



**SNLG17**

**Perioperative antibiotic prophylaxis in adults**

**GUIDELINES**

**Publication date: September 2008**

**Next update: September 2011**

## **Notice to users**

These guidelines are a rapid means of transferring the results of biomedical research to daily clinical practice. The recommendations they contain have been honed through a process of systematically reviewing the literature and expert opinion; they can be used as a tool for physicians and health administrators to improve the quality of care and rationalise the use of resources. When clinical decisions regarding individual patients have to be made, there is a need for recommendations that are based on the soundest scientific evidence, while the clinical experience of the physician and all other relevant circumstances must also be taken into account. Guidelines are a synthesis of the highest quality information and can also be used in medical training and refresher courses. While guidelines comply with standards of quality based on the latest scientific evidence, the skill and experience of the individual clinician will decide how strictly they should be followed in each case.

# **Perioperative antibiotic prophylaxis in adults Guideline**

Date of publication: September 2008

Next update: September 2011

## **Editor**

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## **Layout**

Giovanna Smiriglia This guideline was financed by the Directorate-General for Planning of the Ministry for Health

## **Presentation**

Five years after publication of the guideline “Perioperative Antibiotic Prophylaxis in Adults” by the National Guideline Programme (PNLG) as it was then called, this updated re-edition has been developed. It includes graded recommendations intended to provide healthcare practitioners with a set of evidence-based criteria supplemented with clinical experience as a guide to when and how it is appropriate to administer antibiotic prophylaxis in adult surgery. The guideline is part of the National System of Guidelines (SNLG) programme, fruit of an agreement between the Department for Health Planning, the Ministry for Health and the Italian Health Institute. The aim of this agreement is to produce high-quality publications to promote correct practice throughout the National Health System. The updated guideline responds to a need to assess recently published material regarding perioperative antibiotic prophylaxis in order to verify whether the recommendations proposed in the first edition should be amended in the light of more recent evidence. In response to criticisms of the earlier guideline, the working group decided to extend the recommendations to the first 100 surgical Diagnosis-Related Groups (DRG), analysing newly available evidence and, when there was no evidence base, to formulate recommendations based on the consensus opinion of the panel. Finally, issues relating to the choice, dosage and procedures for the administration of antibiotics have been addressed in greater detail. To this end the present edition includes models that operating units may use as a framework within which to adapt their own guidelines to local settings. The conditions prevailing in individual operating units are in effect a major reason for issuing a new edition of the guideline. The working group has aimed to create a tool that can be used extensively and that will expand knowledge and stimulate debate on an issue – perioperative infections and how best to prevent them – that remains highly topical.

In this regard, the website of the SNLG ([www.snlg-iss-it](http://www.snlg-iss-it)) provides an interactive version of the “Proposals for Local Implementation” (Annex 1), on which users of the guideline are invited to log their comments. It is hoped that numerous suggestions from all quarters may form the basis for the next edition.

## **Foreword to this edition**

At the end of July 2008, when updating of the Italian guideline was virtually completed, the Scottish Intercollegiate Guidelines Network (SIGN) published a new guideline for antibiotic prophylaxis in surgery ([www.sign.ac.uk](http://www.sign.ac.uk)). The earlier version of the SIGN guideline had been used as a model for the first edition of the Italian guideline. In light of the difficulties that had emerged in Italy with local implementation of the guideline, it was decided that the updated version would not include substantial changes to the structure of the first edition but would aim instead to render it more user-friendly. The bibliography has therefore been updated without changing the research strategy used in the first edition of the SIGN guideline; further elaboration of bibliographic searches was instead performed on an *ad hoc* basis. The new SIGN guideline contains several changes to its original structure; recommendations have been extended to cover new topics such as paediatric surgery and certain diagnostic procedures. The odds ratios (OR) have been recalculated, as has the number of patients needed to treat (NNT) on the basis of the expected risk of surgical site infection (SSI), which refers to epidemiological conditions in Britain. As no such figures are available for Italy, the panel decided not to change the method of calculating these parameters. The result is a more noticeable difference between the structure of the two guidelines, which are currently virtually superimposable only when addressing the same question. This is readily understood when it is considered that the SIGN guideline has been widely distributed and local implementation strategies have been applied; for this reason the authors of the new edition aimed to elaborate on and supplement the earlier edition. The Italian guideline, in contrast, has not been adequately implemented and the panel therefore decided that the re-edition should focus on providing more tools for local implementation.

## **Presentation of the first edition**

This volume has been prepared as part of the National Guidelines Programme (PNLG) by a multidisciplinary group of experts representing scientific societies and coordinated by the National Health Institute and the Centre for the Assessment of Healthcare Efficiency (CeVEAS) in Modena. The guideline aims to provide healthcare professionals with evidence-based criteria supplemented by clinical experience to define when and how it is appropriate to administer antibiotic prophylaxis in adult surgery. The proposal to draw up a national guideline arose from the observation that the frequency of perioperative infections in Italy, as deduced from studies conducted or published over the last ten years, is far from negligible and that the use of antibiotics as perioperative prophylaxis, both in Italy and abroad, varies considerably from one healthcare provider to another, with a risk of inequalities in treatment and unnecessary exposure to the risk of hospital infections that may defeat the purpose of surgery and worsen the patient's condition. The indiscriminate use of antibiotics can lead on the one hand to the rapid onset of bacterial resistance, with serious risks of an outbreak of infections that are difficult to deal with and the exposure of surgical patients to possible adverse effects, and on the other hand to an indiscriminate increase in spending on drugs. The aim of the PNLG is thus to reduce this inequality in care. This document presents a number of novel features:

- the broad composition of the working group;
- a procedure based on facts supported and interpreted in the light of clinical experience;
- the cooperation of several bodies and institutions within the PNLG;
- the dissemination of the guideline by means of readily understood material for healthcare professionals;
- ample and representative peer review, aimed at improving quality.

I hope that the users of this guideline will find it really helpful in the fight against perioperative infections and in improving the healthcare offered to the public.

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## GLOSSARY AND ABBREVIATIONS

**Colonisation:** presence of micro-organisms on skin or mucosa but no invasion of tissues or local, regional or systemic clinical signs. **Infection:** presence in an organ or tissue of replicating micro-organisms, marked by clinical signs or immunological response. Defined as sub-clinical or non-apparent when no symptoms are present **SSI:** Surgical Site Infection **SSI Prevention:** body of non-pharmacological measures aimed at preventing germ-patient contact **SSI Antibiotic Prophylaxis:** pharmacological measures aimed at preventing germ-patient contact becoming an infection **Protocols:** binding codes of conduct used during trials or to establish diagnostic or treatment procedures, to be followed strictly. **SSI Antibiotic Therapy:** pharmacological measures adopted to resolve an infection that has become manifest. **ASA:** American Society of Anesthesiologists (see Table 4, p for ASA score). **CDC:** Centers for Disease Control and Prevention **CIO:** Comitato Infezioni Ospedaliere (Hospital Infections Committee). **CTL:** Commissioni Terapeutiche Locali (Local Treatment Committees). **DIP:** Deep Incisional Primary SSI **DIS:** Deep Incisional Secondary SSI **DRG:** Diagnosis Related Group **EBM:** Evidence-based Medicine **HTA:** Health Technology Assessment **IDSA:** Infectious Disease Society of America **MIC:** Minimum Inhibitory Concentration (of antibiotic) **MRSA:** Meticillin-Resistant *Staphylococcus Aureus* **NNT:** Number Needed to Treat **OR:** Odds Ratio

**RCT:** Randomised Clinical (controlled??) Trial  
**SIGN:** Scottish Intercollegiate Guidelines Network  
**SIP:** Superficial Incisional Primary SSI **SIS:**  
Superficial Incisional Secondary SSI

## **Index Summary of the principal recommendations**

General principles of prevention List of principal recommendations Local implementation of the guideline

### **Introduction**

Background Aims and recipients of antibiotic prophylaxis Need for the guideline New features of the updated guideline Issues addressed in the guideline

### **Methods**

Literature search Selection criteria and tools for methodological assessment Levels of evidence and grades of recommendations External review Next update, diffusion, implementation and assessment

**Perioperative antibiotic prophylaxis in adults** **Question 1:** What are the risk factors for surgical site infections and how do they affect the choice of antibiotic prophylaxis? **Question 2:** What are the benefits and risks of perioperative antibiotic prophylaxis? **Question 3:** In which operations has antibiotic prophylaxis been proved to reduce the risk of surgical site infections? **Question 4:** Which type of antibiotic is recommended for perioperative prophylaxis? How and when should it be administered?

### **Implementation of the guideline**

Development of local guidelines Compliance with measures for prevention recommended by the Centers for Disease Control and Prevention (CDC)

Implementation strategies most widely accredited in clinical studies  
Recording of drugs administered and minimum data set Key points and  
core indicators for auditing application of the guideline Data set  
needed to audit perioperative antibiotic prophylaxis

## **Annexes**

1. Proposals for local implementation
2. Recommendations for antibiotic prophylaxis in bacterial endocarditis
3. Antibiotic prophylaxis in patients with prostheses or prosthetic devices
4. CDC/NHSN criteria for the definition of SSI
5. Classification of operations by duration >75<sup>th</sup> percentile
6. Micro-organisms most frequently associated with postoperative infections
7. Auditing compliance with CDC rules for preventing SSI

## **Summary: Summary of the principal recommendations**

This guideline is an update of the earlier guideline published in 2003 by the PNLG (now SNLG); as well as updating the evidence base, the working group decided to make the guideline more user-friendly for operating units by adding annexes containing more detailed information regarding the choice of antibiotic for prophylaxis, dosage and administration procedures. As in all guidelines issued by the SNLG, the strength of recommendations is expressed alphabetically. The new guideline addresses the following questions:

1 What are the risk factors for surgical site infections and how do they affect the choice of antibiotic prophylaxis? (see p..)

2 What are the benefits and risks of perioperative antibiotic prophylaxis? (see p. ..)

3 In which operations has antibiotic prophylaxis been proved to reduce the risk of surgical site infections?

**Bibliography**  
4 Which type of antibiotic is recommended for perioperative prophylaxis? How

and when should it be administered? The issue of local implementation is also addressed. Together with recommendations regarding antibiotic prophylaxis, this guideline describes the general principles of prevention, which are the arbitrary basis for containing complications due to postoperative infections. Antibiotic prophylaxis goes hand in hand with and integrates these measures but does not replace them.

### **General principles of prevention Preoperative measures**

1. Proper preparation of the

patient

2. Proper preparation of the surgical team

3. Management of colonised or infected health personnel so as to minimise the risk of transmission

1. Proper ventilation systems in the operating theatre
2. Proper cleaning and disinfection of the premises
3. Environmental microbiological sampling only during specific epidemiological investigations (not routine)
4. Proper sterilisation of surgical instruments
5. Use of surgical gowns and drapes that minimise the risk of transmission.
6. Asepsis and surgical technique
7. Proper wound medication These measures are described in detail in Table 2, pp

**List of principle recommendations** **Question 1:** What are the risk factors for surgical site infections and how do they affect the choice of antibiotic prophylaxis? Surgical site infections are affected by a number of factors. Those that correlate independently are: class of operation, insertion of prosthetic device, duration of preoperative hospitalisation, duration of surgery, comorbidities. The duration of the operation and comorbidities impact heavily on the risk of infection and are used, together with the class of operation, to define the risk index. **Question 2:** What are the benefits and risks of perioperative antibiotic prophylaxis? The final decision regarding the benefits and risks of antibiotic prophylaxis for each patient depends on:

- the risk of surgical site infection, taking account of both operation-and patient-specific risks;
- the potential seriousness of a possible surgical site infection;
- the efficacy of prophylaxis for that particular operation;
- the consequences of prophylaxis for that particular patient (e.g. increased risk

## **Intraoperative measures**

The following list shows operations for which clinical studies show that antibiotic prophylaxis is effective. The panel has also expressed its opinion (in grey) concerning the expedience of prophylaxis in a number of frequently performed operations for which no clinical studies are available.

### **Chest and thoracic surgery**

Antibiotic prophylaxis is recommended for: **I/A** Cardiac pacemaker/defibrillator insertion Open-heart surgery, including aorto-coronary bypass and prosthetic valve implant **II/A** Pulmonary resection

### **Ear, nose and throat surgery**

Antibiotic prophylaxis is recommended for: **I/A** Head and neck surgery (clean-contaminated and contaminated) Antibiotic prophylaxis is not recommended for: **I/C** Adenotonsillectomy **I/D** Ear surgery (clean and clean-contaminated) including myringoplasty **II/D** Nose or sinus and paranasal surgery (septoplasty/rhinoseptoplasty. **VI/D** Head and neck surgery (clean)

### **General surgery**

Antibiotic prophylaxis is strongly recommended for: **I/A** Colorectal surgery. Antibiotic prophylaxis is recommended for the following, but local antibiotic policy managers must take local infection rates into account (see p. and Table 6, p. , operations marked with an asterisk): **I/A** Breast cancer surgery

of colitis or *Clostridium difficile*-associated diarrhoea. **Question 3:** In which types of

Reductive mammoplasty **II/A** Surgery as antibiotic prophylaxis been proved to reduce the risk of surgical site

Endoscopic gastrostomy

Stomach and duodenal surgery

**VI/B** Clean-contaminated procedures not explicitly mentioned elsewhere.

Oesophageal surgery

Small intestine surgery Antibiotic

prophylaxis is recommended for: **I/A**

Appendicectomy #Open biliary surgery

Resective hepatic surgery

Pancreatic surgery

Additive mastoplasty (breast enlargement)

Antibiotic prophylaxis is not recommended for: **I/D** Inguinal hernia

repair, with or without prosthetic device Laparoscopic inguinal hernia

repair, with or without prosthetic device # Diagnostic laparoscopy

and/or lysis of adhesions

Biopsy of superficial lymphatic structure with excision

Antibiotic Prophylaxis is not recommended for the following, but exceptions may be identified on a local basis (see p. and Table 6, p. , operations with two asterisks): **I/D**

Laparoscopic cholecystectomy

## **Neurosurgery**

Antibiotic prophylaxis is recommended for:

**I/A** Craniotomy

Cerebrospinal fluid shunt

## **Obstetrics and gynaecology**

Antibiotic prophylaxis is recommended for the following, but local antibiotic policy managers must take local infection rates into account (see p. and Table 6, operations marked with an asterisk):

**I/A** Induced abortion **II/A** Abdominal hysterectomy

Vaginal hysterectomy Antibiotic prophylaxis is recommended for: **I/A** Ceasarean section Antibiotic prophylaxis is not recommended for: #Bilateral salpingo-oophorectomy Monolateral salpingo-oophorectomy Removal or local demolition of ovarian lesion or tissue

### **Orthopaedic surgery**

Antibiotic prophylaxis is strongly recommended for: **I/A** Hip prosthesis implant<sup>s</sup> **III/A** Knee prosthesis implant<sup>s</sup> = regardless of whether antibiotic-impregnated cement is used Antibiotic prophylaxis is recommended for: **I/A** Closed fracture fixation

Insertion of prosthetic device when no direct evidence is available

Hip fracture repair **II/A** Rachis surgery Antibiotic prophylaxis is not recommended for: **V/D** Orthopaedic surgery without prosthesis (elective); removal/suture/incision of muscular lesion, tendons and fascia of the hands; other removal or local demolition of wounds or cutaneous or subcutaneous tissue; other repair, section or plasty operations on muscles, tendons and fascia; arthroscopic meniscectomy; arthroscopic sinoviectomy.

### **Urology**

Antibiotic prophylaxis is recommended for:  
**I/A** Transurethral resection of the prostate  
**II/A** Transrectal prostate biopsy

# Radical prostatectomy Radical cystectomy Operations on the renal parenchyma (nephrectomy and nephrostomy) Nephrectomy Removal of hydroceles (of the tunica vaginalis) Antibiotic prophylaxis is recommended for the following, but local antibiotic policy managers should bear local infection rates in mind (see p. .. and Table 6, p. , operations marked with an asterisk): **I/A** Shock-wave lithotripsy Antibiotic prophylaxis is not recommended for **VI/D** Transurethral resection of bladder tumour

### **Vascular surgery**

Antibiotic prophylaxis is recommended for: **II/A**

Lower limb amputation Abdominal or lower limb arterial vascular surgery Antibiotic prophylaxis is

not recommended for: **VI/D**

Thromboendarterectomy Endoarterectomy

#Ligature/stripping of varicose veins Other surgical vessel occlusion

**Question 4** Which type of antibiotic is recommended for perioperative prophylaxis?

How and when should it be administered? **VI/B** The spectrum of the chosen

antibiotic must ensure cover against likely contaminants. #Each local surgery unit should monitor the bacterial species causing post-operative infections and their susceptibility to the antibiotics used in prophylaxis. This means

that material from each SSI must be sent to the microbiology laboratory for culture and an antibiogram. **IV/B** Patients with a history of anaphylaxis, urticaria or exanthema (rash) occurring immediately after penicillin therapy are at increased risk of hypersensitivity and should not receive prophylaxis with a beta-lactam antibiotic. # Where operational antibiotic prophylaxis guidelines recommend beta-lactam antibiotics as first choice, an alternative for patients with an allergy to penicillin or cephalosporins should also be recommended. # Third- and fourth-generation cephalosporins, mono-bactams, carbapenems and piperacillin/tazobactam are not recommended for use in prophylaxis. They should preferably be kept for therapeutic use against multiresistant pathogens. The antibiotics used for prophylaxis should be of proven efficacy for that purpose and should be used therapeutically only to treat infections caused by less resistant pathogens. # Most available studies have failed to demonstrate the superiority of glycopeptides in preventing staphylococcus infections. Excessive use of these drugs risks neutralising their efficacy in the treatment of nosocomial staphylococcus and enterococcus infections. The use of glycopeptides as prophylaxis should be limited exclusively to specific situations and in any case only to major operations that include the insertion of prosthetic devices (cardiac, orthopaedic and vascular surgery, neurosurgery) and only where MRSA colonisation or infection is present or a high rate of MRSA-associated SSI has been confirmed by local clinical and microbiological SSI surveillance. The decision to use glycopeptides should be taken in accordance with local antibiotic policy strategies. # The single dose of antibiotic given as prophylaxis is generally equivalent to a medium-high dose of antibiotic given as therapy. # Antibiotic prophylaxis should be administered intravenously. **II/A** In most cases antibiotic prophylaxis should be initiated immediately prior to anaesthesia and in any case not more than 30-60 minutes before the skin is incised.

**I/A** Antibiotic prophylaxis should be limited to the perioperative period and should be administered immediately before the start of surgery. There is no evidence that prolonged prophylaxis is more effective; in most cases a single dose of antibiotic (administered 30-60 minutes before the skin is incised) is sufficient. There is no justification for continuing prophylaxis beyond the first 24 postoperative hours. # For longer operations most guidelines suggest the administration of an intraoperative dose when the operation has been in progress for double the half-life of the drug administered, although no definitive data are available. **IV/B** The administration of an additional intraoperative dose of antibiotic (to be given after fluid replacement) is indicated for adults if blood loss during surgery exceeds 1,500 ml or if blood dilution has exceeded 15 ml/kg. # Prolongation of prophylaxis to the first 24 postoperative hours may be justified in specific clinical situations when the risk index for postoperative infections is high. Any decision to prolong prophylaxis beyond the time indicated in the local guideline should be justified in the case records.

### **Local implementation of the guideline**

# The implementation strategies most widely supported by evidence of efficacy are: agreement on the protocol regarding prophylaxis between surgeons, anaesthetists and all operating theatre personnel; attention to organisational problems; the specific assignment of responsibility for application of the protocol; the availability of personalised kits from the pharmacy. **VI/A** Auditing the appropriateness of perioperative antibiotic prophylaxis is facilitated if the minimum data set is registered in the case records and treatment chart.

## Introduction

### Background

Infection of the site of incision or of soft tissues is a common but potentially avoidable complication of any surgical procedure. Some bacterial contamination of the surgical site, either from the patient's own bacterial flora or from bacterial flora in the environment, is inevitable. An *ad hoc* search to update the data from epidemiological studies of SSI carried out in Italy from 2003 to the present (Table 1, p. ) revealed 3 new studies. That of Prospero *et al*<sup>2</sup>, conducted in the general surgery unit of Ancona hospital in 2004, found an average rate of SSI of 10,6% (between 0% and 22.2%, depending on the type of operation); many of these infections occurred after discharge from the hospital. Interestingly, for some operations the frequency of infection was greater during hospitalisation while for others it was greater after discharge. A study by Petrosillo *et al*<sup>3</sup> conducted in 2002 found, in the course of one month's surveillance, an average rate of SSI of 5.2% (between 0% and 15.9%, depending on the type of operation), with 38.6% of SSI occurring after discharge (within 30 days). The study by Valentini *et al*<sup>4</sup> carried out between 1999 and 2000 at the Istituto Nazionale "Carlo Besta" involved patients undergoing neurosurgery and found an average rate of SSI of 0.7% (between 0% and 2.1%, depending on the type of operation). Overall, these studies found average rates of SSI that varied between 4.9% and 13.6% for general surgery and between 1.2% and 1.5% for orthopaedic surgery. The variability of average rates is confirmed by studies conducted in the UK<sup>5</sup>. The present guideline uses the expression "surgical site infection" (SSI) unless the evidence of efficacy refers specifically to infections of the surgical wound. In procedures that include the insertion of implants or prosthetic devices the term surgical site infection comprises infections of the surgical wound and/or the implant. The term surgical site infection also includes localised infection in body cavities (e.g. subphrenic abscess), bones, joints, meninges and other tissues involved in surgery. The prophylactic administration of antibiotics is intended to prevent bacteria that have come into

contact with the surgical field during the contaminating phase of the operation<sup>6-8</sup> becoming established at the site of surgery and/or adhering to the prosthetic device implanted. The prophylactic use of antibiotics in surgical units accounts for approximately 40-50% of antibiotics prescribed in hospitals<sup>9</sup>. The indiscriminate use of these drugs has been shown to increase the prevalence of antibiotic-resistant bacterial<sup>10</sup> and to predispose patients to infections such as *Clostridium difficile* associated colitis<sup>11</sup>

### **Aims and recipients of antibiotic prophylaxis**

Antibiotic prophylaxis for surgical patients should aim to:

- reduce the incidence of surgical site infections by using antibiotics in accordance with evidence of their efficacy;
- use antibiotics in accordance with evidence of their efficacy;
- minimise the effects of antibiotics on the patient's bacterial flora;
- minimise adverse effects;

**Table 2.** Principal measures for the prevention of surgical wound infections as indicated in the guideline of the *Centers for Disease Control and Prevention* (chosen from those graded as strongly recommended\*) **PREOPERATIVE MEASURES**

### 1. Preparation of the patient

- identify and treat all infections prior to elective surgery and postpone the operation until the infection has been resolved
- do not remove hair unless the hair around the incision site will interfere with the operation
- if hair must be removed, remove immediately prior to the operation, using electric clippers
- control serum blood glucose levels in diabetic patients and avoid preoperative hyperglycaemia
- encourage smoking cessation, or at least abstinence in the 30 days prior to surgery
- administer blood products where indicated; their use does not increase the risk of SSI
- instruct the patient to shower or bathe with an antiseptic agent at least the night prior to surgery\*\*
- wash and cleanse the incision area thoroughly to remove gross contamination before disinfecting the skin
- cause minimal changes to the patient's host defences. It is important to emphasise that antibiotic prophylaxis is an adjunct to a good surgical technique but does not replace it and that prevention is one of the key elements of an effective policy for the control of hospital-acquired infections. Antibiotic prophylaxis is a component of this policy but does not replace it. Table 2 shows the principal preventive measures that should be adopted during surgery to minimise surgical wound infections. Those listed are taken from the guidelines of the US Centers for Disease Control and Prevention

### 2. Preparation of the surgery team members

- keep nails short and avoid artificial nails
- perform surgical scrub with antiseptic for 2-5 minutes and wash hands and forearms to the elbows. The original recommendations have been changed in light of the results of a recent systematic review<sup>27</sup> of types of soap used for preoperative showering or bathing.
- after scrubbing, keep hands up and away from the body so that the water runs from the fingers towards the elbows, dry with a sterile towel and don sterile gown and gloves

### **3. Management of colonised or infected surgical personnel**

- instruct and encourage operating theatre personnel who have signs of transmissible infections to report them promptly
- develop specific protocols to exclude from or readmit to the operating theatre personnel with transmissible infections
- as a precaution, exclude from duty personnel with draining skin lesions and obtain appropriate cultures of the lesion
- do not exclude from duty personnel colonised with *Staphylococcus aureus* or group A streptococcus unless an epidemiological link has been established with infections in patients.

## **INTRAOPERATIVE MEASURES**

### **1. Ventilation systems**

- maintain operating theatre air at positive pressure in relation to adjacent areas
- ensure at least 15 air changes per hour, with three of fresh air
- use appropriate filters to filter all air, both recirculating and fresh
- ensure that air is introduced through the ceiling and exits via the floor
- do not use UV rays to prevent SSI in the operating theatre
- keep operating theatre doors closed

### **2. Cleaning and disinfection of the environment**

- if the floor, surfaces or equipment are visibly contaminated with blood or other biological fluids, clean with local committee-approved disinfectant before the next operation
- do not adopt special cleaning procedures or close the theatre after contaminated or dirty operations
- do not use tacky mats outside the operating theatre

- do not perform routine sampling; samples of environmental operating theatre air and surfaces should be obtained only as part of specific epidemiological investigations

#### 4. Sterilisation of surgical instruments

- sterilise all surgical instruments as indicated in approved protocols
- perform flash sterilisation of instruments only for items that will be used again immediately

#### 5. Surgical gowns and drapes

• on entering the operating theatre don a mask that properly covers mouth and nose, and a cap or hood to cover hair and beard

- the use of shoe covers does not affect the incidence of SSI
- wear sterile gloves; put them on after donning a sterile gown
- use gowns and drapes that are impermeable to liquids
- change surgical attire that is visibly dirty or contaminated with blood or other material

#### 6. Asepsis and surgical technique

- comply with aseptic principles when placing vascular catheters, spinal or epidural anaesthesia catheters, or when administering drugs intravenously
- handle tissue with care, ensure proper haemostasis, remove devitalised tissues and foreign bodies from the surgical site
- delay closure of the wound or leave the incision open to heal by second intention when the surgical site is heavily contaminated
- where drainage is necessary, use a closed suction drain placed through a separate incision remote from the surgical incision and remove the drain as soon as possible.

#### 7. Medicating the wound

#### 3. Environmental microbiological sampling

- use sterile medication to protect surgical wounds for 24-48 hours
- wash hands before and after medicating or touching the surgical site.

\*measures strongly recommended and supported by well-designed clinical or epidemiological trials or supported by some clinical or epidemiological trials and by strong theoretic rationale. \*\* A recent Cochrane review<sup>17</sup> showed that there is no clear evidence that showering or bathing with chlorhexidine is more effective at reducing SSI than simple detergent.

## **Recommendations**

# Preventive measures are decisive for containing SSI; most studies to assess the efficacy of different perioperative antibiotic prophylaxis procedures are conducted in compliance with these rules # Failure to take preventive measures may neutralise the efficacy of antibiotic prophylaxis.

## **Need for the current guideline**

The proposal to develop a national guideline on perioperative antibiotic prophylaxis sprang from the observation, based on studies conducted in Italy, that behaviour in this field varies considerably<sup>12-16</sup>. Numerous studies published elsewhere<sup>18-20</sup> have confirmed this variability. A survey of over 6,000 surgical operations performed in the Emilia Romagna region in 2000-2001, for example, showed significant variations in the use of surgical chemoprophylaxis and in the duration of antibiotic administration in different regional healthcare centres<sup>16</sup>. A national survey conducted in 2001 by the National Health Institute found that on average only 37% of public hospitals in Italy had written protocols for perioperative chemoprophylaxis: this percentage varied between 20% in hospitals with fewer than 150 beds and 62% in those with more than 1,000 beds<sup>21</sup>. It was therefore thought that the development of an evidence-based guideline could help to reduce this variability and encourage the process of accrediting surgical operating units.

Once the need for a national guideline on surgical chemoprophylaxis was acknowledged, a multidisciplinary working group was formed in 2002-2003 as part of the National Guidelines Programme and charged with developing it. The group's first goal was to identify existing guidelines on the same subject, for which purpose the data banks and sites of international agencies (see p. were reviewed<sup>1, 22-28</sup>). The guidelines thus identified were methodically evaluated and a comparative analysis of the recommendations was made in accordance with the principles described and discussed in the methodological manual of the National Guidelines Programme<sup>29</sup>. Of the different published guidelines, that published in 2000 by the Scottish Intercollegiate Guidelines Network (SIGN)<sup>28,30</sup>, was chosen as being the most suitable, for a number of reasons:

- it was published recently;
- it was developed by a multidisciplinary working group;
- it grades recommendations according to the level of available scientific evidence, in contrast to most earlier guidelines;
- by including the Number Needed to Treat (NNT) for each class of surgical operation, it allows local users to make informed choices when developing protocols;
- it offers suggestions for implementing the guidelines and indicators for

included operations has been undertaken as proposed, it has been improved, possibly, an *ad hoc* guideline) by the system used by SIGN to evaluate the evidence base and to grade it, but where decisions have been significant percentages of systems adopted in the SIGN (key areas); methodological potentials in relation to the risks of SSI and the type of contamination; recommendations would have called for far-reaching changes to the relevant section of the SIGN guideline in order to take Italian conditions into account and the data could not easily have been generalised or applied to different circumstances.

## New features of the updated guideline

The first objective in updating the guideline 5 years after its publication was to bring it up to date with the most recent evidence, while recognising that the consolidation of know-how limits the impact of novelties. The second objective was to address in greater detail the aspects more closely connected with its implementation. To this end it was decided to make the guideline more user-friendly for individual operating units by adding a series of annexes with more detailed information regarding the choice of antibiotic for prophylactic use, dosage and administration procedures. Examples of local implementation have been included for the main types of surgery (described in Table 6, p ); these comprise:

auditing their application. It was therefore decided to adopt the SIGN guideline as the basis for the Italian guideline and to update it in the light of scientific evidence produced after its publication; this was done following the same methodology used in the SIGN guideline (see p. ). It was also decided to adapt the sections dealing with organisational suggestions and the application of indicators to conditions in Italy. The exclusion criteria applied here regarding the issues addressed are the same as those adopted in the Scottish guideline. Recommendations for eye surgery are not a strategy for antibiotic prophylaxis for each group of operations; local working groups may choose between one or more antibiotics chosen from those that have been proved effective in preventing SSI in a particular operation and that are recommended in the main guidelines. Wherever possible, active ingredients not

specifically indicated for surgical prophylaxis are excluded; when this is not practicable (lack of an alternative or there is ample evidence of efficacy) the absence of this specific indication is recorded;

- the initial dosage for each

antibiotic;

- one or more alternatives for each group of operations, for patients allergic to betalactams;

•with regard to intraoperative administration, in cases of prolonged operations (grey area in which evidence of efficacy is not clear) the antibiotic may be chosen at local level, taking into account the prophylactic antibiotic used and its lifespan;

•the possibility to define the duration of prophylaxis at local level, in line with the general recommendations of the guideline: in this regard the local working group may identify patient-specific increased-risk factors (ASA code >3, length of surgical procedure exceeding the 75<sup>th</sup> percentile) or operations for which a single perioperative dose is considered insufficient.

possible, the evidence base for the most frequent procedures and to provide a basis for clinical audits. Table 6 (pp. ) lists the most frequent procedures (taken from the list of the first 100 surgical DRGs) for which either no clinical studies of the efficacy of prophylaxis are available or those that do exist were not conducted correctly. Where a consensus was reached, the panel proposes alternative procedures for prophylaxis in these procedures (Annex 1, p. ) based on the clinical experience of its members and taking into account the risk of infection and most likely type of contamination. Local working groups may evaluate these proposals when developing protocols that reflect specific local conditions. The final decision in each case is the sole responsibility of the surgeon and his clinical judgement. The decision to administer prophylaxis to patients undergoing procedures for which the guideline does not recommend it can be justified if the surgeon deems the individual patient to be at a particularly high risk of SSI. In this case the criteria adopted in evaluating the risk should be recorded in the patient's case records (see p. ).

In consideration of the fundamental changes introduced by the American Heart Association in the new guideline on prophylaxis for bacterial endocarditis during diagnostic or surgical procedures, it was decided to dedicate a special section (annex 2, p. ) to this issue. This section also briefly addresses the appropriateness of antibiotic prophylaxis in patients with prosthetic implants or devices in areas other than the heart.

### **Issues addressed in the guideline**

Both the 2003 guideline and this update deal only with the intravenous administration of antibiotics: other routes of administration (e.g. oral or topical) are not addressed. This is because most evidence of effectiveness relates to intravenous administration. This guideline aims to reduce the incidence of SSI and to identify operations for which there is an evidence base for the effectiveness of prophylaxis; it does not claim to provide an exhaustive guide for every type of surgery, but to indicate, where

1. What are the risk factors for surgical site infections and how do they affect the choice of antibiotic prophylaxis? ( see p..)
2. What are the benefits and risks of perioperative antibiotic prophylaxis? (see p. )
3. In which operations has antibiotic prophylaxis been proved to reduce the risk of surgical site infections? (see p. )
4. Which type of antibiotic is recommended for perioperative prophylaxis? How and when should it be administered? (see p. ..)

The guideline then addresses the problems linked to local implementation, bearing in mind the key factors that must be borne in mind in order to promote the proper implementation of the recommendations and to audit their application (see p. ) Most of the recommendations in this guideline apply to elective surgery, but some emergency procedures are also included (see p. ). The guideline does not cover the following:

- prevention of urinary tract infections, respiratory tract infections or other infections not consequent on surgical procedures, with the exception of urinary tract infections following transurethral prostate resection;
- use of local antiseptics or antibiotics for the prevention of wound infections after elective surgery;
- 
- antibiotic treatment for patients undergoing contaminated or dirty emergency surgery;
- oral administration of antibiotics for bowel preparation or selective decontamination of the gut;
- prevention of infective complications associated with diagnostic procedures or therapy for heart surgery;
- transplant surgery;
- eye surgery

The working group considered that the choice of antibiotic can more appropriately be made at local level, and merely lists antibiotics for which there is an evidence base and which are recommended in the principal international guidelines. Where possible, active principles not specifically indicated for surgical prophylaxis have been omitted.

## Recommendation

Local antibiotic policy managers have the experience and the information needed to recommend specific courses of drugs on the basis not only of local epidemiological conditions, pharmacokinetic characteristics and cost of drugs, but also of an assessment of the evidence base where available and, alternatively, of the suggestions of the national panel.

## Methods

This update was developed by a multidisciplinary panel of experts, including general surgeons, cardiovascular, orthopaedic and ENT surgeons, neurosurgeons, anaesthetists, infectious disease experts, microbiologists and methodologists specialising in guidelines. At its first meeting the panel indicated the criteria to be followed in preparing this update:

- to update the literature search (following the strategy used by SIGN) to identify studies published between 2003 and 2007;
  - to update Table 6 of the earlier document with data on the average frequency of SSI taken from the updated literature or, where necessary, following a search strategy;
  - to propose an appropriate model for implementation.
- The guideline does not systematically address the issue of choosing an antibiotic. There exists a multitude of clinical studies comparing the prophylactic efficacy of various antibiotics, the results of which often differ or even contradict one another. It is difficult to claim that one antibiotic is superior to another for this use. As an example, a systematic review of the literature on antibiotic prophylaxis in colorectal surgery examined 147 studies and found that the various regimens for this single procedure were essentially equivalent: there is thus no evidence to support the choice of any particular antibiotic<sup>C31</sup>.

It was agreed not to make substantial alterations to the central structure of the earlier document, but to amend the chapter headings to the following questions:

1. What are the risk factors for surgical site infections (SSI) and how do they affect the choice of antibiotic prophylaxis?

2. What are the benefits and risks of perioperative antibiotic prophylaxis?

3. In which operations has antibiotic prophylaxis been proved to reduce the risk of SSI

4. Which type of antibiotic is recommended for perioperative prophylaxis?

How

and when should it be administered? The section covering local implementation and audit of the application of the guideline has also been updated. At its second meeting the panel examined the studies identified in the literature and criteria for their inclusion or exclusion were agreed. Further consultations regarding the drawing up of the guideline were conducted by e-mail or telephone.

## **Literature review**

The data banks consulted to update the literature were:

- Medline (PubMed)
- Embase (Embase.com)

omission of more recent studies was covered by consulting *PubMed* and *Embase*, limiting the search to the last 2 years. Guidelines were identified by consulting guideline databases, government agencies and scientific associations. An *ad hoc* search was carried out to update Table 1 regarding data on the distribution of epidemiological studies of SSI in Italy, using the following search strategy: #1 infected wound\* #2 deep wound\* #3 postoperative infection\* #3 “Wound-Infection” [Mesh] #4 «Surgical Wound Infection»[Mesh] #5 «Postoperative Complications»[Mesh] #6 #1 OR # 2 OR #3 OR #4 OR #5 #7 prophylaxis or prophylactic #8 «Anti-Infective Agents»[Mesh] #9 antibiotic prophyl\* #10»Antibiotic Prophylaxis»[Mesh] #11 antimicrobial prophyl\* #12 «Anti-Bacterial Agents/therapeutic use»[Mesh] #13 #7 OR #8 OR #9 OR #10 OR #11 OR #12 #14 «Perioperative Care»[Mesh] #15 perioperative #16 #14 OR #15 #17 Italy [ti/ab] #18 Italy [Mesh] #19 Italy [ad] #20 #17 OR #18 OR #19 #21 #6 AND #13 AND #16 AND #20

- The Cochrane Library The filter used in the search was the same as that used by the *Scottish Intercollegiate Guidelines Network (SIGN)* and already used in the earlier document: (**«Antibiotic Prophylaxis»[Mesh] or «Anti-Bacterial Agents/therapeutic use» [Mesh] or antibiotic prophylaxis**) and (**«Perioperative Care» [Mesh] or perioperative**). Specifically, the search focused on guidelines, systematic reviews and meta-analyses published between 2002 and 2007. *Randomised Controlled Trials (RCTs)* were searched through *Central*, the Cochrane Library’s register of trials, and the possible

**Selection criteria and tools for methodological assessment**

Thirty-four guidelines were identified, 7 were selected and just 2 included as being relevant to the issues covered in this guideline:

- Mariette C, Alves A, Benoist S, Bretagnol F, Mabrut JY, Slim K. Soins périopératoires en chirurgie digestive. Recommandations de la Société française de chirurgie digestive (SFCD1);
- Bratzler DW, Houck PM. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project Clin.Infect.Dis (2004).

particular circumstances. Nonetheless, when experiments are not practicable, the development of recommendations based on best clinical practice may be very useful. When this type of principle is used in the present guideline it is marked with the symbol #

## External Review

The final document agreed by the panel and scientific associations was submitted to external experts, who were explicitly requested to evaluate its legibility and clarity, as well as the clinical relevance and applicability of the recommendations. The group of reviewers comprised an epidemiologist, an anaesthetist and an infectious diseases specialist.

Regarding studies, the research strategy yielded 58 meta-analyses, systematic reviews and 131 RCTs. A selection was then made of those considered more relevant and the complete texts were requested. Analysis of these texts led to a further selection of 36 systematic reviews or RCTs from which data were extracted. The methodological appraisal and extraction of data in each review or RCT were

## Next update, distribution, implementation and evaluation

performed with the support of the methodological checklist of the *National Institute for Health and Clinical Excellence* (NICE). The guideline will next be updated before the end of 2011. Five thousand copies of the guideline will be printed and distributed to hospitals and regional health centres

throughout Italy. Local implementation may take account of epidemiological

## Level of evidence and grades of recommendations

conditions and general antibiotic policies of local health units; using the examples of local implementation attached to the present guideline (of which an interactive version is available on [www.snlg-iss.it](http://www.snlg-iss.it)). The summary tables for each type of study were compiled on the basis of the evidence described in the studies examined. The tables used by NICE were used, with appropriate adaptations. Levels of evidence and grades of recommendation were assigned following the grading method described in the SNLG29 methodological manual, which envisages 6 levels of evidence (I-VI) and 5 grades of recommendation (A-E). Levels of evidence were assigned on the basis of a study's design and methodological assessment; recommendations were graded in consideration of both the strength of the evidence base and the clinical value of the actual recommendations. These

elements were discussed and agreed by the panel. In the current hierarchy of evidence, expert opinion is not rated very highly, but as something to which the proposal is made when the experimental evidence is lacking or in

## Perioperative antibiotic prophylaxis in adults Question 1.

What are the risk factors for surgical site infections (SSI) and how do they affect the choice of antibiotic prophylaxis? For which experimental evidence is lacking or in

- class of operation;
- insertion of prosthetic devices;

- duration of preoperative hospitalisation;
- duration of surgery;
- comorbidities.

### **Class of operation**

Operations can be divided into 4 classes (see Table 3) according to the level of bacterial contamination and consequent incidence of postoperative infection<sup>32</sup>. In elective surgery antibiotic prophylaxis is recommended for clean (only if postoperative complications are life-threatening for the patient) and clean-contaminated surgical procedures. In the case of contaminated operations the decision to administer prophylaxis rather than treatment should be considered separately for each type of operation or situation on the basis of available evidence<sup>33</sup>. In cases of dirty operations immediate treatment is recommended. With regard to emergency surgery, the recommendations indicated in this guideline refer only to clean procedures (e.g. repair of abdominal aortic aneurysm or open fixation of closed fracture) and to caesarean section which, when performed during labour and/or after rupture of the membranes, is considered clean-contaminated.

**Table 3** Classification of operations according to bacterial contamination Class or

operation Definition Clean: operations in which no inflammation is encountered, the respiratory,

alimentary and genitourinary tracts are not entered, and there is no

break in aseptic operating theatre technique

Clean/ operations in which the respiratory, alimentary or genitourinary

Contaminated tracts are entered but there is no significant spillage Contaminated:

operations in which acute inflammation (without pus) is

encountered or there is visible contamination of the wound, such as gross spillage from a hollow viscus during the operation or compound/open injuries operated within four hours

Dirty: operations in the presence of pus or where there is a previously perforated hollow viscus, or compound/open injuries more than four hours old.

Emergency contaminated or dirty operations call for antibiotic therapy rather than prophylaxis and are thus beyond the scope of this guideline.

### **Insertion of prosthetic devices**

The insertion of a prosthetic device increases the risk of wound infection and SSI because it reduces the host's defences<sup>34</sup>. Where a prosthetic device is present even a low bacteria count is sufficient to cause infection. Antibiotic prophylaxis is normally recommended for surgery involving the insertion of prosthetic devices

### **Length of preoperative hospital stay**

In the first 48 hours of his or her stay in hospital the patient's skin is gradually colonised by nosocomial bacterial strains<sup>25</sup>, particularly if he or she is receiving antibiotics as therapy. These strains are often antibiotic-resistant and may cause contamination during the operation, encouraging the onset of multi-resistant germ-associated SSI and increasing the length of postoperative hospital stay<sup>35</sup>. For this reason it is important to limit the preoperative stay; where this is not possible or when subsequent operations are performed during the same stay, this must be taken into account when choosing an antibiotic for prophylaxis<sup>23</sup>.

### **Duration of surgery**

The duration of each operation is directly correlated with the risk of wound infection and this risk is additional to that of the class of operation<sup>32</sup>. In a study by Culver and

colleagues<sup>32</sup>, confirmed by national data<sup>16</sup>, operations lasting more than the 75<sup>th</sup> percentile for the procedure in question are classified as prolonged (see Annex 5, p. ) and therefore at increased risk.

## Comorbidities

The American Society of Anesthesiologists (ASA) has developed a system for scoring preoperative risk based on the presence of comorbidities at the time of surgery (see Table 4, p. ).<sup>36</sup> An ASA score >2 is associated with increased risk of wound infection, which is added to that of the class of operation and its duration<sup>32</sup>.

**Table 4** American Society of Anesthesiologists Classification

Physical status	ASA score
healthy patient	1
patient with mild systemic disease	2
patient with severe systemic disease that limits activity but is not incapacitating	3
patient with incapacitating systemic disease that is a constant threat to life	4
moribund patient who is not expected to survive more than 24 hours with or without surgery	5

- the duration of surgery (when this exceeds the 75<sup>th</sup> percentile the risk of SSI increases). A risk index (with a score from 0 to 3) based on the study by Culver<sup>32</sup> can be calculated as follows:

- a contaminated or dirty operation scores 1 point;
- an ASA score of 3,4 or 5 scores 1 point;
- duration of surgery in excess of the 75<sup>th</sup> percentile for that procedure scores 1

### **Probability of surgical site infection**

Earlier guidelines referred to patients at high risk of SSI but gave no clear information about predicting the risk. This section is intended to illustrate how comorbidity and duration of surgery affect the risk defined by the class of operation. The duration of surgery and comorbidities (according to the ASA score) have the same impact on the risk of wound infection as the class of operation. To define the risk, two factors other than the class of operation need to be considered:

- the presence of comorbidities (with ASA score >2 the risk of SSI increases);



colitis or diarrhoea. The prevalence of *Clostridium difficile* infections generally correlates with the use of all types of antibiotic, and in particular with the use of clindamycin, third-generation cephalosporins and fluoroquinolones<sup>50-54</sup>.

Epidemiological studies of *Clostridium difficile* show that the most frequent reason for prescribing antibiotics is surgical prophylaxis<sup>51</sup>. Although every dose of antibiotic administered increases a patient's risk of becoming a carrier of *Clostridium difficile*, a case-control study of patients who had received prophylaxis for surgery showed that a majority of carriers had received prophylaxis for more than 24 hours (56% compared with 17%)<sup>55</sup>. The consequences of *Clostridium difficile* infection include increased morbidity and mortality, longer hospital stays and generally higher costs<sup>52</sup>. One study of surgical patients showed that patients receiving antibiotic prophylaxis for more than 4 days presented a statistically significantly higher frequency of venous catheter-associated bacteraemia than those who received prophylaxis for one day at most<sup>56</sup>. A prospective cohort study in Israel of 2,641 patients who underwent aorto-coronary bypass and/or valve replacement showed that the administration of antibiotic prophylaxis for more than 48 hours was associated with an increased risk of isolation of antibiotic-resistant bacteria<sup>57</sup>. An observational study conducted in Canada on 7,657 surgical patients showed that the spread of a new hypervirulent strain of *Clostridium difficile* determined a clear increase in the risk of this infection in the area examined (from 0.7 to 14.9 cases per 1,000 operations) and that the other independent variables associated with this infection were older age (> 65) and the use of cefoxitin either alone or in combination as antibiotic prophylaxis or therapy<sup>58</sup>.

## **Recommendation**

# The final decision regarding the benefits and risks of antibiotic prophylaxis for each patient will depend on:

- the patient's risk of SSI, bearing in mind the risks associated with the type of operation and with the patient;
- the potential severity of a possible SSI;
- the efficacy of prophylaxis for that particular operation;
- the consequences of prophylaxis for that particular patient (e.g. increased risk of colitis or *Clostridium difficile*-associated diarrhoea).

**Question 3** In which operations has antibiotic prophylaxis been proved to reduce the risk of surgical site infections? This section sums up the indications for which perioperative antibiotic prophylaxis is recommended. The recommendations are based on evidence of clinical efficacy and cost-effectiveness, as well as on the opinion of the panel. Two types of operation are considered:

- those for which systematic reviews or well-conducted clinical RCTs are available that compare the efficacy of prophylaxis with placebo;
- those for which, albeit in the absence of systematic reviews or *ad hoc* clinical studies, the panel decided to express an opinion in consideration of their relevance in current practice (grey areas).

Where evidence of efficacy is available recommendations were graded in accordance with the most severe complications and hospital costs and probably reduces the overall consumption of antibiotics; which is based not only on the solidity of the scientific evidence but also on the clinical value of the actual recommendations. This procedure envisages simplification of evidence of efficacy (S-I-V) and probability of a reduction in the overall consumption of antibiotics is probable; (A-E). The two elements, “evidence of efficacy” and “strength of recommendation” are conceptually distinct and used independently, in accordance with the explicit criteria underlying grading systems (see p. ..). Recommendations for perioperative antibiotic prophylaxis have been divided into the following 5 grades:

- recommended, but local antibiotic policy managers should decide in the light of local infection rates (see Table 6, p. operations with an asterisk). Where local rates of SSI associated with some of the operations listed are low, a decision to administer perioperative prophylaxis may lead to unnecessary prescribing of antibiotics, particularly in low-risk patients. Where it is decided not to administer antibiotic prophylaxis or to administer it only to high-risk patients, rates of SSI on these operations, a qualitative opinion was expressed based on the general knowledge available and the clinical experience of the individual members. When developing local guidelines for operations regarding which *ad hoc* studies are not available (grey areas), physicians may take the panel’s opinion into account, together with their own experience and local epidemiological conditions. It is to be hoped that the grey areas were conducted on too small a scale. Here, too, a decision not to administer prophylaxis may be the gaps in our knowledge of antibiotic prophylaxis in surgery.

justified, but constant surveillance systems must be put in place to monitor the situation; not recommended, but exceptions may be allowed at local level (see Table 6, p operations with two asterisks). In these cases the decision must be based on local rates of SSI. The only recommendation in this category refers to laparoscopic cholecystectomy, for which the recommendation not to administer prophylaxis is based on the results of two systematic reviews of the literature, in which the studies examined excluded patients with complications (cholecystitis, pancreatitis, jaundice, immunodeficiency, biliary prosthesis) and the duration of the operation. In light of this and in consideration of possible variations in local rates of postoperative infections, the working group resolved to allow local operating units to decide whether or not to administer prophylaxis in patients with complications; not recommended, when there is evidence that prophylaxis is not clinically effective. Because the consequences of possible infection associated with these operations are both limited and short-term, a decision to administer prophylaxis to all patients would increase the consumption of antibiotics in return for a very small clinical benefit.

(1-expected baseline risk) x expected baseline risk x (1-odds ratio) § expected baseline risk = % of ISS in the hospital §§ Odds ratio = ratio between the odds of an event occurring in the treated group and the odds of the same event occurring in a control group (an odds ratio of 1 means that there is no difference between the groups).

Wherever possible, the odds ratio and NNTs shown in Table 6 were derived from the most recently published meta-analyses. In some cases, however, data from different trials were pooled and no formal meta-analysis was performed. The NNT is only one of the elements necessary to estimate the cost-benefit ratio. Additional information is needed to evaluate the clinical consequences of the outcome (specifically, a wound infection or SSI) measured in the trial(s) and used to calculate the NNT. For example, the NNT derived from studies of implants of hip prostheses is much higher than that derived from studies of transvaginal hysterectomy: 30 patients need to be treated to prevent one case of infection associated with hip prosthesis implant, while 4 patients need to be treated with antibiotic prophylaxis to prevent one episode of infection following transvaginal hysterectomy (see Table 6). It should nonetheless be borne in mind that whereas an infection following arthroprosthesis implant is a severe

The panel notes that data are currently available for only a few types of surgery, and that evidence for antibiotic prophylaxis is generally weak. The table below indicates the odds ratios for the risk of wound infection and the number of patients who must receive prophylaxis to prevent one wound infection (NNT). The odds ratio for the risk of wound infection in patients receiving antibiotic prophylaxis compared with those not receiving it is a **1**. Indications for periprocedural antibiotic prophylaxis used together with the panel's list of both operations for which direct evidence is available and those for which direct evidence is lacking but which the panel decided to include on account of their impact in current practice (grey areas).

$$1 - [\text{expected baseline risk} \times (1 - \text{odds ratio}^{\text{§§}})] \text{NNT} =$$

In the latter group of operations clinicians may base their decisions not only on the opinion of the panel but also on their own experience and local epidemiological conditions.

**(Table 6 Indications for perioperative antibiotic prophylaxis)**  
**(la tabella viaggia a parte)**

**Question 4** Which type of antibiotic is recommended for perioperative prophylaxis?  
How and when should it be administered?

**Choice of antibiotic**

The process of choosing an appropriate antibiotic should include an overall evaluation of the risk<sup>135</sup>. As shown in Table 7, a number of elements need to be considered. This section examines the factors that affect the choice of antibiotic in light of the available evidence. Annex 1 lists a number of surgical procedures, together with the antibiotics for which evidence of efficacy is available and which the panel considers useful as prophylaxis.

**Table 7** Factors that affect the choice of antibiotic for prophylaxis

- the bacteria that cause SSI
- the operative site
- the pharmacokinetic features of the antibiotic
- possible allergies to the antibiotic
- intrinsic toxicity of antibiotics and possible cross-reactivity
- effectiveness, based on RCTs
- the effects on the ecosystem
- cost

Contamination of the operative site is a frequent occurrence during surgery, where it is largely an inevitable consequence of surgical procedures to enter a non-sterile organ or tissue; alternatively, it may be due to failure to observe the rules of asepsis. This can allow micro-organisms to settle in the surgical site, or lead to bacteraemia and consequent settling of bacteria in organs or tissues remote from the operative site. Contamination may be either endogenous or exogenous. **Endogenous contamination** occurs when the micro-organisms responsible for the contamination are saprophytes present on the skin and/or mucosa at the operative site (e.g. *Staphylococcus aureus* or *Staphylococcus epidermidis* in the case of contamination of the skin, or *Escherichia coli* or other enterobacteria or an anaerobe in the case of operations on the intestine). Exogenous contamination<sup>1,25</sup> is caused by environmental micro-organisms or others that do not originate from the patient's own bacterial flora and is the consequence of failure to comply with standards of prevention. Because endogenous contamination is expressed by saprophytic bacterial flora, the micro-organisms responsible for it can be predicted for each type of operation. Although infections in surgical patients can theoretically be caused by a large number of micro-organisms, SSI is in fact generally due to a limited number of pathogens<sup>136,137</sup> (see Annex 6, p. ). If the patient has not spent a long time in hospital prior to the operation and/or has not been treated with antibiotics, the contaminating micro-organism is not usually antibiotic-resistant<sup>138</sup>. It is always advisable for each local surgical unit to carry out periodic monitoring of the bacteria responsible for postoperative infections and their susceptibility to the antibiotics used as prophylaxis. Exogenous contamination is caused by micro-organisms that come into contact with the patient accidentally and cannot therefore be predicted. They are often picked up in the operating theatre (staphylococci, gram-negative aerobes and others) and their susceptibility to antibiotics depends on local prescriptive practices<sup>1,25</sup>.

### **Bacteria that cause contamination of the surgical field and SSI**

The antibiotic chosen for prophylaxis must cover the probable pathogens. The efficacy of prophylaxis has been shown to be limited to endogenous contaminants; only these pathogens can reasonably be predicted and thus covered by antibiotic prophylaxis<sup>36</sup>. In the event that environmental contamination causes epidemics of postoperative infection, the antibiotic used for prophylaxis must be effective against the microorganism causing the epidemic, until the cause of contamination can be identified and removed.

**Recommendations VI/B** The antibiotic selected must be effective against probable pathogens. # It is advisable for every local surgical unit to monitor the bacteria causing postoperative infections and their susceptibility to the antibiotics used for prophylaxis. It is therefore absolutely essential that material from each SSI be submitted to microbiological culture tests and antibiogram.

### **Operative site and pharmacokinetics of the antibiotic**

The kinetics of the chosen antibiotic must be such that it reaches the operative site in concentrations exceeding the Minimal Inhibitory Concentration (MIC) for the target pathogens<sup>25,26</sup>. The effective concentration must be maintained throughout the operation

<sup>139</sup>.

### **Possible allergies to beta-lactams**

Allergic reactions to penicillin may depend on the molecule as such or on its metabolites. Past symptoms most frequently associated with subsequent immediate hypersensitivity to penicillin are, in order of frequency<sup>7140-142</sup>:

- anaphylaxis
- urticaria

- exanthema (rash) Other less specific symptoms are either not associated or only weakly associated with a subsequent allergic reaction. Patients should not be given any antibiotic or class of antibiotics to which they have had a past adverse reaction.

## **Recommendations**

IV/B Patients with a history of anaphylaxis, urticaria or exanthema (rash) immediately following treatment with penicillin are at greater risk of immediate hypersensitivity and should not be given prophylaxis with beta-lactams.

# Whenever the guidelines for surgical antibiotic prophylaxis recommend a beta-lactam antibiotic as first-line agent, an alternative for patients with an allergy to penicillins or cephalosporins should always be recommended.

## **Intrinsic toxicity of antibiotics and possible cross-reactivity**

The chosen antibiotic must be one of those with the most advantageous risk-benefit ratios; where two or more drugs are equally effective, the one least likely to cause organic disease or to cross-react with other drugs administered to the patient, in particular those used for anaesthesia, must be chosen<sup>1,23,27</sup>. If the chosen antibiotic is one that can cross-react with other therapeutic drugs currently being administered, the dosage should be adjusted accordingly.

## **Evidence-based effectiveness and effects on the environment**

Numerous RCTs in recent years have demonstrated that antibiotics are more effective than a placebo in preventing postoperative infections. The first to be proved effective were the first- and second-generation cephalosporins, penicillins, lincosamides and aminoglycosides, particularly gentamicin. More recent studies have demonstrated the efficacy in prophylaxis of antibiotics normally used in

the treatment of multi-resistant nosocomial infections, such as some penicillins associated with a beta-lactamase inhibitor, third-and fourth-generation cephalosporins, carbapenems, glycopeptides<sup>76,94,143-146</sup>. Far fewer studies have compared the prophylactic efficacy of recent drugs and traditionally used drugs. No well-designed studies are available to demonstrate the superiority of more recent drugs in preventing SSF<sup>21,147-149</sup>; specifically, no well-designed studies or reviews have demonstrated that third-and fourth-generation cephalosporins are more effective than other antibiotics<sup>150-151</sup>. There is a, however, a large body of evidence demonstrating the negative effects on bacterial flora (in individual patients and in the environment) caused by the excessive use of some antibiotics<sup>10,20,44,45,47,152</sup>; the frequency of MRSA, for example, has been shown to be directly in proportion to consumption of third-generation cephalosporins<sup>46,153,154</sup>.

## **Recommendation**

#Third-and fourth-generaton cephalosporins, monobactams, carbapenems, piperacillin/tazobactam are not recommended for use in prophylaxis. They should preferably be reserved for therapeutic use against multiresistant pathogens. For prophylactic use, it is preferable to use antibiotics that are known to be effective for prophylaxis and that are used therapeutically only for the treatment of infections caused by not particularly resistant pathogens.

Most available clinical studies do not show that glycopeptides are more effective than beta-lactams against *Staphylococcus aureus* and *Staphylococcus epidermidis*<sup>147,154,161</sup>. A recent review of the literature on vascular and prosthetic orthopaedic surgery found no difference between the prophylactic use of a first-or second-generation cephalosporin and teicoplanin<sup>162</sup> in terms of either overall mortality or the incidence of infections of the surgical or distant sites.

The steady increase in the frequency of postoperative infections with MRSA and the results of a randomised controlled study published in 1992<sup>138</sup> (this study of patients undergoing major cardiac or vascular surgery showed that vancomycin was more effective in prophylaxis than either cefazoline or cefamandole) persuaded the authors of some guidelines to recommend glycopeptides for prophylaxis in high-risk surgery with prosthetic device implant where there is a particularly high frequency of MRSA-associated SSI. However, no criteria have yet been established to define a threshold for the meticillin-resistance of staphylococcus and different studies and guidelines have different approaches to defining a high percentage of meticillin-resistance. In addition, two published studies showed no difference between glycopeptides and cephalosporins in preventing SSI, even in the presence of a high incidence of MRSA. The first was an RCT that compared cefazoline and teicoplanin in 3,027 patients undergoing aorto-coronary bypass and/or valve replacement or plasty. The results showed that one month after surgery there were no differences in the incidence of SSI between the two prophylactic regimens, while at six months the incidence of SSI was lower for the cefazoline-treated patients<sup>147</sup>. The second study, performed in a hospital in Israel with a high prevalence of MRSA, compared the efficacy of prophylaxis with vancomycin and with cefazoline in preventing SSI in 885 patients undergoing sternotomy. The results showed superimposable efficacy of the two antibiotics<sup>149</sup>. These recent findings seem to confirm that beta-lactams are effective in preventing staphylococcal SSI even in the presence of a high frequency of meticillin-resistance. It is also known that the excessive use of glycopeptides is one of the causes of the development of resistance in enterococci (vancomycin-resistant enterococci) and staphylococci (vancomycin-resistant staphylococci and vancomycin-intermediate susceptible staphylococci). The Centers for Disease Control and Prevention recommendations indicate glycopeptides as the prophylaxis of choice only in particular circumstances, such as the presence of a cluster of MRSA-associated

mediastinitis or of meticillin-resistant coagulase-negative staphylococcus-associated SSI<sup>1</sup>. When the use of glycopeptides for prophylaxis is considered indispensable its use should nonetheless be limited to a single dose<sup>163</sup> (2 doses if the operation lasts more than 6 hours and if vancomycin is administered). The recently updated guidelines<sup>164</sup> published jointly by the *British Society for Antimicrobial Chemotherapy*, the *Hospital Infection Society* and the *Infection Control Nurses Association* also recommend limiting the use of glycopeptides to individual patients with a history of uneradicated MRSA colonisation/infection<sup>161</sup> or from areas where MRSA infections are frequent. Once again, it is noted that no agreement has been reached on when MRSA infections are to be considered frequent and that local epidemiological information is important when deciding the most appropriate prophylactic strategy.

## **Recommendation**

Most available evidence does not show that glycopeptides are more effective in preventing staphylococci-associated SSI. Excessive use of these drugs risks neutralising the efficacy of therapy for staphylococcus- or enterococcus-associated nosocomial infections. The decision to use a glycopeptide for prophylaxis must be limited exclusively to specific situations and in any case to major surgery with prosthetic device insertion (cardiac, orthopaedic or vascular surgery, neurosurgery) and only in the presence of MRSA colonisation/infection or when a high incidence of MRSA-associated SSI has been confirmed by local clinical and microbiological SSI surveillance. The choice must be made in accordance with local antibiotic policy strategies<sup>1</sup>.

## **Cost**

In choosing which antibiotic to use for prophylaxis the economic aspect should not be overlooked: where two or more drugs are equally effective and their environmental

impact is the same, preference should be given to the one with the lowest purchase price and the lowest costs of preparation and administration<sup>135</sup>.

### **Dosage selection**

It is generally accepted as good practice that the dosage of an antibiotic required for prophylaxis is the same as that used in therapy; the dosage selected should ensure serum levels of antibiotic exceeding the MIC for the pathogens likely to be encountered<sup>22,25,26</sup>. Annex 1 shows the antibiotics recommended by the panel and the initial doses that should be administered, based on dosages used in clinical studies and those recommended in the major guidelines. If it is decided to prolong prophylaxis for 24 hours, the dosages and intervals of administration are generally the same as those used for treatment.

### **Recommendation**

# The single dose of antibiotic used as prophylaxis is, in most cases, the same as a medium-high therapeutic dose.

### **Route of administration**

The most reliable means of ensuring effective levels of the antibiotic in the blood and operative site tissues is an intravenous administration 30-60 minutes before the skin is incised<sup>23</sup>. Serum levels after oral or intramuscular administration, on the other hand, are affected not only by the dosage administered but also by the speed of absorption and the bio-availability of the drug, and may therefore vary between individuals. It is also important to remember that organisational considerations make it more difficult to respect the timing if the antibiotic is administered outside the operating theatre. The intravenous administration of antibiotic prophylaxis inside the operating theatre is thus the only method supported by a substantial evidence base.

## **Recommendation**

# Antibiotic prophylaxis should be administered intravenously

### **The timing of administration**

Some animal models<sup>165-167</sup> have demonstrated the existence of a critical period for the occurrence of SSI and that for antibiotic prophylaxis to be most effective there must be an appropriate concentration in the tissues from the moment of the incision until completion of the surgical procedure. These studies have also shown that effectiveness decreases rapidly and is eventually eliminated if prophylaxis is initiated some hours after the start of the operation or in the postoperative period<sup>67,88</sup>. These findings are confirmed by a prospective cohort study in humans<sup>168</sup> in which, as can be seen in Figure 1, the frequency of SSI increases in parallel with the time between the incision of the skin and administration of the antibiotic; an antibiotic administered more than 2 hours before, or one or two hours after the skin is incised is less likely to be effective. A recent observational study of patients undergoing arthroplasty showed that inappropriate timing of the antibiotic administration is the error that most seriously affects the frequency of prosthesis infections<sup>169</sup>. It is advisable, in clinical practice, to include antibiotic administration among the procedures to be performed immediately prior to beginning the operation, avoiding possible cross-reactions with other drugs administered at that time (mainly anaesthetics).

**Figure 1** Frequency of SSI in relation to the timing of administration of the first dose of antibiotic Amended by D.C. Classen et al <sup>168</sup>.

## **Recommendation**

**II/A** In most cases antibiotic prophylaxis should be initiated immediately prior to the anaesthetic procedures and in any case 30-60 minutes before the skin is incised. Particular clinical situations may nonetheless arise that make it advisable to vary the timing of antibiotic administration. In caesarean section, for example, prophylaxis may be delayed until after the cord-clamp in order to prevent the drug reaching the neonate. When a pneumatic tourniquet is applied, as in orthopaedic surgical procedures on a bloodless limb, the necessary tissue levels should be reached before the tourniquet is applied (it will prevent any antibiotic circulating in the blood from reaching the surgical field). This probably happens within 30 minutes of administering an antibiotic via intravenous bolus. There is also the possibility that an operation with a low risk of infection and for which it was decided not to administer antibiotic prophylaxis is prolonged beyond the usual duration, thereby increasing the risk index. In such cases antibiotic prophylaxis may be given during the operation as soon as the over-run becomes inevitable.

### **Additional doses during surgery**

Many of the drugs used for prophylaxis have a relatively short half-life (calculated as 1-2 hours in studies of healthy volunteers). In light of this it is logical to administer a further dose of antibiotic if the operation lasts more than 2-4 hours. However, patients undergoing surgery eliminate drugs more slowly than do healthy volunteers<sup>170-171</sup>, probably on account of a combination of factors. For example, surgical patients are probably generally older than healthy volunteers (and therefore have decreased renal function), and comorbidities are often present. The few available data show that drugs such as cefuroxim, which has a half-life of 1-2 hours in healthy volunteers, has a half-life of 2-4 hours in surgical patients and that effective levels of antibiotic are maintained for at least 5 hours after the start of surgery<sup>170-171</sup>. The search strategy used in developing this guideline (see p. ) found no clear evidence either for or against the administration of additional intraoperative doses of antibiotics. The few studies available<sup>145,172-174</sup> are methodologically questionable;

either they were not specifically designed with this issue in mind or, if they were, they were methodologically unreliable. In a recent cohort study of patients undergoing cardiac surgery, an analysis of subgroups showed that the risk of SSI was reduced by an intraoperative dose of antibiotic only when the operation lasted more than 400 minutes from the first administration<sup>175</sup>. A systematic review of the literature referring to patients receiving prophylaxis for colorectal surgery found no evidence that drugs with a long half-life were more effective than those with a short half-life<sup>31</sup>; this is further evidence of the limited usefulness of maintaining high serum levels of antibiotic for a long time. In conclusion, no clear evidence has yet emerged for or against the administration of additional doses of antibiotic during surgery. However, most guidelines<sup>1,22,23,25,26</sup>, endorse the 1984 recommendation of Stone<sup>176</sup> to administer a second, intraoperative dose if the operation is still in progress when the period since it began is equivalent to double the half-life of the antibiotic used.

## **Recommendation**

Albeit in the absence of definitive data, most guidelines suggest administering an intraoperative dose of antibiotic when the duration of the operation is equal to double the half-life of the drug used.

Serum antibiotic levels are reduced by blood loss and fluid replacement, particularly if these occur during the first hour of surgery, when plasma drug levels are high<sup>177,178</sup>. The precise effects of blood loss and fluid replacement are difficult to predict and will depend on the particular antibiotic used, the timing and extent of blood loss and fluid replacement<sup>136</sup>. In any case, the effect of intraoperative bleeding and fluid replacement on serum drug levels in adults is generally negligible<sup>179,180</sup>.

For heart surgery performed with extracorporeal circulation there is no evidence that an additional intraoperative administration of antibiotic is effective; the working group suggests that a higher dose of antibiotic be administered at the beginning of the anaesthetic procedures.

### **Recommendation**

An additional intraoperative dose of antibiotic (to be administered after fluid replacement) is indicated for adults if blood loss during surgery exceeds 1,500 ml or blood dilution has exceeded 15 ml/kg..

### **Duration of prophylaxis**

The administration of additional, postoperative doses has not generally been proved effective in further reducing the incidence of SSI<sup>117,136,181-185</sup>. Individual studies that suggest the administration of additional postoperative antibiotics are methodologically questionable. For example, the use of observers who were non-blind to the allocation of treatment and the use of a wound swab as an indicator of infection are not acceptable<sup>186</sup>. The latter test is specifically excluded from most definitions of wound infection because it does not distinguish between colonisation and infection<sup>187,188</sup>. Additionally, in patients receiving prolonged antibiotic therapy bacteria are certainly less likely to be isolated from a wound swab. The study by Gatell *et al*<sup>189</sup> is often cited to support the efficacy of administering additional doses of antibiotic in patients with closed fracture. In the case in question the regimen included an intraoperative dose (two hours after the start of the operation) and a postoperative dose, the benefit of which is not clear. Two studies of patients undergoing heart surgery found that longer prophylaxis duration has no impact on the frequency of SSI even in the long term<sup>57,148</sup>. A medium-sized Italian study (206 patients) that compared a single dose of piperacillin with 3 doses in patients undergoing caesarean section found no differences between the two groups<sup>185</sup>. A larger study of 2,651 operations for hip

arthroplasty<sup>183</sup> found no difference in wound infection rates after administration of 1 or 3 doses of cefuroxim. The study found that infection of the joint was less frequent in the group who received three doses (0.45% compared with 0.83%), but the difference was not statistically significant (OR 0.54;95% CI 0.20-1.48). A recent observational study of patients undergoing cemented hip arthroplasty found fewer repeat operations for the removal or replacement of the prosthesis when prophylaxis was continued for 24 hours and antibiotic was added to the cement<sup>190</sup>. Three recent studies, including one of patients undergoing appendicectomy (for non-perforated appendix), one of patients undergoing surgery for gastric carcinoma and a third of patients undergoing gynaecological surgery, confirm that the administration of a single perioperative dose of antibiotic has the same effect in preventing SSI as repeated doses<sup>191-193</sup>. There is no evidence to show that continuing antibiotic prophylaxis reduces postoperative infections when drainage is used.

**Recommendations I/A** Antibiotic prophylaxis should be limited to the perioperative period and should be administered immediately before the operation begins. There is no evidence to support the increased effectiveness of prolonged prophylaxis; in most cases a single dose of antibiotic is sufficient (administered within 30-60 minutes before the skin is incised). A decision to continue prophylaxis beyond the first 24 postoperative hours is not justified.

# Prolonging prophylaxis for the first 24 postoperative hours may be justified in specific clinical situations with a high risk of postoperative infections. Every decision to prolong prophylaxis beyond the duration indicated in local guidelines should be justified in the case notes.

## **Implementation of the guideline**

### **Development of local guidelines**

This guideline can serve as the basis for the development and implementation of local guidelines. For this guideline to be useful in clinical practice, clinicians, healthcare managers and local working groups should adapt the national guideline to local conditions. Locally developed guidelines should reflect local epidemiological conditions and the antibiotic policy strategies of individual healthcare structures. Individual operating units should use the examples of local implementation attached to this guideline (Annex 1 p..) to develop their own detailed operating protocol, which should indicate the first choice of antibiotic, dosage, administration procedures and duration of prophylaxis for each type of operation or group of operations. The protocol should be agreed with the experts involved in administering the antibiotics and should be approved and signed by the manager of the operating unit. Local therapeutic and hospital infection committees should be involved in validating and developing a strategy for the implementation of the guideline. Responsibility for the application and implementation of the guideline in each operating unit must be clearly assigned.

### **Compliance with measures for prevention suggested by the *Centers for Disease Control and Prevention* (CDC)**

The administration of antibiotic prophylaxis cannot in any way replace the correct adherence to preventive measures, which are fundamental in limiting the development of SSI. It is important to remember that most findings of clinical studies of prophylaxis are the result of both the application of preventive measures and the actual pharmacological prophylaxis.

The Atlanta-based CDC have developed a series of recommendations for prevention based on sound evidence of efficacy. The experts who drew up this guideline decided to include only recommendations supported by strong evidence of efficacy and to refer the solution of specific problems to the CDC guideline. The CDC recommendations are listed in Table 2 on page . Because the CDC guidelines have not been updated since 1999, the panel has made additions to the table included in the first edition. Specifically, the recommendation regarding the efficacy of using antiseptic soaps for preoperative showering has been modified. A review by *Cochrane* published in 2007<sup>17</sup> evaluated 6 clinical studies for a total of approximately 10,000 patients but found no clear evidence that chlorhexidine-based soaps are more effective than soaps that do not contain a disinfectant. Application of the key rules for prevention listed in Table 2 (p. ) calls for a considerable degree of coordination between medical and nursing staff in the operating theatre and on the ward, and may be facilitated by the development of agreed rules of conduct. It is in any case of fundamental importance that all the personnel involved in the operating theatre and the ward adhere scrupulously to the rules. The conduct of clinical audits may help to verify the application and awareness of the recommendations<sup>194</sup>. Annex 7 (page ) provides a checklist of information needed to complete a clinical audit. Health managers should promote, monitor and evaluate the correct application of measures to prevent the occurrence of SSI (including through the use of resources and of various organisational tools).

## **Most widely accredited implementation strategies in clinical trials**

### **Circulation, dissemination and educational initiatives**

This type of strategy usually has a limited effect. In the case of perioperative antibiotic prophylaxis, departmental meetings, possibly with the attendance of experts

in the field, and the distribution of easy-reference versions of the guideline have proved fairly effective at modifying surgeons' behaviour<sup>195-197</sup>.

## **Reminder**

Paper-based systems to alert staff when it is time to administer an antibiotic have not proved very effective. Electronic reminders give better results, particularly those with a vocal alert or an <sup>alarm system</sup><sup>173,198,200</sup>. However, the installation of electronic reminders calls for computerised systems to manage operating theatre paperwork.

## **Audit and feedback**

The impact of this procedure tends to vary according to context<sup>201,202</sup>. For audit and feedback to be effective the data collection procedures must be carefully planned so that they are easy to implement and acceptable to professionals within the operating unit context. If the provision of data is seen not as a form of control but rather as an opportunity for comparison and discussion, it should be effective.

## **Assignment of responsibility**

The administration of antibiotic prophylaxis in the operating theatre may, in certain circumstances, lead to tension between the surgeon, who usually decides it, and the anaesthetist, who administers it. To ensure that prophylaxis is given in accordance with the procedures and timing indicated in the relevant guideline there must be: effective cooperation between the anaesthetist and nursing staff on the ward and in the operating theatre, all of whom should take part in the preparation and agreement of the guideline; resolution of organisational problems associated with antibiotic administration (particularly when there are special circumstances or it is prolonged); and the assignment of specific responsibilities for the administration of the antibiotic<sup>203</sup>.

## **Personalised antibiotic kits**

The most efficient means of ensuring the correct dosage and duration of prophylaxis would appear to be restrictive measures. The supply of personalised kits by hospital pharmacies has proved particularly effective. These kits are dispensed each day by the pharmacy in accordance with the local antibiotic prophylaxis guideline and a list of operations scheduled for the next day, and contain the correct number of phials of the antibiotics to be administered to each patient at the recommended dosage. Any additional doses of the same antibiotic can be obtained only on presentation of a motivated request<sup>204-205</sup>.

## **Recommendation**

# The most reliably accredited strategies for implementing guidelines are: agreement of a protocol for prophylaxis between surgeons, anaesthetists and operating theatre personnel; resolution of organisational problems; assignment of specific responsibilities for application of the guideline, and the preparation of personalised kits by pharmacies.

## **Recording of drugs used and minimum data set**

All information relating to antibiotic prophylaxis should be recorded in the case records and/or treatment chart<sup>206-209</sup>. To facilitate this procedure it is recommended that stickers be applied to the case records (for easy recording of the agreed administration procedures and proper controls), or reminders be used for nursing staff. Alternatively, the information could be recorded by hand in the case records and/or treatment chart. The guideline working group is aware that the routine collection of detailed information on operative procedures or postoperative complications is still difficult to achieve in most situations. The minimum data set that must be recorded whenever antibiotic prophylaxis is administered is summarised at the end of this chapter.

If the recommendations indicated in the guideline are not followed (the suggested antibiotic prophylaxis is not given or an agent not indicated in the guideline is given) the reasons should be clearly set out in the case records.

**Recommendation VI/A** The recording of a minimum data set in the case records and treatment charts facilitates the performance of audits to assess the appropriateness of perioperative antibiotic prophylaxis. Numerous methods of measuring outcome have been suggested<sup>152</sup>: the most commonly used is the rate of SSI<sup>152</sup>. The measurement and comparison of these rates are complicated by the fact that different groups may use different definitions of wound infection. This working group suggests adopting the definition of SSI developed by the CDC/NHSN (see Annex 4, page ). This envisages monitoring postoperative infections one month after the operation; when the operation includes the insertion of a prosthetic device, monitoring should be performed one month and again one year after the operation.

## **Key points and core indicators for audit of application of the guideline**

### **Core indicators for audit**<sup>19,152,194,210,211</sup>

#### Indicators of procedures The

following must be recorded:

- whether or not prophylaxis was prescribed as indicated in the local guideline;
- whether or not, when the choice of prophylaxis was different from the indications in the local guideline, a clinical justification for that choice was recorded in the case notes and/or other case records;
- whether or not the first dose of antibiotic was given within 60 minutes before the start of surgery;

- whether or not the prescription was written in the case notes and/or in the special forms contained in the case notes;
- whether or not an additional dose of antibiotic was given during the operation;
- whether or not the duration of prophylaxis was longer than 24 hours. If so, the reasons should be indicated.

### Outcome measures The following

should be indicated:

- the incidence of SSI (defined as the ratio between the number of surgical site infections occurring postoperatively and the total number of surgical procedures);
- the ratio between the incidence of SSI occurring postoperatively in patients who received inappropriate antibiotic prophylaxis (as defined in the guideline) and in patients who received appropriate antibiotic prophylaxis;
- the ratio between the incidence of *Clostridium difficile* infections occurring postoperatively in patients who received inappropriate antibiotic prophylaxis (as defined in the guideline) and in patients who received appropriate antibiotic prophylaxis.

## **Data set needed to audit perioperative antibiotic prophylaxis**

As well as the information normally contained in patients' case notes, the following should also be available:

- patient information -patient's ASA code at time of surgery
- surgery information -type of operation  
-elective or emergency operation -duration of operation
- information on antibiotic prophylaxis given

- type of antibiotic, dosage and route of administration;
- time and procedure of administration of first dose
- number of doses effectively administered in the operating theatre and in the ward;
- justification for not following the guideline
- written justification for not following the guideline

## **Annexes**

### **Annex 1 Proposals for local implementation**

The guidelines should be transformed into operating instructions that define the following for every specific local context: • operations for which prophylaxis is always indicated; • operations for which prophylaxis should be limited to patients at risk; • operations for which prophylaxis should not be given.

The following pages show examples of operating instructions for specific surgical procedures; further details should be added in light of local epidemiological conditions. For instance:

- the list of operations can be extended on the basis of cases actually treated in local units; additional procedures should, where possible, be included among one of the types of operation listed;
- one of the antibiotics listed as an alternative can be chosen;
- decisions can be taken on when and how to organise the intraoperative administration of antibiotic in cases of prolonged operations;

- the instructions be defined at local level with the participation of surgeons, anaesthetists, nursing staff and theatre personnel, the hospital pharmacy and infection control personnel;
- organisational problems relating to antibiotic administration be identified and resolved;
- specific responsibilities for antibiotic administration be assigned. It is also important that the operating instructions be signed by the Manager of the Operating Unit and contain the date of issue and of the next update.

NB: In the following pages some active principles are marked with the symbol ^.

Although there is evidence that these are effective in perioperative antibiotic prophylaxis, they are not indicated for that purpose in the relative data sheets.

Paragraph Z of the 2007 Finance Bill states that these active principles may not be used if another active principle is registered for the same indication. The working group therefore recommends the use of antibiotics not registered for prophylaxis only in selected situations (for example for patients who are allergic to beta-lactams or for certain operations where anaerobes are present) for which either no alternatives are available or evidence of their efficacy is less reliable.

## **Annex 2 Recommendations for antibiotic prophylaxis in bacterial**

### **endocarditis**

In 1955 the American Heart Association issued a first series of recommendations for prophylaxis for bacterial endocarditis. Subsequent revisions have gradually amended and supplemented the original recommendations, suggested different methods of administration and introduced dosages for children. The levels of risk associated with different cardiopathies and with procedures involving the oral cavity or genitourinary apparatus that necessitate antibiotic prophylaxis have also been better defined. These recommendations were the product of expert opinion and were mainly for medical-legal use as a source of evidence supporting the relation defined in Table 2.1.1.1

implementation of operating instructions, it is essential that:

diagnostic or surgical procedures and on the efficacy of prophylaxis were still lacking. The 1997 update, while not substantially altering prophylactic strategy, acknowledged for the first time that most cases of endocarditis are the result of randomly occurring bacteraemias rather than of particular diagnostic procedures. This and a series of other considerations listed below were formulated over the years and led to a radically new approach in the update published by the AHA in August 2007<sup>212</sup>.

- the occurrence of bacterial endocarditis is much more likely to result from exposure to episodes of bacteraemia associated with daily activities than from bacteraemia caused by diagnostic or surgical procedures in the mouth, GI tract or GU tract,
- antibiotic prophylaxis can prevent an exceedingly small number of cases of bacterial endocarditis in patients undergoing dental, GI tract or GU tract diagnostic or surgical procedures;
- the risk of adverse events associated with antibiotic prophylaxis is greater than the benefits;
- maintenance of optimal oral health and hygiene and periodic odontoiatric check-ups may reduce the incidence of bacteraemia associated with daily activities and are more important and effective than antibiotic prophylaxis administered in association with odontoiatric procedures.

The following are the latest recommendations for antibiotic prophylaxis to prevent bacterial endocarditis published by the AHA in August 2007<sup>212</sup>.

**Patients at high risk of developing endocarditis: antibiotic prophylaxis is recommended only for patients with these cardiac conditions**

- prosthetic cardiac valve
- previous history of endocarditis (including without valve lesion)
- congenital heart disease, in particular:

- unrepaired cyanotic heart disease or disease for which only palliative treatment was given;
- completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure
- repaired congenital heart disease with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialisation);

cardiac transplantation recipients who develop cardiac valvulopathy

## **RECOMMENDATIONS FOR PATIENTS AT HIGH RISK OF ENDOCARDITIS UNDERGOING PROCEDURES/OPERATIONS IN THE MOUTH OR RESPIRATORY TRACT**

### DENTAL PROCEDURES

Prophylaxis is recommended for:

- procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa

Prophylaxis is NOT recommended for:

- anaesthetic injections through non-infected tissue
- dental radiographs
- placement of removable prosthodontic or orthodontic appliances
- adjustment of orthodontic appliances
- extraction of deciduous teeth
- bleeding from trauma to the lips or gums

## RESPIRATORY TRACT PROCEDURES AND OPERATIONS

Prophylaxis is recommended for:

- invasive procedures involving an incision or biopsy of the mucosa (e.g. tonsillectomy and/or adenoidectomy).

Prophylaxis is NOT recommended for:

- bronchoscopy (unless it involves incision of the mucosa).

**N.B.:** For operations where an infection is present (e.g. drainage of an abscess or empyema) the chosen antibiotic should be active against beta-haemolytic streptococci. If a staphylococcus-associated infection is suspected the treatment should include a penicillin active against staphylococcus or a cephalosporin. If the staphylococcus is likely to be meticillin-resistant or the patient is allergic to betalactams, treatment should include vancomycin.

## **RECOMMENDATIONS FOR PATIENTS AT HIGH RISK OF ENDOCARDITIS UNDERGOING PROCEDURES/OPERATIONS ON INFECTED GI OR GU TRACT OR ON INFECTED SKIN OR MUSCOSKELETAL TISSUE**

### **DIAGNOSTIC/SURGICAL PROCEDURES ON INFECTED GI OR GU TRACT**

Prophylaxis should be considered EXCLUSIVELY when an infection or colonisation is present in :

- patients undergoing diagnostic or surgical procedures; it is reasonable that the therapeutic regimen include an antibiotic active against enterococci, such as ampicillin, piperacillin, vancomycin;
- patients undergoing cystoscopy or other elective manipulations of the urinary tract when an enterococcal colonisation or infection is present: it is reasonable to administer an effective antibiotic prior to the procedure.

**N.B.:** It is very important that patients at risk of endocarditis maintain healthy teeth.

This can be ensured through regular cleaning of the teeth (with an ordinary or electric toothbrush) and regular dental check-ups.

In emergency surgery it is reasonable to choose a treatment that includes an antibiotic active against enterococci.

**SURGICAL PROCEDURES/OPERATIONS ON INFECTED SKIN OR MUSCOSKELETAL TISSUE** Prophylaxis should be considered EXCLUSIVELY when an infection or colonisation is present in:

- patients undergoing surgery who have infections of the skin, skin structure or musculoskeletal tissue: it is reasonable that the choice of treatment include an antibiotic active against staphylococci and beta-haemolytic streptococci, such as penicillin or a cephalosporin; clindamycin or vancomycin may be administered respectively to patients allergic to beta-lactams or when the infection is known or suspected to be caused by a <sup>high</sup> ~~meticillin-resistant~~ staphylococcus.

**RISK  
OF  
ENDOCARDITIS**

**ANTIBIOTICS RECOMMENDED FOR ~~PROPHYLAXIS~~ IN PATIENTS AT  
PROCEDURES/OPERATIONS  
ON  
THE  
MOUTH  
OR  
RESPIRATORY  
TRACT**

**STANDARD TREATMENT**

cephalexin<sup>s</sup> 2 g 30-

60 minutes before

azithromycin/clarithromycin 500 mg 30-60 minutes before the procedure/operation  
the procedure Or

*Parenteral alternative:*

-clindamycin 600 mg iv 30-60 minutes before the procedure

Or

- cefazolin<sup>s</sup> or ceftriaxone<sup>s</sup> 1 g im/iv 30-60 minutes before the procedure

<sup>s</sup> Cephalosporins should not be given to patients with a history of allergic reactions such as urticaria, angioedema or anaphylaxis.

### **Annex 3 Antibiotic prophylaxis in patients with prosthetic devices or extracardiac prosthetic material.**

A systematic review published in April 2007<sup>213</sup> examined available evidence regarding the efficacy of antibiotic prophylaxis for odontostomatological procedures in the following clinical conditions:

- prostheses or prosthetic devices in the heart (cardiac-native heart valve disease, prosthetic heart valves, pacemakers)
- hip, knee or shoulder prosthetic joints
- vascular grafts
- cerebrospinal fluid shunts, renal dialysis shunts

Amoxicillin, oral administration: 2 g 30-60 minutes before the procedure

- immunosuppression secondary to cancer or chemotherapy
- systemic lupus erythematosus
- type 1 diabetes mellitus

**PATIENTS UNABLE TO TAKE ORAL MEDICINE**

Ampicillin im/iv: 2 g 30-60 minutes before the procedure

**PATIENTS ALLERGIC TO AMPICILLIN/AMOXICILLIN**

*Oral alternative:*

clindamycin 600 mg 30-

60 minutes before the

procedure Or

efficacy was graded according to the system used by the American College of Cardiology/American Heart Association. The results of their review are as follows:

- Presence of cardiac-native heart disease or prosthetic heart valves No randomised controlled studies exist, but one case-control study is available, as is a series of observational studies and case reports. The available studies were appraised in a review published by Cochrane of 980 references, and revealed poor preventive efficacy of antibiotic prophylaxis <sup>213</sup>. The recommendations are based only on expert opinion, clinical cases or prescriptive practices. There is some evidence of efficacy in high-risk patients.
- Presence of pacemakers The available evidence of efficacy is derived from retrospective reviews of case histories, and shows that procedures on the oral cavity have little effect on bacteraemia associated with staphylococcus (the agent that causes most pacemaker infections) The American Heart Association, in agreement with most of the literature, therefore recommends not giving antibiotic prophylaxis for procedures on the oral cavity, even in immunocompromised patients with pacemakers.
- Prosthetic joints No randomised controlled studies exist, only observational studies, case reports and numerous citations in books or treatises. The limited evidence base shows that infections of joint prostheses are often caused by a staphylococcus and rarely by micro-organisms typically found in the bacterial flora of the oral cavity, although cases that contradict this statement have been reported. Over the years guidelines issued by orthopaedic societies and developed in cooperation with odontoiatric societies have produced occasionally conflicting recommendations and the absence of an evidence base makes it impossible to agree an approach. The recommendations are based only on expert opinion, clinical cases or prescriptive practices. The authors searched Medline for the period 1998-2005 for guidelines issued by scientific associations and references in books or treatises. They were able to limit the search to a systematic review without producing quantitative data. The evidence of

- Vascular grafts No randomised controlled studies exist, only very few observational studies or case reports and some citations in books or treatises. The AHA does not recommend antibiotic prophylaxis in these patients even if immunosuppression, diabetes mellitus or renal insufficiency are present. Existing recommendations are based only on expert opinion, clinical cases or prescriptive practices.

- CSF shunts No randomised controlled studies are available, only one prospective study of 14 children with peritoneal shunts. Very few observational studies or case reports and some citations in books or treatises are available. Existing recommendations are based only on expert opinion, clinical cases or prescriptive practices.

Of the clinical conditions considered, the only cases in which the administration of antibiotic prophylaxis is based on weak evidence are:

- serious immunosuppression following chemotherapy;
- high-risk patients with prosthetic heart valves or other cardiac prosthetic device.

-micro-organisms isolated from aseptically obtained culture of fluid or tissue from the site of incision;

- at least one of the following signs or symptoms of infection:

- pain or tenderness to pressure;
- localised swelling;
- redness;
- heat;
- deliberate re-opening of the wound by a surgeon (in which case the culture must be positive). If the culture is negative this criterion has not been met;
- diagnosis of superficial wound infection made by the surgeon or attending physician.

#### **Annex 4 CDC/NHSN criteria for defining a surgical site infection<sup>214</sup>. Superficial infection**

The infection occurs within 30 days of the operation and involves only the skin and subcutaneous tissue at the site of incision, plus one of the following: -purulent drainage;

- infection of both superficial and deep tissues at the incision site (defined as a deep infection).

### Deep infection

Infection occurs within 30 days of the operation if no implant is in place, or within one year if an implant is in place and the infection appears related to the operation and involves deep soft tissues (e.g. fascial or muscle layers). At least one of the following conditions must also be present:

- purulent drainage from the deep incision but not from the organ/space component of the surgical site;
  - a deep incision spontaneously dehisces or is deliberately re-opened by the surgeon when one of the following signs or symptoms is present (a culture-negative finding does not meet this criterion):
    - fever ( $>38^{\circ}\text{C}$ )
    - localised pain
    - abscess or other sign of infection found on direct examination, during re-operation, or by histopathological or radiological examination;
- There are two types of superficial infection: -superficial incisional primary SSI (SIP) affects the site of the primary incision of a patient receiving one or more incisions (e.g. a superficial infection of chest incision in a patient operated for aorto-coronary bypass);

- diagnosis of deep incisional SSI by surgeon or attending physician
- superficial incisional secondary SSI (SIS) occurs at the site of a secondary

There are 2 types of deep infection:

- deep incisional primary (DIP) occurs at the primary incision in a patient who received one or more incisions (e.g. deep infection of chest incision in patient undergoing aorto-coronary bypass);
  - deep incisional secondary (DIS) occurs at the secondary incision in a patient who received more than one incision (deep wound infection following harvesting of the saphenous vein in a patient undergoing aorto-coronary bypass).
- The following are not considered superficial surgical site infections:

- stitch abscess (minimal inflammation and discharge confined to the points of suture)
- localised infection of the drainage incision (this may be an infection of the skin or of the subcutaneous tissue, according to depth);
- infection of a newborn circumcision site; infected burn wound; infection that extends to the fascial or muscle layers (see deep incision);

This may involve any part of the anatomy other than the incision site or fascial or muscle layers that were manipulated during surgery. Site-specific definitions are assigned to these infections (see below). A typical example is an intra-abdominal abscess following appendicectomy. An SSI is defined as an organ/space infection when all the following conditions are met:

- the infection occurs within 30 days of the operation if no implant is left in place or within one year if an implant is in place and the infection is related to the operation;
- the infection involves any part of the anatomy other than the incision site or fascial or muscle layers that was opened or manipulated during surgery;
- at least one of the following is present: -purulent drainage from a drainage tube placed in the organ/space; -micro-organisms isolated from aseptically obtained culture of fluid or

**N.B:** if the infection affects both the superficial and deep portions of the incision it is classified as deep SSI.

**Organ/space SSI**

- myocarditis, pericarditis
- endocarditis -arterial infections or mediastinitis

### **Gastrointestinal tract infections**

- GI tract infections -Unspecified abdominal infections

### **Reproductive tract infections**

- Endometritis -Vaginal cuff infection -Other male or female reproductive apparatus infections

### **Infections of the skin and soft tissue**

- Breast abscess or mastitis

### **Infections of the upper or lower respiratory tract**

- Pneumonia (with specific laboratory finding in immunocompromised patients) -Infections of the upper airways (pharyngitis, laryngitis, epiglottitis) -abscess or other sign of infection involving the organ/space found on direct examination, during re-operation or by histopathological or radiological examination

### **CNS infections**

- Meningitis, or ventriculitis -Spinal abscess without meningitis

-diagnosis of a wound/space SSTI by a surgeon or attending physician. **N.B.:**

organ/space infections occasionally drain through the incision. This does not generally involve re-operation and the infection is considered a complication of the incision and classified as a deep (incision SSTI).

### **Urinary tract infections**

Urinary tract infections (excluding SS) symptomatic bacteriuria or urinary tract infection)

### **Infections of eye, ear, nose, throat, mouth and face surgical site infections**

#### **Infections in bones or joints**

- Otitis, mastoiditis -Oral cavity infections (mouth, tongue, gums) -Eye, other than conjunctivitis, sinus or bursae

### **Cardiovascular system infections**

## Annex 5 Classification of operations by duration > 75<sup>th</sup>

### percentile

Operations are classified according to the categories of the *National Nosocomial Infections Surveillance* (NNIS): the times shown below are the duration beyond which an operation is defined as prolonged and the risk of SSI increases. The NNIS figures are compared with those from an Italian study. Duration of operations beyond the 75<sup>th</sup>

percentile Type of operation Cardiac surgery Aorto-coronary bypass with extrathoracic incision Aorto-coronary bypass with sternotomy Vascular surgery Other cardiac or vascular surgery Thoracic surgery Other respiratory tract operations Head and neck Other otorhinolaryngoiatric (ENT) operations Mastectomy Laparotomy Hernia repair Colon surgery Liver/pancreas Other intestinal surgery Nephrectomy Prostatectomy Other GU tract surgery Craniotomy Ventricular shunt

Other CNS surgery Caesarean section Abdominal hysterectomy Other  
obstetric operations Limb amputation Open fracture reduction Knee  
prosthesis Hip prosthesis Laminectomy Other prosthetic implants Other  
musculoskeletal operations Other haemolympathic system operations Skin  
transplant Splenectomy Other endocrine system operations Other  
tegument operations Organ transplant

## **Annex 6 Micro-organisms most frequently associated with postoperative infections**

The table that follows shows the micro-organisms most frequently associated with postoperative infections and the antibiotic or combination of antibiotics recommended by the major guidelines and agreed by the panel.

## **Annex 7 Auditing compliance with CDC rules for preventing SSI**

The list that follows shows aspects that should be investigated in order to assess how far surgical operating units comply with the recommendations issued by the Centers for Disease Control and Prevention (CDC) for the prevention of surgical site infections (SSI). The list includes questions that refer to negative recommendations, in other words measures that have been shown not to be effective in preventing SSI and that should therefore not be adopted (e.g. tacky mats and routine microbiological sampling). In some cases relevant information can be obtained by a single visit to the operating theatre or technical department to check the structural (ventilation system) or organisational (existence of protocols, environmental microbiological sampling practices, etc.) details. In other cases the information should be obtained by planning a number of visits in proportion to the expected frequency of an event or by examining case records: for example, to elicit information regarding behaviour that is not routine for all operations (such as normal practice following visible contamination of the floor or surfaces with biological fluids during an operation, or customary care of diabetic patients). The following list of questions indicates only some of the aspects to be examined and should not be considered or used as an operational tool.

1. Preparation of the patient

- Is the hair around the incision site removed? If so, how long before the operation?
- Is the blood sugar level checked in diabetic patients? When? Are these patients given continuous infusions of insulin in the operating theatre?
- If the patient is a smoker, how long before the operation was the last cigarette smoked?
- Do patients take a shower prior to the operation? If so, how long before? What type of soap is used for the shower?
- Was the incision site washed before the surgical field was disinfected?

## 2. Preparation of the surgical team

- Are the nails of medical and nursing operating theatre staff properly cut?
- Have all surgical team members involved in the operation completed a proper surgical scrub of their hands?
- Are all the surgical team members involved in the operation wearing sterile gloves and gowns?

## 3. Management of infected or colonised surgical personnel

- Have any team members reported signs or symptoms of transmissible diseases? -Are specific protocols in place to exclude personnel from the operating theatre or readmit them in the event of transmissible infectious diseases? -Have any surgical team members been excluded from the operating theatre over a specific period on account of suspected or confirmed draining skin lesions?
- Have any surgical team members been excluded from the operating theatre over a specific period on account of colonisation with *Staphylococcus aureus* or Group A streptococcus epidemiologically unrelated to cases of infection?

## 4. Ventilation systems

- Is the operating theatre equipped with a positive-pressure ventilation system?
- Is the air changed 15 times per hour, with three changes of fresh air?
- Is all the air in the operating theatre filtered?
- Is the air introduced at the ceiling and expelled through the floor?
- Is UV radiation used in the operating theatre to prevent SSI?

-Is the operating theatre closed or subjected to special cleaning after contaminated or dirty operations?

- Are tacky mats used at the entrance to the operating theatre?

#### 6. Environmental microbiological sampling

-Is sampling of the air and of the surfaces of the operating theatre routinely performed? If so, how often?

#### 7. Sterilisation of surgical instruments

- Are protocols in place for the sterilisation of surgical instruments?

-Is flash sterilisation performed? If so, is it limited to instruments for immediate re-use?

#### 8. Surgical attire and gowns

- Did all personnel in the operating theatre wear a mask and a cap or hood?
- Did all personnel in the operating theatre wear shoe covers?

-Are the doors to the operating theatre generally open, generally closed, always open, always closed?

5. Environmental cleaning and disinfecting -Was there any visible contamination of the floor or other surfaces by organic fluids during the operation?

-If contamination occurred, were the affected areas cleaned before the next operation with a disinfectant approved by the relevant committee?

-For how many hours does the protocol indicate that the surgical wound should be covered with a sterile dressing?

- Does the protocol require that hands be washed before and after medication?

- Did all personnel in the operating theatre wear sterile gloves? -During the operation were surgical gowns or drapes necessary as barriers? If so, were they available?

-During the operation did surgical attire become dirty or contaminated with blood or other biological materials? If so, was it changed?

#### 9. Asepsis and surgical technique

-During diagnostic and therapeutic procedures (placing of venous catheters, spinal or epidural anaesthesia catheters, etc.) were the principles of asepsis adhered to?

-During the operation was adequate haemostasis maintained? Were tissues manipulated with care? Were devitalised tissues and foreign bodies removed? -If the surgical site was heavily contaminated, was the wound left open to heal by second intention?

- Was an open drain used? Was the drainage removed soon after the operation?

#### 10. Medication of the wound



11. Jobe BA, Grasley A, Deveney KE, Deveney CW, Sheppard BC. Clostridium difficile colitis: an increasing hospital-acquired illness. *Am J Surg* 1995;169:480-83.
12. Greco D, Moro ML, Tozzi AE, De Giacomi GV. Effectiveness of an intervention italiana: P Colombini e PL Viale (a cura di) Linee guida per la prevenzione delle program in reducing postoperative infections. Italian PRINOS Study Group. *Am J infezioni del sito chirurgico dei Centers for Disease Control and Prevention*, 1999. *Med* 1991;91:164S-169S.
13. *Giornale italiano delle Infezioni Ospedaliere* 1999; 6: 157-195.
14. *Journal of Hospital Infection* 2006; 62: 1313-1317
15. Agenzia regionale della sanità, Regione Friuli Venezia Giulia. Programma di *infezioni della ferita chirurgica. Report anno 2000.*
16. Moro ML, Morsillo F, Ragni P, Tangenti M. Regione Emilia Romagna, Agenzia *infezioni ospedaliere in*
17. *National Prevalence Study of Infections in Hospital-Sanitarie del Friuli Venezia Giulia* ISSN 1591-223x Dossier 63; 2002. (<http://www.regione.emilia-romagna.it/ermes/cerca/default.asp?query=63&O=ERMES&Pg=C&root=PhARMAS>)
18. *Preoperative bathing or showering with skin antiseptics to prevent surgical site infections.* *Cochrane Database Syst Rev* 2007;2:CD004985.
19. *Some effects of subinhibitory concentrations of antibiotics on bacteria.* *Bull NY Acad Med* 1975;51:1046-55.
20. *The post-antibiotic sub-MIC effect in vitro and in vivo.* *J Antimicrob Chemother* 1993;31:159-66.
21. *Survey of antibiotic prescribing in a district general hospital. I. Pattern of use.* *Lancet* 1981;2:349-52.
22. *Outpatient antibiotic use in Europe and association with resistance: a crossnational database study.* *Lancet* 2005;365:579-87.



30. Scottish Intercollegiate Guidelines Network (SIGN). SIGN Guidelines: An introduction to SIGN methodology for the development of evidence-based clinical guidelines. Edinburgh: SIGN, 1999 (SIGN publication no.39).
31. Song F, Glenny AM. Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomised controlled trials. Health Technol Assessment South Hampton NY 1998;2:1-110.
32. Culver DH, Horan TC, Gaynes RP, Eykyn SJ, Littler WA, McGowan DA et al. Surgical wound infection rates by wound class, operative procedure and patient risk index. National Nosocomial Infections Surveillance System. Am J Med 1991;91:152-57.
33. Taylor E, Dev V, Shah D et al. Complicated appendicitis: is there a minimum intravenous antibiotic requirement? A prospective randomized trial. Am Surg 2000;66:887-90.
34. Gristina AG, Costerton JW. Bacterial adherence and the glycocalyx and their role in musculoskeletal infection. Orthop Clin North Am 1984;15:517-35.
35. McGowan JE. Cost and benefit in control of nosocomial infection: methods for analysis. Rev Infect Dis 1981;3:790-97.
36. American Society of Anesthesiologists. New classification of physical status. Anesthesiology 1963;24:111.
37. Haley RW, Culver DH, Morgan WM, White JW, Emori TG, Hooton TM. Identifying patients at high risk of surgical wound infection. A simple multivariate index of patient susceptibility and wound contamination. Am J Epidemiol 1985;121:206-15.
38. Baum ML, Anish DS, Chalmers TC, Sacks HS, Smith H, Fagerstrom RM. A survey of clinical trials of antibiotic prophylaxis in colon surgery: evidence against further use of no-treatment controls. N Engl J Med 1981;305:795-99.
39. Lidwell OM. Air, antibiotics and sepsis in replacement joints. J Hosp Infect 1988;11:18-40.

40. Coello R, Glenister H, Fereres J, Bartlett C, Leigh D, Sedgwick J et al. The cost of infection in surgical patients: a case control study. *J Hosp Infect* 1993;25:239-50.
41. Davies TW and Cottingham J. The cost of hospital infection in orthopaedic patients. *J Infect* 1979;1:329-38.
42. Lynch W, Malek M, Davey PG, Byrne DJ, Napier A. Costing wound infection in a Scottish hospital. *Pharmacoeconomics* 1992;2:163-70.
43. Davey PG, Duncan ID, Edward D, Scott AC. Cost-benefit analysis of cephradine and mezlocillin prophylaxis for abdominal and vaginal hysterectomy. *Br J Obstet Gynaecol* 1988;95:1170-77.
44. Gold HS, Moellering RC. Antimicrobial drug resistance. *N Engl J Med* 1996; 335: 1445-53.
45. American Society for Microbiology. Report of the ASM Task Force on antimicrobial resistance. Washington: The Society, 1994.
46. Austin DJ, Kakehashi M, Anderson RM. The transmission dynamics of antibiotic-resistant bacteria: the relationship between resistance in commensal organisms and antibiotic consumption. *Proc R Soc Lond B Biol Sci* 1997;264:1629-38.
  
47. Schwartz B, Bell DM, Hughes JM. Preventing the emergence of antimicrobial resistance. A call for action by clinicians, public health officials, and patients. *JAMA* 1997;278:944-45.
48. McCaig LF, Hughes JM. Trends in antimicrobial drug prescribing among office-based physicians in the United States. *JAMA* 1995;273:214-19.
49. Kato D, Maezawa K, Yonezawa I, Iwase Y, Ikeda H, Nozawa M, Kurosawa H. Randomized prospective study on prophylactic antibiotics in clean orthopedic surgery in one ward for 1 year. *J Orthop Sci.* 2006 Jan;11:20-7.
50. Wilcox MH, Smyth ET. Incidence and impact of *Clostridium difficile* infection in the UK, 1993-1996. *J Hosp Infect* 1998;39:181-87.
51. Zadik PM, Moore AP. Antimicrobial associations of an outbreak of diarrhoea due to *Clostridium difficile*. *J Hosp Infect* 1998;39:189-93.

52. Wilcox MH, Cunniffe JG, Trundle C, Redpath C. Financial burden of hospital-acquired *Clostridium difficile* infection. *J Hosp Infect* 1996;34:23-30.
53. Pépin J, Saheb N, Coulombe MA, Alary ME, Corriveau MP, Authier S, Leblanc M, Rivard G, Bettez M, Primeau V, Nguyen M, Jacob CE, Lanthier L. Emergence of fluoroquinolones as the predominant risk factor for *Clostridium difficile*-associated Diarrhea: a cohort study during an epidemic in Quebec. *Clin Infect Dis* 2005;41:1254-60.
54. Owens RC Jr, Donskey CJ, Gaynes RP, Loo VG, Muto CA. Antimicrobial associated risk factors for *Clostridium difficile* infection. *Clin Infect Dis* 2008;46:S19-31
55. Privitera G, Scarpellini P, Ortisi G, Nicastro G, Nicolini R, de Lalla F. Prospective study of *Clostridium difficile* intestinal colonisation and disease following single dose antibiotic prophylaxis in surgery. *Antimicrob Agents Chemother* 1991;35:208-10.
56. Namias N, Harvill S, Ball S, McKenney MG, Salomone JP, Civetta JM. Cost and morbidity associated with antibiotic prophylaxis in the ICU. *J Am Coll Surg* 1999;188:225-30.
57. Harbarth S, Samore MH, Lichtenberg D, Carmeli Y. Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance. *Circulation* 2000;101:2916-21.
58. Carignan A, Allard C, Pépin J, Cossette B, Nault V, Valiquette L. Risk of *Clostridium difficile* Infection after perioperative antibacterial prophylaxis before and during an outbreak of infection due to a hypervirulent strain. *Clin Infect Dis* 2008;46:1838-43.
59. Kolben M, Mandoki E, Ulm K, Freitag K. Randomized trial of cefotiam prophylaxis in the prevention of postoperative infectious morbidity after elective cesarean section. *Eur J Clin Microbiol Infect Dis* 2001;20:40-42.
60. Cook RJ, Sackett DL. The number needed to treat: a clinically useful measure of treatment effect. *Brit Med J* 1995;310:452-54.

61. Berbari EF, Hanssen AD, Duffy MC, Steckelberg JM, Ilstrup DM, Harmsen WS et al. Risk factors for prosthetic joint infection: case-control study. *Clin Infect Dis* 1998;27:1247-54.
62. Monif RG, Lowenkron JD. Temperature and fever in ob-gyn patients. In: G. Pastorek (ed) *Obstetric and gynaecologic infectious disease*. New York: Raven Press, 1994.
63. Da Costa A, Kirkorian G, Cucherat M, Delahaye F, Chevalier P, Cerisier A et al. Antibiotic prophylaxis for permanent pacemaker implantation: a meta-analysis. *Circulation* 1998;97:1796-801.
64. Kreter B, Woods M. Antibiotic prophylaxis for cardiothoracic operations. Meta-analysis of thirty years of clinical trials. *J Thorac Cardiovasc Surg* 1992;104:590-99.
65. Fong IW, Baker CB, McKee DC. The value of prophylactic antibiotics in aorta-coronary bypass operations: a double-blind randomized trial. *J Thorac Cardiovasc Surg* 1979;78:908-13.
66. Austin TW, Coles JC, Burnett R, Goldbach M. Aortacoronary bypass procedures and sternotomy infections: a study of antistaphylococcal prophylaxis. *Can J Surg* 1980;23:483-85.
67. Penketh AR, Wansbrough-Jones MH, Wright E, Imrie F, Pepper JR, Parker DJ. Antibiotic prophylaxis for coronary artery bypass graft surgery. *Lancet* 1985;1:1500.
68. Amoury RA, Bowman FO Jr, Malm JR. Endocarditis associated with intracardiac prostheses. Diagnosis, management, and prophylaxis. *J Thorac Cardiovasc Surg* 1966;51:36-48.
69. Stein PD, Harken DE, Dexter L. The nature and prevention of prosthetic valve endocarditis. *Am Heart J* 1966;71:393-407.
70. Ilves R, Cooper JD, Todd TR, Pearson FG. Prospective, randomised, double-blind study using prophylactic cephalothin for major, elective, general thoracic operations. *J Thorac Cardiovasc Surg* 1981;81:813-17.

71. Aznar R, Mateu M, Miro JM, Gatell JM, Gimferrer JM, Aznar E et al. Antibiotic prophylaxis in noncardiac thoracic surgery: cefazolin versus placebo. *Eur J Cardiothorac Surg* 1991;5:515-18.
72. Velanovich V. A meta-analysis of prophylactic antibiotics in head and neck surgery. *Plast Reconstr Surg* 1991;87:429-34.
73. Dor P, Klastersky J. Prophylactic antibiotics in oral, pharyngeal and laryngeal surgery for cancer:(a double-blind study). *Laryngoscope* 1973;83:1992-98.
74. Becker GD, Parell GJ. Cefazolin prophylaxis in head and neck cancer surgery. *Ann Otol Rhinol Laryngol* 1979;88:183-86.
75. Johnson JT, Yu VL, Myers EN, Muder RR, Thearle PB, Diven WF. Efficacy of two third generation cephalosporins in prophylaxis for head and neck surgery. *Arch Otolaryngol* 1984;110:224-27.
76. Zijderveld SA, Smeele LE, Kostense PJ, Tuinzing DB. Preoperative antibiotic prophylaxis in orthognathic surgery: a randomized, double-blind, and placebo-controlled clinical study. *J Oral Maxillofacial Surgery* 1999;57:1403-06.
77. Skitarelic N, Morovic M, Manestar D. Antibiotic prophylaxis in clean-contaminated head and neck oncological surgery. *Journal of Cranio-Maxillofacial Surgery* 2007;35:15-20.
78. Ong SK, Morton RP, Kolbe J, Whitlock RM, McIvor NP. Pulmonary complications following major head and neck surgery with tracheostomy: a prospective, randomized, controlled trial of prophylactic antibiotics. *Arch. Otolaryngol. Head Neck Surg.* 2004;130:1084-7.
79. Carroll WR, Rosenstiel D, Fix JR, de la TJ, Solomon JS, Brodish B et al. Three-dose vs extended-course clindamycin prophylaxis for free-flap reconstruction of the head and neck. *Arch. Otolaryngol. Head Neck Surg.* 2003;129:771-4
80. Verschuur HP, de Wever WW, van Benthem PP. Antibiotic prophylaxis in clean and cleancontaminated ear surgery. *Cochrane Database Syst Rev* 2004;3:CD003996.
81. Johnson JT, Wagner RL. Infection following uncontaminated head and neck surgery. *Arch Otolaryngol Head Neck Surg* 1987;113:368-69.

82. Legent F, Arnould JF. Antibiotic prophylaxis in ORL surgery and oral medicine. [French] *Ann Fr Anaesth Reanim* 1994;13:5100-09.
83. Iyer S, DeFoor W, Grocela J, Kamholz K, Varughese A, Kenna M. The use of perioperative antibiotics in tonsillectomy: does it decrease morbidity? *Int. J. Pediatr. Otorhinolaryngol.* 2006;70:853-61
84. Burkart CM, Steward DL. Antibiotics for reduction of posttonsillectomy morbidity: a metaanalysis. *Laryngoscope* 2005;115:997-1002
85. Andersen BR, Kallehave FL, Andersen HK. Antibiotics versus placebo for prevention of postoperative infection after appendectomy. *Cochrane Database Syst Rev* 2005;3:CD001439.
86. Willis AT, Ferguson IR, Jones PH, Phillips KD, Tearle PV, Berry RB. Metronidazole in prevention and treatment of bacteroides infections after appendicectomy. *Brit Med J* 1976;1:318-21.
87. Winslow RE, Dean RE, Harley JW. Acute non perforating appendicitis. Efficacy of brief antibiotic prophylaxis. *Arch Surg* 1983;118:651-55.
88. Donovan IA, Ellis D, Gatehouse D, Little G, Grimley R, Armistead S et al. One-dose antibiotic prophylaxis against wound infection after appendicectomy: a randomised trial of clindamycin, cefazolin sodium and a placebo. *Br J Surg* 1979;66:193-96.
89. Koch A, Zippel R, Marusch F et al. Prospective multicenter study of antibiotic prophylaxis in operative treatment of appendicitis. *Dig Surg* 2000;17:370-78.
90. Meijer WS, Schmitz PI, Jeekel J. Meta-analysis of randomised, controlled clinical trials of antibiotic prophylaxis in biliary tract surgery. *Br J Surg* 1990;77:283-90.
91. Cunningham M, Bunn F, Handscomb K. Prophylactic antibiotics to prevent surgical site infection after breast cancer surgery [Systematic Review]. *Cochrane Database Syst Rev* 2007;2:CD005360.
92. Ahmadi AH, Cohen BE, Shayani P. A prospective study of antibiotic efficacy in preventing infection in reduction mammoplasty. *Plastic & Reconstructive Surgery* 2005;116:126-31.

93. Preclik G, Grune S, Leser HG, Lebherz J, Heldwein W, Machka K et al. Prospective, randomised, double blind trial of prophylaxis with single dose of co-amoxiclav before percutaneous endoscopic gastrostomy. *Brit Med J* 1999;319:881-84.
94. Dormann AJ, Wigglinghaus B, Risius H et al. Antibiotic prophylaxis in percutaneous endoscopic gastrostomy (PEG) -results from a prospective randomized multicenter trial. *Z Gastroenterol* 2000;38:229-34.
95. Sharma VK, Howden CW. Meta-analysis of randomized, controlled trials of antibiotic prophylaxis before percutaneous endoscopic gastrostomy. *Am J Gastroenterol* 2000;95:3133-36.
96. Polk HC Jr, Lopez-Mayor JF. Postoperative wound infection: a prospective study of determinant factors and prevention. *Surgery* 1969;66:97-103.
97. Evans C, Pollock AV. The reduction of surgical wound infections by prophylactic parenteral cephaloridine. A controlled clinical trial. *Br J Surg* 1973;60:434-37.
98. Lewis RT, Allan CM, Goodall RG, Lloyd-Smith WC, Marien B, Wiegand FM. Discriminate use of antibiotic prophylaxis in gastroduodenal surgery. *Am J Surg* 1979;138:640-43.
99. Bricard H, Deshayes JP, Sillard B, Lefrancois C, Delassus P, Lochu T et al. Antibiotic prophylaxis in surgery of the oesophagus.[French] *Ann Fr Anaesth Reanim* 1994;13:161-68.
100. Aufenacker TJ, Koelemay MJ, Gouma DJ, Simons MP. Systematic review and meta-analysis of the effectiveness of antibiotic prophylaxis in prevention of wound infection after mesh repair of abdominal wall hernia. *British Journal of Surgery* 2006;93:5-10.
101. Sanchez-Manuel FJ, Seco-Gil JL. Antibiotic prophylaxis for hernia repair. *Cochrane Database Syst Rev* 2003;2:CD003769. Update in *Cochrane Database of Syst Rev* 2004;4:CD003769

102. Catarci M, Mancini S, Gentileschi P, Camplone C, Sileri P, Grassi GB. Antibiotic prophylaxis in elective laparoscopic cholecystectomy. Lack of need or lack of evidence? *Surgical Endoscopy* 2004;18:638-41.
103. Goldfaden A, Birkmeyer JD Evidence-based practice in laparoscopic surgery: perioperative care. *Surgical innov* 2005;12:51-61.
104. Barker FG. Efficacy of prophylactic antibiotics for craniotomy: a meta-analysis. *Neurosurgery* 1994;35:484-90.
105. Langley JM, LeBlanc JC, Drake J, Milner R. Efficacy of antimicrobial prophylaxis in placement of cerebrospinal fluid shunts: a meta analysis. *Clin Infect Dis* 1993;17:98-103.
106. Haines SJ, Walters BC. Antibiotic prophylaxis for cerebrospinal fluid shunts: a meta-analysis. *Neurosurgery* 1994;34:87-92.
107. Ratilal B, Costa J, Sampaio C. Antibiotic prophylaxis for surgical introduction of intracranial ventricular shunts. *Cochrane Database Syst Rev.* 2006;3:CD005365.
108. Smaill F, Hofmeyr GJ. Antibiotic prophylaxis for cesarean section. *Cochrane Database Syst Rev.* 2000;2:CD000933. Update in: *Cochrane Database Syst Rev.* 2002;3:CD000933.
109. Tanos V, Rojansky N. Prophylactic antibiotics in abdominal hysterectomy. *J Am Coll Surg* 1994;179:593-600.
110. Mittendorf R, Aronson MP, Berry RE, Williams MA, Kupelnick B, Klickstein A et al. Avoiding serious infections associated with abdominal hysterectomy: a meta-analysis of antibiotic prophylaxis. *Am J Obstet Gynecol* 1993;169:1119-24.
111. Allen JL, Rampone JF, Wheelless CR. Use of a prophylactic antibiotic in elective major gynaecologic operations. *Obstet Gynecol* 1972;39:218-24.
112. Ledger WJ, Sweet RL, Headington JT. Prophylactic cephaloridine in the prevention of postoperative pelvic infections in premenopausal women undergoing vaginal hysterectomy. *Am J Obstet Gynecol* 1973;115:766-74.

113. Sawaya GF, Grady D, Kerlikowske K, Grimes DA. Antibiotics at the time of induced abortion: the case for universal prophylaxis based on a meta-analysis. *Obstet Gynecol* 1996;87:884-90.
114. Glenny AM, Song F. Antimicrobial prophylaxis in total hip replacement: a systematic review. *Health Technol Assess* 1999;3:21-47.
115. Hill C, Flamant R, Mazas F, Evrard J. Prophylactic cefazolin versus placebo in total hip replacement. Report of a multicentre double-blind randomised trial. *Lancet* 1981;1:795-96.
116. Lidwell OM, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D. Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement: a randomised study. *Brit Med J* 1982;285:10-14.
117. Gillespie WJ, Walenkamp G. Antibiotic prophylaxis for surgery for proximal femoral and other closed long bone fractures. *Cochrane Database Syst Rev*. 2000;2:CD000244. Update in: *Cochrane Database Syst Rev*. 2001;1:CD000244.
118. Southwell-Keely JP, Russo RR, March L, Cumming R, Cameron I, Brnabic AJ. Antibiotic prophylaxis in hip fracture surgery: a metaanalysis. *Clinical Orthopaedics & Related Research* 2004;419:179-84.
119. Boxma H, Broekhuizen T, Patka P, Oosting H. Randomised controlled trial of single dose antibiotic prophylaxis in surgical treatment of closed fractures: the Dutch Trauma Trial. *Lancet* 1996;347:1133-37.
120. Beaupre LA, Jones CA, Saunders LD, Johnston DWC, Buckingham J, Majumdar SR. Best practices for elderly hip fracture patients: A systematic overview of the evidence. *Journal of General Internal Medicine* 2005;20:1019-25.
121. Barker IF, McCormick PC, Haines SJ, Benzel EC. Efficacy of prophylactic antibiotic therapy in spinal surgery: A meta-analysis. *Neurosurgery* 2002;51:391-401.
- 122 Bert J, Giannini D, Nace L. Antibiotic prophylaxis for arthroscopy of knee: is it necessary. *Arthroscopy* 2007;23:1-3



123. Pugh BA, Potter HG, McGowan AW, Faglia L, W. S. Anako A, B. Stizans I, V. et al. Prophylactic sulfamethoxazole prophylaxis. Topical systemic or intravenous? *Ann Surg* 1985;192:356-64.

124. Stewart AD, Hayes PSL, Jr, Strydom WJ, Brennan T. Prevention of urinary tract infection in the community. *Database of Syst Rev* 2006;3:CD003073;127:449-51.

125. MacGowan MS, Johnson C. Benefit of perioperative antibiotic prophylaxis in antibiotic prophylaxis for patients: a meta-analysis. *Rev Infect Dis* 1991;13:879-89.

126. Draft of the National Nosocomial Infection Survey (NNIS) System. *Respon, Inf Data* 1998;6:1167-92. Antibiotic prophylaxis in transurethral resection of the prostate. *National Nosocomial Infection Survey (NNIS) System. Respon, Inf Data* 1998;6:1167-92. January 1992 to June 2002. *Am J Infect Control* 2002;30:458-75.

127. Magiera TG, Bott M, H, R. K. S. M. G. H. K. H. M. R. A. M. D. C. W. T. F. M. J. M. D. L. O. K. M. P. A. L. E. U. S. P. A. C. I. L. L. A. B. E. T. A. I. N. S. T. U. D. Y. A. N. A. D. U. L. I. A. N. D. P. R. O. P. H. Y. L. A. X. I. S. F. O. R. F. O. R. S. S. U. R. G. I. C. A. L. P. R. O. C. E. D. U. R. A. N. D. U. R. O. L. O. G. Y. *J Thorac Cardiovasc Surg* 1992;104:1423-31.

128. Miller JB, Golji H, Dunshee CJ. Comparison of single-dose antibiotic prophylaxis in transurethral prostatectomy. *Urology* 1987;6:196-201.

129. Bekris A, Ferratt R. Risk factors for antibiotic allergy. In *Allergy Clin Immunol* 1984;70:567-72.

130. Davi P, Reid D, Hailberg B, Childers G, Lancaster D, Mangin P. The value of antibiotic prophylaxis in the treatment of bacterial meningitis. *Am J Clin Pathol* 1993;97:82-8.

131. S. O. G. A. H. 1968;38:159-88.

132. S. O. G. A. H. 1968;38:159-88.

133. P. A. S. P. H. A. C. A. N. T. I. B. I. O. T. I. C. S. I. N. G. A. T. I. O. N. O. F. T. H. E. N. E. E. F. F. E. C. T. I. V. E. P. R. O. P. H. Y. L. A. X. I. S. A. N. D. T. H. E. I. M. P. A. C. T. I. V. E. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Arch Surg* 2000;135:674-9.

134. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

135. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

136. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

137. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

138. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

139. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

140. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

141. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

142. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

143. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

144. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

145. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

146. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

147. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

148. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

149. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

150. A. N. T. I. B. I. O. T. I. C. P. R. O. P. H. Y. L. A. X. I. S. I. N. T. H. E. T. R. E. A. T. M. E. N. T. *Ann Surg* 1978;188:283-9.

with polypropylene mesh: the randomized, double-blind, prospective trial. *Ann Surg* 2001;233:26-33.

145. Whitby M, Johnson BC, Atkinson RL, Stuart G. The comparative efficacy of intravenous cefotaxime and trimethoprim/sulfamethoxazole in preventing infection after neurosurgery: a prospective, randomized study. Brisbane Neurosurgical Infection Group *Br J Neurosurg* 2000;14:13-18.

146. Zhu XL, Wong WK, Yeung WM et al. A randomized, double-blind comparison of ampicillin/sulbactam and ceftriaxone in the prevention of surgical-site infections after neurosurgery. *Clin Ther* 2001;23:1281-91.

147. Saginur R, Croteau D, Bergeron MG. Comparative efficacy of teicoplanin and cefazolin for cardiac operation prophylaxis in 3,027 patients. The ESPRIT Group. *J Thorac Cardiovasc Surg* 2000;120:1120-30.

148. Kriaras I, Michalopoulos A, Turina M, Geroulanos S. Evolution of antimicrobial prophylaxis in cardiovascular surgery. *Eur J Cardiothorac Surg* 2000;18:440-46.

149. Finkelstein R, Rabino G, Mashiah T, Bar-El Y, Adler Z, Kertzman V, Cohen O, Milo S. Vancomycin versus cefazolin prophylaxis for cardiac surgery in the setting of a high prevalence of methicillin-resistant staphylococcal infections. *J Thor Cardiovasc Surg* 2002;123:326-32.

150. Dietrich ES, Bieser U, Frank U, Schwarzer G, Daschner FD. Ceftriaxone versus other cephalosporins for perioperative antibiotic prophylaxis: A meta-analysis of 43 randomized controlled trials. *Chemotherapy* 2002;48:49-56.

151. Esposito S, Noviello S, Vanasia A, Venturino P. Ceftriaxone versus Other Antibiotics for Surgical Prophylaxis: A Meta-Analysis. *Clinical Drug Investigation* 2004;24:29-39.

152. Goldman DA, Weinstein RA, Wenzel RP, Tablan OC, Duma RJ, Gaynes RP et al. Strategies to prevent and control the emergence and spread of antimicrobial resistant microorganisms in hospitals. A challenge to hospital leadership. *JAMA* 1996;275:234-40.

153. Ballow CH, Schentag JJ. Trends in antibiotic utilisation and bacterial resistance. Report of the National Nosocomial Resistance Surveillance Group. *Diagn Microbiol Infect Dis* 1992;15:37S-42S.
154. Salminen US, Viljanen TU, Valtonen VV, Ikonen TE, Sahlman AE, Harjula AL. Ceftriaxone versus vancomycin prophylaxis in cardiovascular surgery. *J Antimicrob Chemother* 1999;44:287-90.
155. den Hoed PT, Boelhouwer RU, Veen HF, Hop WC, Bruining HA. Infections and bacteriological data after laparoscopic and open gallbladder surgery. *J Hosp Infect* 1998;39:27-37.
156. Sanderson PJ. Prophylaxis in orthopaedic implant surgery -should we use a glycopeptide? *J Antimicrob Chemother* 1998;41:322-25.
157. Scottish Office Department of Health. Hospital acquired infection -a framework for a national system of surveillance for the NHS in Scotland. Edinburgh: Scottish Office, 1999.
158. Marroni M, Cao P, Fiorio M, Maghini M, Lenti M, Repetto A, Menichetti F. Prospective, randomized, double-blind trial comparing teicoplanin and cefazolin as antibiotic prophylaxis in prosthetic vascular surgery. *Eur J Clin Microbiol Infect Dis* 1999;18:175-78.
159. Periti P, Stringa G, Mini E. Comparative multicenter trial of teicoplanin versus cefazolin for antimicrobial prophylaxis in prosthetic joint implant surgery. Italian Study Group for Antimicrobial Prophylaxis in Orthopedic Surgery. *Eur J Clin Microbiol Infect Dis* 1999;18:113-19.
160. Vuorisalo S, Pokela R, Syrjala H. Comparison of vancomycin and cefuroxime for infection prophylaxis in coronary artery bypass surgery. *Infect Control Hosp Epidemiol* 1998;19:234-39.
161. Bolon MK, Morlote M, Weber SG, Koplan B, Carmeli Y, Wright SB. Glycopeptides are no more effective than beta-lactam agents for prevention of surgical site infection after cardiac surgery: A meta-analysis. *Clin Infect Dis* 2004;38:1357-63.

162. Vardakas KZ, Soteriades ES, Chrysanthopoulou SA, Papagelopoulos PJ, Falagas ME. Perioperative anti-infective prophylaxis with teicoplanin compared to cephalosporins in orthopaedic and vascular surgery involving prosthetic material. *Clinical Microbiology and Infection* 2005;11:775-7.
163. Recommendations for preventing the spread of vancomycin resistance. Recommendations of the Hospital Infection Control Practices Advisory Committee (HICPAC) US Department of Health and Human Service, Centers for Disease Control and Prevention, September 1995. (<http://www.cdc.gov/drugresistance/technical/clinical.htm>)
164. Gemmell CG, Edwards DI, Fraise AP, Gould KF, Ridgway GL, Warren RE. Guidelines for the prophylaxis and treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in the UK. *Journal of Antimicrobial Chemotherapy* (2006);57:589–608.
165. Burke JF. The effective period of preventive antibiotic action in experimental incision and dermal lesions. *Surgery* 1961;50:161-68. 166. Weinstein WM, Onderdonk AB, Bartlett JG, Gorbach SL. Experimental intra-abdominal abscesses in rats: development of an experimental model. *Infect Immun* 1974;10:1250-55.



170. van Dijk-van Dam MS, Moll FL, de Letter JA, Langemeijer JJ, Kuks PF. The myth of the second prophylactic antibiotic dose in aortoiliac reconstructions. *Eur J Vasc Endovasc Surg* 1996;12:428-30.
171. Vuorisalo S, Pokela R, Syrjala H. Is single-dose antibiotic prophylaxis sufficient for coronary artery bypass surgery? An analysis of peri-and postoperative serum cefuroxime and vancomycin levels. *J Hosp Infect* 1997;37:237-47.
172. Cuthbertson AM, McLeish AR, Penfold JC, Ross H. A comparison between single and double dose intravenous Timentin for the prophylaxis of wound infection in elective colorectal surgery. *Dis Colon Rectum* 1991;34:151-55.
173. Scher KS. Studies on the duration of antibiotic administration for surgical prophylaxis. *Am Surg* 1997;63:59-62.
174. Zanetti G, Flanagan J, Cohn LH, Giardina R, Platt R. Improvement of intraoperative antibiotic prophylaxis in prolonged cardiac surgery by automated alerts in the operating room. *Infection Control and Hospital Epidemiology* 2003;24:13-6.
175. Zanetti G, Giardina R, Platt R. Intraoperative redosing of cefazolin and risk for surgical site infection in cardiac surgery. *Emerging Infectious Diseases* 2001;7:828-31.
176. Stone H.H. Basic principles in the use of prophylactic antibiotics. *J Antimicrob Chemother* 1984;14:335-51.
177. Gately M, Edgers J, Stroh J, Spino M, Bannatyne R et al. The timing of prophylactic antimicrobial agents and the risk of surgical-wound infection. *Am J Surg* 1992;164:281-86.
178. Wollins KH, Bachler M, Kluger P, Mehrkens HH, Marre R et al. Antipostoperative wound infections: the most important factor. *Clin Infect Dis* 2007;44:921-7.
179. Van Kesteren IJ, Maoniefu O, Ome A, Kelsberg B, de Boer AS, Gysse JG. Antipostoperative wound infections: the most important factor. *Clin Infect Dis* 2007;44:921-7.
180. Verhoef J. Single-dose prophylaxis with broad-spectrum penicillins (piperacillin and

mezlocillin) in gynaecologic oncological surgery, with observation on serum and tissue concentrations. *Eur J Obstet Gynecol Reprod Biol* 1990;36:137-45.

180. Sue D, Salazar TA, Turley K, Guglielmo BJ. Effect of surgical blood loss and volume replacement on antibiotic pharmacokinetics. *Ann Thorac Surg* 1989;47:857-59.

181. Culver DH, Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG et al. Surgical wound infection rates by wound class, operative procedure, and patient risk index. National Nosocomial Infections Surveillance System. *Am J Med* 1991;91:152-57.

182. McDonald M, Grabsch E, Marshall C, Forbes A. Single-versus multiple-dose antimicrobial prophylaxis for major surgery: a systematic review. *Aust NZ J Surg* 1998;68:388-96.

183. Wymenga A, van Horn J, Theeuwes A, Muytjens H, Slooff T. Cefuroxime for prevention of postoperative coxitis. One versus three doses tested in a randomized multicenter study of 2,651 arthroplasties. *Acta Orthop Scand* 1992;63:19-24.

184. Zelenitsky SA, Silverman RE, Duckworth H, Harding GK. A prospective, randomized, double-blind study of single high dose versus multiple standard dose gentamicin both in combination with metronidazole for colorectal surgical prophylaxis. *J Hosp Infect* 2000;46:135-40

185. Patacchiola F, Di Paolantonio L, Palermo P, Di Stefano L, Mascaretti G, Moscarini M. Profilassi antibiotica delle complicanze infettive dopo taglio cesareo. Nostra esperienza. [Antibiotic prophylaxis of infective complications after caesarean section. Our experience]. *Minerva Ginecol* 2000;52:385-89.

186. Hall JC, Christiansen KJ, Goodman M, Lawrence-Brown M, Prendergast FJ, Rosenberg P et al. Duration of antimicrobial prophylaxis in vascular surgery. *Am J Surg* 1998;175:87-90.

187. Steering Group of the Second National Prevalence Survey. National prevalence survey of hospital acquired infections: definitions. *J Hosp Infect* 1993;24:69-76.

188. Crowe MJ, Cooke EM. Review of case definitions for nosocomial infection -towards a consensus. Presentation by the Nosocomial Infection Surveillance Unit (NISU) to the Hospital Infection Liaison Group, subcommittee of the Federation of Infection Societies (FIS). *J Hosp Infect* 1998;39:3-11.
189. Gatell JM, Garcia S, Lozano L, Soriano E, Ramon R, SanMiguel JG. Perioperative cefamandole prophylaxis against infections. *J Bone Joint Surg Am* 1987;69:1189-93.
190. Engesaeter IB, lie SA, Espehaug B, Furnes o, vollset SE, Havelin II. Antibiotic prophylaxis in total hip arthroplasty: effects of antibiotic prophylaxis systemically and in bone cement on the revision rate of 22.170 primary hip replacements followed 0-14 years in the Norwegian Arthroplasty Register. *Acta orthopaedica Scandinavica* 2003;74:644-51.
191. Mui LM, Ng CS, Wong SK, Lam YH, Fung TM, Fok KL et al. Optimum duration of prophylactic antibiotics in acute non-perforated appendicitis. *ANZ. J. Surg.* 2005;75:425-8.
192. Mohri Y, Tonouchi H, Kobayashi M, Nakai K, Kusunoki M; Mie Surgical Infection Research Group. Randomized clinical trial of single-versus multiple-dose antimicrobial prophylaxis in gastric cancer surgery. *Br J Surg.* 2007;94:683-8
193. Su HY, Ding DC, Chen DC, Lu MF, Liu JY, Chang FY Prospective randomized comparison of single-dose versus 1-day cefazolin for prophylaxis in gynecologic surgery. *Acta Obstet Gynecol Scand.* 2005;84:384-9.
194. Davey P, Dodd T, Kerr S, Malek M. Audit of IV antibiotic administration. *Pharm J* 1999;244:793-96.
195. Talon D Evaluation of current practices in surgical antimicrobial prophylaxis before and after implementation of local guidelines. *J of Hosp Inf* 2001;49:193-98.
196. Alerany C, Campany D, Monterde J, Semeraro C. Impact of local guidelines and an integrated dispensing system on antibiotic prophylaxis quality in a surgical centre. *J Hosp Infect* 2005;60:111-117.

197. Brusaferrò S, Rinaldi O, Pea F, Faruzzo A, Barbone F. Protocol implementation in hospital infection control practice: an Italian experience of preoperative antibiotic prophylaxis. *J of Hosp Inf* 2001;47:288-293.
198. Wax DB, Beilin Y, Levin M, Chadha N, Krol M, Reich DL. The effect of an interactive visual reminder in an anaesthesia information management system on timeliness of prophylactic antibiotic administration. *Int Anaest Res Soc* 2007;104:1462-1465.
199. O'Reilly M, Talsma A, VanRiper S, Kheterpal S, Burney R. An Anesthesia Information System Designed to Provide Physician-specific feedback improves timely administration of prophylactic antibiotic. *Int Anaest Res Soc* 2006;103:908-12.
200. Wax DB, Beilin Y, Levin M, Chadha N, Krol M, Reich DL. The effect of an interactive visual reminder in an anaesthesia information management system on timeliness of prophylactic antibiotic administration. *Int Anaest Res Soc* 2007;104:1462-146.
201. Capuano A, Noviello S, Avolio A, Mazzeo F, Ianniello F, Rinaldi B, Ferrante L, Capuano M, Esposito S, Rossi F. Antibiotic prophylaxis in surgery: an observational prospective study conducted in a large teaching hospital in Naples. *Journal of Chemotherapy* 2006;18:293-297
202. Foy R, Penney GC, Grimshaw JM; Ramsay CR.; Walker AE, MacLennan G, Stearns SC, McKenzie L. A randomized controlled trial of a tailored multifaceted strategy to promote implementation of a clinical guideline on induced abortion care. *BJOG* 2004;111:726-733.
203. Tan JA, Naik VN, Lingard L. Exploring obstacles to proper timing of prophylactic antibiotics for surgical site infections. *Qual Saf Health Care*. 2006;15:32-8.
204. Carlès M, Gindre S, Aknouch N, Goubaux B, Mousnier A, Raucoules-Aimé M. Improvement of surgical antibiotic prophylaxis: a prospective evaluation of personalized antibiotic kits. *J of Hosp Inf* 2006;62:372-375.

205. White A, Schneider T Improving compliance with prophylactic antibiotic administration guidelines. *AORN J* 2007;85:173-180.
206. Au P, Salama S, Rotstein C. Implementation and evaluation of a preprinted perioperative antimicrobial prophylaxis order form in a teaching hospital. *Can J Infect Dis* 1998;9:157-66.
207. Soumerai SB, Avorn J, Taylor WC, Wessels M, Maher D, Hawley SL. Improving choice of prescribed antibiotics through concurrent reminders in an educational order form. *Med Care* 1993;31:552-58.
208. Marr JJ, Moffet HL, Kunin CM. Guidelines for improving the use of antimicrobial agents in hospitals: a statement by the Infectious Diseases Society of America. *J Infect Dis* 1988;157:869-76.
209. Girotti MJ, Fodoruk S, Irvine-Meek J, Rotstein OD. Antibiotic handbook and preprinted perioperative order forms for surgical antibiotic prophylaxis: do they work? *Can J Surg* 1990;33:385-88.
210. Martin C, Pourriat JL. Quality of perioperative antibiotic administration by French anaesthetists. *J Hosp Infect* 1998;40:47-53.
211. Dobranski S, Lawley DI, McDermott I, Selby M, Ausobsky JR. The impact of guidelines on peri-operative antibiotic administration. *J Clin Pharm Therap* 1991;16:19-24.
212. Wilson W, MD, Taubert KA, Gewitz M et al. Prevention of Infective Endocarditis. Guidelines From the American Heart Association. A Guideline From the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group *Circulation* 2007;116:1736-54
213. Lockhart PB, Loven B, Brennan MT, Fox FC. The evidence base for the efficacy of antibiotic prophylaxis in dental practice. *JADA* 2007;138:458-474.

214. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008;36:309-32.

215. Bratzler DW, Houck PM, for the Surgical Infection Prevention Guidelines Writers Workgroup. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Clin Infect Dis.* 2004;38:1706-15.