbenicillin, piperacillin and cefamandole), *Acinetobacter* spp. (n = 2, resistant to ampicillin, cefamandole and gentamicin) and *Pseudomonas maltophilia* (n = 1, resistant to nitrofurantoin, cotrimoxazole, gentamicin, tobramycin, amikacin, ampicillin and cefamandole); these seven isolates were all sensitive to norfloxacin. Two multiply resistant isolates from prophylaxis patients comprised an *Acinetobacter* sp. (resistant to gentamicin, cefamandole, ampicillin, tobramycin, amikacin and norfloxacin) and a *Pseudomonas maltophilia* strain (resistant to nitrofurantoin, gentamicin, tobramycin, amikacin, ampicillin, cefamandole and norfloxacin). In general, bacteria isolated from patients treated with norfloxacin were less sensitive or completely resistant to this quinolone, whereas bacteria isolated from control patients were at least moderately sensitive to this drug (data not shown).

Table 2: Bacteria isolated from urine of norfloxacin-treated and control patients. All isolates from catheter urine, regardless of their colony count, are listed. Figures in parenthesis indicate isolates found in urine samples with significant bacteriuria ($> 10^3$ CFU/ml).

Species	Norfloxacin-treated group	Control group
Enterobacteriaceae		
Escherichia coli	1	18 (15)
Citrobacter freundii	0	4 (4)
Klebsiella oxytoca	0	2 (2)
Proteus mirabilis	0	1
Gram-positive cocci		
Staphylococcus aureus	0	5 (5)
Staphylococcus epidermidis	1 (1)	17 (11)
Haemolytic streptococci	1	5 (4)
Streptococcus faecalis	3 (1)	6 (4)
Glucose non-fermenting species		
Pseudomonas	3	2 (2)
Acinetobacter	5 (3)	2 (2)
Alcaligenes	13 (6)	0
Flavobacterium	1	0
Achromobacter	4 (1)	0
Other	1 (1)	1 (1)
Yeast		
Candida albicans	1	0
Total	34 (13)	63 (50)
Multi-resistant strains	2	7

None of the prophylaxis patients complained of potentially drug-related side-effects, nor did any patient develop dysuria after catheter removal before discharge. At the six-week follow-up dysuria was reported by one prophylaxis patient versus three control patients ($p > 0.1$). No differences were found in the median number of days of postoperative stay in the hospital, the figures being 11 days (range 6–28) for prophylaxis patients versus 11 days (range 9–27) for the control group.

Discussion

This study demonstrates that catheter-associated urinary tract infection following gynaecological surgery can be prevented using low-dose prophylactic norfloxacin therapy. Previous studies using nitrofurantoin or cefazolin (19) have shown antibiotic prophylaxis to be effective in reducing the rate of urinary tract infection in this patient group. This was not the case in studies using chloramphenicol (15), oxytetracycline (20) or sulphonamides (21). Even if an effective prophylactic regimen is found, however, the desirability of such a preventive strategy is still debatable. Several authors have previously argued that antibiotic prophylaxis should not be used to prevent catheter-associated urinary tract infection (2–4, 5, 9, 14). Their main objections are that the composition of the microbial flora in prophylaxis patients and, perhaps more importantly, the composition of the hospital bacterial flora could change to include other more resistant species of bacteria or (multipy) resistant mutant strains of bacterial species commonly causing nosocomial infections. Furthermore, antibiotic prophylaxis may lead to an increased incidence of drug-toxicity and protects the catheterised urinary tract for a limited period only. Finally, some authors argue that catheter-associated urinary tract infections are, for the most part, relatively benign afflictions that need treatment only when they become symptomatic, and are then easy to treat (5, 19).

Changes in the composition of patients' microbial flora have, indeed, been detected in this and previous studies of catherized patients who were given antibiotics (4, 8, 9, 10, 15, 16, 21) or underwent bladder irrigation with disinfectants (22–25). However, other investigators have found that the composition of patients' (gut) flora returns to normal once the short-term prophylactic therapy is stopped (26). Furthermore, controlled studies that link the emergence and epidemic spread of drug-resistant bacteria in hospitals to the use of a short-term prophylactic antibiotic regimen for prevention of urinary tract infection are, to our knowledge, lacking.

The selection of the antimicrobial agents and patient groups for prophylaxis is of great importance. We tested the efficacy of antibiotic prophylaxis in female patients following gynaecological surgery because they form a well-defined group of patients suffering from a high rate of catheter-associated infection, such infections constituting a significant proportion of the total number of hospital-acquired urinary tract infections in our hospital. Moreover, these patients were previously given routine therapeutic courses of nitrofurantoin after catherisation because many of them acquired symptoms of urinary tract infection. The isolation of seven multi-resistant bacteria from our control patients further indicated that some patients become infected with strains circulating in the hospital environment. These patients may thus serve as important reservoirs for nosocomial pathogens from which other infections with these organisms could originate (6). Furthermore, urinary tract infections, even asymptomatic infections acquired during bladder catheterisation, may predispose patients to other infection and lead to mortality (27). Finally, these patients are scheduled to have bladder drainage for only a limited number of days, usually seven or less, there thereby being no grounds for the objection that antibiotics afford protection only to patients with short-term catheters.

It should be noted, however, that the large majority of patients catheterised in hospitals have bladder drainage for less than fourteen days (4, 9). It is thus reasonable to assume that other groups of patients can be defined which likewise require short-term bladder drainage, and have an unacceptably high incidence of urinary tract infection, and therefore would potentially benefit from prophylaxis with a well-chosen antibiotic regimen (11–13). Efficacy and toxicity of antibiotic prophylaxis primarily depends on the choice of the antimicrobial agent and the dose given. For this study we elected to use norfloxacin, one of the new fluorinated quinolones. Norfloxacin is active against a wide range of urinary pathogens and is recommended for therapy of urinary tract infections (28–30); it is not used to treat systemic infections or infections at other body sites. However, it has been prescribed for so-called selective decontamination of the gut flora in immunocompromised patients (31) and for treatment of acute diarrheal disease (32). Development of resistance to norfloxacin, especially in glucose-non-fermenting gram-negative bacilli, can occur in vitro, albeit at a relatively low rate (33). Clinically, resistance to norfloxacin in species normally sensitive to the drug does not often occur; rather, species with an inherently higher resistance to norfloxacin, such as *Alcaligenes* spp., *Acinetobacter* spp. and other glucose-non-fermenting species, are sometimes selected, as we found in this study. It should be noted that resistance to the quinolones is mediated by chromosomal genes, and not by genes found in plasmid or transposon DNA which are potentially transferable to other bacteria of the same or even other species (33). Control patients, but not norfloxacin-treated patients, had infections with a multi-resistant *Citrobacter freundii* strain that is endemic in our hospital and contains R-plasmids. We used a dose of 200 mg norfloxacin given orally once daily because with this dose the urine levels maintained over 24 h adequately suppress sensitive organisms (MIC < 2 µg/ml), and because the cost and potential side-effects are lower (34, 35). None of the patients showed drug-related toxicity. However, bacteriological data indicated that this dose of norfloxacin was selecting bacterial species with moderate sensitivity to the drug. Significant bacteriuria caused by bacterial species normally sensitive to norfloxacin but now resistant to it was not found. In addition, none of the eight prophylaxis patients with significant bacteriuria (10^4–10^5 CFU/ml) due to the selected non-fermenting strains had symptomatic or persistent infection after prophylactic therapy and bladder drainage were discontinued. Further study is needed to test the hypothesis that these strains may have less pathogenic potential at this site compared to *Escherichia coli* or other common urinary pathogens. Finally, we would like to caution against the uncritical use of antimicrobial prophylaxis based on the data presented in this study. The study did not attempt to give a complete evaluation of all benefits versus costs and adverse effects of prophylaxis in this setting. Rather, further study of the potential role of antibiotics in the prevention of catheter-associated urinary tract infection is encouraged.

Continued prophylactic use of norfloxacin after termination of the trial has significantly reduced the proportion of gynaecologic patients with hospital-acquired urinary tract infection. Of equal importance is the observation made in our ongoing surveillance of hospital-acquired infections that the gynaecological wards as well as other wards have so far not experienced an increase in the level or spectrum of antibiotic resistance of the organisms causing infections. Rather, the rate of isolation of *Enterobacteriaceae* resistant to multiple antibiotics has significantly decreased (data not shown).

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Impact of concurrent antimicrobial therapy on catheter-associated urinary tract infection

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Summary: Results of a survey in two Dutch district hospitals which investigated the impact of concurrent administration of antibiotics on the incidence of catheter-associated urinary tract infection (UTI), showed that 61% of catheterized patients received antibiotics at some stage during bladder drainage. The use of antibiotics within 48 hours prior to catheter removal reduced the risk of bacteriuria fivefold. Multivariate analysis of patients who were catheterized for 3–14 days indicated that, apart from the duration of catheter employment, the use of antibiotics was the only variable significantly and independently associated with the development of bacteriuria. The power of this association varied inversely with increasing duration of catheterization but remained significant throughout the 3–14-day interval. Patients with bacteriuria at the time of catheter removal were more likely to have a febrile illness compared to those who remained free of catheter-associated UTI.

Keywords: Catheter-associated urinary tract infections; antibiotics; prophylaxis; survey.

Introduction

Indwelling bladder catheters are implicated in 40–75% of all hospital-acquired urinary tract infections (UTI).[1–4] Nosocomial UTI is the leading cause of Gram-negative bacteraemia[5–7] and prolongs the duration of hospital stay by 1 to 5 days.[8–10] Catheter-associated UTI has been reported to increase the risk of Gram-negative bacteraemia by as much as fivefold when compared with patients without UTI.[11] A near threefold increase in mortality was found to be associated with catheter-related UTI,[12] although this excess mortality may be limited to high-risk patients with poor prognoses due to their underlying diseases.[13]

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In 1966 Kunin & McCormack[14] introduced the closed sterile drainage (CSD) technique for which they claimed considerable efficacy in preventing catheter-associated UTI. Several other measures proposed since, to further reduce these infections, have either proven unsatisfactory[15–20] or have yet to gain wide acceptance.[21–24] In their study Kunin & McCormack[14] found that only 23·1% of 580 patients with sterile initial cultures became bacteriuric over the course of CSD. Their results compared favourably with the much higher incidences of UTI reported by previous investigators using open drainage systems. However, Kunin & McCormack also noted that patients given antimicrobial agents (mostly penicillin and streptomycin) retained a sterile urine longer than those left untreated. Importantly, CSD failed to prevent urinary infection in those patients who were on CSD for more than 7–14 days unless they had received concurrent antibiotic therapy as well. Because 84% of the patients in their study had actually received one or more antimicrobial agents during the course of CSD, the relative contributions of CSD and concurrent antimicrobial treatment, in preventing UTI, could not be fully ascertained. Kunin & McCormack commented that the partial effectiveness of antimicrobials justified further prospective controlled studies. Unfortunately, few other studies have focused on the possible impact of concurrent antimicrobial therapy on the incidence of catheter-associated UTI. We therefore prospectively surveyed all patients receiving bladder-catheters in two general hospitals over a 2-month period. Multivariate analysis of the data suggests that, apart from the duration of catheterization, the concurrent use of antibiotics is the only other variable significantly and independently associated with the occurrence of UTI in patients catheterized from 3 to 14 days.

Materials and methods

Use of indwelling urinary tract catheters (IUTCs) and IUTC-associated bacteriuria were recorded over a period of 2 months in two general Dutch hospitals, (the Diakonessen- and Oudenrijn- Hospitals, Utrecht, The Netherlands). Relevant demographic and medical data, with special emphasis on the concurrent administration of antimicrobial agents, were recorded through daily visits to all wards by a single person throughout the surveillance period. A specimen of catheter urine was taken for culture at the time of IUTC insertion (hereafter called 'initial culture') and again just prior to final IUTC removal (hereafter called 'final culture'). If more than 24 hours had elapsed between removal of the IUTC and insertion of a new one, this was counted as a new catheterization episode. If this interval was less than 24 hours an 'exchange of catheter' was recorded. Urine was distributed over a dipslide ('Urotube', Hoffman-La Roche, FRG); for culture and colony-counting. Significant bacteriuria was defined as $\geqslant 10^3$ colony forming units (cfu) ml^{-1} (this definition being based on earlier work by Platt[25] and Stark & Maki[26]). All microorganisms were identified to at

least the genus level and their antimicrobial resistance tested, using Microscan Microdilution Panels (Baxter, The Netherlands) that permitted minimum inhibitory concentration (MIC) determinations for ampicillin, nitrofurantoin, cotrimoxazole, sulpha group, gentamicin and norfloxacin. Ciprofloxacin was tested separately by standardized agar diffusion assay using Rosco tablets (International Medical, The Netherlands). Multiple resistance was defined as resistance to at least ampicillin, cefamandole and one of the aminoglycoside antibiotics. Pyuria was considered to exist if $\geqslant 8$ leucocytes/high power field were seen in a Gram-stained sediment. Catheterizations were considered evaluable for the purposes of this study only if culture results were available of both the 'initial' and 'final' urine specimens. The term 'potentially effective antibiotics' refers to those antibiotics covering most of the pathogens commonly found in catheter-associated UTI. These included the following groups of antibiotics: penicillins, aminoglycosides, cephalosporins, quinolones, cotrimoxazole and nitrofurantoin. Febrile morbidity was defined as a rectal temperature $\geqslant 38°C$ on the day of catheter removal. The following immunocompromising host-factors were taken into account in the multivariate analysis: disseminated malignancy, administration of cytotoxic drugs and/or high dose steroids, diabetes mellitus, current or past irradiation therapy of the lower genitourinary tract and known deficiencies of humoral or cellular immunity.

Statistical analysis

Univariate analysis by χ^2 tests was used to assess the relationship between concurrent use of antibiotics at some stage during catheterization and the results of urinary cultures taken on catheter removal. It was also used to analyse the association between febrile morbidity and culture results on catheter removal.

Stepwise logistic regression analysis was used to judge the influence of the following variables on the results of final cultures: age, gender, number of days on IUTC drainage, immunocompromising host factors, known anatomical abnormalities of the urinary tract, and concurrent use of antimicrobials during catheterization.

Results

Three hundred and sixty-four catheterizations were recorded between 1 June and 5 August (Diakonessenhuis) and 15 June and 1 August (Oudenrijn-Ziekenhuis) 1988, involving 342 patients (median age 68 years, range 37–99). For these hospitals this means that 14·2% and 10·8%, respectively, of all admitted patients received an IUTC at some stage during their hospital stay. Excluding catheterizations with IUTCs in place at discharge from the hospital or at the end of the survey ($N=25$) and those of less than 24 hours duration ($N=7$) the remaining 332 catheterizations

Table I. *Frequency, incidence and duration of catheter use, and its indications*

Service	No. of patients (A)	No. of IUTC used (B)	B/A (%)	Duration of IUTC use (days) Mean	Median	Range	Indication for IUTC use* 1	2	3	4	5	6	Incidence of IUTC**
Gynaecology	262	78	29·7	4·2	2·0	1–17	72	6	–	–	–	–	11·7
Internal medicine	524	71	13·5	9·9	7·5	1–53	9	29	11	21	1	–	9·6
Urology	131	52	39·7	3·6	3·0	1–21	13	7	–	1	29	2	15·2
Surgery	426	50	11·7	9·3	7·0	1–62	20	22	3	3	1	1	9·1
Obstetrics	353	45	12·7	1·4	1·0	1– 4	44	1	–	–	–	–	3·4
Cardiology	275	26	9·4	4·4	3·0	1–17	–	7	–	18	–	1	4·3
Orthopaedics	134	17	12·6	7·5	5·0	2–21	8	4	1	2	–	2	5·0
Neurology	203	16	7·8	14·7	11·0	2–43	1	6	7	2	–	–	6·3
Other	585	9	1·5	6·0	5·0	1–15	–	7	2	–	–	–	NE
Total	2893	364	12·6	6·2	4·0	1–62	167	89	24	47	31	6	NE

NE = not evaluable; incomplete registration data.

* Explanation of code: 1, perioperative drainage; 2, urinary retention; 3, incontinence; 4, fluid balance monitoring; 5, bladder irrigation; 6, other.

** Mean number of days IUTC in place per 100 nursing days.

had a median duration of 3 days (range 1–62). Of the total catheterizations 103 (28%) were not completely evaluable for the following reasons: initial culture specimen missing ($N = 14$), both initial and final culture specimens missing ($N = 12$), only final culture specimen missing ($N = 77$). Unavoidable reasons for failure to obtain final culture specimens were: patient died with catheter in place ($N = 25$), still on drainage at the end of the survey ($N = 13$), discharged with catheter in place ($N = 12$), accidental removal of catheter not followed by reinsertion within 24 hours ($N = 7$). For the non-evaluable patients median age (73 years, range 21–97), duration of catheterization (3 days, range 0–53) and female to male ratio (2·2) were not significantly different from those that were evaluable. The remaining 261 evaluable catheterizations (72%) had a median duration of 4 days. In this latter subgroup female to male ratio (2·6 overall) was 2·7 in those with a negative initial culture and 5·1 in those with a positive initial culture ($P > 0{\cdot}1$).

The survey data clearly showed that the incidence (per 100 nursing days) and frequency (per 100 admitted patients) of catheter use was highest in the departments of gynaecology and urology and that there were considerable differences in the duration of catheter usage between the various specialities (Table I).

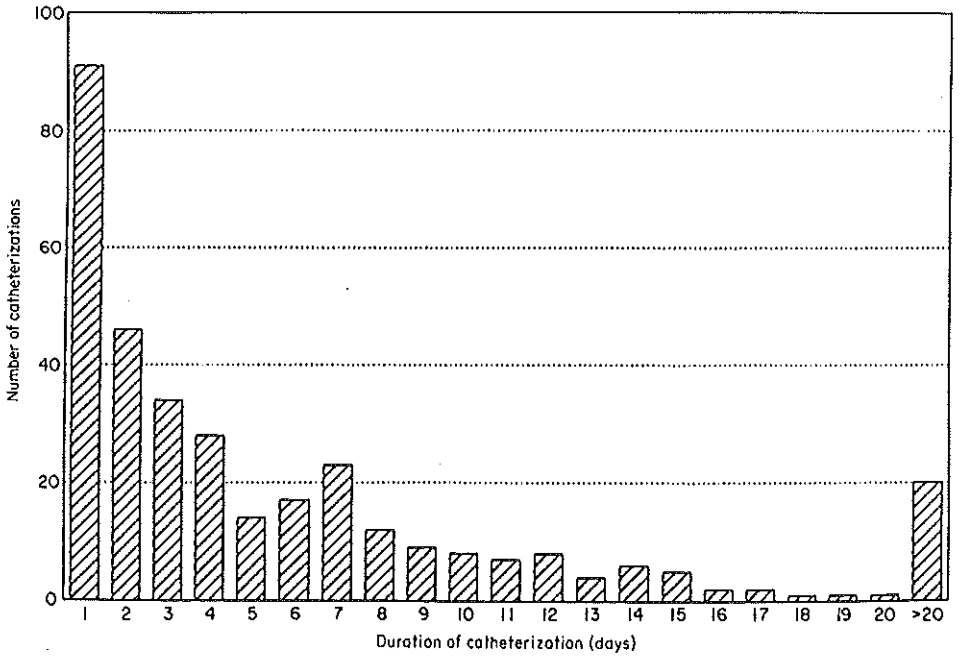

Figure 1. Distribution of the duration of catheterizations. Data pertain to all catheterizations of known duration (⩾ 1 day), irrespective of evaluability. Of all catheterizations recorded, 90% lasted 14 days or less and 50% lasted between 3 and 14 days.

Overall 40%, 75% and 90% of patients were catheterized for $\leqslant 2$, $\leqslant 7$ and $\leqslant 14$ days, respectively (Figure 1). Perioperative drainage (45%) and urinary retention (24%) were the major indications for IUTC use. Incontinence was the indication in only 7% of catheterizations. A positive initial culture was found in 57 catheterizations overall (16%) and in 37/261 (14%) of evaluable cases. Positive final cultures occurred in 113 cases (31%). Of all 224 evaluable cases with negative initial cultures, 78 (35%) showed significant bacteriuria at the time of catheter removal. In infected urine specimens the mean colony count was 10^5 cfu ml^{-1} which was associated with pyuria in 27% of cases.

Use of antimicrobial agents at some stage during IUTC drainage was recorded in 226 of 364 cases (62%), in 170 of 261 evaluable cases (65%) and in 144 of 224 (64%) evaluable cases with a sterile initial culture. In the latter subgroup, potentially effective antibiotics were used in 100 of 146 (68%) cases with negative final cultures versus 31 of 78 (40%) cases who became bacteriuric; focusing on the use of antibiotics within 48 hours prior to catheter removal, we found this to be the case in 59% and 17% of cases, respectively, for the same subgroup ($P < 0{\cdot}001$).

The association between concurrent use of antibiotics, the duration of catheterization and the culture results at the time of catheter removal in patients with negative initial cultures was further analysed (Figure 2). The majority (61%) of patients who had negative final urinary cultures were receiving antibiotics at that time or had been receiving antibiotics within 48 hours prior to catheter removal, irrespective of duration of catheterization. In contrast, this was the case in only 26% of patients with positive final cultures ($P < 0{\cdot}001$).

The effect of antibiotic usage, and its timing in relation to catheter removal on the occurrence of catheter-associated UTI was also analysed in a subgroup of patients with a negative initial culture and duration of catheter drainage between 3 and 14 days ($N = 89$). In this subgroup 43 positive final cultures were recorded, constituting 55% of all cases with negative initial culture who became bacteriuric while on catheter drainage (Table II). For the same subgroup, univariate analysis showed that not using antibiotics was associated with a 3·7-fold increased risk of having a positive final culture ($P = 0{\cdot}0041$).

Multivariate regression analysis including age, gender, immunocompromising host factors, known anatomical abnormalities of the urinary tract, duration of catheter use and use of antibiotics as variables, showed that the use of antibiotics within 48 hours prior to catheter removal and the duration of catheter use were the only variables significantly and independently associated with the development of bacteriuria. The use of antibiotics within 48 hours prior to catheter removal increased the likelihood of a negative final culture result by fivefold [95% confidence intervals (CIs) 1·82–13·6] in comparison with those cases in whom antibiotics were last administered more than 48 hours prior to IUTC removal or those in whom no antibiotics were used at all. This association

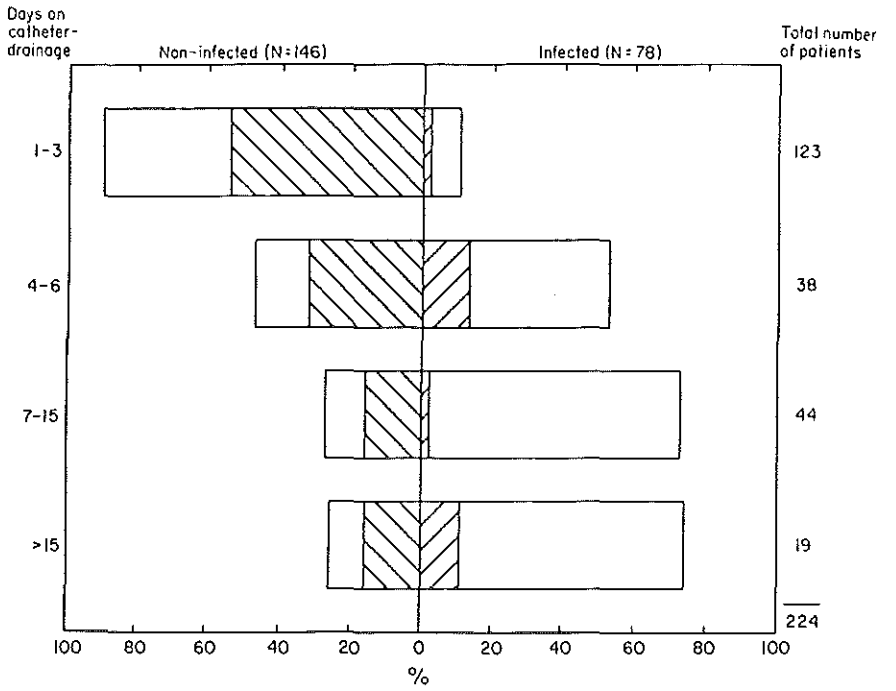

Figure 2. Prevalence of infected *vs* non-infected bladder urine at the time of catheter removal in relation to the duration of bladder drainage. The hatched sectors of each bar denote the proportion of patients that had received concurrent antimicrobial therapy within 48 hours prior to catheter removal. Note that each bar has equal length, corresponding to 100%, and that the majority of patients receiving antibiotics will have sterile urines on catheter removal, irrespective of the duration of catheterization. All patients had sterile urines at the time of catheter insertion.

was shown to be modified, but not reduced to a non-significant level, by the duration of catheter-use. The duration of drainage itself carried a 3·4-fold increased risk for a positive final culture if it exceeded 5 days as compared to 5 days or less ($P = 0{\cdot}005$).

Neither repeated insertions nor exchange of catheter could be demonstrated to affect culture results in any way. However, the small number of such manipulations in the evaluable subgroup may have biased this finding.

In the subgroup with sterile initial culture and a duration of catheter drainage of between 3 and 14 days, febrile morbidity was found to exist in one of 45 cases (2%) with sterile final cultures versus 6 of 43 cases (14%) who became bacteriuric ($P < 0{\cdot}05$).

Three hundred and twenty-seven microorganisms belonging to 30 different species were retrieved from 170 positive cultures. The distribution of species found in positive initial cultures was slightly different from that

Table II. *The effect of antibiotic usage, and its timing in relation to catheter removal on the development of bacteriuria in patients catheterized for 3–14 days*

Antibiotic usage	Number of patients	Patients developing UTI	
		No.	%
None	34	23	67·7
Yes, >48 h*	19	11	57·9
Yes, ⩽48 h**	36	9	25·0

* Use of antimicrobials ended more than 48 hours prior to catheter removal.
** Use of antimicrobials (ABs) ended within 48 hours prior to IUTC removal.
Difference between 'none' and 'ABs>48 hours' non-significant ($P>0·2, <0·5$); between 'ABs>48 hours' and 'ABs<48 hours' significant ($P<0·05$); and between 'none' and 'ABs<48 hours' significant ($P<0·001$). Note that all patients had negative initial urine cultures.

Table III. *Microorganisms cultured from positive catheter-urine specimens*

Species	Urine specimen		*P* value
	initial (%)	final (%)	
Gram-negative rods	49 (48)	88 (39)	NS
Escherichia coli	36 (35)	50 (22)	$P<0·05$
Other *Enterobacteriaceae*	12 (12)	27 (12)	NS
Glucose non-fermenting	1 (1)	11 (5)	NS
Gram-positive bacteria	49 (48)	119 (53)	NS
Staphylococcus epidermidis	10 (10)	47 (21)	$P<0·05$
Staphylococcus aureus	2 (2)	10 (4)	NS
Enterococcus	17 (16)	43 (19)	NS
Haemolytic streptococci	9 (9)	5 (2)	$P<0·05$
Other streptococci	5 (5)	7 (3)	NS
Diphtheroids	5 (5)	6 (3)	NS
Other	1 (1)	1 (–)	NS
Yeasts	5 (5)	17 (8)	NS
Total	103	224	

found in positive final urines (Table III). Only the differences in frequency with which *Staphylococcus epidermidis*, haemolytic streptococci and *Escherichia coli* were cultured proved to be significant. Interestingly, catheter-associated UTI in final cultures was caused more frequently by staphylococci and less often by *E. coli*.

In three cases the microorganism cultured (*Pseudomonas aeruginosa* from an initial specimen; *Citrobacter freundii* and a diphtheroid from two final specimens) was considered multiresistant. One of the three patients involved had received antimicrobial treatment (cotrimoxazole) for a period of 10 days preceeding catheter removal and collection of the urine specimen. Interestingly, all three patients were diabetics.

Discussion

Over the past 40 years a large body of literature has been published on the subject of preventing catheter-associated UTI. The classical study by Kunin & McCormack, published in 1966, made the use of CSD a universally accepted measure against catheter-associated UTI. However, 84% of the patients in their study received antimicrobials at some stage during catheter drainage and the relative contribution of CSD and antimicrobials in preventing catheter-associated UTI could not be fully ascertained. In 1984 Kunin wrote: 'even with the best methods of aseptic closed drainage, colonization of bladder urine will occur in half the patients within 10 days to 2 weeks', by which he clearly indicated that CSD alone was not sufficient to tackle the problem of catheter-related UTI.

The possible role of antibiotic prophylaxis as an additional measure in the prevention of catheter-associated UTI has remained a highly controversial and unresolved issue. One of the reasons for the ongoing discussion seems to be that many authors[2,6,27] declared themselves principally opposed to it on the grounds that it will lead to induction and subsequent spread of multiresistant bacterial strains. This argument, though understandable from a theoretical point of view, has to our knowledge yet to be substantiated by well-controlled prospective studies that are accompanied by concurrent nosocomial infection surveillance. On the contrary, several authors[28,29] have noted the association between IUTC use and spread of resistant *Pseudomonas, Serratia* and *Citrobacter* species. Seen from this point of view, one might even argue in favour of antibiotic prophylaxis in clinical settings with high rates of cross-infection between catheterized patients.

Secondly, an unpredictable relationship exists between IUTC-related bacteriuria and the incidence of infectious morbidity and mortality. This fact seems, even today, to induce a wait-and-see attitude towards IUTC-related bacteriuria in many clinicians. For reasons already mentioned and the fact that costs involved in the treatment of nosocomial UTI by now probably exceed the figures published some years ago,[9,30,31] another attitude clearly seems warranted. Finally, in reviewing the literature, it becomes clear that most controlled prospective antibiotic prophylaxis studies in selected patient groups do not permit adequate comparison and often show varying degrees of conflicting results, a problem noted by several authors.[14,32] Major reasons for this seem to be the non-comparability of the prophylaxis regimens used and differences regarding the inclusion criteria used, the number of days on drainage and the definitions as to which colony count constitutes significant bacteriuria.

Nevertheless, it has become generally accepted that antibiotics are of little or no use in preventing UTI in catheterizations of less than 3 days duration[33–36] and in those of more than 14 days duration.[37–39] Their role in catheterizations of 3–14 days duration, however, remains an issue of considerable controversy although several prospective trials[24,40] have

demonstrated their effectiveness in preventing catheter-associated UTI in this subgroup.

It is for this reason that, in analysing the association between culture outcome and concurrent use of antibiotics, we focused on the subgroup with sterile initial culture and duration of catheter use ranging from 3 to 14 days. As pointed out earlier, the results from multivariate analysis indicate that, with respect to that subgroup, use of antimicrobials and duration of catheter use were the only variables independently and significantly associated with culture outcome. Similar findings have been reported by some,[11,41,42] but not all,[6,43] authors. The impact of concurrent use of antibiotics on culture results remained significant throughout the 3–14 days interval. Beyond 5 days of catheter drainage, however, this impact was only apparent if antibiotics had been continued to within 48 hours prior to catheter removal.

In our opinion these results justify further controlled and prospective trials of antibiotic prophylaxis in catheterized patients. Such studies may serve to find answers to some of the following questions concerning the clinical implications of catheter-associated bacteriuria: (i) what and how much is actually being prevented in terms of morbidity and mortality?; (ii) how do costs and benefits relate?; (iii) will surveillance of nosocomial infections show that routine use of prophylactic antibiotics in selected patient groups indeed leads to considerable induction and spread of multiresistant bacteria?; (iv) which categories of patients are most likely to benefit from such prophylactic measures?

Regarding the last question we suggest that, in order to become eligible for antibiotic prophylaxis, these patients should undergo bladder drainage for a predetermined period of 3–14 days and belong to well-defined, easily identifiable, patient groups, thus permitting selection in advance. The fact that 68% of all hospital-acquired catheter-associated UTIs were recorded in patients with bladder drainage for 3 to 14 days would support this view.

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Prophylactic ciprofloxacin for catheter-associated urinary-tract infection

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Patients receiving antibiotics during bladder drainage have a lower incidence of urinary-tract infections compared with similar patients not on antibiotics. However, antibiotic prophylaxis in patients with a urinary catheter is opposed because of the fear of inducing resistant bacterial strains. We have done a double-blind, placebo-controlled trial of prophylactic ciprofloxacin in selected groups of surgical patients who had postoperative bladder drainage scheduled to last for 3 to 14 days. Patients were randomly assigned to receive placebo (n = 61), 250 mg ciprofloxacin per day (n = 59), or 500 mg ciprofloxacin twice daily (n = 64) from postoperative day 2 until catheter removal.

75% of placebo patients were bacteriuric at catheter removal compared with 16% of ciprofloxacin-treated patients (relative risk [RR] [95% CI] 4·7 [3·0–7·4]). The prevalence of pyuria among placebo patients increased from 11% to 42% while the catheter was in place; by contrast, the rate of pyuria was 11% or less in patients receiving ciprofloxacin (RR 4·0 [2·1–7·3]). 20% of placebo patients had symptomatic urinary-tract infections, including 3 with septicaemia, compared with 5% of the ciprofloxacin groups (RR 4·0 [1·6–10·2]). Bacteria isolated from urines of placebo patients at catheter removal were mostly species of enterobacteriaceae (37%), staphylococci (26%), and *Entercoccus faecalis* (20%), whereas species isolated from urines of ciprofloxacin patients were virtually all gram-positive. Ciprofloxacin-resistant mutants of normally sensitive gram-negative bacteria were not observed.

Ciprofloxacin prophylaxis is effective and safe in the prevention of catheter-associated urinary tract infection and related morbidity in selected groups of patients requiring 3 to 14 days of bladder drainage.

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Introduction

Urinary-tract infection is the most common type of hospital-acquired infection, accounting for more than 30% of all cases.[1] Presence of a urinary catheter is an important risk factor for acquisition of nosocomial urinary-tract infection.[2-6] Of the measures that have been proposed to reduce the incidence of catheter-associated urinary-tract infection only the sterile closed drainage system has gained wide acceptance.[7,8] Even with a closed drainage system the risk of urinary-tract infection remains high at an estimated 5–10% for each day the catheter is in place.[2,9]

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Patients taking antibiotics while they have a catheter in place have a much lower incidence of urinary-tract infection compared with similar patients not receiving antimicrobial agents.[6,7,10-12] However, the prophylactic use of antibiotics during bladder drainage remains controversial. Antibiotic prophylaxis is opposed because of the fear of induction and subsequent spread of resistant bacterial strains that may cause serious infections.[2,3,13,14] This objection must be carefully balanced against the potential benefits of prophylaxis. We have therefore done a prospective study that compares the benefits and hazards of prophylactic ciprofloxacin versus placebo in patients requiring temporary bladder drainage following surgery.

Patients and methods

Study design

Patients were enrolled from those admitted to two acute-care general hospitals (Diakonessen Hospital and Oudenrijn Hospital) in Utrecht, Netherlands, for vaginal repair, total hip replacement, or colorectal surgery (in Oudenrijn Hospital, only patients admitted for vaginal repair participated). In these patients, bladder drainage for more than 2 days but less than 14 days was planned. The pattern of use of indwelling urinary catheters in the two hospitals was known from an earlier survey.[11]

Patients were eligible for enrolment if they were at least 18 years old and had given informed consent. Exclusion criteria were pregnancy, impaired renal or hepatic function (serum creatinine >150 mmol/l, serum transaminases >75 IU/l, respectively), symptomatic urinary-tract infection, fever, or antibiotic use. If antibiotics had been stopped at least 48 h before the study drug was given patients were not excluded. Similarly, 24 h perioperative antibiotic prophylaxis with cefotetan (single preoperative intravenous dose of 2 g), amoxycillin/clavulanic acid (single preoperative intravenous dose of 1·2 g), lincomycin (three doses of 600 mg starting preoperatively), or cephalothin (1 g every 6 h starting preoperatively) did not lead to exclusion. Patients were randomly assigned to receive either placebo or 250 mg once daily or 500 mg twice daily of ciprofloxacin. Medication was given from the second postoperative day until catheter removal. Randomisation was achieved with separate lists with permuted blocks of 12 random numbers for each of the two hospitals and for each hospital service (gynaecology, surgery, orthopaedics) participating in the study. Assignment to one of the study groups was done with these lists by the hospital pharmacy at the time of drug delivery to the wards. Patients and the doctors and nurses involved in their care were all unaware of the nature of the medication being given. All tablets were identical and contained either 250 mg ciprofloxacin or no active drug. Patients received two doses of two tablets per day; thus, patients assigned to the lower dose of ciprofloxacin received one tablet of drug and three of placebo per day. Ciprofloxacin and placebo tablets were provided by Bayer AG (Leverkusen, Germany) and were individually wrapped in identical blister packs by an independent pharmacy.

Clinical and laboratory assessments

The past medical history, Apache II score, and any drugs being taken were recorded for each patient at enrolment. Patients were visited daily by an investigator to record the occurrence of infectious morbidity and adverse events. Hospital-acquired infections were defined according to recognised criteria.[15] Febrile illness was defined as two successive episodes at least 6 h apart during which the patient's temperature exceeded 38°C, excluding episodes within 48 h of surgery. Adverse events were assessed by interview and, if present, classified as possibly study drug-related or not. Daily visits continued until the patient was discharged from hospital.

Specimens of urine were taken for quantitative culture within 24 h of insertion of the catheter, just before its removal, and if requested by the treating physicians. A clean-catch urine sample was obtained at six-weeks' follow-up. Significant bacteriuria was defined as $\geq 10^3$ colony-forming units (cfu)/ml of catheter urine or $\geq 10^5$ cfu/ml clean-catch urine.[16] All microorganisms were identified to at least the genus level. All coagulase-negative staphylococci were considered to be *Staphylococcus epidermidis*. A minimum inhibitory concentration (MIC) of ≤ 2 mg/l ciprofloxacin denoted sensitivity of a bacterial strain. Multiple resistance was defined as resistance to at least ampicillin, cefamandole, and one of the aminoglycoside antibiotics. Urine containing more than 8 leucocytes/µl by a standardised sedimentation technique was considered pyuric. To monitor the effects of study drug on aerobic faecal flora, faecal specimens for quantitative culture were obtained at the same time as urine specimens from 41 consecutively randomised patients admitted for gynaecological or orthopaedic procedures to the Diakonessen Hospital. Quantitative culture of faeces was done by serial dilutions. Only the predominant isolates—ie, those present at the highest dilution—were speciated and counted.

Blood samples were taken before surgery and on the day of catheter removal for measurement of total and differential leucocyte count, haemoglobin, packed cell volume, erythrocyte sedimentation rate, bilirubin, liver transaminases, and creatinine. If abnormal values were found, a third blood sample was obtained at six-weeks' follow-up.

About six weeks after discharge, patients were seen in the outpatient clinic and checked for symptoms of urinary-tract

TABLE I—INTENTION-TO-TREAT ANALYSIS OF RANDOMISED PATIENTS ACCORDING TO PROPHYLACTIC REGIMEN

Characteristic	Prophylaxis with: Placebo (n=68)	Ciprofloxacin 250 mg/day (n=66)	Ciprofloxacin 1000 mg/day (n=68)
Age (yr)			
Median (range)	65 (31–90)	68 (31–91)	64 (39–90)
Female/male	64/4	60/6	64/4
No (%) with surgical procedure:			
Burch or MMK*	28 (41·1)	21 (31·8)	23 (33·8)
Anterior colporraphy	17 (25·0)	20 (30·3)	22 (32·4)
Total hip replacement	18 (26·5)	17 (25·8)	17 (25·0)
Colorectal surgery	4 (5·9)	7 (10·6)	6 (8·8)
No surgery	1 (1·5)	1 (1·5)	0
Bladder drainage			
Suprapubic/urethral	17/51	16/50	12/56
Median no days	7·5	7·0	7·0
No (%) with adverse outcome:			
Infectious morbidity	16 (23·5)†	5 (7·6)	5 (7·4)
Side-effects	2 (2·9)	1 (1·6)	2 (2·9)

*Burch or Marshall-Marchetti-Krantz retropubic urethral suspension
†RR (95% CI) *vs* 250 mg ciprofloxacin group = 3·1 (1·2–8·0), *vs* 1000 mg ciprofloxacin group = 3·2 (1·2–8·2)

TABLE II—CHARACTERISTICS OF 184 EVALUABLE PATIENTS ACCORDING TO PROPHYLACTIC REGIMEN

Characteristic	Prophylaxis with: Placebo (n=61)	Ciprofloxacin 250 mg/day (n=59)	Ciprofloxacin 1000 mg/day (n=64)
Age (yr)			
Median (range)	63 (31–90)	67 (31–91)	65 (39–90)
Female/male	58/3	54/5	60/4
No (%) with surgical procedure:			
Burch or MMK*	28 (45·9)	21 (35·6)	21 (32·8)
Anterior colporraphy	15 (24·6)	19 (32·2)	21 (32·8)
Total hip replacement	14 (22·9)	12 (20·3)	16 (25·0)
Colorectal surgery	4 (6·6)	7 (11·9)	6 (9·4)
Bladder drainage			
Suprapubic/urethral	17/44	16/43	11/53
Median (range) days	8·0 (3–16)	7·0 (3–18)	7·0 (3–15)
Follow-up days			
Median (range)	46·0 (18–70)	45·5 (19–102)	45·0 (13–80)

*Burch or Marshall-Marchetti-Krantz retropubic urethral suspension

infection. They were asked to bring a clean-catch midstream urine specimen and complete a questionnaire dealing with the post-discharge frequency of urination, dysuria, fever, and use of antibiotics. An investigator visited patients who were unable to come to the outpatient clinic at home and collected specimens.

Surveillance of nosocomial infections

The incidence of hospital-acquired infections in the two hospitals has been under constant surveillance since January, 1984. Surveillance is done by methods modified from those of Wenzel et al[17] through weekly visits to each ward by the infection-control nurse.

Statistical analysis

Statistical analysis of numerical data was done with SPSS software (version 3.1, SPSS Inc, Chicago, USA). Variables such as age, number of days catheter in place, number of ciprofloxacin doses, Apache II score, and follow-up days were compared with median tests. The mean and range were also determined for these variables. Univariate analysis by the chi-squared test was used to assess differences in the occurrence of bacteriuria, pyuria, infectious morbidity, and adverse events. The magnitude of differences was estimated by relative risk (RR) with 95% confidence intervals (CI). Fisher's test and Student's *t* test were used to determine the influence of the study medication on laboratory variables. The influence on infectious outcome of age, sex, hospital, type of surgery, type of catheter, and duration of catheter insertion was assessed by stepwise logistical regression analysis.

Results

Between December 1, 1988, and June 1, 1990, 142 patients in Diakonessen Hospital and 60 patients in Oudenrijn Hospital were enrolled in the study. Table I shows the characteristics of all randomised patients and an intention-to-treat analysis of infectious morbidity and side-effects in each of the three study groups. Patients given placebo had a threefold increased risk of infectious morbidity, but were in their other characteristics comparable to patients given active drug. 18 patients were excluded from further analysis because of protocol errors (16) or because they refused further participation (2). These patients were evenly distributed over the three study arms. Characteristics of the 184 evaluable patients are shown in table II. The placebo and two treatment groups were comparable in terms of age, gender, type of surgery, type of bladder drainage, duration catheter in place, and the number of follow-up days. The median Apache II score of all patients was 5 (range 0–9).

14 patients (4 placebo, 5 receiving 250 mg per day ciprofloxacin, and 5 receiving 1000 mg per day) were not evaluable for occurrence of bacteriuria and pyuria because a second specimen of catheter urine was not obtained at the time of catheter removal, usually because the patient had accidentally removed the catheter. Of the 170 patients evaluated, 11% or less in each group were bacteriuric at the time of catheter insertion. However, at catheter removal, 75% of placebo patients were bacteriuric ($\geq 10^3$ cfu/ml) compared with 19% of patients who received 250 mg per day ciprofloxacin and 14% who received 1000 mg per day (RR [95% CI] *vs* 250 mg = 4·1 [2·3–7·3] and *vs* 1000 mg = 5·6 [2·9–10·8]). Furthermore, a striking difference in urine colony count was seen at catheter removal: in 70% of patients receiving placebo the colony count was at least 10^5 cfu/ml, but only 7% of the group receiving 250 mg ciprofloxacin and 3% of those on 1000 mg had the same level of bacteriuria. Patients receiving placebo had a fourfold to fivefold greater risk of pyuria or bacteriuria at the time of catheter removal compared with all those receiving ciprofloxacin (table III).

TABLE III—EFFECT OF CIPROFLOXACIN ON PYURIA AND BACTERIURIA

Analysis of urine at catheter removal	Placebo (n = 57)	Ciprofloxacin (n = 113)	Relative risk (95% CI)
Pyuria			
No	33	101	4·0
Yes	24	12	(2·1–7·3)
Bacteriuria $\geq 10^3$ *cfu/ml*			
No	14	95	4·7
Yes	43	18	(3·0–7·4)
Bacteriuria $\geq 10^5$ *cfu/ml*			
No	17	107	13·2
Yes	40	6	(6·0–29·3)

14 patients were not evaluable at the time of catheter removal (see text).

Symptomatic infections or fever developed in 16 (26%) patients in the placebo group but in only 10 (8%) of those receiving ciprofloxacin. Urinary-tract infection accounted for 67% (12/18) of the episodes of infectious morbidity in the placebo group and surgical wound infections for 22% (4/18) of episodes. 2 patients in the placebo group had two separate infectious episodes. Therapeutic courses of antibiotics were given to placebo-group patients for surgical wound infections (2 patients), pneumonia (two courses in 1 patient), and for urinary-tract infection (8 patients of whom 3 were septicaemic). 4 patients receiving 250 mg ciprofloxacin had febrile episodes (1 urinary-tract infection, 2 wound infections, 1 fever of unknown origin), and 1 had a urinary-tract infection without fever. Only 2 patients on 250 mg ciprofloxacin received therapeutic antibiotics, both because of urinary-tract infection, of whom 1 had septicaemia that was associated with ciprofloxacin-resistant *S epidermidis* bacteriuria. No patients in the group given 1000 mg per day ciprofloxacin had febrile episodes ($p \leq 0{\cdot}023$ compared with placebo and 250 mg groups), although a phlebitis was seen in 1 patient and 4 had urinary-tract infection for which antibiotics were prescribed.

There was no relation between the onset of febrile morbidity and either the time of insertion or of removal of the bladder catheter; however, non-febrile morbidity usually occurred a few days before or within 1–4 days after catheter removal (data not shown). Patients receiving ciprofloxacin prophylaxis (both doses) had a fourfold lower risk of symptomatic urinary-tract infection compared with those on placebo (table IV), giving an absolute risk reduction of 15%. Clinically, this suggests that only 7 patients need to be given prophylaxis to prevent 1 from having infectious morbidity. The difference in infectious morbidity remained

TABLE IV—EFFECT OF CIPROFLOXACIN PROPHYLAXIS ON SYMPTOMATIC URINARY-TRACT INFECTIONS

Prophylaxis	Patients with symptomatic urinary-tract infection	Patients without symptomatic urinary-tract infection
Placebo (n = 61)	12	49
250 mg/day ciprofloxacin (n = 59)	2	57
1000 mg/day ciprofloxacin (n = 64)	4	60
250 mg or 1000 mg/day ciprofloxacin (n = 123)	6	117

RR (95% CI) for placebo *vs* 250 mg/day ciprofloxacin = 5·8 (1·4–24·8), *vs* 1000 mg/day ciprofloxacin = 3·2 (1·1–9·2), and *vs* 250 or 1000 mg/day ciprofloxacin = 4·0 (1·6–10·2)

TABLE V—NUMBER OF ISOLATES OF MICROORGANISMS IN URINE SPECIMENS ACCORDING TO PROPHYLACTIC REGIMEN

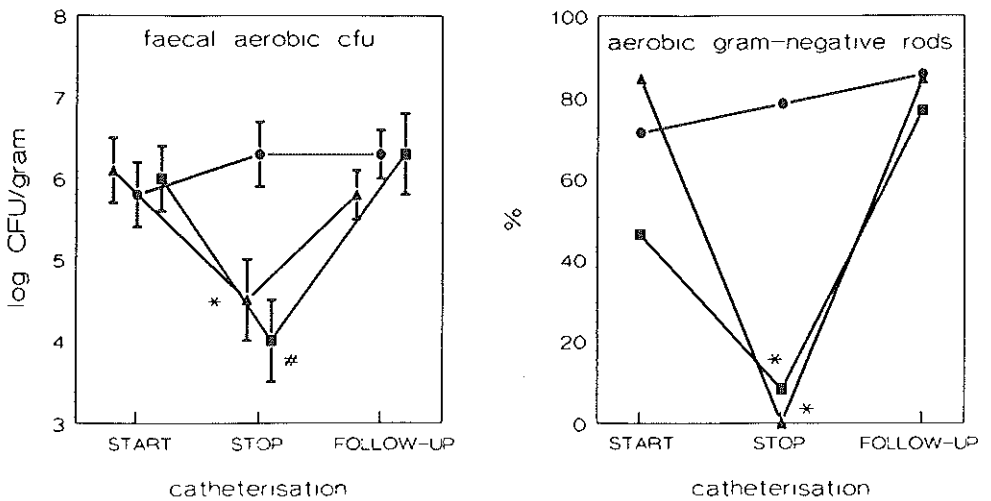
Microorganisms	Prophylaxis with: Placebo			250 mg/day ciprofloxacin			1000 mg/day ciprofloxacin		
	After catheter insertion (n=57)	Before catheter removal (n=57)	Six-weeks' follow-up (n=54)	After catheter insertion (n=54)	Before catheter removal (n=54)	Six-weeks' follow-up (n=53)	After catheter insertion (n=59)	Before catheter removal (n=59)	Six-weeks' follow-up (n=58)
Enterobacteriaceae									
E coli	4	20	14	10	0	3	9	0	5
Other	0	6	6	0	0	1	2	0	6
Glucose-non-fermenting									
Pseudomonas sp	0	2	4	0	0	0	0	0	2
Other	0	1	3	0	0	3	0	0	4
Gram-positive bacteria									
Diphtheroids	1	1	7 (1)	0	1 (1)	9 (1)	0	0	10 (5)
S aureus	0	2	0	0	0	0	0	0	2
S epidermidis	0	16	8	3 (1)	6 (5)	14 (6)	2	5 (5)	22 (7)
E faecalis	1	14 (1)	4	2	2	6 (1)	1	0	9 (1)
Beta streptococcus	0	3 (2)	1	1	1	7 (2)	0	0	9
Other streptococci	0	1	1	0	0	4	0	0	6 (2)
Lactobacillus sp	0	2 (2)	0	0	0	1 (1)	0	0	2
Micrococcus luteus	0	0	0	0	0	1	0	0	0
Candida sp	1 (1)	2 (2)	3 (3)	1 (1)	3 (3)	0	1	5 (5)	0
Total isolates	7 (1)	70 (7)	51 (4)	17 (2)	13 (9)	49 (11)	15	10 (10)	77 (15)

Figures in parentheses are the number of isolates resistant to ciprofloxacin

highly significant when data were adjusted for age, sex, hospital, type of surgery, type of catheter, and duration catheter in place by stepwise logistical regression analysis. Placebo patients were more likely to need therapeutic antibiotics for symptomatic urinary-tract infection (RR 2·7, 95% CI 1·0–7·4).

3 patients on ciprofloxacin experienced moderate gastrointestinal symptoms, including nausea and vomiting, on the second day of prophylaxis, and medication was discontinued. These complaints resolved without further treatment. No other laboratory values were remarkable.

The effect of prophylaxis with ciprofloxacin on the distribution of bacterial species in patients' urine is shown in table V. At the time of catheter insertion, the number of isolates and their species distribution were comparable between the three study groups. The predominant species of bacteria found in urine samples from placebo patients at cather removal were *Escherichia coli* and other enterobacteriaceae (37% of all isolates), staphylococci (26%), and *Enterococcus faecalis* (20%); the total number of isolates increased tenfold during catheter insertion. By contrast, in patierits taking ciprofloxacin the number of isolates from urines did not increase during catheter insertion and aerobic gram-negative rods were not found. The few culture-positive urines from ciprofloxacin-treated patients yielded, predominantly, *S epidermidis* and *Candida*



Effect of ciprofloxacin prophylaxis on aerobic faecal flora.

The total number of aerobic organisms per g faeces was transiently reduced by ciprofloxacin prophylaxis (left panel). Ciprofloxacin virtually eradicated aerobic gram-negative rods (right panel), an effect that was fully reversed at six-weeks' follow-up (% on y-axis = % of faecal samples with predominance of gram-negative rods). Patients received placebo (●), 250 mg ciprofloxacin (▲), or 1000 mg ciprofloxacin (■) daily while a catheter was in place
*$p < 0.0001$ and #$p < 0.001$ compared with placebo

species. At six-weeks' follow-up, gram-positive bacteria predominated in the urine of patients who had received ciprofloxacin, but ciprofloxacin-sensitive gram-negative bacteria were again cultured from the urine of these patients. Resistance to ciprofloxacin was not found among aerobic gram-negative bacteria cultured from urine. The aerobic gram-positive microorganisms cultured from urine samples at the end of ciprofloxacin prophylaxis were largely resistant to ciprofloxacin (table v). However, at six-weeks' follow-up, nearly 75% of isolates of gram-positive bacteria were sensitive to ciprofloxacin, indicating repopulation of the urinary tract with ciprofloxacin-sensitive organisms.

The effect of ciprofloxacin prophylaxis on the aerobic faecal flora manifested itself as a transient reduction in the number of all aerobic organisms, and as almost complete eradication of aerobic gram-negative rods (figure). Before prophylaxis, enterobacteriaceae or glucose-non-fermenting species were usually the predominant aerobic bacteria in faeces from all three groups of patients (between 59 and 82% of patients' samples). At the end of prophylaxis, no enterobacteriaceae and only a single ciprofloxacin-sensitive pseudomonas were isolated from the faeces of ciprofloxacin-treated patients. By contrast, at the same time, enterobacteriaceae species and aerobic glucose-non-fermenting gram-negative bacilli predominated in 79% and 5%, respectively, of faecal samples from placebo patients. Streptococci (usually α-haemolytic) were the predominant aerobic organisms in 63% or faecal samples from patients given 250 mg per day ciprofloxacin and in 54% of faecal samples from patients given 1000 mg per day ciprofloxacin. Yeasts predominated in the faeces of 13% of patients on 250 mg per day ciprofloxacin and 31% of those on 1000 mg per day, but were not found in faecal samples from placebo patients.

No ciprofloxacin-resistant enterobacteriaceae species emerged in the faecal flora as a consequence of antibiotic prophylaxis. At the time of catheter insertion, a ciprofloxacin-resistant *E faecalis* was found in the faeces of 1 patient in the ciprofloxacin-treated groups. After prophylaxis, 8 of 23 (35%) faecal isolates of aerobic gram-positive bacteria from ciprofloxacin-treated patients were resistant to ciprofloxacin. 1 ciprofloxacin-resistant strain of a β-haemolytic streptococcus (group D) was isolated from the faeces of a placebo patient after prophylaxis. The effect of ciprofloxacin on the aerobic faecal flora was fully reversed at six-weeks' follow-up: 1 ciprofloxacin-resistant *E faecalis* and 1 resistant strain of an α-haemolytic streptococcus were cultured from the faecal specimens of a placebo patient and a ciprofloxacin-treated patient, respectively.

Data for follow-up analysis were available from 164 patients. Patients were recorded as lost to follow-up if a completed questionnaire was not obtained. No episodes of dysuria were observed between catheter removal and discharge from hospital in patients that had received ciprofloxacin, but 2 patients in the placebo group complained about dysuria and urinary frequency. 1 of these patients received nitrofurantoin at discharge; the other was not given antibiotics and was readmitted within 4 days because of septicaemia. At six-weeks' follow-up dysuria, urinary frequency, and fever were reported by patients in each of the three study arms. Bacteriuria ($\geq 10^5$ cfu/ml) was more prevalent in the placebo group (28%) than in patients who had received 250 mg per day (13%) or 1000 mg per day (21%) ciprofloxacin. In addition, pyuria was more prevalent among placebo patients (24%) than among either the 250 mg (9%) or 1000 mg (7%) treatment groups, and placebo patients were more likely to have received therapeutic antibiotics between discharge and follow-up (22%, 13%, and 14%, respectively). Compared with all ciprofloxacin-treated patients, placebo patients were significantly more prone to bacteriuria (RR [95% CI] 1·7 [1·2–2·5]) and pyuria (RR 3·0 [1·4–6·5]) at follow-up, and to have had dysuria (RR 1·8 [1·0–3·2]) after discharge.

The overall incidence of hospital-acquired infections in 1988, before the start of this study, was about 5% in each hospital.[12] The rate of nosocomial infections, other than those found in the study groups, did not vary substantially during the trial. Importantly, multiple-antibiotic resistance did not emerge among aerobic gram-negative bacilli causing nosocomial infections in other patients admitted to the hospitals during the study.

Discussion

This study shows that postoperative catheter-associated urinary-tract infection in patients requiring temporary bladder drainage can be prevented with prophylactic ciprofloxacin. Prophylaxis with ciprofloxacin significantly reduced the incidence of bacteriuria and pyuria and gave a fourfold lower incidence of urinary-tract-associated infectious morbidity.

The sterile closed drainage system has been the only accepted measure thought to be effective in lowering the incidence of catheter-associated urinary-tract infection. This method was introduced after a non-comparative study in which 82% of patients received antibiotics at some stage during catheterisation,[7] and it was noted that patients given antimicrobial agents (mostly penicillin and streptomycin) had sterile urine for longer than those left untreated. Sterile closed drainage failed to prevent urinary-tract infection in patients with a catheter in place for 7 to 14 days unless they had also received antimicrobial therapy. Although the reduction in catheter-associated infections in patients given antibiotics was confirmed by other studies,[6,10,11] controlled prospective trials of antibiotic prophylaxis in selected groups of patients with a catheter did not produce unequivocal results.[5,18-22] Differences in prophylactic regimens, inclusion criteria, the number of days catheters were in place, and the definitions of significant bacteriuria do not allow comparison of these studies. Nevertheless, it appears that antimicrobial prophylaxis is of no value in patients with a catheter in place for more than 14 days.[4,5] However, most patients will have bladder drainage for less than 14 days,[7,11] and we found that 90% of patients in our institutions had bladder drainage for less than 14 days. Importantly, 68% of all hospital-acquired catheter-associated urinary-tract infections were recorded in patients with bladder drainage for 3 to 14 days.[11]

Antibiotic prophylaxis during temporary bladder drainage has been opposed on the grounds that multiple-antibiotic-resistant bacteria might emerge in hospitals leading to serious infections, and because of fear of a higher incidence of drug-related toxicity.[2,3,14] It has also been argued that catheter-associated urinary-tract infections are usually benign, they need treatment only when symptomatic, and are then easy to treat.[4,18] In addressing these objections, the selection of patient groups and the choice of antimicrobial agent for prophylaxis is of great importance. Based on the results of our previous survey,[11] we focused on surgical patients who were scheduled to have postoperative bladder drainage for 3 to 14 days. All patients

belonged to well-defined, easily identifiable groups that permitted selection in advance. Ciprofloxacin was chosen for prophylaxis because it is easy to administer, is well absorbed orally, is effective in the treatment of uncomplicated and complicated urinary-tract infection,[23] has been used prophylactically in patients with granulocytopenia with success,[24] and because it has few side-effects.[25]

Ciprofloxacin prophylaxis caused a complete but transient disappearance of enterobacteriaceae species and glucose-non-fermenting gram-negative bacilli from the faecal flora, confirming previous findings.[24,26] Eradication of the aerobic gram-negative gut flora may be an important determinant of ciprofloxacin's efficacy in preventing nosocomial infection since most urinary-tract infections are thought to be due to bacteria from the gut. At six-weeks' follow-up, bacteriuria and pyuria were less common in patients that had received ciprofloxacin than in placebo patients, indicating that the protective effect of ciprofloxacin may last for weeks after its discontinuation. Since dysuria was also prevented this long-lasting effect seems clinically relevant.

Development of resistance to ciprofloxacin among initially sensitive, clinically important bacteria is uncommon. Bacterial resistance to fluoroquinolones is mediated by chromosomal mutations altering DNA gyrase, which confer resistance to quinolones alone, or by changes in the permeability of the cell wall, which may prevent penetration of other antibiotics and thus confer cross-resistance.[27] Ciprofloxacin-resistant strains of enterobacteriaceae or glucose-non-fermenting gram-negative species were not observed in this study. Yet, ciprofloxacin-resistant aerobic gram-positive bacteria, mostly α-haemolytic streptococci and *S epidermidis*, were cultured from the faecal and urine samples of pateints given ciprofloxacin; ciprofloxacin-resistant *S aureus* was not found. Thus, ciprofloxacin prophylaxis altered the aerobic microflora of patients in favour of those species that are inherently less sensitive or completely resistant to fluoroquinolones, but did not lead to the emergence of resistant strains of species that are normally sensitive to fluoroquinolones. Surveillance of hospital-acquired infections showed that wards that took part in the study and other wards in our hospitals did not experience an increase in the frequency, or changes in the spectrum, of antibiotic-resistant organisms causing nosocomial infections.

We conclude that ciprofloxacin can be safely prescribed postoperatively to selected patients receiving bladder drainage; once daily doses of 250 mg are probably sufficient. Although we have not observed emergence of ciprofloxacin-resistant strains of aerobic gram-negative bacteria, we must caution against overinterpretation of our results. The use of other classes of antimicrobials (eg, β-lactams or sulphonamides) in this setting has been associated with failure of prophylaxis and emergence of resistance.[28] We believe that ciprofloxacin prophylaxis should be reserved for well-defined groups of patients that will have bladder drainage for more than 2 days but less than two or three weeks. Active surveillance of hospital-acquired infections, including monitoring for resistant nosocomial pathogens, is essential.

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Estimation of extra charges, extra nursing procedures and prolongation of stay attributable to hospital-acquired infections

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Abstract

Objective: To estimate the extra charges, extra nursing procedures and prolongation of stay attributable to nosocomial infections in an acute care hospital in the Netherlands.

Design: Prospective and descriptive study.

Method: From January to April 1993, concurrent with the surveillance of hospital-acquired infections, data were gathered on the extra charges for diagnostic and therapeutic procedures, nursing procedures and prolongation of hospital stay attributable to nosocomial infections in the Oudenrijn Hospital, Utrecht, the Netherlands.

Results: 75 nosocomial infections were found in 2,871 admissions and 27,566 hospital days, for an incidence of 2.6 per 100 admissions and 2.7 per 1,000 days. Extra charges attributable to nosocomial infections were calculated to be dfl. 39,280.- for medical procedures, 820 extra nursing procedures and 195 days

prolongation of hospital stay (per infection dfl. 524.-, 11 extra nursing procedures and 3 hospital days). The extra charges ranged from dfl. 5.- to dfl. 3,046.- for medical procedures, from 0 - 79 extra nursing procedures and from 0 - 30 extra hospital days. Calculation for the major sites of infections showed surgical wound, lower respiratory tract and bloodstream infections to be relatively expensive and urinary tract and miscellaneous other infections to have relatively low associated cost-profile. This type of information may be useful as a management tool in infection control.

Introduction

In 1990 the Health Council of the Netherlands issued a report "Prevention and Control of nosocomial infections" [1]. The committee made recommendations regarding the continuous surveillance of nosocomial infections and the evaluation on study of the costs of the several types of nosocomial infections [1](p.89).

Information on costs of nosocomial infections in the Netherlands is rare. Most estimations of costs are still based on figures collected in the USA [2]. Sometimes cost-effectiveness studies for specific control measures have been published from the Netherlands [3 4]. These studies, however, are of no help in estimating the costs of nosocomial infections in an individual hospital. Therefore, a study was undertaken to estimate the costs of hospital-acquired infections (HAI) in Oudenrijn Hospital, an acute care hospital in the Netherlands.

Costs of hospital-acquired infections are defined as the costs that are generated by the HAI, and would not have been generated if no HAI had occurred. Actually, the real costs are often not evaluated, but rather the hospital charges are taken, since true costs are difficult to measure. The terms are, however, often used interchangeably [5].

Costs of HAI can be expressed in direct costs of HAI that include costs of

medical-diagnostic and therapeutic procedures, and prolongation of hospital stay [6 7 8 9 10]. Indirect costs of HAI include costs of morbidity and postoperative absenteism from work [1 8]. Intangible costs are those that carry no price tag but relate to the physical and psychological costs of discomfort, pain, and other problems the patient would not have to face if no infection had occurred [11]. Finally, ecological costs can be defined as those due to environmental pollution of the extra disposables, desinfectants and antibiotics needed to treat patients with HAI [12].

Patients and methods

The costs of HAI were studied prospectively using a concurrent, non-comparative method. Costs were defined in terms of those generated by medical-therapeutic and medical-diagnostic procedures and tests in the radiology department, the clinical chemistry and medical microbiology laboratory, and in the hospital pharmacy. Prolongation of hospital stay and extra nursing interventions needed in patient care were tabulated separately.

The choice of these categories was based upon the literature and a two-month pilot study in the Oudenrijn hospital (not published) [9 10].

The study took place in a four-month period in the Oudenrijn hospital in 1993, a general 270-bed hospital with 12 medical specialties, 8,000 admissions and 79,000 patient days per year. As soon as the CDC criteria for a given nosocomial infection were met the patient was included in the study in sequence of the date of onset of infection [13]. In this way a convenient sample cohort was created of patients with one or more HAI's.

The consequences of HAI in terms of medical-diagnostic procedures consisted of procedures in the radiology department, and tests in the chemical and microbiological laboratories. The calculation of costs was based upon the

prices as determined by the Central Organisation Charges in Health Care (COTG). These prices exclude specialists' fees and are assumed to give a more or less correct estimation of the true costs in terms of the hospital budget [14]. For the calculation of the costs in the laboratories, a system which allocates points to specific laboratory tests was used; these so called "Spaanderpoints" were multiplied with the price per point (dfl. 1.70 /point for clinical chemistry and dfl. 2.33 /point for medical microbiology).

The medical-therapeutical procedures consisted of medications delivered by the hospital pharmacy department. The costs of medications were based upon the pharmacists' 1993 retrieval price (AIP) and included 6% tax. Costs of preparing, delivering and administration of medications were not included in these calculations.

The consequences of HAI for the nurses' workload were expressed in extra nursing interventions. These interventions included the nursing techniques the patient needed because of the HAI. The type of interventions were not further specified in advance, but consisted mainly of intravenous administration of antibiotics, monitoring of heart rate, bloodpressure and temperature, and wound care.

Extra patient days were defined as the number of days the patient's hospital stay was prolonged because of the HAI, without the primary diagnosis or underlying disease being a valid reason for hospital stay. A system was used that applied criteria to determine the need for hospital admission for each day of in-patient care according to an appropriateness evalution protocol modified from Gertman and Restuccia [15]. A HAI lasted as long as the CDC criteria of HAI were met or the therapy, to cure the HAI, was continued.

The collection of data on costs, extra nursing procedures and prolonged stay was linked to the ongoing routine surveillance of HAI [16]. As soon as the diagnosis of the nosocomial infection was confirmed, the medical record and the nursing

cardex were reviewed every second day, along with other relevant information until the infection was resolved or the patient discharged. Whenever things were unclear, the medical or nursing staff was questioned on the subject. Roentgenograms and laboratory tests were only considered performed, and antibiotics were only considered administered when a written order as well as a result from the laboratory or radiology department, or a medication order from the pharmacy were present in the medical record or nursing cardex. When a patient was discharged with an unresolved nosocomial infection, then the costs were counted until the moment of discharge.

Costs of two or more nosocomial infections in one patient were counted separately. If this proved impossible, the costs were attributed to the infection with the most serious signs and symptoms.

The data on costs were coded according to a model used for registration and estimation of costs of clinical and out-patient activities for patients with HIV infection [17]. Reflex® and SPSS® software was used for data management and statistical tests (Mann-Whitney U - Wilcoxon Rank Sum W test, two-tailed)[18].

Results

In the study period 2,871 patients were admitted, with 27,566 patient days, in which 75 HAI were found; an incidence of 2.6 per 100 admissions and 2.7 per 1,000 patient days.

The nosocomial infections that were found were 8 surgical site infections, 28 urinary tract infections, 17 respiratory tract infections, 4 bloodstream infections, and 18 other types of infection (Table 1).

The surgical site infections developed after colon surgery (3 times), skin and soft tissue surgery (3 times), gynecological surgery (1 time) and after orthopedic surgery (1 time, no implant). The category of "other infections" consisted of

stomatitis (3 times), gastrointestinal system infections (3 times), conjuntivitis, skin and soft tissue infections (9 times), upper respiratory tract infection (2 times) and one patient with an intra-abdominal infection.

Table 1. Number of laboratory tests, roentgenograms and pharmacy prescriptions due to hospital-acquired infections.

	number of procedures by			
type of infection	*radiology*	*chemistry lab*	*bacteriology lab*	*pharmacy*
surgical site (n=8)	15	109	20	18
urinary tract (n = 28)	9	67	35	26
respiratory tract (n = 17)	44	110	52	35
bacteremia (n = 4)	5	12	20	8
other (n = 18)	8	16	24	17
all (n = 75)	81	314	151	104
per infection	**1,1**	**4,2**	**2,0**	**1,4**

The 75 HAI generated 81 extra roentgenograms (Table 1) Of these, 72% were X-thorax, accounting for more than half of the extra costs in the X-ray department generated by HAI. In the laboratories 465 extra tests were carried out on behalf of the HAI. A total of 7,145 of the so called "spaanderpoints" were included in the calculation. The pharmacy delivered 104 extra medication courses, of which 98 % were antibiotics, half of which consisted of only four types of antibiotics (Ceftriaxon, Norfloxacin, Netilmicin and Amoxicillin/clavulanic acid). The total amount of extra roentgenograms, laboratory tests and medication courses was d*f*l. 39,280.-, this means d*f*l. 524.- per HAI. This would mean an amount of d*f*l. 117,840.-per year, if the observed incidence and types of infection would be extrapolated over the full year.

10% of the total amount was on account of extra roentgenograms, 40 % on account of the laboratory tests and 50% on account of the extra medications.

These percentages differed depending on the type of nosocomial infection.

The 75 HAI generated 820 extra nursing interventions. If extrapolated to a full year this would mean 2,460 extra nursing interventions, when the incidence and type of infection stayed the same as in the study period. Most nursing interventions were required by patients with surgical wound infections. When a nursing intervention takes about 15 minutes nursing time, then the total of 820 nursing interventions required 205 hours, this is 25.6 working days of 8 hours [19]. This means that 6 days per month were spent on nursing care of HAI, this is a mean of $2^{3/4}$ hours per infection.

The HAI resulted in a total number of 195 extra patient days in the four-month study period. This would mean 585 days for an entire year, if the incidence and types of infections would remain stable over one year. These 195 extra patient days were divided over 19 patients, of whom 13 patients were 65 years and over, half of all the costs of diagnostic and therapeutic interventions and also half of all the extra nursing care were spent on these 19 patients. Ten of these patients had a respiratory nosocomial infection, four had a surgical site infection, three of them a urinary tract infection, one patient had a gastro-intestinal infection and one patient an intra-abdominal infection. Patients with surgical site infections and respiratory infections required the most extra patient days; in contrast, no extra days were allocated to patients with nosocomial bacteremia. Eight patients were discharged during the therapy of the nosocomial infection. No single patient required transfer to another hospital because of the HAI. Five patients with a nosocomial infection died, one patient had a respiratory infection, one patient had a respiratory and a urinary tract infection, and one patient had a surgical site infection. No attempt was made to decide whether or not the nosocomial infection had contributed to the demise of these patients.

The extra costs, extra nursing care and extra days caused by the HAI's showed a wide range (Table 2). The costs for extra diagnostic and therapeutic procedures ranged from dfl. 5.- to dfl. 3,046.-, the number of nursing inter-

ventions from 0 to 79 and the number of extra patient days from 0 to 30 days per infection.

Table 2. Summary of the consequences of hospital acquired infections per type of infection.

type of infection	*type of costs*	*totals*	*mean*	*median*	*range*
surgical site	interv dfl	7,026	878	635	54 - 1,858
n = 8	nurs care	226	28	25	0 - 73
	days	64	8	3	0 - 30
urinary tract	interv dfl	7,664	274	213	31 - 758
n = 28	nurs care	51	2	0	0 - 11
	days	7	0	0	0 - 4
respiratory tract	interv dfl	15,264	898	756	12 - 3,046
n = 17	nurs care	261	15	10	0 - 77
	days	106	6	2	0 - 30
bacteremia	interv dfl	4,879	1,220	1,165	947 - 1,602
n = 4	nurs care	57	14	14	7 - 23
	days	0	0	0	0
other	interv dfl	4,447	247	145	5 - 1,168
n = 18	nurs care	225	13	8	0 - 79
	days	18	1	0	0 - 10
all	interv dfl	39,280	524	228	5 - 3,046
n = 75	nurs care	820	11	7	0 - 79
	days	195	3	0	0 - 30

interv dfl = costs of diagnostic and therapeutic interventions in Dutch guilders
nurs care = number of extra nursing interventions
days = number of extra patient days

The more serious the infection, the more extra costs, days and nursing care. Thus surgical site infections were different from urinary tract infections; in that surgical site infections carried more pharmaceutical costs (p= 0,0492), extra

patient days (p= 0,006) and nursing procedures (p= 0,0001). Compared to respiratory infections surgical site infections required on average a higher number of nursing procedures (p= 0,0472). Surgical site infections were also more expensive than infections in the category "other infections" (p= 0,0324) generating significantly more nursing procedures (p= 0,0240) and extra patient days (p= 0,0394).
No statistical difference was found between costs of respiratory tract infections and bacteremias.

Discussion

75 HAI in a 270-bed general hospital in a four month period generated dfl. 39,280.- due to extra medical-diagnostic and therapeutic interventions. Mean costs were dfl. 524.- per HAI. Half of the costs was spent on antibiotics, nosocomial infections being responsible for 12% of all antibiotics delivered by the pharmacy in the same period. In the laboratories 2.8% of all so called "spaanderpoints" were spent on tests on behalf of HAI. The radiology department spent 2.4% of their roentgenograms in the same period on HAI.
Three factors are influencing the amount of costs of HAI found in a hospital: the incidence of HAI, the types of HAI and the method used to assess extra costs of HAI.
To our surprise only 2.6 HAI per 100 admissions (2.7 per 1000 patient days) were observed during the study period which is rather low compared to the rates previously published from this hospital [16]. Relatively few urinary tract infections, surgical site infections and bacteremias were found compared to respiratory tract infections and "other infections". Thus, the "expensive" infections were a minority [3 20 21].
In this study a non-comparative method was used to assess costs of HAI. Two

methods are recognised to assess the effects of HAI in terms of extra costs and patient days: a comparative and a non-comparative method [22]. In the comparative method a group of patients with is compared to a group without nosocomial infections; the difference between the groups in costs and prologation of stay being attributed to the nosocomial infections. The better the matching, the smaller the difference between the two groups. However, in spite of accurate matching methods, it is felt that patients who acquire a nosocomial infection are sicker than patients without infection for reasons unknown until now [8 22 23]. Unless other factors predisposing for prolongation of hospital stay, are corrected for, the estimates of prolongation of stay attributed to nosocomial infections in comparative studies are considered to be overestimates [22]. Much lower estimations are generated by the non-comparative method; every infected patient is screened for costs and prolongation of stay attributable to his or her nosocomial infection(s) [22 24]. In a small hospital the non-comparative method is preferable since finding a matching control group may be a problem due to the relatively small number of admissions.

Because of the low incidence of HAI in the study period together with the relatively small number of "expensive" infections and the method used in this study, the amount of dfl. 39,280.- is to be considered a minimum of costs attributable to HAI in this hospital over a four-month period [16 22]. Half of all costs were spent on antibiotics and the most "expensive" infections turned out to be respiratory tract infections, bacteremias and surgical site infections. This is in agreement with other studies [8 22].

To our knowledge no other studies are available in which the effects of HAI in terms of extra nursing procedures are described. The extra nursing care generated by HAI adds to the workload of nurses. So called "cheap" infections may not be so cheap if extra nursing workload is also considered. In our study for example the infections in the category "other" were not expensive in terms of laboratory costs, but were expensive in the sense that they consumed extra nursing care.

The HAI generated 195 extra patient days (0.7% of the total number of patient days) with a mean range of 2.6 (0-30) days per infection. It is curious that a clinically serious infection such as bacteremia did not result in prolongation of stay, unlike what is reported in the literature [22 25]. This effect may be caused by the difference in methods used in the assessment of prolongation of stay. In the non-comparative study by Haley et al. extra days were assessed by a physician-epidemiologist who reviewed the medical records [10 22]. In our study, all bacteremic patients stayed appropriately in the hospital because of their underlying disease according to the criteria used in the appropriateness evaluation protocol [15]. The total of 195 extra patient days was found in 19/64 (30%) of the infected patients. These patients accounted for half of the extra costs and half of the extra nursing care. Haley et al. also found that a relatively small percentage (10%) of the patients is responsible for a large share of the costs [22]. Five patients died during an episode of HAI, to what degree the HAI contributed to the death of these patients was not studied. Mortality influences the direct hospital costs "favourably". The extra costs and extra days were studied as long as the patients stayed alive.

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Chapter 5.

Towards a national network of standardised surveillance of hospital-acquired infections in the Netherlands

Abstract

The surveillance in the Oudenrijn Hospital (chapter 3) had a spin-off effect into the "Project Surveillance of hospital-acquired infections in the region of Utrecht" (PSZU). The feasibility was studied of conducting standardised surveillance of hospital-acquired infections (HAI) in a network of eight hospitals in the province of Utrecht. Standardisation was obtained by training and use of written protocols. Data on HAI were collected in the hospitals, data on the population under surveillance were obtained from the National Medical Registry. Analysis was done at the National Institute of Public Health and Environmental Protection. Privacy of patients, physicians and hospitals was guaranteed by anonimisation of data and written agreements with participants. During a 9-16 months period of surveillance of all sites of infection 526 HAI were found among 8,922 patients admitted to the gynaecology and orthopedic surgery services in these hospitals (incidence 5.9 [CI_{95} 5.7-6.7] per 100 admissions, 6.3 [CI_{95} 5.7-6.9]) per 1000 patient days). Of these were 56 % urinary tract infections, 34 % surgical wound infections, 2 % infections of the bloodstream, and 1% lower respiratory infections. The incidence of HAI increased with age. Incidences differed widely per hospital and per service due in part to differences in patient-mix and diagnostic medical practices. The sensitivity of the method was 87.5 % and the specificity 99.3 %. Data analysis was hampered by long delays in obtaining the denominator data

through the National Medical Registry. Also, the continuity of surveillance was regularly interrupted by illness and other unforeseen events preventing Infection Control Practitioners to proceed. Recommendations for a future National Nosocomial Infections Surveillance System are given.

Introduction

The preamble to the "Project Surveillance of hospital-acquired infections in the region of Utrecht" (PSZU) was the hospital wide surveillance in the Oudenrijn Hospital, which was initiated in 1984 [1].

Publication of the first results in 1987 awoke the interest of infection control practitioners (ICP's) that much, that the Oudenrijn infection control team decided to give additional information in the form of a training course in 1988 [2 3]. This fullfilled a need, since few hospitals conducted surveillance at that time, and methods and definitions were not standardised [4 5 6]. On request of the ICP's a more comprehensive course was to be repeated, but funds were lacking [7]. From that moment the idea grew of starting a multicenter surveillance project within the Utrecht region, and in 1990 the National Institute of Public Health and Environmental Protection (RIVM) was invited to participate in such a study [8]. The RIVM embraced this private initiative following the publication of the Report of the National Health Council in december 1990 [9]. This Health Council report strongly advocated that a national body be created to conduct standardised surveillance of HAI's in a network of sentinel hospitals, and suggested that the RIVM should act accordingly. This way the PSZU project was born [10]. The study was supported by a grant from the Ministry of Public Health, Welfare and Sports. As model for such a network stood the National Nosocomial Infections Surveillance system (NNIS) of the Centers for Disease Control (CDC) in the US [11].

The primary goal of this study was to investigate the feasibility of developing and implementing a system of standardised surveillance of HAI in eight hospitals all located in the province of Utrecht. A detailed set of research questions was defined in a series of meetings of the participants. The standardisation and efficiency of data collection on infected and non-infected patients had to be addressed, as was the quality of data gathered. Potential problems in aggregating and analysing the surveillance data at the Center of Infectious Disease Epidemiology (CIE) of the RIVM had to be addressed. Also the privacy of the patient, the attending physician and the hospital were major concerns.

Patients and methods.

The ICP's and microbiologists participating in the project discussed the project with their Infection Control Committees. The hospitals were formally invited to cooperate by contacting the administrators and physicians involved. Written permission was obtained to conduct surveillance in the services of Gyneacology and Orthopedic Surgery.

The clinical patients of Gynaecology and Orthopedics were included in the surveillance of all types of hospital-acquired infections in eight hospitals in the region of Utrecht. Patients admitted for day care only were excluded from the study. The hospitals had different characteristics and were located in towns within a 20 miles radius around the city of Utrecht (table 1).

Table 1. Hospitals participating in the Project of surveillance of hospital-acquired infections in the region of Utrecht.

Hospital	*City*	*Hospital characteristics*	*number of beds*
University Hospital Utrecht	Utrecht	university hospital	858
St. Antonius	Nieuwegein	university-affiliated	584
Diakonessenhuis	Utrecht	university-affiliated	378
Eemland-Elisabeth	Amersfoort	general hospital	320
Eemland-Lichtenberg	Amersfoort	general hospital	500
Hofpoort	Woerden	general hospital	262
Lorentz	Zeist	general hospital	243
Oudenrijn	Utrecht	general hospital	270

The surveillance was conducted for at least nine months in the period from the 1st of March 1992 until July 1993.

Data on nosocomial infections were collected by the ICP's according to a written protocol. Data were collected from medical and nursing charts in twice-weekly ward rounds. These charts contained information on clinical signs and symptoms of the patient and on the results of diagnostic and therapeutic procedures. When information was unclear or lacking, the attending physician or nurse was consulted. The use of the definitions of HAI from the Working Party Infection Prevention (WIP) was agreed upon since these were largely based upon the definitions of the Centers for Disease Control, USA [12 13]. Only two adjustments were made; bacteremia following an infection at another site was not considered as complication of the initial infection but was recorded separately, and the isolation of a pathogenic organisms from washed sputum samples was accepted as one of the criteria for the diagnosis of pneumonia and other lower respiratory tract infections.

Data on the patient, the infection, and patient-related and infection-related riskfactors were recorded on a worksheet. The layout of the worksheet matched the data-entry screen on the computer (Epi-Info, version 5) [14]. Error checks were

applied where appropriate. The anonimised monthly data were sent on diskettes to the RIVM.

Information on all (infected and non-infected) patients under surveillance consisted of the data routinely collected by the hospital administration for the National Medical Registry (SIG, Utrecht). These data were not sent by the ICP's but were directly sent from the SIG to the RIVM. The denominator data set contained selected information on the hospitalisation, the patient, and surgery (table 2).

Complementary to the use of written definitions and protocols standardisation was enhanced by training. Before the start of the project ICP's were trained on the spot in casefinding, and during the course of the project problems with the application of definitions and other problems were discussed during the monthly meetings between the ICP's and medical microbiologists of the participating hospitals.

Table 2. Data from the National Medical Registry selected as denominators for the Project of surveillance of hospital-acquired infections in the region of Utrecht. (ref. 10)

Hospitalisation	*Patient*	*Surgery*
patient ID #	patient ID #	patient ID #
admission #	admission #	admission #
hospital #	service #	service #
type of admission	physician	rank # of surgery
date of admission	primary diagnosis	type of surgery
date of discharge	secondary diagnoses (up to 10)	date of surgery
lenght of stay	main surgery	surgeon
birth date	date main surgery	
sex	transferred from other service	
discharge service	transferred to other service	
primary diagnosis	lenght of stay per service	
outcome		

Number

The sensitivity and specificity for identifying patients with nosocomial infections was assessed twice by concurrent surveillance by a "golden standard " team, consisting of an experienced ICP and medical microbiologist. To estimate the proportion of clinical patients missed in the surveillance the ICP's recorded during two months all patients seen and compared these with the population reported by the SIG in the same period.
At the RIVM the data on infected patients, sent by the ICP's, were checked and linked with the population data sent by the SIG, using SAS software package. The results of the analysis were fed back regularly to the hospitals.

Results

All hospitals and professionals who were invited agreed to participate in the surveillance feasibility study. The ICP's from the eight hospitals completed the minimum of nine months of surveillance within the required period of 15 months. At the beginning of the study a maximum of 468 weeks of surveillance were planned, of which 37 weeks (8%) could not be realised due to unforeseen problems including illnesses of the ICP's or overriding outbreaks in the hospitals. A total number of 8,922 patients were included in the surveillance, of which 470 patients were infected with 526 (5.9% [CI_{95} 5.4-6.5]) hospital-acquired infections. The incidence calculated using the total number of 83,597 patient days was 6.3% (CI_{95} 5.7-6.9). Of these infections 56% were urinary tract infections, 34% were surgical woundinfections, 2% were bloodstream infections, 1% lower respiratory infections and 6% were other types of infections (table 3).

Table 3. Hospital-acquired infection in gyneacologic and orthopedic patients in eight hospitals in the Utrecht region, the Netherlands. (ref. 10)

	orthopedic surgery				
	male	*female*	*gynaecology*	*all*	
number of patients	2,042	3,257	3,623	8,922	
patients with nosocomial infections	52	168	250	470	
number of nosocomial infections	59	188	279	526	(100%)
surgical wound infections	22	50	108	180	(34,2%)
urinary tract infections	27	117	151	295	(56,1%)
lower respiratory infections	2	3	2	7	(1,3%)
bloodstream infections	0	6	5	11	(2,1%)
other types of infections*	6	14	13	33	(6,3%)

* included skin & soft tissue infection, gastrointestinal tract infection, and genital tract infection predominantly.

Incidences of nosocomial urinary tract infections and surgical wound infections were higher in gynaecologic patients than in orthopedic patients (table 4).

Table 4. Incidences of nosocomial surgical wound and urinary-tract infections in gyneacologic and orthopedic patients in eight hospitals in the Utrecht region, the Netherlands. (ref. 10)

Infections	*orthopedics male n=2,042*	*orthopedics female n=3,257*	*gynaecology n=3,623*	*All patients n=8922*
all infections	2.8*	5.8	7.7	5.9
	(2.3-3.8)	(4.9-6.7)	(6.8-8.7)	(5.4-6.5)
surgical wound infections	1.1	1.5	3.0	2.0
	(0.6-1.6)	(1.1-2.0)	(2.5-3.6)	(1.7-2.3)
urinary tract infections	1.3	3.6	4.2	3.3
	(0.9-1.8)	(2.9-4.2)	(3.6-4.8)	(2.9-3.7)

* All data are numbers (CI_{95}) per 100 patients admitted.

Increased age was associated with higher incidence of HAI (table 5).

Table 5. Incidences of hospital-acquired infections per age-class in orthopedic and gynaecologic patients in eight hospitals in the Utrecht region. (ref. 10)

	age-class in years							
	0-19	20-29	30-39	40-49	50-59	60-69	70-79	>80
number of patients	463	1107	1501	1761	1229	1197	1179	485
incidence per 100 patients	1.3	1.0	3.3	4.4	4.5	6.4	10.4	14.4
incidence per 1,000 patient days	2.0	1.7	5.0	5.8	5.2	5.8	6.9	7.8

In 8,898/8,922 patients (97%) denominator data were found in the National Medical Registry. In 3.4% of this population a secondary diagnosis such as diabetes, malignities or chronic obstructive pulmonary disease was present: in this subgroup 12.1% (CI_{95} 8.2-15.5) of the patients were infected versus 4.8% (CI_{95} 4.4-5.3) in the group without such underlying diseases. The age-standardised incidences of HAI varied considerably from hospital to hospital, from 1.8 to 12.6 per 100 admissions (data not shown). Likewise, the incidences of wound-infections in patients following hysterectomy varied widely between hospitals from 0.0 to 23.2 per 100 hysterectomies and from 0.0 to 6.1 per 100 patients following total hip surgery (data not shown).

Validation of "patient finding" in 1946 patients showed that 68% of the population was present in both the National Medical Registry and in the ICP's registry. 23% was present only in the national data set, and not in ICP's dataset; this difference was due to shortness (< 2-3 days) of hospital stay (15%) or unknown reasons (8%). On the other hand 9% of those seen by the ICP's were absent in the national data set. Validation of "case-finding" in 316 patients showed full agreement on 28/32 (sensitivity 87.5%) HAI, and on 284/286 of those without HAI (specificity 99.3%).

Linkage of infection data from the hospitals and population data from the National Medical Registry at the CIE proved to be feasible. A check on the variables birth-date, age and sex in 446 patients showed discrepancies in only

6% of cases.

The data of the National Medical Registry of specified months arrived at the CIE within a lapse of three to twelve months. Further analysis showed that these delays were primarily due to variability in the individual hospitals' ability to deliver these data to the National Medical Registry in a timely fashion.

Discussion

The goal of this study was to investigate the feasibility of standardised, multicenter surveillance rather than collection and comparison of infection rates among hospitals itself. It proved to be feasible to conduct standardised surveillance of HAI on two services in a network of eight hospitals in the Utrecht region. The validity of the method was satisfactory. Surveillance was not conducted in approximately 8% of the surveillance weeks planned; failure to screen was due to unforeseen absence or increased workload of the ICP. Thus, requirements should be formulated on the future availability of personel such that the continuity of surveillance can be guaranteed.

Beforehand much attention was given to inform the administrators and professionals involved correctly and completely, in order to increase the acceptance of the surveillance activities. The surveillance offered information on the incidence of nosocomial infections and riskfactors including age, surgical procedure and underlying disease. This information was used in individual hospitals to reflect upon their own infection rates. However, to allow more meaningful comparisons of infection rates between hospitals more detailed information on patient- and procedure-related riskfactors and diagnostic medical practices would be needed in the future. The efficiency of the surveillance was enhanced by the use of data on the population under surveillance already collected by the National Medical Registry. Disadvantageous were the delays in obtaining such denominator data

from the Registry since this caused the analysis phase to be inappropriately postponed as well. However, much can be gained if the hospitals would be able to deliver their data to the National Medical Registry in a more timely fashion. A more timely feed back of analysed data should be a future aim and options for data analysis in the individual hospital should be improved.

The experiences and recommendations of the PSZU project contributed much to the recent initiative for a national "Project Surveillance of Hospital-acquired infections" that was started in 1996. This initiative was also supported by a similar surveillance project initiated in the Medical Centre Alkmaar (MCA) in another part of the Netherlands (Alkmaar, province of Northern Holland) [15 16 17]. This project, called SWIFT, was coordinated by the National Organization for Quality Assurance in hospitals (CBO) [18]. Although the goals and scopes of these two separate projects differed somewhat (table 6), both recommended to improve the feed-back of the results and the efficiency of data collection, and to concentrate on risk-factors for HAI.

In these two projects the first steps were set in the proces of surveillance, that is the collection and analysis of data and the dissemination of those who need to know. To what extent the surveillance data were used for planning, execution and evaluation of policies in the participating hospitals was not investigated. However, some hospitals mentioned to have identified problems through the surveillance and to have changed their policies, which may have resulted in a reduction in infection rates. But sofar no reports have been published yet.

The efforts needed to collect data on HAI by the ICP are considerable and may be acceptable only for a time-limited project [19 20]. If such data are to be collected for longer time-periods, the data collection method chosen should be highly effective and efficient [21]. The use of existing, electronic data bases may help improve efficiency of data collection. For example Glenister found that 3.0 -6.8 hours per week /100 beds spent on data collection (infected patients only) was considered

acceptable by the ICP's [22]. The decision to opt for time-consuming collection of riskfactors should be based on the goals of the surveillance, which should be made clear in advance [23]. If the purpose of surveillance is the identification of problem areas for further study and intervention, monitoring the effect of these interventions, and detecting trends in incidences of HAI, then only a limited number of known riskfactors may be needed [24 25]. In contrast, if surveillance data are to be used as indicators of quality and to detect new determinants of HAI then collection of all potentially relevant risk factors will be needed. If the purpose of surveillance is to identify patients at increased risk for HAI, then the collection of riskfactors is especially important. It is, thus, essential to explicitely state the purpose of surveillance such that one can choose an adequate level of detail of data to be collected.

The surveillance should generate feed-back information that is meaningful to the professional in providing targets for prevention. Only the prevention of HAI legitimizes the effort of surveillance.

Table 6. Comparison between the "Project surveillance of hospital-acquired infections in the region of Utrecht" (PSZU) and the "Project of surveillance of surgical woundinfections" (SWIFT) in the Netherlands.

	PSZU project	*SWIFT project*
Goal	feasibility of surveillance of HAI in a network of hospitals	support hospitals in implementing limited surveillance; produce comparable infection rates
Scope	8 hospitals 2 services all sites of infection 8,922 clinical patients	26 hospitals surgical procedures surgical site infections only 18,612 clinical patients
Methods	active prospective surveillance numerator data by ICP denominator data from National Registry Epi-info software	active prospective surveillance numerator data by ICP denominator data by ICP WHOCARE software
Validation	patient-finding by national Registry case-finding by golden standard team	patient-finding by questionnaire case-finding by questionnaire
Results	526 HAI (5.9%)	488 woundinfections (2.7%)
Analysis	incidences of all sites * per 100 admissions * per 1,000 patient days * per surgical procedure * per age-class * length of stay * with secondary diagnosis	incidences of surgical wound -infections * per surgical procedure * per risk-index * per elective/emergency * per use antibiotic prophylaxis * per age class * per lenght of stay
Pro's	all sites use of existing database as denominator validated	(crude) interhospital comparisons allowed crude reference infection rates per surgical procedure
Con's	no interhospital comparison allowed due to differences in medical diagnostic practices and patient mix	not validated labour intensive due to collection of denominator data by ICP's.
Recommendations	improve: * feed-back * efficiency * risk-factor analysis * software	improve: * feed-back * efficiency * risk factor analysis * preventive actions

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Chapter 6.

General Discussion and Conclusion

Surveillance of HAI is the systematic monitoring, analysis, action, and feedback regarding the "event" HAI. The information fed back must be professionally meaningful, based on good quality data, and not be too costly to obtain.

Unlike in the USA[1] and perhaps other countries as well there was little incentive from the governement or from any accreditation institution to promote surveillance in the Netherlands; the reports from the National Health Council have occasionally addressed the surveillance of HAI [2 3]. However, this situation may be changing with the upcoming Law on Quality, that, among other things, requires a working system of quality control in hospitals [4]. Moreover, national activities aimed at the development and implementation of standardized surveillance of HAI have been supported by the governement. The activities include those of the Working party on Infection Prevention (WIP) which develops infection control guidelines[5] and the Working party on the Implementation of Surveillance of Nosocomial infections (WIRZI), that is preparing a handbook on standardized surveillancesystems [6 7].
In August 1995 several institutions including the National Organization for Quality Assurance in Hospitals (CBO) and the National Institute of Public Health and Environmental Protection (RIVM) joined forces in a governement-supported "Project Surveillance of hospital-acquired infections".

The feasibility of a surveillance system depends on the fit between the hospital and the system, on the availability of personnel and other resources. Several surveillance methods are available. Methods that require less time compared to active hospital-wide tracking of HAI usually have to accept lower sensitivity. Glenister compared six different methods to a reference method [8]. Of the more

selective surveillance methods, those based on the review of microbiology reports with regular ward liaison identified the highest proportion (71%) of HAI; this system closely resembled the one we used in the Oudenrijn hospital. The time required was 6.4 hours per 100 beds per week, the wards were visited twice weekly. The reported sensitivity was 76% (CI_{95} 59-88%), the specificity 100% (CI_{95} 98-100%). Surveillance systems using total chart review may have sensitivities approaching 90 % [9]. We spent 6 to 8 hours each week collecting data during the ward rounds in a 270 bed hospital [10]. The sensitivity of the method used in Oudenrijn hospital was studied at the time the hospital participated in a regional project on standardized surveillance of nosocomial infections [11]. Sensitivity (probability that a hospital acquired infection is correctly recorded as such) was 87,5% (CI_{95} 71,0-96,5) and the specificity (probability that a nosocomial infection was justly not recorded) was 98,6% (CI_{95} 96,5-99,6).

Performing continuous hospital-wide surveillance requires the following elements[9]: definitions of categories of infection, systematic case finding and data collection, tabulation of data, analysis and interpretation of data, reporting of relevant infection surveillance data to individuals and groups for appropriate action, appropriately trained personnel, and a computer and software.

In the Oudenrijn Hospital all these requirements were met. Personnel required for an effective surveillance and control program is a hospital epidemiologist (trained infection control physician or medical microbiologist) and one infection control practitioner per 250 beds [12]. The application of computers is essential for the efficient tabulation and analysis of data, and programs to produce graphs will improve the quality of reports. Information derived from electronic data bases already present in the hospital will increase the efficiency of surveillance[13 14 15], e.g by providing denominators, demographic and economic data on (groups of) patients. Another aspect important for the succes of surveillance is the acceptance and full cooperation of the physicians[16]. Acceptance of the surveillance system by the hospital administration and physicians is a conditio sine qua non.

The targets for interventions are derived from the analysis of surveillance data. The SENIC report provided for each type of nosocomial infection the proportion that could be prevented by an effective surveillance and control program (Table 1) [12].

Table 1. percentage of nosocomial infections prevented by the most effective infection surveillance and control program. From reference 12.

type of infection	*components of program*	*percent prevented*
Surgical Wound Infections	An organized hospital wide program with: *intensive surveillance and control *reporting SWI to surgeons	20
	Plus: *physician with interest and knowledge in infection control	35
Urinary Tract Infections	An organized hospital-wide program with: *intensive surveillance in operation for at least a year *an ICN per 250 beds	38
Bloodstream Infections	An organized hospital-wide program with: *intensive control alone	15
	Plus: *moderately intensive surveillance in operation for at least a year *an ICN per 250 beds *an infection control physician or microbiologist	35
Postoperative Pneumonia	An organized hospital-wide program with: *intensive surveillance * an ICN per 250 beds	27
Pneumonia in medical patients	An organized hospital-wide program with: *intensive surveillance and control	13

In Oudenrijn Hospital targets were set at 1) reducing urinary tract infections; after analyzing the surveillance data priority was given to reducing such infections in gynaecologic patients, 2) reducing surgical wound infections; analysis of surveillance data indicated that action should be focussed on patients undergoing appendectomy, and subsequently those having hysterectomy, 3) reducing bacteremias; surveillance data pointed out that central-catheter associated

bacteremia was a major problem. Ongoing surveillance has subsequently shown that the rate of urinary tract infections in gynaecologic patients was reduced by 93 %, the wound infection rate in appendectomy by 99 % and the wound infections following hysterectomy by virtually 100 %. Although the numbers of HAI involved are relatively small the figures indicated that through such efforts HAI can be prevented to a significant extent.

The choice for targets for preventive action is based upon the severity of the HAI and the magnitude of the problem, and the availability of cost-effective options for prevention. Such options for prevention can be found in the available scientific literature or by performing research in one's own institution. In OudenrijnHospital the measures for prevention of urinary tract infections were the result of research performed in Oudenrijn Hospital itself [17 18 19], while the measures to prevent wound infections and bacteremia were based upon reports in the scientific literature [20 21]. Thus, the literature-based introduction of cefotetan-prophylaxis before appendectomy was shown to prevent 4 surgical site infections per 100 patients so treated (chapter 3), for a drug versus HAI associated cost calculation that showed a cost saving (data not given).

Did the surveillance and control activities have a noticeable impact on the infection rates? The following factors influencing changes in infection rates have previously been recognised in the SENIC study [12]. Infection rates in hospitals starting with high base-line rates tended to decrease and vice versa. This can be seen as a characteristic example of "regression to the mean". Changes in diagnostic medical practices influenced the rates of urinary tract infection, postoperative pneumonia, pneumonia in medical patients, and bacteremia. In general the risk of infection increases with new invasive practices and procedures introduced.

Changes in length of stay did decrease the observed surgical wound infection rate in patients at low risk for surgical wound infections. However, reduction in the length of stay did not affect the wound infection rate or rates of infection at other

sites in high-risk surgical patients. The length of hospital stay may be considered an effect modifier of some risk factors for nosocomial infection (e.g. age, operation, underlying disease)[22].

Surveillance bias may occur due to changes in staffing or surveillance practices resulting in better detection of infections associated with an apparent increase in the number of HAI. For example, when a hospital epidemiologist took a training course in hospital infection control, the rate of urinary tract infections in high-risk patients tended to increase afterwards in his/her institution [12].

Increased infection rates were associated with a change in underlying nosocomial infection risks of the patient population. The increasing proportion of elderly, debilitated patients, occupying hospital beds is an example of such changes.

A rise in percentage of patients who underwent surgery was associated with a decrease in surgical wound infection rate. Increases in the ratio of nurses to patients and house staff to patients were strongly associated with changes in urinary tract infection rates and rates of bacteremia.

Hospitals affiliated with medical schools tended to have increased adjusted infection rates of urinary tract infection, pneumonia and bacteremia.

However, the SENIC study found that the establishment of intensive surveillance and control programs was strongly associated with reductions in rates of nosocomial urinary tract infection, surgical wound infection, pneumonia and bacteremia after controlling for these factors.

Although some of the above mentioned factors may have influenced the infection rate in the Oudenrijn Hospital over time independent of our surveillance and control efforts, the infection rates decreased significantly after the establishment of the surveillance and control program in 1984, strongly suggesting that our program has had a major impact. Our prospectively collected data, therefore, corroborate the results of the SENIC study, that was largely based on retrospective chart review.

However, crude overall infection rates of a given hospital or a service, and

even site specific infection rates by service, should not be used for direct comparisons since such data are never properly adjusted for specific infection risks [23]. Whenever comparing infection rates intrahospital or interhospital adjustments should be made for known riskfactors. The denominator should reflect the appropriate population at risk for the type of infection in the numerator. All patients admitted to the hospital are potentially at risk of a HAI, but their risks are certainly not equal. Risks are significantly related to to age, sex, service, the duration of total and of preoperative hospitalization, the presence of previous nosocomial or community-acquired infection, the type of underlying disease and invasive procedures, the duration of each surgery, the use of urinary tract catheters, continuous ventilatory support, antibiotics and immunosuppressive medications [24 25 26].

Our data showed a decrease in infection rates in all agegroups except for those less than 14 years of age. Service-specific infection rates did decrease for Gynaecology and General Surgery, in which targeted interventions were aimed at specific patientgroups. The efficacy of these interventions was proven by well-controlled clinical trials, not by surveillance data. The success of these interventions was evidenced in downward trends or a trend breach in the ongoing surveillance data, suggesting a causal relationship between the intervention and the reduction in infection rate. As was noted much earlier by Lister in 1870, often the numbers will be "too small for satisfactory statistical comparison; but when details are considered, they are highly valuable with reference to the question we are considering" [27].

Treatment-specific infection rates have decreased following targeted interventions in patients with urinary tract catheters, appendectomy, hysterectomy and central lines for total parenteral nutrition.

The decrease in the all-over infection rate is due to a decrease in infection rates in these subgroups and a stable infection rate in most other areas. Surveillance data provided insight in the long-standing effect of these interventions and will provide

recognition of the emergence of new problems, which allows immediate appropriate preventive action. The goals and data of surveillance have to be sufficiently communicated with those who need to know, using proper feedback methods. We have greatly emphasised this feedback, thus increasing the awareness of the problem of hospital-acquired infections and amplifying the willingness of physicians and other healthcare workers to cooperate in preventive action and to comply with the guidelines on infection control. In this manner hospital-wide surveillance may be a valuable tool in continuous quality improvements.

Conclusion

We conclude, after having performed surveillance of hospital-acquired infections for over ten years, that a system of hospital wide-surveillance was feasible in an acute care hospital, with one Infection Control Practioner per 250 beds and a medical microbiologist with special interest in infection control, together with the support of an appropriate electronic data management system. We found that continuous surveillance of hospital-acquired infections did provide relevant targets for intervention and was very valuable in estimating the effect of the interventions placed. This system of continuous surveillance and control did have noticeable impact on the incidence of hospital-acquired infections in Oudenrijn Hospital, it is, thus, a very valuable tool in improving the quality of care.

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Summary

Quality of care in hospitals is impaired by adverse patient outcomes, such as hospital-acquired infections. These infections, also called nosocomial infections, occurr in patients during their stay in hospital and should be prevented as much as possible. Insight in the type and magnitude of the problem is required before one is able to solve the problem. Data collections on hospital acquired infections are known from the eighteenth century onwards (Chapter 1). Specific interventions did reduce the risk on nosocomial infections. After the introduction of antisepsis, asepsis and antibiotics the interest in nosocomial infection control decreased until the 1950s. At that time Staphylococcal infections began to plague hospitalized patients and renewed efforts were directed at prevention and control of nosocomial infections. It was understood that assessment of the frequency of hospital-acquired infections is a prerequisite for judging if infection control measures have been succesful or need to be adjusted. The continuous collection, collation and analysis of data on hospital acquired infections, and, subsequently, the planning, execution and evaluation of infection control policies, with dissemination to those who need to know, became known as "surveillance". The "Study on the efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals" (SENIC) showed that surveillance is an essential element for any infection control program to be effective.

An infection surveillance and control program was started in 1984 in the 270-bed Oudenrijn Hospital, Utrecht, the Netherlands.
The ultimate goal was to reduce the risk on nosocomial infections. To estimate the magnitude of the problem a study on the incidence of all types of bacteremia was started along with hospital-wide surveillance of all types of nosocomial infections (Chapter 2). In 1984, 197 episodes of bacteremia occurred in 174 patients admitted to two general hospitals. The sources of infection and the

moments of occurrence were studied. The incidence of bacteremia was 1.15 per 100 admissions in the larger university- affiliated hospital and 0.84 in the smaller non-teaching hospital. 43% of these bacteremias were due to urogenital tract infections, virtually always caused by *Escerichia coli* and other Gram negative bacteria of the family of Enterobacteriaceae. In 20% of the bacteremias the source of infection was an infected wound, a decubitus ulcer or an intravascular catheter. The predominant causative agents isolated in these cases were *Staphylococcus aureus* and *Staphylococcus epidermidis*. 29 of the 174 (17%) patients died, 23 (13%) of them as a consequence of sepsis. 68 % of the bacteremias could be classified as nosocomial. A continuous active surveillance system for hospital acquired-infections was felt to be of prime importance.

Consequently hospital-wide surveillance and control of hospital-acquired infections in the Oudenrijn hospital was continued and evaluated after 10 years (Chapter 3). From 1984 onwards surveillance-based preventive actions were targeted at nosocomial urinary tract infections, postoperative wound infections and central venous catheter-related sepsis.

From 1984-1993 a total number of 2,772 HAI were found among 56,410 admissions representing 611,310 patientdays in 92 months of hospital-wide surveillance. The overall incidence in these 10 years was 4.9 (CI_{95} 4.7-5.0) per 100 admissions and 4.5 (CI_{95} 4.4-4.7) per 1,000 patient days.

The incidence of HAI increased with the age of the patients. The lowest incidence was found in the age category 1-14 years: 1.1 % (CI_{95} 0.8-1.6) and the highest incidences were found to be 7.0 % (CI_{95} 5.4- 8.8) in patients from 65-74 years and 10.7 % (CI_{95} 8.5-13.6) in patients above 75 years.

Infections most frequently found were urinary tract infections (43%), followed by surgical wound infections (19%), lower respiratory infections (11%), cutaneous infections (11%) and bacteremias (10%).

Post-discharge infections were not included unless the patient was readmitted

because of the HAI.

The incidence decreased from 7.6 per 100 admissions in 1984 to 3.6 per 100 admissions in 1993; a 53% decrease. The incidence per 1,000 patient days (days at risk) decreased from 6.1 per 1,000 patient days in 1984 to 3.7 in 1993, a 39% decrease. The decrease in incidence of urinary tract per 100 admissions was 68%, the decrease per 1,000 patient days was 60%).

The predominant type of infections differed among the services. The high incidence in urinary tract infections in gynaecology was due to catheter-related urinary tract infections in the first years of surveillance. The infection rates in gynaecology decreased over the years from 16.5 per 100 admissions (19.4 per 1,000 patient days) in 1984 to 2.2 per 100 admissions (2.7 per 1,000 patient days) in 1993. In the medical service urinary tract infections, lower respiratory tract infections and bloodstream infections were mostly found. In surgical patients the infections most frequently found were surgical wound infections and urinary tract infections. The overall surgical woundinfection rate remained rather stable varying from 2.4 to 1.1. However, the rates of infection following appendectomy and hysterectomy decreased by 46% and 80% respectively following the institution of antimicrobial prophylaxis. Efforts were applied to decrease central-line associated bloodstream infections.

A total number of 2,176 cultures were taken from 2,772 infections, this means that no cultures were taken in 22 % of the cases of hospital-acquired infections. The number of pathogens cultured was 3,318; 18 % were *Escherichia coli*, 16 % were miscellaneous , 13 % were *Staphylococcus aureus* and 11 % were coagulase negative staphylococci.

Multiresistance in Gram-negative pathogens did occur sporadically, primarily in the first years of surveillance. No large shifts in the distribution of pathogens did occur over the years.

Surveillance data triggered three in-depth studies on the prevention of catheter-

related urinary tract infections (Chapter 4). The effect of once daily dosis of 200 mg oral norfloxacin on the occurrence of catheter-associated bacteriuria (>1,000 CFU/ml) and pyuria was studied in 105 postoperative gynecologic patients. Norfloxacin was given from the second day after surgery until catheter removal. Bacteriuria developed in 32 of 51 (63%) control patients compared to 8 of 54 (15%) patients receiving norfloxacin ($p< 0.001$). Bacteria isolated from control patients comprised species of *Enterobacteriacae* (40%), *Staphylococcus* (35%), and *Streptococcus* (17%); seven isolates were resistant to multiple antibiotics reflecting their nosocomial origin. In contrast, strains isolated from norfloxacin-treated patients comprised non-fermenting gram-negative rods (79%, usually *Alcaligenes* or *Acinetobacter* spp) and faecal streptococci (12%). It is concluded that once daily doses of 200 mg oral norfloxacin are effective in reducing the rate of catheter-associated bacteriuria and pyuria following reconstructive gynaecologic surgery.

The impact of concurrent antimicrobial therapy on catheter-associated urinary tract infection was studied in more detail (Chapter 4). A survey in two Dutch district hospitals which was focused on the impact of concurrent administration of antibiotics on the incidence of catheter-associated urinary tract infection showed that 61% of catheterized patients received antibiotics at some stage during bladder drainage. The use of antibiotics within 48 hours prior to catheter removal reduced the risk of bacteriuria five-fold. Multivariate analysis of patients who were catheterized for 3-14 days indicated that the use of antibiotics was the only variable, apart from the duration of catheterization, that was significantly and independently associated with bacteriuria. The power of this association varied inversely with increasing duration of catheterization but remained significant throughout 3-14 days interval. Patients with bacteriuria at the time of catheter removal were more likely to have febrile illness compared to those who remained free of catheter-associated urinary tract infection.

The use of antibiotic prophylaxis in patients with a urinary catheters is opposed because of fear of inducing resistant bacterial strains. Therefore we performed a double blind-placebo controlled trial of prophylactic ciprofloxacin in selected groups of surgical patients with postoperative bladder drainage scheduled for 3 to 14 days (Chapter 4). Patients were randomly assinged to receive placebo (n=61), 250 mg ciprofloxacin per day (n= 59), or 500 mg ciprofloxacin twice daily (n= 64) from postoperative day until the day of catheter removal. 75% of placebo patients were bacteriuric at the time of catheter removal compared with 16% of ciprofloxacin treated patients (relative risk [RR] [CI_{95}] 4.7 [3.0-7.4]). The prevalence of pyuria among placebo patients increased from 11% to 42% while the catheter was in place; by contrast, the rate of pyuria was 11% or less in patients receiving ciprofloxacin (RR 4.0 [2.1-7.3]). 20 % of placebo patients had symptomatic urinary tract infections, including 3 with septicemia, compared with 5% of the ciprofloxacin groups (RR 4.0 [1.6-10.2]). Bacteria isolated from urines at the time of catheter removal were mostly species of enterobacteriacea (37%), staphylococci (26%), and *Enterococcus faecalis* (20%), whereas species isolated from urines of ciprofloxacin were virtually all gram-positive. Ciprofloxacin-resistant mutants of normally sensitive bacteria were not observed. Ciprofloxacin prophylaxis is effective and safe in the prevention of catheter-associated urinary tract infection and related morbidity in selected groups of patients requiring 3 to 14 days of bladder drainage.

In order to be able to evaluate the financial consequences of infection control measures a study was conducted on the extra charges, extra nursing procedures and prolongation of stay, attributable to hospital acquired infections in Oudenrijn hospital (Chapter 4).

From January to April 1993, concurrent with the surveillance of hospital acquired infections, data were collected on the extra charges for diagnostic and therapeutic procedures, nursing procedures and prolongation of hospital stay

attributable to nosocomial infections. In the study period 75 nosocomial infections were found in 2,871 admissions and 27,566 hospital days, for an incidence of 2.6 per 100 admissions and 2.7 per 1,000 days. Extra charges attributable to these nosocomial infections were calculated to be d*fl*. 39,280.- for medical procedures, 820 extra nursing procedures and 195 days prolongation of hospital stay. The extra charges per infection ranged from d*fl*. 5.- to d*fl*. 3,046.- for medical procedures, from 0 - 79 for nursing procedures and from 0 - 30 extra hospital days. Calculation for the major sites of infections showed surgical wound, lower respiratory tract and bloodstream to be relatively expensive and urinary tract and miscellaneous infections to have relatively low associated costs. This type of information may be highly useful as a management tool in infection control.

The surveillance in the Oudenrijn Hospital had a spin-off effect into the "Project Surveillance in the region of Utrecht" (Chapter 5). The feasibility was studied of conducting standardised surveillance of hospital-acquired infections (HAI) in a network of eight hospitals in the province of Utrecht. Standardisation was obtained by training and use of written protocols. Data on HAI were collected in the hospitals, data on the population under surveillance were obtained from the National Medical Registry. Analysis was done at the National Institute of Public Health and Environmental Protection. Privacy of patients, physicians and hospitals was guaranteed by anonimisation of data and written agreements with participants. During a 9-16 months period of surveillance of all sites of infection 526 HAI were found among 8,922 patients admitted to the gynaecology and orthopedic surgery services in these hospitals (incidence 5.9 [CI_{95} 5.7-6.7] per 100 admissions, 6.3 [CI_{95} 5.7-6.9]) per 1000 patient days). Of these were 56 % urinary tract infections, 34 % surgical wound infections, 2 % infections of the bloodstream, and 1% lower respiratory infections. The incidence of HAI increased with age. Incidences differed widely per hospital and per service due in part to diffe-

rences in patient-mix and diagnostic medical practices. The sensitivity of the method was 87.5 % and the specificity 99.3 %. Data analysis was hampered by long delays in obtaining the denominator data through the National Medical Registry. Also, the continuity of surveillance was regularly interrupted by illness and other unforeseen events preventing Infection Control Practitioners to proceed. Recommendations for a future National Nosocomial Infections Surveillance System are given.

In Chapter 6 the feasibility, the requirements and the efficacy of surveillance of hospital-acquired infections in general and in Oudenrijn Hospital in particular are discussed.

It is concluded that a system of hospital-wide surveillance of nosocomial infections is feasible with one Infection Control Practitioner per 250 beds and a microbiologist with special interest in infection control, together with the support of appropriate software. Continuous surveillance does provide relevant targets for intervention and is very valuable in estimating the effect of the interventions placed. The system of continuous surveillance and control did have a noticeable impact on the incidence of hospital-acquired infections in an acute-care facility in the Netherlands. It is, thus, a very valuable tool in improving the quality of care.

Samenvatting

Kwaliteit van zorg in ziekenhuizen wordt bedreigd door het optreden van ongewenste gebeurtenissen, zoals het ontstaan van ziekenhuisinfekties. Deze infekties ontstaan bij patiënten tijdens hun opname in het ziekenhuis en moeten zoveel mogelijk voorkomen worden. Inzicht in de aard en grootte van het probleem zijn noodzakelijk alvorens het probleem te kunnen oplossen. Gegevensverzamelingen over ziekenhuisinfekties zijn bekend vanaf de achttiende eeuw (Hoofdstuk 1). Specifieke maatregelen deden het risico op nosocomiale infekties dalen. Na de invoering van antisepsis, asepsis en antibiotica daalde de belangstelling tot aan de vijftiger jaren. Toen werden ziekenhuizen geplaagd door Staphylococceninfekties en met hernieuwde kracht werden bestrijding en preventie van nosocomiale infekties ter hand genomen. Duidelijk was dat het vaststellen van de frequentie van ziekenhuisinfekties een voorwaarde is om te kunnen beoordelen of infektiepreventieve maatregelen effect hebben gesorteerd of moeten worden aangepast. Het doorlopend verzamelen, verwerken en analyseren van gegevens over ziekenhuisinfekties, en vervolgens het plannen, uitvoeren en evalueren van het infektiepreventie beleid, met informatieverstrekking aan de betrokkenen, werd bekend onder de naam "surveillance". De Amerikaanse SENIC "Studie over de effectiviteit van het systeem van surveillance en preventie van ziekenhuisinfekties in Amerikaanse ziekenhuizen" toonde aan dat surveillance een essentieel onderdeel is van infektiepreventie in ziekenhuizen.

Een systeem van surveillance en preventie van ziekenhuisinfekties werd in 1984 ingevoerd in het 270 bedden tellend ziekenhuis Oudenrijn, Utrecht, Nederland. Het uiteindelijke doel was om het risiko op ziekenhuisinfekties te doen dalen. Om inzicht te krijgen in de grootte van het probleem werd begonnen met een onderzoek naar de incidentie van bacteriaemieën, gelijk met ziekenhuisbrede

surveillance van alle soorten ziekenhuisinfekties (Hoofdstuk 2). In één jaar traden 197 episoden van bacteriaemie op bij patiënten die waren opgenomen in twee algemene ziekenhuizen. Het tijdstip van ontstaan en de infektiebron werden bestudeerd. De incidentie van bacteriaemie was 1,15 per 100 opgenomen patiënten in het centrumziekenhuis en 0,85% in het basisziekenhuis. Van deze bacteriaemieën was 43% het gevolg van infecties in de tractus urogenitalis, vrijwel steeds veroorzaakt door *Escherichia coli* en andere Gram-negatieve bacteriën uit de familie der Enterobacteriacae. De infectiebron van 20% van de bacteriaemiën was een geïnfecteerde wond, decubitus-ulcus of intravasculaire catheter; hieruit werden vooral *Staphylococcus aureus* en *Staphylococcus epidermidis* als verwekkers geïsoleerd. Van de 174 patiënten overleden 29 (17%) van wie 23 (13%) tengevolge van de sepsis. 68% van de bacteriëmiën was ontstaan in het ziekenhuis. Een doorlopend actief registratiesysteem werd van maximaal belang geacht.

Vervolgens werd ziekenhuisbrede surveillance van ziekenhuisinfekties in het ziekenhuis Oudenrijn voortgezet en na 5 en 10 jaar geëvalueerd (Hoofdstuk 3). Vanaf 1984 werden op basis van de surveillance gegevens preventieve maatregelen gericht op nosocomiale urineweginfekties, postoperatieve wondinfekties, en centraal-veneus catheter gerelateerde sepsis. Van 1984-1993 werden totaal 2772 ziekenhuisinfekties gevonden bij 56410 opnamen met 611310 verpleegdagen in 92 maanden van ziekenhuisbrede surveillance. De incidentie in deze 10 jaar was 4,9 per 100 opnamen en 4,5 per 1000 verpleegdagen. De incidentie nam toe met de leeftijd van de patiënten. De laagste incidentie werd gevonden in de leeftijdscategorie van 1-14 jaar,: 1,1 % (95% CI 0,8-1,6) en de hoogste incidenties waren 7% (95% CI 5,4-8,8) bij patiënten van 65-74 jaar en 10,7% (95% CI 8,5-13,6) bij patiënten boven de 75 jaar. Urineweginfekties werden het meest gevonden (43%), gevolgd door postoperatieve wondinfekties (19%), lage luchtweginfekties (11%), infekties aan bedekkend weefsel (11% en bacteriaemieën (10%).

Infekties die zich openbaarden na ontslag werden niet meegerekend, tenzij dit een reden was voor heropname. De incidentie nam af van 7,6 per 100 opnamen in 1984 tot 3,6 per 100 opnamen in 1993; een daling met 53%. De incidentie per 1000 verpleegdagen (risicodagen) nam af van 6,1 per 1000 verpleegdagen in 1984 tot 3,7 in 1993, een daling met 39%. De daling in incidentie urineweginfekies per 100 opnamen was 68% (daling per 1000 verpleegdagen bedroeg 60%). Welk type infektie overheerste hing samen met het specialisme. De hoge incidentie urineweginfekties bij gynaecologie hing samen met catheter-gerelateerde urineweginfekties in de eerste jaren van de surveillance. De infektiepercentages bij gynaecologie namen in de loop der jaren af van 16,5 per 100 opnamen (19,4 per 1000 verpleegdagen) in 1984 tot 2,2 per 100 opnamen (2,7 per 1000 verpleegdagen) in 1993. Bij het interne specialisme werden vooral urineweginfekties, luchtweginfekties en bacteriaemiën gevonden. Bij chirurgische patiënten werden vooral postoperatieve wondinfekties en urineweginfekties gevonden. Het overall percentage postoperatieve wondinfekties varieerde van 2,4 tot 1,1% . De infektiepercentages bij appendectomie en uterusextirpaties daalden met respectievelijk 46% en 80%, deze daling werd gerealiseerd na het instellen van antimicrobiële profylaxe. Gerichte aktie werd ondernomen om het aantal centraal-venueuze lijn gerelateerde infekties in de bloedbaan terug te dringen. In totaal 2176 kweken werden afgenomen bij 2772 ziekenhuisinfekties, 22% van alle ziekenhuisinfekties werd niet bacteriologisch gedocumenteerd. Het aantal geïsoleerde microorganismen bedroeg 3318; hiervan was 18% *Escherichia coli*, 16% overige gemengde soorten, 13% *Staphylococcus aureus* en 11% coagulase negatieve staphylococcen. Multiresistentie in Gram negatieve pathogenen kwamen sporadisch voor in de eerste jaren van de surveillance. Geen grote verschuivingen in de verdeling van soorten pathogenen werden in de loop der jaren gezien.

De surveillance gegevens instigeerden drie dieptestudies met betrekking tot de preventie van catheter-gerelateerde urineweginfekties (Hoofdstuk 4). Het effect

werd bestudeerd van een dosis van eenmaal daags 200 mg norfloxacin oraal op het vòòrkomen van catheter geassocieerde bacteriurie (>1000 CFU/ml) en pyurie bij 105 gynaecologische postoperatieve patiënten. Norfloxacin werd gegeven vanaf de tweede dag na operatie tot het moment van verwijderen van de catheter.Bacteriurie trad op bij 32 van de 51 controlepatiënten (63%) vergeleken met 8 van de 54 (15%) patiënten die norfloxacin kregen ($p < 0.001$). Bacteriën geïsoleerd bij de controle patiënten bestonden uit soorten *Enterobacteriacae* (40%), *Staphylococcus* (35%) en *Streptococcus* (17%); zeven isolaten waren resistent voor meerdere soorten antimicrobiële middelen, hun nosocomiale oorsprong doen vermoedend. Daartegenover waren de stammen, geïsoleerd bij de met norfloxacin behandelde patiënten, gewoonlijk non-fermenterende gram negatieve staven (79%, meestal *Alcaligenes* of *Acinetobacter* species) en faecale streptococcen (12%). De conclusie is dat een dosis van 200 mg oraal eenmaal daags effectief is om het percentage te reduceren van catheter-geassocieerde bacteriurie en pyurie bij patiënten na gynaecologische hersteloperaties.

Het effect van antimicrobiële therapie tijdens catheter gebruik op het het ontstaan van catheter-geassocieerde urineweginfekties werd verder bestudeerd (Hoofdstuk 4). Een survey in twee Nederlandse regionale ziekenhuizen toonde aan dat 61% van de gecatheriseerde patiënten een bepaalde tijd met antibiotica werd behandeld in de periode dat de catheter aanwezig was. Het gebruik van antibiotica 48 uur voor het verwijderen van de catheter reduceerde de kans op bacteriurie vijfvoudig. Multivariate analyse van de gecatheteriseerde patiënten toonde aan dat het gebruik van antibiotica de enige variabele was, behalve de duur van de blaasdrainage, die significant en onafhankelijk was geassocieerd met bacteriurie. De sterkte van deze associatie varieerde omgekeerd evenredig met de duur van de blaasdrainage maar bleef significant tijdens de periode van 3-14 dagen. Patiënten met bacteriurie op het moment dat de catheter verwijderd werd hadden meer kans op koorts dan diegenen die geen catheter-geassocieerde

urineweginfektie kregen.

Het gebruik van antimicrobiële prophylaxe bij patiënten met urinewegcatheters wordt ontraden uit angst voor de ontwikkeling van resistente bacteriestammen. Daarom werd een dubbel blind placebo-gecontroleerd onderzoek gedaan met toediening van ciprofloxacin profylaxe aan geselecteerde chirurgische patiënten met een urinecatheter die naar verwachting 3 tot 14 dagen in situ bleef (Hoofdstuk 4). Patiënten werden willekeurig ingedeeld in groepen voor toediening van placebo (n=61), van 250 mg ciprofloxacin eenmaal daags (n=59), of van 500 mg ciprofloxacin tweemaal daags (n=64) vanaf de dag na operatie tot aan de dag van catheterverwijdering. 75% van de patiënten uit de placebogroep hadden bacteriurie ten tijde van het verwijderen van de catheter, vergeleken met 16% uit de met cirpofloxacin behandelde groep (RR [95% CI] 4,7 [3,7-7,4]). De prevalentie van pyurie in de placebogroep steeg van 11% tot 42% in de periode dat de catheter in situ was; in tegenstelling tot de groep patiënten die ciprofloxacin kreeg, waarvan 11% of minder pyurie had (RR 4,0 [2,1-7,3]). 20% van de patienten uit de placebogroep had een symptomatische urineweginfektie, waarvan 3 met een sepsis, vergeleken met 5% uit de ciprofloxacin groepen (RR 4,0 [1,6-10,2]). Bacteriën die geïsoleerd werden uit de urine op het moment van verwijderen van de catheter waren meestal enterobacteriacae soorten (37%), staphylococcen (26%), en enterococcus faecalis (20%), terwijl de species uit de ciprofloxacin groep vrijwel allemaal gram positieven waren. Mutaties van bacteriën die normaal gevoelig zijn voor ciprofloxacin zijn niet waargenomen. Ciprofloxacin profylaxe bleek een effectief en veilig middel ter preventie van catheter geassocieerde urineweginfekties en daaraan gerelateerde morbiditeit, bij toepassing in groepen patiënten die naar verwachting een blaascatheter krijgen gedurende 3-14 dagen.

Ter ondersteuning van het beleid werd een onderzoek gedaan naar de gevolgen

van ziekenhuisinfekties in termen van kosten voor medisch-diagnostische en -therapeutische verrichtingen, extra verpleegtechnische zorghandelingen en extra ligdagen (Hoofdstuk 4).
Van januari tot en met april 1993 zijn prospectief gegevens verzameld over de gevolgen van alle ziekenhuisinfekties die in die periode konden worden vastgesteld. Er werden 75 ziekenhuisinfekties gevonden bij 2871 opgenomen patiënten, incidentie 2,6 per 100 opnamen. De kosten van verrichtingen die aan de ziekenhuisinfekties konden worden toegeschreven bedroegen *f* 39280,-. De ziekenhuisinfekties genereerden 820 extra verpleegtechnische zorghandelingen en 195 extra ligdagen. Per ziekenhuisinfektie betekende dit gemiddeld *f* 524,-, 11 verpleegtechnische zorghandelingen en 3 extra dagen. De variabiliteit in kosten is groot. De bedragen variëren van *f* 5,- tot *f* 3046,- per ziekenhuisinfektie, het aantal extra zorghandelingen van 0 tot 79 en het aantal extra ligdagen van 0 tot 30 dagen. De kosten zijn berekend voor de verschillende soorten ziekenhuisinfekties: postoperatieve wondinfekties, urineweginfekties, luchtweginfekties, bacteriaemiën, en overige infekties. Deze kosteninformatie is een indicatie voor de kosten die de verschillende soorten ziekenhuisinfekties in het Ziekenhuis Oudenrijn met zich meebrengen.

De surveillance in het Ziekenhuis Oudenrijn had een spin-off effect naar het "Project Surveillance in de regio Utrecht" (Hoofdstuk 5). Dit was een studie naar de haalbaarheid van gestandaardiseerde surveillance van ziekenhuisinfekties in een netwerk van acht ziekenhuizen in de provincie Utrecht. Standaardisatie werd verkregen door middel van training en gebruik van schriftelijke protocollen. De gegevens over ziekenhuisinfekties werden verzameld in de ziekenhuizen, de gegevens over de gesurveilleerde patiënten werden verkregen van de Landelijke Medische Registratie (LMR) van de Stichting Informatievoorziemningen in de Gezondheidszorg (SIG). De gegevens werden bewerkt in het Rijksinstituut voor Volksgezondheid en Milieuhygiëne (RIVM).

De privacy van de patienten, de specialisten en de ziekenhuizen werd gewaarborgd door anonimisering van de gegevens en schriftelijke overeenkomsten met de deelnemers. Gedurende 9-16 maanden van surveillance van alle soorten ziekenhuisinfekties werden 526 infekties gevonden bij 8922 patients, opgenomen bij de specialismen gynaecology and orthopedie (incidentie 5,9 [CI_{95} 5,7-6,7] per 100 opnamen, 6,3 [CI_{95} 5,7-6,9]) per 1000 verpleegdagen). Hiervan bestond 56 % uit urineweginfekties, 34% uit postoperatieve wondinfekties, 2 % uit infekties in de bloedbaan, en 1% uit infekties in de lagere luchtwegen. De incidentie van ziekenhuisinfekties nam toe met de leeftijd. De incidenties varieerden in hoge mate per ziekenhuis en per specialisme, deels vanwege verschil in samenstelling van de patientenpopulatie en deels vanwege verschillen in medisch diagnostische praktijkvoering. De sensitiviteit van de methode was 87,5 % en de specificiteit 99,3 %. Een storende factor bij de analyse van gegevens was de langdurige vertraging in de aanlevering van de noemergegevens door de LMR. Eveneens belemmerende factoren waren ziekte en andere onvoorziene gebeurtenissen, die de hygiënist beletten de surveillance voort te zetten. Aanbevelingen voor een toekomstig nationaal systeem voor surveillance van ziekenhuisinfekties worden gegeven.

Hoofdstuk 6 is de bespreking van de haalbaarheid, de voorwaarden en de doeltreffendheid van doorlopende surveillance van ziekenhuisinfekties in het algemeen en in het Ziekenhuis Oudenrijn in het bijzonder.
Geconcludeerd wordt dat in een algemeen ziekenhuis in Nederland een systeem van ziekenhuisbrede surveillance van ziekenhuisinfecties haalbaar is met één ziekenhuishygiënist per 250 bedden en een medisch microbioloog met speciale belangstelling voor infektiepreventie, en met beschikbaarheid over adequate software. Doorlopende surveillance van ziekenhuisinfekties verschaft onderwerpen voor specifieke preventieve maatregelen en maakt het effect van die maatregelen zichtbaar. Het systeem van doorlopende opsporing van ziekenhuisinfekties

en toepassing van gerichte preventieve maatregelen heeft een aantoonbaar effect gehad op de incidentie van ziekenhuisinfekties in het Ziekenhuis Oudenrijn. Het is een waardevol instrument ter verbetering van de kwaliteit van zorg.

Appendix A

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CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

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SPECIAL ARTICLE

CDC definitions for nosocomial infections, 1988

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The Centers for Disease Control (CDC) has developed a new set of definitions for surveillance of nosocomial infections. The new definitions combine specific clinical findings with results of laboratory and other tests that include recent advances in diagnostic technology; they are formulated as algorithms. For certain infections in which the clinical or laboratory manifestations are different in neonates and infants than in older persons, specific criteria are included. The definitions include criteria for common nosocomial infections as well as infections that occur infrequently but have serious consequences. The definitions were introduced into hospitals participating in the CDC National Nosocomial Infections Surveillance System (NNIS) in 1987 and were modified based on comments from infection control personnel in NNIS hospitals and others involved in surveillance, prevention, and control of nosocomial infections. The definitions were implemented for surveillance of nosocomial infections in NNIS hospitals in January 1988 and are the current CDC definitions for nosocomial infections. Other hospitals may wish to adopt or modify them for use in their nosocomial infections surveillance programs. (AM J INFECT CONTROL 1988;16:128-40)

During the past two decades, the Centers for Disease Control (CDC) has published several sets of definitions for nosocomial infections. The definitions used during the Comprehensive Hospital Infections Project (CHIP) from 1969 to 1972 and in the National Nosocomial Infections Study (NNIS) from 1970 to 1974 appeared in the Proceedings of the First International Conference on Nosocomial Infections conducted by CDC in 1970.[1] They were subsequently expanded in 1974 for hospitals participating in NNIS.[2] Algorithms were used for diagnosing infections in the Study on the Efficacy of Nosocomial Infection Control (SENIC Project)[3] in 1975-1976.

From the Hospital Infections Program, Center for Infectious Diseases, Centers for Disease Control, Public Health Service, U.S. Department of Health and Human Services.

Reprint information on p. 33.

The Hospital Infections Program, Center for Infectious Diseases, CDC, has developed a new set of definitions for surveillance of nosocomial infections. The definitions were introduced into hospitals participating in NNIS in 1987 and were modified based on comments from infection control personnel in NNIS hospitals and others involved in surveillance, prevention, and control of nosocomial infections. The definitions were implemented in NNIS hospitals in January 1988 and are the current CDC definitions for nosocomial infections.

PRINCIPLES USED IN DEFINITIONS

The definitions are based on several important principles. First, information used to determine the presence and classification of an infection involves various combinations of clinical findings and results of laboratory and other diagnostic tests. Clinical evidence is derived

from direct observation of the patient or review of information in the patient's chart or other ward or unit records, for example, temperature sheet or Kardex. Laboratory evidence consists of results of cultures, antigen- or antibody-detection tests, and microscopic visualization methods. Supportive data are derived from other diagnostic studies, such as results of x-ray studies, ultrasound examination, computed tomography (CT) scan, magnetic resonance imaging, radiolabel scans, endoscopic procedures, biopsies, and needle aspiration. For infections in which clinical manifestations are different in neonates and infants than in older persons, specific criteria are included.

Second, a physician's or surgeon's diagnosis of infection derived from direct observation during surgery, endoscopic examination, or other diagnostic study, or based on clinical judgment, is an acceptable criterion for an infection, unless there is compelling evidence to the contrary (e.g., information written on the wrong patient's record or a presumptive diagnosis that was not substantiated by subsequent studies). For infections at some sites, however, a physician's clinical diagnosis in the absence of supportive data must be accompanied by initiation of appropriate antimicrobial therapy to satisfy the criterion.

Third, for an infection to be defined as nosocomial, there must be no evidence that the infection was present or incubating at the time of hospital admission. An infection that occurs in the following special situations is considered nosocomial: (1) infection that is acquired in the hospital and becomes evident after hospital discharge and (2) newborn infection that is the result of passage through the birth canal.

Fourth, infection that occurs as the result of the following special situations is not considered nosocomial: (1) infection that is associated with a complication or extension of infection(s) already present on admission, unless a change in pathogen or symptoms strongly suggests the acquisition of a new infection and (2) infection in an infant that is known or proved to have been acquired transplacentally (e.g., herpes simplex, toxoplasmosis, rubella, cytomegalovirus, and syphilis) and becomes evident shortly after birth.

Fifth, except for a few situations that are referred to in the definitions, no specific time during or after hospitalization is given to determine whether an infection is nosocomial or community-acquired. Thus each infection must be assessed for evidence that links it to hospitalization.

DEFINITIONS FOR NOSOCOMIAL INFECTIONS

Definitions for surgical wound infection, primary bloodstream infection, pneumonia, and urinary tract infection are presented first and are followed by other sites of infection listed alphabetically.

SURGICAL WOUND INFECTION

Surgical wound infection includes incisional surgical wound infection and deep surgical wound infection.

Incisional surgical wound infection must meet the following criterion: Infection occurs at incision site within 30 days after surgery AND involves skin, subcutaneous tissue, or muscle located above the fascial layer AND any of the following:

1. Purulent drainage from incision or drain located above fascial layer
2. Organism isolated from culture of fluid from wound closed primarily
3. Surgeon deliberately opens wound, unless wound is culture-negative
4. Surgeon's or attending physician's diagnosis of infection

Deep surgical wound infection must meet the following criterion: Infection occurs at operative site within 30 days after surgery if no implant* is left in place or within 1 year if implant is in place AND infection appears related to surgery AND infection involves tissues or spaces at or beneath fascial layer AND any of the following:

1. Purulent drainage from drain placed beneath fascial layer
2. Wound spontaneously dehisces or is delib-

*A nonhuman-derived implantable foreign body (e.g., prosthetic heart valve, nonhuman vascular graft, mechanical heart, or hip prosthesis) that is permanently placed in a patient during surgery.

crately opened by surgeon when patient has fever (>38° C) and/or localized pain or tenderness, unless wound is culture-negative
3. An abscess or other evidence of infection seen on direct examination, during surgery, or by histopathologic examination
4. Surgeon's diagnosis of infection

PRIMARY BLOODSTREAM INFECTION

Primary bloodstream infection includes laboratory-confirmed bloodstream infection and clinical sepsis. The definition of clinical sepsis is intended primarily for infants and neonates.

Laboratory-confirmed bloodstream infection must meet one of the following criteria:

1. Recognized pathogen isolated from blood culture AND pathogen is not related to infection at another site.*
2. One of the following: fever (>38° C), chills, or hypotension AND any of the following:
   a. Common skin contaminant† isolated from two blood cultures drawn on separate occasions AND organism is not related to infection at another site*
   b. Common skin contaminant isolated from blood culture from patient with intravascular access device AND physician institutes appropriate antimicrobial therapy
   c. Positive antigen test on blood‡ AND organism is not related to infection at another site
3. Patient ≤12 months of age§ has one of the following: fever (>38° C), hypothermia (<37° C), apnea, or bradycardia AND any of the following:
   a. Common skin contaminant isolated from two blood cultures drawn on separate occasions AND organism is not related to infection at another site*
   b. Common skin contaminant isolated from blood culture from patient with intravascular access device AND physician institutes appropriate antimicrobial therapy
   c. Positive antigen test on blood AND pathogen is not related to infection at another site

Clinical sepsis must meet either of the following criteria:

1. One of the following clinical signs or symptoms with no other recognized cause: fever (>38° C), hypotension (systolic pressure ≤90 mm Hg), or oliguria (>20 ml/hr) AND all of the following:
   a. Blood culture not done or no organism or antigen detected in blood
   b. No apparent infection at another site
   c. Physician institutes appropriate antimicrobial therapy for sepsis
2. Patient ≤12 months of age has one of the following clinical signs or symptoms with no other recognized cause: fever (>38° C), hypothermia (<37° C), apnea, or bradycardia AND all of the following:
   a. Blood culture not done or no organism or antigen detected in blood
   b. No apparent infection at another site
   c. Physician institutes appropriate antimicrobial therapy for sepsis

PNEUMONIA

Pneumonia is defined separately from other infections of the lower respiratory tract. The criteria for pneumonia involve various combinations of clinical, radiographic, and laboratory evidence of infection. In general, expecto-

*When an organism isolated from blood culture is compatible with a related nosocomial infection at another site, the bloodstream infection is classified as a secondary bloodstream infection. Exceptions to this are intravascular device–associated bloodstream infections, all of which are classified as primary even if localized signs of infection are present at the access site.

†Organisms that are normal skin flora (e.g., diphtheroids, *Bacillus* sp., *Propionibacterium* sp., coagulase-negative staphylococci, or micrococci).

‡Detection of bacterial, fungal, or viral antigen (e.g., *Candida* sp., herpes simplex, varicella zoster, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, group B streptococci) by rapid diagnostic test (e.g., counterimmunoelectrophoresis, coagulation, or latex agglutination).

§These criteria apply specifically to infants ≤12 months of age; they may infrequently apply to older infants and children.

*When an organism isolated from blood culture is compatible with a related nosocomial infection at another site, the bloodstream infection is classified as a secondary bloodstream infection. Exceptions to this are intravascular device–associated bloodstream infections, all of which are classified as primary even if localized signs of infection are present at the access site.

rated sputum cultures are not useful in diagnosing pneumonia but may help identify the etiologic agent and provide useful antimicrobial susceptibility data. Findings from serial chest x-ray studies may be more helpful than those from a single x-ray film.

Pneumonia must meet one of the following criteria:

1. Rales or dullness to percussion on physical examination of chest AND any of the following:
   a. New onset of purulent sputum or change in character of sputum
   b. Organism isolated from blood culture
   c. Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy
2. Chest radiographic examination shows new or progressive infiltrate, consolidation, cavitation, or pleural effusion AND any of the following:
   a. New onset of purulent sputum or change in character of sputum
   b. Organism isolated from blood culture
   c. Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy
   d. Isolation of virus or detection of viral antigen in respiratory secretions
   e. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen
   f. Histopathologic evidence of pneumonia
3. Patient ≤12 months of age has two of the following: apnea, tachypnea, bradycardia, wheezing, rhonchi, or cough AND any of the following.
   a. Increased production of respiratory secretions
   b. New onset of purulent sputum or change in character of sputum
   c. Organism isolated from blood culture
   d. Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy
   e. Isolation of virus or detection of viral antigen in respiratory secretions
   f. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen
   g. Histopathologic evidence of pneumonia
4. Patient ≤12 months of age has chest radiologic examination that shows new or progressive infiltrate, cavitation, consolidation, or pleural effusion AND any of the following:
   a. Increased production of respiratory secretions
   b. New onset of purulent sputum or change in character of sputum
   c. Organism isolated from blood culture
   d. Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy
   e. Isolation of virus or detection of viral antigen in respiratory secretions
   f. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen
   g. Histopathologic evidence of pneumonia

URINARY TRACT INFECTION

Urinary tract infection includes symptomatic urinary tract infection, asymptomatic bacteriuria, and other infections of the urinary tract.

Symptomatic urinary tract infection must meet one of the following criteria:

1. One of the following: fever (>38° C), urgency, frequency, dysuria, or suprapubic tenderness AND a urine culture* of $\geq 10^5$ colonies/ml urine with no more than two species of organisms
2. Two of the following: fever (>38° C), urgency, frequency, dysuria, or suprapubic tenderness AND any of the following:
   a. Dipstick test positive for leukocyte esterase and/or nitrate
   b. Pyuria (≥10 white blood cells [WBC]/ml^3 or ≥3 WBC/high-power field of unspun urine)
   c. Organisms seen on Gram stain of unspun urine
   d. Two urine cultures with repeated isolation of the same uropathogen† with $\geq 10^2$ colonies/ml urine in nonvoided specimens

*For urine specimens to be of value in determining whether a nosocomial infection exists, they must be obtained aseptically using an appropriate technique, such as clean catch collection, bladder catheterization, or suprapubic aspiration.

†Gram-negative bacteria or *Staphylococcus saprophyticus*.

e. Urine culture with $\leq 10^5$ colonies/ml urine of single uropathogen in patient being treated with appropriate antimicrobial therapy
f. Physician's diagnosis
g. Physician institutes appropriate antimicrobial therapy

3. Patient ≤12 months of age has one of the following: fever (>38° C), hypothermia (<37° C), apnea, bradycardia, dysuria, lethargy, or vomiting AND urine culture of $\geq 10^5$ colonies/ml urine with no more than two species of organisms
4. Patient ≤12 months of age has one of the following: fever (>38° C), hypothermia (<37° C), apnea, bradycardia, dysuria, lethargy, or vomiting AND any of the following:
   a. Dipstick test positive for leukocyte esterase and/or nitrate
   b. Pyuria
   c. Organisms seen on Gram stain of unspun urine
   d. Two urine cultures with repeated isolation of same uropathogen with $\geq 10^2$ organisms/ml urine in nonvoided specimens
   e. Urine culture with $\leq 10^5$ colonies/ml urine of a single uropathogen in patient being treated with appropriate antimicrobial therapy
   f. Physician's diagnosis
   g. Physician institutes appropriate antimicrobial therapy

Asymptomatic bacteriuria must meet either of the following criteria:

1. An indwelling urinary catheter is present within 7 days before urine is cultured AND patient has no fever (>38° C), urgency, frequency, dysuria, or suprapubic tenderness AND has urine culture of $\geq 10^5$ organisms/ml urine with no more than two species of organisms.
2. No indwelling urinary catheter is present within 7 days before the first of two urine cultures with $\geq 10^5$ organisms/ml urine of the same organism with no more than two species of organisms, AND patient has no fever (>38° C), urgency, frequency, dysuria, or suprapubic tenderness.

Other infections of the urinary tract (kidney, ureter, bladder, urethra, or tissues surrounding the retroperitoneal or perinephric spaces) must meet one of the following criteria:

1. Organism isolated from culture of fluid (other than urine) or tissue from affected site
2. An abscess or other evidence of infection seen on direct examination, during surgery, or by histopathologic examination
3. Two of the following: fever (>38° C), localized pain, or tenderness at involved site AND any of the following:
   a. Purulent drainage from affected site
   b. Organism isolated from blood culture
   c. Radiographic evidence of infection*
   d. Physician's diagnosis
   e. Physician institutes appropriate antimicrobial therapy
4. Patient ≤12 months of age has one of the following: fever (>38° C), hypothermia (<37° C), apnea, bradycardia, lethargy, or vomiting AND any of the following:
   a. Purulent drainage from affected site
   b. Organism isolated from blood culture
   c. Radiographic evidence of infection
   d. Physician's diagnosis
   e. Physician institutes appropriate therapy

BONE AND JOINT INFECTION

Bone and joint infection includes osteomyelitis, joint or bursa infection, and vertebral disk infection.

Osteomyelitis must meet one of the following criteria:

1. Organism cultured from bone
2. Evidence of osteomyelitis seen during surgery or by histopathologic examination
3. Two of the following with no other recognized cause: fever (>38° C), localized swelling, tenderness, heat, or drainage at suspected site of infection AND any of the following:
   a. Organism isolated from blood culture
   b. Positive antigen test on blood
   c. Radiographic evidence of infection

Joint or bursa infection must meet one of the following criteria:

1. Organism isolated from culture of joint fluid or synovial biopsy
2. Evidence of joint or bursa infection seen

*Radiographic evidence of infection includes abnormal results of ultrasound examination, CT scan, magnetic resonance imaging, or radiolabel scan (e.g., gallium or technetium)

during surgery or by histopathologic examination
3. Two of the following with no other recognized cause: joint pain, swelling, tenderness, heat, evidence of effusion or limitation of motion AND any of the following:
   a. Organisms and white blood cells seen on Gram stain of joint fluid
   b. Positive antigen test on blood, urine, or joint fluid
   c. Cellular profile and chemistries of joint fluid compatible with infection and not explained by underlying rheumatologic disorder
   d. Radiographic evidence of infection

Vertebral disk space infection must meet one of the following criteria:
1. Organism isolated from culture of involved site tissue obtained during surgery or needle aspiration
2. Evidence of infection at involved site seen during surgery or by histopathologic examination
3. Fever (>38° C) with no other recognized cause or pain at involved site AND radiographic evidence of infection
4. Fever (>38° C) with no other recognized cause AND pain at involved site AND positive antigen test on blood or urine.

CARDIOVASCULAR SYSTEM INFECTION

Cardiovascular system infection includes arterial or venous infection, endocarditis, myocarditis or pericarditis, and mediastinitis. Mediastinitis is grouped with cardiovascular system infections because it most often occurs after cardiac surgery.

Arterial or venous infection must meet one of the following criteria:
1. Organism isolated from culture of arteries or veins removed during surgery AND blood culture not done or no organism isolated from blood culture
2. Evidence of infection at involved vascular site seen during surgery or by histopathologic examination
3. One of the following: fever (>38° C), pain, erythema, or heat at involved vascular site AND both of the following:
   a. More than 15 colonies cultured from intravascular cannula tip using semiquantitative culture method
   b. Blood culture not done or no organism isolated from blood culture
4. Purulent drainage at involved vascular site AND blood culture not done or no organism isolated from blood culture
5. Patient ≤12 months of age has one of the following: fever (>38° C), hypothermia (<37° C), apnea, bradycardia, lethargy, pain, erythema, or heat at involved vascular site AND both of the following:
   a. More than 15 colonies cultured from intravascular cannula tip using semiquantitative culture method
   b. Blood culture not done or no organism isolated from blood culture

Endocarditis of natural or prosthetic heart valve must meet one of the following criteria:
1. Organism isolated from culture of valve or vegetation
2. Two of the following with no other recognized cause: fever (>38° C), new or changing murmur; embolic phenomena, skin manifestations (i.e., petechiae, splinter hemorrhages, painful subcutaneous nodules), congestive heart failure, or cardiac conduction abnormality AND physician institutes appropriate antimicrobial therapy if diagnosis is made antemortem AND any of the following:
   a. Organism isolated from two blood cultures
   b. Organisms seen on Gram stain of valve when culture is negative or not done
   c. Valvular vegetation seen during surgery or autopsy
   d. Positive antigen test on blood or urine
   e. Evidence of new vegetation seen on echocardiogram
3. Patient ≤12 months of age has two or more of the following with no other recognized cause: fever (>38° C), hypothermia (<37° C), apnea, bradycardia, new or changing murmur, embolic phenomena, skin manifestations, congestive heart failure, or cardiac conduction abnormality AND physician institutes appropriate antimicrobial therapy if diagnosis is made antemortem AND any of the following:
   a. Organism isolated from two blood cultures
   b. Organisms seen on Gram stain of valve when culture is negative or not done

c. Valvular vegetation seen during surgery or autopsy
d. Positive antigen test on blood or urine
e. Evidence of new vegetation seen on echocardiogram

Myocarditis or pericarditis must meet one of the following criteria:

1. Organism isolated from culture of pericardial tissue or fluid obtained by needle aspiration or during surgery
2. Two of the following with no other recognized cause: fever (>38° C), chest pain, paradoxical pulse, or increased heart size AND any of the following:
   a. Abnormal electrocardiogram (ECG) consistent with myocarditis or pericarditis
   b. Positive antigen test on blood
   c. Evidence of myocarditis or pericarditis on histologic examination of heart tissue
   d. Fourfold rise in type-specific antibody with or without isolation of virus from pharynx or feces
   e. Pericardial effusion identified by echocardiogram, CT scan, magnetic resonance imaging, angiography, or other radiographic evidence of infection
3. Patient ≤12 months of age has two of the following with no other recognized cause: fever (>38° C), hypothermia (<37° C), apnea, bradycardia, paradoxical pulse, or increased heart size AND any of the following:
   a. Abnormal ECG consistent with myocarditis or pericarditis
   b. Positive antigen test on blood
   c. Histologic examination of heart tissue shows evidence of myocarditis or pericarditis
   d. Fourfold rise in type-specific antibody with or without isolation of virus from pharynx or feces
   e. Pericardial effusion identified by echocardiogram, CT scan, magnetic resonance imaging, angiography, or other radiographic evidence of infection

Mediastinitis must meet one of the following criteria:

1. Organism isolated from culture of mediastinal tissue or fluid obtained during surgery or needle aspiration
2. Evidence of mediastinitis that is seen during surgery or by histopathologic examination
3. One of the following: fever (>38° C), chest pain, or sternal instability AND any of the following:
   a. Purulent drainage from mediastinal area
   b. Organism isolated from blood culture or culture of drainage from mediastinal area
   c. Mediastinal widening on x-ray examination
4. Patient ≤12 months of age has one of the following: fever (>38° C), hypothermia (<37° C), apnea, bradycardia, or sternal instability AND any of the following:
   a. Purulent drainage from mediastinal area
   b. Organism isolated from blood culture or culture of drainage from mediastinal area
   c. Mediastinal widening on x-ray examination

CENTRAL NERVOUS SYSTEM INFECTION

Central nervous system infection includes intracranial infection, meningitis or ventriculitis, and spinal abscess without meningitis.

Intracranial infection (brain abscess, subdural or epidural infection, and encephalitis) must meet one of the following criteria:

1. Organism isolated from culture of brain tissue or dura
2. Abscess or evidence of intracranial infection seen during surgery or by histopathologic examination
3. Two of the following with no other recognized cause: headache, dizziness, fever (>38° C), localizing neurologic signs, changing level of consciousness, or confusion, AND physician institutes appropriate antimicrobial therapy if diagnosis is made antemortem AND any of the following:
   a. Organism seen on microscopic examination of brain or abscess tissue obtained by needle aspiration or by biopsy during surgery or autopsy
   b. Positive antigen test on blood or urine
   c. Radiographic evidence of infection
   d. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen

4. Patient ≤12 months of age has two of the following with no other recognized cause: fever (>38° C), hypothermia (<37° C), apnea, bradycardia, localizing neurologic signs, or changing level of consciousness AND physician institutes appropriate antimicrobial therapy if diagnosis is made antemortem AND any of the following:
   a. Organisms seen on microscopic examination of brain or abscess tissue obtained by needle aspiration or by biopsy during surgery or autopsy
   b. Positive antigen test on blood or urine specimen
   c. Radiographic evidence of infection
   d. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen

Meningitis or ventriculitis must meet one of the following criteria:

1. Organism isolated from culture of cerebrospinal fluid (CSF)
2. One of the following with no other recognized cause: fever (>38° C), headache, stiff neck, meningeal signs, cranial nerve signs, or irritability, AND physician institutes appropriate antimicrobial therapy if diagnosis is made antemortem AND any of the following:
   a. Increased white cells, elevated protein, and/or decreased glucose in CSF
   b. Organisms seen on Gram stain of CSF
   c. Organism isolated from blood culture
   d. Positive antigen test on CSF, blood, or urine
   e. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen
3. Patient ≤12 months of age has one of the following with no other recognized cause: fever (>38° C), hypothermia (<37° C), apnea, bradycardia, stiff neck, meningeal signs, cranial nerve signs, or irritability AND physician institutes appropriate antimicrobial therapy if diagnosis is made antemortem AND any of the following:
   a. Increased white cells, elevated protein, and/or decreased glucose in CSF
   b. Organisms seen on Gram stain of CSF
   c. Organism isolated from blood culture
   d. Positive antigen test on CSF, blood, or urine
   e. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen

Spinal abscess without meningitis (an abscess of the spinal epidural or subdural space, without involvement of the CSF or adjacent bone structures) must meet one of the following criteria:

1. Organism isolated from culture of abscess in spinal epidural or subdural space
2. Abscess in spinal epidural or subdural space seen during surgery or autopsy or by histopathologic examination
3. One of the following with no other recognized cause: fever (>38° C), back pain, focal tenderness, radiculitis, paraparesis, or paraplegia AND physician institutes appropriate antimicrobial therapy if diagnosis is made antemortem AND either of the following:
   a. Organism isolated from blood culture
   b. Radiographic evidence of spinal abscess

EYE, EAR, NOSE, THROAT, AND MOUTH INFECTION

Eye infection includes conjunctivitis and other eye infections. Ear infections include otitis externa, otitis media, otitis interna, and mastoiditis. Nose, throat, and mouth infections include oral cavity infections, upper respiratory infections, and sinusitis.

Conjunctivitis must meet either of the following criteria:

1. Pathogen isolated from culture of purulent exudate obtained from conjunctiva or contiguous tissues, such as eyelid, cornea, meibomian glands, or lacrimal glands
2. Pain or redness of conjunctiva or around eye AND any of the following:
   a. WBCs and organisms seen on Gram stain of exudate
   b. Purulent exudate
   c. Positive antigen test on exudate or conjunctival scraping
   d. Multinucleated giant cells seen on microscopic examination of conjunctival exudate or scrapings
   e. Positive viral culture on conjunctival exudate

f. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen

Eye infections other than conjunctivitis must meet either of the following criteria:

1. Organism isolated from culture of anterior or posterior chamber or vitreous fluid
2. Two of the following with no other recognized cause: eye pain, visual disturbance, or hypopyon AND any of the following:
   a. Physician's diagnosis
   b. Positive antigen test on blood
   c. Organism isolated from blood culture

Otitis externa must meet either of the following criteria:

1. Pathogen isolated from culture of purulent drainage from ear canal
2. One of the following: fever (>38° C), pain, redness, or drainage from ear canal AND organisms seen on Gram stain of purulent drainage

Otitis media must meet either of the following criteria:

1. Organism isolated from culture of fluid from middle ear obtained by tympanocentesis or surgery
2. Two of the following: fever (>38° C), pain in eardrum, inflammation, retraction or decreased mobility of eardrum, or fluid behind eardrum

Otitis interna must meet either of the following criteria:

1. Organism isolated from culture of fluid from inner ear obtained at surgery
2. Physician's diagnosis

Mastoiditis must meet either of the following criteria:

1. Organism isolated from culture of purulent drainage from mastoid
2. Two of the following with no other recognized cause: fever (>38° C), pain, tenderness, erythema, headache, or facial paralysis AND either of the following:
   a. Organisms seen on Gram stain of purulent material from mastoid
   b. Positive antigen test on blood

Oral cavity infection (mouth, tongue, or gums) must meet one of the following criteria:

1. Organism isolated from culture of purulent material from tissues or oral cavity
2. Abscess or other evidence of oral cavity infection seen on direct examination, during surgery, or by histopathologic examination
3. One of the following: abscess, ulceration, or raised white patches on inflamed mucosa, or plaques on oral mucosa AND any of the following:
   a. Organisms seen on Gram stain
   b. Positive potassium hydroxide (KOH) stain
   c. Multinucleated giant cells seen on microscopic examination of mucosal scrapings
   d. Positive antigen test on oral secretions
   e. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen
   f. Physician's diagnosis and treatment with topical or oral antifungal therapy

Sinusitis must meet either of the following criteria:

1. Organism isolated from culture of purulent material obtained from sinus cavity
2. One of the following: fever (>38° C), pain or tenderness over the involved sinus, headache, purulent exudate, or nasal obstruction AND either of the following:
   a. Positive transillumination
   b. Radiographic evidence of infection

Upper respiratory tract infection (pharyngitis, laryngitis, epiglottis) must meet one of the following criteria:

1. Two of the following: fever (>38° C), erythema of pharynx, sore throat, cough, hoarseness, or purulent exudate in throat, AND any of the following:
   a. Organism isolated from culture of specific site
   b. Organism isolated from blood culture
   c. Positive antigen test on blood or respiratory secretions
   d. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen
   e. Physician's diagnosis
2. Abscess seen on direct examination, during surgery, or by histopathologic examination
3. Patient ≤12 months of age has two of the following: fever (>38° C), hypothermia (<37° C), apnea, bradycardia, nasal discharge, or purulent exudate in throat, AND any of the following:

a. Organism isolated from culture of specific site
b. Organism isolated from blood culture
c. Positive antigen test on blood or respiratory secretions
d. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen
e. Physician's diagnosis

GASTROINTESTINAL SYSTEM INFECTION

Gastrointestinal system infections include gastroenteritis, hepatitis, necrotizing enterocolitis, gastrointestinal tract infections, and intraabdominal infections not specified elsewhere.

Gastroenteritis must meet either of the following criteria:

1. Acute onset of diarrhea (liquid stools for more than 12 hours) with or without vomiting or fever (>38° C) AND no likely noninfectious cause (e.g., diagnostic tests, therapeutic regimen, acute exacerbation of a chronic condition, psychologic stress)
2. Two of the following with no other recognized cause: nausea, vomiting, abdominal pain, or headache AND any of the following:
   a. Enteric pathogen isolated from stool culture or rectal swab
   b. Enteric pathogen detected by routine or electron microscopy examination
   c. Enteric pathogen detected by antigen or antibody assay on feces or blood
   d. Evidence of enteric pathogen detected by cytopathic changes in tissue culture (toxin assay)
   e. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen

Hepatitis must meet the following criterion: Two of the following with no other recognized cause: fever (>38° C), anorexia, nausea, vomiting, abdominal pain, jaundice, or history of transfusion within the previous 3 months AND any of the following:

1. Positive antigen or antibody test for hepatitis A, hepatitis B, or delta hepatitis
2. Abnormal liver function tests (e.g., elevated alanine/aspartate aminotransferase [ALT/AST] and bilirubin)
3. Cytomegalovirus (CMV) detected in urine or oropharyngeal secretions

Infant necrotizing enterocolitis must meet the following criterion: Two of the following with no other recognized cause: vomiting, abdominal distention, or prefeeding residuals AND persistent microscopic or gross blood in stools AND any of the following abdominal radiographic abnormalities:

1. Pneumoperitoneum
2. Pneumotosis intestinalis
3. Unchanging "rigid" loops of small bowel

Gastrointestinal (GI) tract infection (esophagus, stomach, small bowel, large bowel, and rectum), excluding gastroenteritis and appendicitis, must meet either of the following criteria:

1. Abscess or other evidence of infection seen during surgery or by histopathologic examination
2. Two of the following with no other recognized cause and compatible with infection of the organ or tissue involved: fever (>38° C), nausea, vomiting, abdominal pain, or tenderness AND any of the following:
   a. Organism isolated from culture of drainage or tissue obtained during surgery or endoscopy or from surgically placed drain
   b. Organisms seen on Gram or KOH stain or multinucleated giant cells seen on microscopic examination of drainage or tissue obtained during surgery or endoscopy or from surgically placed drain
   c. Organism isolated from blood culture
   d. Radiographic evidence of infection
   e. Pathologic findings on endoscopic examination (e.g., *Candida* esophagitis or proctitis)

Intraabdominal infection (including gallbladder, bile ducts, liver [other than viral hepatitis], spleen, pancreas, peritoneum, subphrenic or subdiaphragmatic space, or other intraabdominal tissue or area not specified elsewhere) must meet one of the following criteria:

1. Organism isolated from culture of purulent material from intraabdominal space obtained during surgery or needle aspiration

2. Abscess or other evidence of intraabdominal infection seen during surgery or by histopathologic examination
3. Two of the following with no other recognized cause: fever (>38° C), nausea, vomiting, abdominal pain, or jaundice AND any of the following:
   a. Organism isolated from culture of drainage from surgically placed drain (e.g., closed suction drainage system, open drain, or T-tube drain)
   b. Organisms seen on Gram stain of drainage or tissue obtained during surgery or needle aspiration
   c. Organism isolated from blood culture and radiographic evidence of infection

LOWER RESPIRATORY TRACT INFECTION (EXCLUDING PNEUMONIA)

Lower respiratory tract infection (excluding pneumonia) includes infections such as bronchitis, tracheobronchitis, bronchiolitis, tracheitis, lung abscess, and empyema.

Bronchitis, tracheobronchitis, bronchiolitis, tracheitis, without evidence of pneumonia, must meet either of the following criteria:

1. Patient has no clinical or radiographic evidence of pneumonia AND has two of the following: fever (>38° C), cough, new or increased sputum production, rhonchi, wheezing, AND either of the following:
   a. Organism isolated from culture obtained by deep tracheal aspirate or bronchoscopy
   b. Positive antigen test on respiratory secretions
2. Patient ≤12 months of age has no clinical or radiographic evidence of pneumonia AND has two of the following with no other recognized cause: fever (>38° C), cough, new or increased sputum production, rhonchi, wheezing, respiratory distress, apnea, or bradycardia AND any of the following:
   a. Organism isolated from culture of material obtained by deep tracheal aspirate or bronchoscopy
   b. Positive antigen test on respiratory secretions
   c. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen

Other infections of the lower respiratory tract must meet one of the following criteria:

1. Organisms seen on smear or isolated from culture of lung tissue or fluid, including pleural fluid
2. Lung abscess or empyema seen during surgery or by histopathologic examination
3. Abscess cavity seen on radiographic examination of lung

REPRODUCTIVE TRACT INFECTION

A group of infections that occur in obstetric and gynecology patients and in male urology patients is defined as reproductive tract infection. Such infections include endometritis, episiotomy infection, vaginal cuff infection, and other infections of the male or female reproductive tract.

Endometritis must meet either of the following criteria:

1. Organism isolated from culture of fluid or tissue from endometrium obtained during surgery, by needle aspiration, or by brush biopsy
2. Purulent drainage from uterus AND two of the following: fever (>38° C), abdominal pain, or uterine tenderness

Episiotomy site infection must meet either of the following criteria:

1. Purulent drainage from episiotomy
2. Episiotomy abscess

Vaginal cuff infection must meet one of the following criteria:

1. Purulent drainage from vaginal cuff
2. Abscess at vaginal cuff
3. Pathogen isolated from culture of fluid or tissue obtained from vaginal cuff

Other infections of the male or female reproductive tract (epididymis, testes, prostate, vagina, ovaries, uterus, or other deep pelvic tissues, excluding endometritis or vaginal cuff infection) must meet one of the following criteria:

1. Organism isolated from culture of tissue or fluid from affected site
2. Abscess or other evidence of infection seen during surgery or by histopathologic examination
3. Two of the following: fever (>38° C), nausea, vomiting, pain, tenderness, or dysuria AND either of the following:
   a. Organism isolated from blood culture
   b. Physician's diagnosis

SKIN AND SOFT TISSUE INFECTION

Skin and soft tissue infection includes skin infection (other than incisional wound infection), soft tissue infection, decubitus ulcer infection, burn infection, breast abscess or mastitis, omphalitis, infant pustulosis, and newborn circumcision infection. Separate criteria are presented for each infection.

Skin infection must meet either of the following criteria:

1. Purulent drainage, pustules, vesicles, or boils
2. Two of the following at affected site: localized pain or tenderness, swelling, redness, or heat AND any of the following:
   a. Organism isolated from culture of aspirate or drainage from affected site; if organism is normal skin flora, must be pure culture of single organism
   b. Organism isolated from blood culture
   c. Positive antigen test on infected tissue or blood
   d. Multinucleated giant cells seen on microscopic examination of affected tissue
   e. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen

Soft tissue infection (necrotizing fasciitis, infectious gangrene, necrotizing cellulitis, infectious myositis, lymphadenitis, or lymphangitis) must meet one of the following criteria:

1. Organism isolated from culture of tissue or drainage from affected site
2. Purulent drainage from affected site
3. Abscess or other evidence of infection seen during surgery or by histopathologic examination
4. Two of the following at affected site: localized pain or tenderness, redness, swelling, or heat AND any of the following:
   a. Organism isolated from blood culture
   b. Positive antigen test on blood or urine
   c. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen

Decubitus ulcer infection, including both superficial and deep infection, must meet the following criterion: Two of the following: redness, tenderness, or swelling of wound edges AND either of the following:

1. Organism isolated from culture of fluid obtained by needle aspiration or biopsy of tissue obtained from ulcer margin
2. Organism isolated from blood culture

Burn infection must meet one of the following criteria:

1. Change in burn wound appearance or character, such as rapid eschar separation, or dark brown, black, or violaceous discoloration of the eschar, or edema at wound margin, AND histologic examination of burn biopsy specimen that shows invasion of organisms into adjacent viable tissue
2. Change in burn wound appearance or character, such as rapid eschar separation, or dark brown, black, or violaceous discoloration of the eschar, or edema at wound margin AND either of the following:
   a. Organism isolated from blood culture in absence of other identifiable infection
   b. Isolation of herpes simplex virus, histologic identification of inclusions by light or electron microscopy, or visualization of viral particles by electron microscopy in biopsy specimens or lesion scrapings
3. Burn patient has two of the following: fever (>38° C) or hypothermia (<36° C), hypotension (systolic pressure ≤90 mm Hg), oliguria (<20 ml/hr), hyperglycemia at previously tolerated level of dietary carbohydrate, or mental confusion AND any of the following:
   a. Histologic examination of burn biopsy specimen that shows invasion of organisms into adjacent viable tissue
   b. Organism isolated from blood culture
   c. Isolation of herpes simplex virus, histologic identification of inclusions by light or electron microscopy, or visualization of viral particles by electron microscopy in biopsy specimens or lesion scrapings

Breast abscess or mastitis must meet one of the following criteria:

1. Organism isolated from culture of affected breast tissue or fluid obtained by incision and drainage or needle aspiration
2. Breast abscess or other evidence of infection seen during surgery or by histopathologic examination
3. Fever (>38° C), local inflammation of the breast, and physician's diagnosis

Omphalitis in newborn (≤30 days of age) must meet either of the following criteria:

1. Erythema and/or serous drainage from umbilicus and either of the following:
   a. Organism isolated from culture of drainage or needle aspirate
   b. Organism isolated from blood culture
2. Erythema and purulent drainage at umbilicus

Pustulosis in infant (≤12 months of age) must meet the following criterion:

1. Infant has pustules AND physician's diagnosis or
2. Physician institutes appropriate antimicrobial therapy

Circumcision infection in new born (≤30 days of age) must meet one of the following criteria:

1. Newborn has purulent drainage from circumcision site.
2. Newborn has one of the following: erythema, swelling, or tenderness at circumcision site AND pathogen isolated from culture of site.
3. Newborn has one of the following: erythema, swelling, or tenderness at circumcision site, and skin contaminant isolated from culture of site AND physician's diagnosis or physician institutes appropriate antimicrobial therapy.

SYSTEMIC INFECTION

Systemic infection is defined as infection that involves multiple organs or systems, without an apparent single site of infection. Such infections are usually of viral origin and can usually be identified by clinical criteria alone (e.g., measles, mumps, rubella, and varicella); they occur infrequently as nosocomial infections.

COMMENTS

Although the definitions presented here were developed for use in hospitals participating in NNIS to standardize and improve the quality of nosocomial infection data reported to CDC, other hospitals may wish to adopt these definitions for use in their surveillance programs. By doing so and by using similar surveillance methods, comparisons may be made with NNIS data. In addition to use in routine surveillance programs for endemic nosocomial infections, these definitions can be used for prevalence surveys, special studies, and outbreak investigations.

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Erratum: The second criterion under "pustulosis in infant" should read:

2. Infant has pustules AND physician institutes appropriate antimicrobial therapy.

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Report From the CDC

CDC Definitions of Nosocomial Surgical Site Infections, 1992: A Modification of CDC Definitions of Surgical Wound Infections

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In 1988, the Centers for Disease Control (CDC) published definitions of nosocomial infections.[1] However, because of journalistic style and space constraints, these definitions lacked some of the detail provided to National Nosocomial Infections Surveillance (NNIS) System hospitals in the *NNIS Manual* (unpublished). After the NNIS System hospitals had had considerable experience with the definitions and in response to a request for review by The Surgical Wound Infection Task Force,[2] a group composed of members of The Society for Hospital Epidemiology of America, the Association for Practitioners in Infection Control, the Surgical Infection Society, and the CDC, we slightly modified the definition of surgical wound infection and changed the name to surgical site infection (SSI).

The changes were made for two reasons. First, in the 1988 definitions, it was not clear that for deep surgical wound infections, specifying the anatomic location of the deep infection was necessary. For example, NNIS System hospitals would report osteomyelitis as the specific site of a deep surgical wound infection if it followed an orthopedic operative procedure. Hospitals unfamiliar with this two-level designation might not have gleaned this information from the 1988 definitions. In this revision, we have included a Table listing specific sites. Second, we have removed the term "wound," because in surgical terminology, "wound" connotes only the incision from skin to deep soft tissues. We introduce the term "organ/space" to define any part of the anatomy (e.g., organs or spaces), other than the incision, opened or manipulated during the operative procedure. The distinction between this component of the surgical site and the incision is important in the pathogenesis of SSI following certain operative procedures.

The following revised definitions should be used for surveillance of SSI by hospitals wishing to compare their SSI data with NNIS System SSI data. This article includes some additional considerations when comparing hospital data to NNIS System data.

GENERAL CRITERIA

The American College of Surgeons, in the *Manual on Control of Infection in Surgical Patients*, classified surgical infections into the following groups according to anatomical location and pathophysiologic changes: wound infection, regional extension, organ or visceral infection, systemic infection, and remote coexisting or complicating infections.[3] The first three groups are covered in the following definitions of SSI and involve the skin, subcutaneous tissue, deep soft tissues (e.g., fascial and muscle layers) of the incision, and organs or spaces opened or manipulated during an operative procedure. Systemic and remote or complicating infections that follow an operative procedure (e.g., postoperative pneumonia following cholecystectomy) are

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considered surgical patient infections but are not classified as SSI because they are not associated with the surgical site. The exception is a bloodstream infection secondary to an incisional or organ/space SSI.

As with all CDC definitions of nosocomial infections, a physician's or surgeon's diagnosis of infection is an acceptable criterion for an SSI unless there is compelling evidence to the contrary (e.g., information written on the wrong patient's record or presumptive diagnosis not substantiated by subsequent studies).[1]

DEFINITIONS OF SSI

For surveillance classification purposes, SSI are divided into incisional SSI and organ/space SSI. Incisional SSI are further classified into those involving only the skin and subcutaneous tissue (called superficial incisional SSI) and those involving deep soft tissues of the incision (called deep incisional SSI [e.g., fascial and muscle layers]). Organ/space SSI involve any part of the anatomy (e.g., organs or spaces), other than the incision, opened or manipulated during the operative procedure (Figure).

Superficial Incisional SSI

Superficial incisional SSI must meet the following criteria: the infection occurs within 30 days after the operative procedure and involves only skin or subcutaneous tissue of the incision. In addition, it must meet at least one of the following: purulent drainage from the superficial incision; organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision; at least one of the following signs or symptoms of infection—pain or tenderness, localized swelling, redness or heat, and the superficial incision is deliberately opened by surgeon unless the incision is culture-negative; or diagnosis of superficial incisional SSI by the surgeon or attending physician.

The following are not reported as superficial incisional SSI: stitch abscess (minimal inflammation and discharge confined to the points of suture penetration); infection of an episiotomy or newborn circumcision site (episiotomy and circumcision are not considered NNIS System operative procedures); infected burn wound; and incisional SSI that extends into the fascial and muscle layers (see deep incisional SSI). (Note: specific criteria are used for infected episiotomy and circumcision sites and burn wounds.)

Deep Incisional SSI

Deep incisional SSI must meet the following criteria: the infection occurs within 30 days after the operative procedure if no implant (i.e., a nonhuman-derived implantable foreign body [e.g., prosthetic heart valve, nonhuman vascular graft, mechanical heart, or hip prosthesis] that is permanently placed in a patient during surgery) is left in place or within one year if an implant is in place and the infection appears to be related to the operative procedure and the infection involves deep soft tissues (e.g., fascial and muscle layers) of the incision. In addition, it must meet at least one of the following: purulent drainage from the deep incision but not from the organ/space component of the surgical site; a deep incision that spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms—fever (>38°C), localized pain, or tenderness, unless the incision is culture-negative; an abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination; or diagnosis of a deep incisional SSI by a surgeon or attending physician

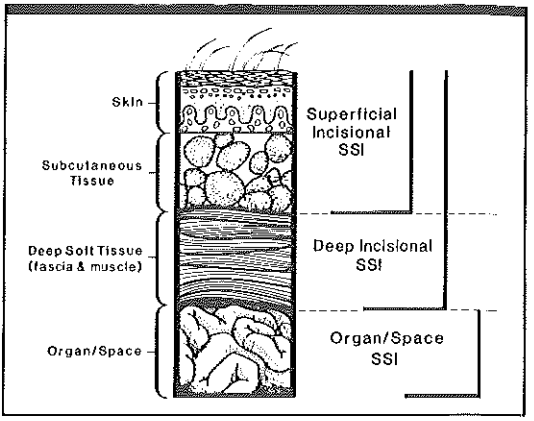

FIGURE. Schematic of SSI anatomy and appropriate classification.

Organ/Space SSI

An organ/space SSI involves any part of the anatomy (e.g., organs or spaces), other than the incision, opened or manipulated during the operative procedure. Specific sites are assigned to organ/space SSI to further identify the location of the infection. The Table lists the specific sites that must be used to differentiate organ/space SSI. An example is appendectomy with subsequent subdiaphragmatic abscess, which would be reported as an organ/space SSI at the intra-abdominal specific site.

Organ/space SSI must meet the following criteria: the infection occurs within 30 days after the operative procedure if no implant is left in place or within one year if implant is in place and the infection appears to be related to the operative procedure and the infection involves any part of the anatomy (e.g., organs or spaces), other than the incision, opened or manipulated

TABLE
SPECIFIC SITES OF ORGAN/SPACE SSI

Arterial or venous infection	Meningitis or ventriculitis
Breast abscess or mastitis	Myocarditis or pericarditis
Disc space	Oral cavity (mouth, tongue, or gums)
Ear, mastoid	Osteomyelitis
Endometritis	Other infections of the lower respiratory tract
Endocarditis	Other infections of the urinary tract
Eye, other than conjunctivitis	Other male or female reproductive tract
Gastrointestinal tract	Sinusitis
Intra-abdominal, not specified elsewhere	Spinal abscess without meningitis
Intracranial, brain abscess or dura	Upper respiratory tract, pharyngitis
Joint or bursa	Vaginal cuff
Mediastinitis	

during the operative procedure. In addition, it must meet at least one of the following: purulent drainage from a drain that is placed through a stab wound into the organ/space (if the area around a stab wound becomes infected, it is not an SSI—it is considered a skin or soft tissue infection, depending on its depth); organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space; an abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination; or diagnosis of an organ/space SSI by a surgeon or attending physician.

SSI Involving More Than One Specific Site

An infection that involves *both* superficial and deep incision sites is classified as deep incisional SSI.

Occasionally, an organ/space infection drains through the incision. Such infection generally does not involve reoperation and is considered a complication of the incision. Therefore, it is classified as a deep incisional SSI.

COMPARING HOSPITAL SSI DATA TO NNIS SYSTEM SSI DATA

SSI and all other types of nosocomial infections reported to the NNIS System are collected on patients whose date of admission to and date of discharge from an acute-care hospital are different calendar days (i.e., SSI resulting from outpatient or same-day surgery are not included). Further, to be classified as having an SSI in the NNIS System, a patient has to have undergone an operation, which is defined as a single trip to the operating room (this includes the delivery room if a cesarean section is performed), where a surgeon makes at least one incision through skin or mucous membrane and closes the incision primarily before the patient leaves the operating room. In addition, in the NNIS System System, an SSI can only be reported if it follows one of the NNIS System-designated operative procedures.[4]

In January 1992, the NNIS System began distinguishing between deep incisional SSI of the chest and leg (donor) site after coronary artery bypass graft procedures involving both of these sites to acknowledge that two incisions are made and that infection risks may differ at these sites. Hospitals wishing to compare their data to those of the NNIS System in the future should adopt this practice.

DISCUSSION

To clarify the definitions of surgical wound infections and to be more consistent with surgical terminology, we have eliminated the use of the word "wound" when defining postoperative infections and have more clearly distinguished between superficial and deep infections of the incision. For infections involving the incision, we use the term "incisional SSI." The previous definitions of incisional surgical wound infection and deep soft tissue surgical wound infection[1] are replaced by superficial incisional SSI and deep incisional SSI. Infections that involve the organ/space component of the surgical site were previously called deep surgical wound infections at specific sites other than soft tissue. These are now termed organ/space SSI and use the same specific sites as before.

Two recent reports from the CDC gave data on surgical wound infection rates.[5,6] Because the infections included in those reports were not stratified by incisional and deep, the rates are not affected by the change from surgical wound infection to SSI.

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Curriculum Vitae

Adriana Johanna de Groot werd geboren op 24-11-1945 te Velsen-Noord. Na het behalen van het diploma gymnasium-α volgde zij de opleiding tot verpleegkundige aan de Verpleegstersschool van de Vrije Universiteit te Amsterdam (1964-1968). Als verpleegkundige werkte zij in verschillende functies in het Academisch Ziekenhuis der Vrije Universiteit, het Anthoni van Leeuwenhoekziekenhuis en de Lutherse Diakonesseninrichting, alle te Amsterdam. Van 1977-1983 werkte zij als staffnurse in het St.Joseph's Hospice, Rawalpindi, Pakistan, en was tevens coördinator van een Klein Ambassade Projekt (KAP) voor Moeder- en Kindzorg in Rawalpindi. Na terugkeer uit het buitenland behaalde zij het Diploma Ziekenhuishygiënist A en B te Breda, C te Groningen, en werkte als ziekenhuishygiënist in het Ziekenhuis Oudenrijn te Utrecht. Daar ontwikkelde zij samen met de toenmalige arts-microbioloog van het Ziekenhuis Oudenrijn, prof.dr.H.A.Verbrugh, het systeem van surveillance van ziekenhuisinfekties. Ook bekleedde zij verschillende functies in de Vereniging voor Hygiëne en Infektiepreventie in de Gezondheidszorg (VHIG), waaronder die van voorzitter van het bestuur. Zij participeerde in de projektleiding (prof. dr.H.A.Verbrugh, prof.dr.C.M.J.E.Vandenbroucke-Grauls, dr.A.J.Severijnen) van het Projekt Surveillance Ziekenhuisinfekties in de regio Utrecht (PSZU projekt) onder auspiciën van het Rijksinstituut voor Volksgezondheid en Milieuhygiëne en het Streeklaboratorium voor de Volksgezondheid Nieuwegein (1992\1993). In 1993 behaalde zij het Doctoraal diploma Gezondheidswetenschappen, afstudeerrichting verplegingswetenschappen, aan de Rijksuniversiteit Limburg, lokatie Utrecht. Vanaf 1994 is zij coördinator kwaliteitszorg in het Ziekenhuis Oudenrijn en projektmedewerker bij het Centraal Begeleidingsorgaan voor de Intercollegiale Toetsing (CBO). In 1995 behaalde zij het Diploma Kwaliteitsfunctionaris Intramurale Gezondheidszorg, georganiseerd onder auspiciën van de Nederlandse Vereniging van Ziekenhuizen (NVZ).

Zij is getrouwd en heeft twee dochters.

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