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July 2006, Volume 96, No. 7 (Part 2)

ISSN 0256-9574

PRINTED BY TANDYM PRINT

GUIDELINE FOR THE MANAGEMENT OF NOSOCOMIAL INFECTIONS IN SOUTH AFRICA

Published by Media Outsourcing on behalf of SAMA Health and Medical Publishing Group, Suites 1-2, Lonsdale Building, Gardener Way, Pinelands, 7405. Tel. (021) 530-6520. Fax (021) 531-4126. E-mail: publishing@samedical.org
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CLINICAL GUIDELINE

Guideline for the Management of Nosocomial Infections in South Africa

Adrian Brink, Charles Feldman, Adriano Duse, Dean Gopalan, David Grolman, Mervyn Mer, Sarala Naicker, Graham Paget, Olga Perovic, Guy Richards

Objective. To write a guideline for the management and prevention of nosocomial infections in South Africa in view of the following:

- Nosocomial infections are a common and increasing problem globally, including South Africa
- Widely varying standards of prevention and management of these important infections
- Increasing and emerging antimicrobial resistance among commonly isolated pathogens
- The significant economic burden of these infections on the health care system as well as their impact on patient morbidity and mortality.

The main aims of the guideline are to provide recommendations for the initial choice of antimicrobial agents and the appropriate management of these infections encompassing the following conditions: (*i*) nosocomial pneumonia, health care-associated pneumonia and ventilator-associated pneumonia; (*ii*) nosocomial bloodstream infections; (*iii*) nosocomial intravascular infections; (*iv*) nosocomial urinary tract infections; (*v*) nosocomial intra-abdominal infections; and (*vi*) nosocomial surgical skin and soft-tissue infections.

Evidence. Working group of clinicians from relevant disciplines, following detailed literature review.

Recommendations. These include details of the likely pathogens, an appropriate diagnostic approach, antibiotic treatment options and appropriate preventive strategies.

Endorsement. The guideline document was endorsed by the South African Thoracic Society, the Critical Care Society of Southern Africa and the Federation of Infectious Diseases Societies of Southern Africa.

Guideline sponsor. The meeting of the Working Group and the guideline publication were sponsored by an unrestricted educational grant from Sanofi Aventis South Africa.

S Afr Med J 2006; **96:** 642-652.

1. Process of guideline development

The South African Thoracic Society (SATS) was offered an unconditional educational grant from Sanofi-Aventis to develop a guideline for the management of nosocomial infections in South Africa. Professor Charles Feldman, as Council Member of SATS, offered to organise the development of such a guideline. On invitation, Professor Guy Richards (Critical Care Society of Southern Africa) and Dr Adrian Brink (Infectious Diseases Society of South Africa) agreed to co-organise the guideline development.

Members of the editorial board prepared draft documents on the various topics. These were circulated initially to the editorial board for comment and then to a working group drawn from professionals around the country, representing the private and public sector and including individuals from various disciplines, viz. physicians, infectious disease specialists, pulmonologists, intensivists, trauma surgeons, cardiothoracic surgeons, clinical microbiologists, and nephrologists.

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A workshop meeting was held at Caesar's Palace, Johannesburg, in February 2005 at which the papers were presented to the group, critiqued, and specific final decisions were taken on the various recommendations. Changes were made to the original draft documents by the editorial team, and the documents were then re-circulated to the workshop group for comment.

The complete and detailed background guideline was published in the June 2005 issue of the *Southern African Journal of Epidemiology and Infection* (*SAJEI* 2005; **20:** 37-76 (**www.fidssa.co.za**), link to guidelines). The guideline presented here is a summarised version, and includes antibiotic dosages.

2. Statement

This statement is published for educational purposes only. The recommendations are based on currently available scientific evidence together with the consensus opinion of the authors and the working group. The guideline is not meant to replace clinical judgement, but rather to give logical framework to the evaluation of patient management.

3. Authors of the guideline

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4. Working group members

The authors above plus: V Ballhausen, A L Biebuyck, D J du Toit, P J du Toit, L Fingelson, P Grolman, G Hammond, E Hodgson, I Hunt, J Kilian, G Kretsmer, L Krige, G Lups, G Maartens, A Mackinlay, D Muckart, H Pahad, A Pieterse, A Roodt, G Schleicher, M A Seedat, M Senekal, W Sieling, M Sussman, M van der Heiden, H van Straaten, J A Venter, L A Venter, P Williams.

5. Infection control in developing countries, with particular emphasis on South Africa

Health care-associated infections (HAIs) are a cause of significant morbidity and mortality in patients receiving health care, and the costs (direct and indirect) of these infections deplete the already limited financial resources allocated to health care delivery.

- Approximately 1 in 7 patients entering South African hospitals are at high risk of acquiring an HAI.
- Lower respiratory tract infections, urinary tract infections, bloodstream infections and post-surgical infections account for the majority (about 80%) of HAIs.
- Indiscriminate and inappropriate use of antibiotics leads to the selection of antimicrobial-resistant organisms.
- Bi-directional flow of resistance from hospitals into communities and vice versa makes it difficult to distinguish community-acquired multidrug-resistant pathogens from those that are nosocomial.
- To counter the emergence and spread of multidrug-resistant pathogens the only feasible strategy is the implementation of an effective and integrated programme that involves antimicrobial resistance surveillance, a rational antimicrobial-use programme, and infection control.
- Infection control activities on their own are primarily centred around the goal of decreasing or preventing the transmission of nosocomial (health care-associated) pathogens to patients and staff, irrespective of whether these organisms are multidrug-resistant or not.
- To further reduce and control the emergence of antimicrobial resistance it is therefore essential that infection control activities be coupled with an optimised, effective and highly restrictive antimicrobial-use programme.
- Most importantly, such a programme must be realistic, adaptable, and take cognisance of the severe limitation of resources characteristic of many developing countries.

In order to develop simple, effective and sensible infection control interventions it is necessary to understand the sources of HAIs and their modes of transmission.

5.1 Transmission of HAIs

HAIs are transmitted in three ways.

- **Contact spread** involves skin-to-skin contact and the direct physical transfer of micro-organisms from one patient to another or by a health care worker (HCW). Examples of direct contact include patient examination, with cross-infection occurring from contaminated hands of the HCW. Although hand washing is singly the most important, evidence-supported intervention for the prevention of transmission of organisms as a consequence of direct contact, compliance is only 40% in intensive care units (ICUs). Indirect contact refers to contact with inanimate objects or surfaces such as bedpans, thermometers, etc. that are contaminated with microbes. Organisms such as methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, extended-spectrum beta-lactamase (ESBL)-producing Gram-negatives, and *Clostridium difficile* are typically spread by direct and/or indirect contact routes.
- **Droplet spread** involves spread of pathogens by respiratory droplets produced during coughing, sneezing, talking, respiratory therapy and procedures such as bronchoscopy. Respiratory droplets larger than 5 microns do not remain suspended (airborne) in the air for long periods of time and fairly close contact with patients (within 1 - 2 m) is required for transmission to occur. Organisms such as *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Mycoplasma pneumoniae*, infections such as pneumonic plague and streptococcal pharyngitis and viral infections such as influenza virus infections are spread via this route.
- **Airborne spread** occurs when droplets less than 5 microns in size are produced by coughing, sneezing, or consequent to procedures such as bronchoscopy and suctioning. These small droplets desiccate to form droplet nuclei that remain suspended in the air for long periods and travel long distances. The airborne nature of these contaminated droplet nuclei enables them to infect susceptible hosts several metres away from where they are produced. Organisms typically spread by this route include *Mycobacterium tuberculosis*, measles virus and varicella-zoster virus.

5.2 Prevention and control of HAIs

- All patients presenting to health care facilities, irrespective of their diagnoses, must be treated using standard precautions. These include hand washing (using either aqueous or non-aqueous hand decontamination agents), wearing of personal protective equipment as necessary (gloves, masks, gowns, and eye protection), safe disposal of waste, appropriate

cleaning, disinfection, or sterilisation of equipment and patient-care items as well as appropriate decontamination of linen and the environment. Stringent attention to aseptic technique is crucial.

- In addition to standard precautions, additional patient isolation procedures (contact isolation, droplet isolation and airborne isolation) are required, depending on the mode of transmission of the suspected micro-organism.
- The judicious use of preoperative prophylaxis to prevent post-surgical infections cannot be overemphasised.

5.3 Infection control and prevention programmes

- The efficacy of infection control and prevention programmes in decreasing HAIs (especially in outbreak situations), patient morbidity and mortality, and cost to health care institutions is well established.
- Regrettably the implementation and/or quality of such programmes is variable across South African health care facilities.
- Good and standardised surveillance systems for HAIs are not currently in place in most South African health care institutions.
- HAIs are under-reported and data on antimicrobial resistance trends are only available for academic hospitals and from private-sector microbiology laboratories.
- It is crucial that the true impact of HAIs and of antimicrobial resistance on health care delivery be documented accurately and that strategies be formulated to minimise these problems.
- Education on infection control and correct antimicrobial prescribing is often neglected in undergraduate curricula of the health sciences.

Multiple interventions are available that may help to minimise or control nosocomial infections and the development and spread of microbial resistance to antimicrobial agents. Strategies to prevent and control the emergence and spread of antimicrobial-resistant micro-organisms may be grouped into those aimed at optimising antimicrobial use and those preventing the transmission of resistant organisms.

5.4 Interventions aimed at optimising antimicrobial use

- Optimising antimicrobial prophylaxis for operative procedures.
- Optimising the choice and duration of empirical treatment.
- Improving antimicrobial prescribing by educational and administrative means.
- Monitoring and providing feedback on antibiotic resistance.
- Defining and implementing health care delivery system guidelines for important types of antimicrobial use.

5.5 Interventions aimed at preventing nosocomial transmission of resistant organisms

- Developing systems to recognise and report trends in antimicrobial resistance within institutions.
- Developing systems to rapidly detect and report resistant micro-organisms in individual patients and ensuring rapid response by caregivers.
- Increasing adherence to basic infection control policies and procedures.
- Incorporating detection, prevention, and control of antimicrobial resistance into institutional strategic goals and providing the required resources.
- Developing a plan for identifying, transferring, discharging, and readmitting patients colonised with specific antimicrobial-resistant pathogens.

As we are seeing increasing numbers of vulnerable individuals at our health care facilities we should be continuously aware of the consequences of poor infection control practices and the misuse and abuse of the antimicrobial armamentarium. Good infection control practices can usually contain the majority of infections, including those caused by multidrug-resistant organisms, using simple measures. An infection control programme is as effective as the personnel responsible for its implementation: dedication, knowledge, education, constructive feedback and sensitivity to the needs of both patients and health care workers are essential. Furthermore, rational and restrictive antibiotic prescribing strategies together with continuing developments in the search for new antimicrobials must ensure that these so-called miracle drugs will retain their value in the treatment of infections in years to come. Education in infection control practices, nosocomial infection epidemiology, and antimicrobial resistance is critically important. The development of these guidelines is a step in the right direction.

6. Antimicrobial resistance in nosocomial infections in South Africa

In South Africa the following patterns of antimicrobial resistance have recently been noted:

- A dramatic increase in ESBL production, particularly in *Klebsiella* and *Enterobacter* spp.
- An increase in carbapenem resistance, including multidrug resistance in *Pseudomonas aeruginosa* and *Acinetobacter baumanii*.
- Emergence of carbapenem resistance in strains of *Enterobacter* spp. and *Klebsiella pneumoniae*.
- An increase in multidrug-resistant *Escherichia coli*.
- Emerging resistance among Gram-positive isolates including an increased prevalence of methicillin-resistant *S. aureus* (MRSA) and emergence of glycopeptide-resistant enterococci (GRE).

Antibiotic resistance is an inevitable consequence of the inappropriate use of antibiotics, and impacts on every hospital to varying degrees.

6.1 Risk factors for inappropriate antibiotic use

- Not using local epidemiological and antibiotic susceptibility data.
- Use of broad-spectrum antibiotics when not absolutely necessary.
- Treatment of contamination or colonisation rather than invasive infection.
- Inappropriate surgical prophylaxis.
- Excessive antimicrobial treatment (i.e. continuing antibiotics when infection is cured).

6.2 Recommendations for the antimicrobial management of nosocomial infections

- Early appropriate empirical antibiotic therapy for severe nosocomial infections reduces mortality.
- Timeous broad-spectrum empirical therapy must be utilised for nosocomial infections until the pathogen is identified.
- Prescribe an initial antibacterial regimen that will cover the most likely pathogens associated with infection, based on local surveillance ('know your bugs').
- However, increased use of antimicrobial therapy with this practice ('getting it right the first time') may inevitably lead to increase in resistance.
- Therefore antibiotic therapy is subsequently scaled down, de-escalated or tailored to a narrow spectrum once identity and susceptibility patterns of the infecting pathogen(s) are known.
- Shorter duration of therapy is currently recommended because antibiotics that are continued after an infection has resolved are harmful in that they predispose to superinfection with more resistant bacteria.

6.3 General principles for the duration of antibiotic treatment

- If a response to a particular antibiotic is seen within 48 hours, treatment should be continued for another 5 - 7 days after which it should be discontinued.
- Prolonged use beyond a week is therefore strongly discouraged for most nosocomial infections.
- If no response is seen in 48 hours:
  - Discontinue the antibiotic
  - Re-culture the patient
  - Review source control
  - Switch to another class of antibiotic.
- If septic markers worsen on an antibiotic, resistance should be considered and a change to another class also made.

6.4 Measures to reduce nosocomial infections

In the past not enough attention was given to prevention of infection. Accepted practices include:

- Elevation of the head of the bed in ventilated patients
- Perioperative normothermia
- Restriction of blood transfusions
- Early enteral nutrition
- Avoidance of urinary catheters wherever possible
- Recently, intensive insulin therapy in critically ill patients has been shown to reduce mortality
- Implementation of special 'programmes' such as for the prevention of ventilator-associated pneumonia (VAP) or central venous catheter infections.

6.5 Dilemmas in the antimicrobial management of nosocomial infections

- Combination versus monotherapy – 'should antibiotics be combined?'
  - There is no evidence that a combination of antibiotics increases efficacy or decreases resistance, particularly when using the newer antimicrobial agents such as the 4th generation cephalosporins (i.e. cefepime), beta-lactam/betalactamase inhibitor combination agents (i.e. piperacillin/tazobactam), fluoroquinolones (i.e. ciprofloxacin, levofloxacin) and the carbapenems (i.e. imipenem, meropenem).
  - Controversy still currently exists with regard to whether mono- or combination therapy is optimal for pseudomonal infections, particularly in the critically ill patient.
- Antibiotic cycling – 'should antibiotics be rotated?'
  - Antibiotic cycling has been suggested as a means of reducing antibiotic pressure and selection of resistant mutants. A recent review of antibiotic cycling or rotation concluded that studies do not permit reliable conclusions regarding efficacy of cycling. Therefore routine implementation of cycling as a means of reducing antibiotic resistance rates is currently not advised.

6.6 A systematic approach in selecting an antibiotic for nosocomial infections

A systematic approach in selecting an antibiotic promotes appropriate antimicrobial use. The following should be considered:

- Which pathogens are likely to be encountered?
- What are the likely susceptibility patterns of these

pathogens?

- What is the antimicrobial spectrum of the chosen antibiotic?
- Use appropriate dosing schedules based on the pharmacokinetic and pharmacodynamic properties of the chosen agent.
- What are the pharmacological considerations in the patient?
- Direct therapy to a narrow spectrum once microbiology results are available.
- But foremost, always consider whether an antibiotic is really necessary.

7. Management of nosocomial pneumonia, health care-associated pneumonia, and ventilator-associated pneumonia

7.1 Definitions

- Nosocomial pneumonia (NP) or hospital-acquired pneumonia (HAP) is a pneumonia occurring ≥ 48 hours after hospital admission that was neither present nor incubating at the time of admission to hospital.
- VAP is a pneumonia occurring in a patient undergoing mechanical ventilation that was neither present nor incubating at the time of intubation (occurring > 48 hours after intubation).
- Health care-associated pneumonia (HCAP) is a pneumonia occurring in a patient who has: (*i*) been hospitalised in an acute care hospital for 2 or more days within 90 days of the infection; (*ii*) resided in a nursing home or long-term care facility (LTCF); or (*iii*) received intravenous antibiotic therapy, chemotherapy, or wound care within the past 30 days of the current infection, or attended a hospital or haemodialysis clinic.

Microbiology of nosocomial pneumonia

- Early-onset bacterial NP occurring within the first 4 days in patients with no risk factors for multidrug-resistant bacteria is more frequently due to *S. pneumoniae, Haemophilus influenzae*, methicillin-sensitive *S. aureus* and *Moraxella catarrhalis* and antibiotic-sensitive aerobic, enteric Gram-negative bacilli. The latter include *Enterobacter* spp., *E. coli*, *Klebsiella* spp., *Proteus* spp., and *Serratia marcescens* ('core pathogens').
- Late-onset bacterial NP can occur with the same pathogens but is more commonly due to MRSA and multidrug-resistant pathogens including *Pseudomonas* spp., *Acinetobacter* spp., and *Klebsiella* spp. (including isolates producing ESBLs).
- The elderly residents of LTCFs have a spectrum of pathogens that more closely resemble that of late-onset HAP or VAP than early-onset HAP.

7.2 Diagnosis

- The most commonly used clinical definition of NP includes the following:
  - New or progressive radiographical shadowing

    Plus at least 2 of the following:
  - Fever ≥ 38.3ºC or hypothermia < 35ºC
  - Leukocytosis > 12 x 10^9/l or leukopenia < 4 x 10^9/l
  - Purulent respiratory secretions.
- Although a controversial area, more recent studies and guidelines suggest that invasive diagnostic techniques are not essential or routinely recommended for diagnosis of VAP.
- A fresh specimen of lower respiratory secretions should be submitted at the time of clinical diagnosis of possible NP (e.g. through a sterile suction catheter in patients who are intubated), before initiating antibiotic treatment.
- A chest radiograph, blood cultures and evaluation of oxygenation should also be undertaken and may be helpful in management of these cases.

7.3 Management

- Initiate antibiotics as soon as possible once the presence of an active infection is suspected as the early initiation of antibiotics (within 24 hours and preferably 12 hours) to which the causative organisms are sensitive is associated with the best outcome.
- In the choice of empirical antibiotic therapy, consideration should be given to which antibiotics the patient has had in the recent past; it is preferable that an agent from a different class be used.
- Factors to consider in empirical therapy include:
  - Whether the pneumonia is of 'early' or 'late' onset
  - The severity of illness of the individual patient, including a consideration of whether the patient is in or out of the ICU, and
  - Whether there are any specific risks factors for infection with severe Gram-negative pathogens such as *Acinetobacter* and *Pseudomonas* spp.
- In patients not in an ICU, with an early and/or mild to moderately severe NP, and without specific risk factors for resistant pathogens such as *Pseudomonas* and *Acinetobacter* spp., initial antibiotic treatment should target the so-called 'core pathogens', which may be accomplished with the following various agents:
  - 3rd generation cephalosporins, particularly in regional centres outside the central academic and private sectors (i.e. ceftazidime, ceftriaxone, or cefotaxime)
  - 4th generation cephalosporin (i.e. cefepime)

- Beta-lactam/beta-lactamase inhibitor (i.e. piperacillin/tazobactam)
- Group 1 carbapenem (i.e. ertapenem)
- Fluoroquinolones (i.e. ciprofloxacin or levofloxacin), particularly if there is severe allergy to beta-lactams.

- In patients with additional risk factors for specific pathogens, cover for the 'core pathogens' and add specific treatment indicated below, if also required:
  - Anaerobes – piperacillin/tazobactam or ertapenem alone will be sufficient, or add metronidazole or clindamycin to cephalosporin- or fluoroquinolone-containing regimens
  - *S. aureus* – for methicillin-sensitive isolates add cloxacillin and for methicillin-resistant isolates add a glycopeptide (teicoplanin or vancomycin) or linezolid
  - ESBL-producing isolates – ertapenem.
- In patients with severe HAP, particularly those treated in the ICU, cases with VAP and cases with risk factors for infections with resistant Gram-negative pathogens, treatment should be instituted using one of the following agents:
  - 4th generation cephalosporin (i.e. cefepime)
  - Beta-lactam/beta-lactamase inhibitor (i.e. piperacillin/tazobactam)
  - Group 2 carbapenem (i.e. meropenem or imipenem/cilastatin)
  - Fluoroquinolone (ciprofloxacin or levofloxacin)
  - ± combinations of the above, such as with the addition of an aminoglycoside
  - Add vancomycin only if MRSA is strongly suspected. Alternatives include teicoplanin and linezolid. There is some emerging evidence of the possible advantage of linezolid over vancomycin for the treatment of proven HAP or VAP due to MRSA.
- Specific risk factors for resistant pathogens such as *Pseudomonas* and *Acinetobacter* spp. include:
  - Recent antibiotic treatment (preceding 90 days)
  - Present hospitalisation for a period of $\geq$ 5 days
  - Structural lung disease
  - High levels and frequency of antibiotic resistance in the community or the specific unit
  - Immunosuppression
  - HCAP.

7.4 Duration of therapy

- The general consensus is that treatment of NP, including VAP, has traditionally been longer than is required and the currently recommended treatment duration is 5 - 7 days.

7.5 Prevention

- The most important currently recommended preventive measures for VAP are:
  - Hand washing
  - Application of general infection control measures
  - General aseptic techniques
  - Judicious antibiotic use
  - Semi-recumbent patient positioning
  - Oral endotracheal tube
  - Oral gastric tube
  - Aseptic tracheal suctioning
  - Avoiding unplanned extubation
  - Less frequent ventilator tube changing
  - Heat and moisture exchangers with bacteriological filters.

8. Management of nosocomial bloodstream infections

8.1 Definition

- Bloodstream infection is referred to as being primary when there is no obvious source, or secondary when arising as a complication of infection elsewhere.

Microbiology of nosocomial bloodstream infections

- The micro-organisms responsible include Gram-positive and Gram-negative bacteria and/or fungi.
- The most common Gram-positive organisms include *S. aureus*, coagulase-negative staphylococci and enterococci
- The most common Gram-negative organisms include *Enterobacter* spp., *P. aeruginosa*, *E. coli*, *Klebsiella* spp., and *Acinetobacter* spp.

8.2 Management

- Seek a potential source of origin.
- Institute appropriate source control measures.
- The importance of source control cannot be overemphasised.
- Initiate appropriate antimicrobial therapy.
- Give suitable supportive interventions and care.
- Factors involved in the initial antimicrobial choice should include:
  - Consideration of the site of infection
  - Knowledge of prevalent and likely pathogens and their susceptibility patterns
  - Whether or not the patient is immunosuppressed.

9. Management of nosocomial intravascular infections

9.1 Definitions

- Catheter colonisation: growth of ≥ 15 colony-forming units (semi-quantitative culture) or ≥ 10^3 colony-forming units (quantitative culture) from a proximal or distal catheter segment in the absence of local or systemic infection.
- Local infection: erythema, tenderness, induration or purulence within 2 cm of the skin-insertion site of the catheter.
- Catheter-related bloodstream infection (CRBSI): isolation of the same organism (i.e. the identical species as per antibiogram) from culture (semi-quantitative or quantitative) of a catheter segment and from the blood of a patient with accompanying clinical symptoms and signs of bloodstream infection and no other apparent source of infection.

Microbiology of nosocomial intravascular infections

- Coagulase-negative staphylococci
- *S. aureus*
- *Candida* spp.
- *Acinetobacter* spp.
- *P. aeruginosa*
- *Stenotrophomonas maltophilia*
- *Klebsiella* spp.
- *Enterobacter* spp.
- *S. marcescens*
- *Citrobacter freundii*
- *Enterococcus* spp.
- *Bacillus* spp. (especially JK strains)

9.2 Diagnosis

- The clinical features are generally nonspecific and include fever, rigors, hypotension and confusion.
- Fundoscopy should always form part of the clinical examination.
- Blood cultures are central to the diagnosis of CRBSI.
- Paired quantitative cultures, which involve taking blood from both the catheter and a peripheral site, may be particularly useful where luminal colonisation is predominant.
- The most widely used laboratory technique for culturing the catheter is the semi-quantitative roll-plate method.
- Newer diagnostic culture techniques include the endoluminal brush and the Gram's stain and acridine-orange leukocyte cytospin (AOLC) test.

9.3 Management

- Treatment depends on the stage of infection and the pathogen.
- As a general rule, if CRBSI is suspected, the catheter must be removed and replaced only if necessary.
- Most of the infectious complications are self-limited and resolve after removal of the catheter.
- Empirical antibiotic therapy is not recommended unless there are specific indications. Indications for antibiotic therapy include:
  - Persistent sepsis despite catheter removal
  - Evidence of septic thrombosis of the great veins
  - Clinical or echocardiographic evidence of endocarditis
  - Metastatic foci of infection
  - Underlying valvular heart disease (especially prosthetic valves)
  - Underlying immunosuppressed state.
- In the setting of uncomplicated *S. aureus* CRBSI, the catheter should be removed and at least 2 weeks (and preferably 4 weeks) of parenteral antibiotics given because of a higher relapse rate with shorter courses.
- Systemic antifungal therapy (together with removal of the catheter) should be given in all cases of catheter-related candidaemia in view of the potentially significant sequelae. Amphotericin B and fluconazole (except for fluconazole-resistant organisms such as *Candida glabrata* and *C. krusei*) for at least 14 days have been shown to be equally effective. Newer antifungal agents such as voriconazole may also be considered.

9.4 Duration of central venous catheter (CVC) use

- The duration of CVC use has remained controversial.
- Several studies have shown the duration of catheterisation to be a risk factor for infection.
- Scheduled replacement remains widely practised.
- No catheter should be left in place longer than absolutely necessary.
- Over the past few years, antimicrobial-impregnated catheters have been introduced in an attempt to limit catheter-related infections (CRIs) and increase the time that CVCs can safely be left in place.

9.5 Prevention

- The protocol for insertion and maintenance of CVCs and recommendations regarding insertion, maintenance and use of intravascular devices in general, may be found in the original publication (**www.fidssa.co.za**).
- Strict adherence to hand washing and aseptic technique remains the cornerstone of prevention of CRI.
- Infusion therapy teams.
- Maximum sterile barriers with use of gloves, gowns, masks,

cap and large drape for line insertion.
- Cutaneous antimicrobials and antiseptics for skin decontamination before line insertion.
- Dressing: there has been ongoing debate concerning the best method of catheter dressing.

10. Management of nosocomial urinary tract infections (NUTIs)

10.1 Definitions

The urinary tract is usually sterile except for the distal urethra.

- Colonisation is defined as the presence of micro-organism/s in the urine without clinical manifestations.
- Urinary tract infection (UTI) is defined as invasive disease by micro-organisms, inducing an inflammatory response and symptoms and signs such as fever > 38°C, urgency, frequency, and dysuria without any other cause.
- Nosocomial urinary tract infection (NUTI) refers to a UTI acquired in a hospital setting.

Microbiology of NUTI

- Gram-negative pathogens, especially *E. coli* (50% of infections), also *Klebsiella, Proteus, Enterobacter* spp.
- Staphylococci
  - *S. aureus* (including MRSA)
  - Coagulase-negative staphylococci.
- Enterococci
  - *Enterococcus faecalis*.
- *P. aeruginosa*.
- *Candida* spp.
- Urinary tract pathogens such as *S. marcescens* and *Burkholderia cepacia* have special epidemiological significance; their isolation from catheterised patients suggests acquisition from an exogenous source.

10.2 Diagnosis

- Non-catheterised patients
  - In non-catheterised patients, significant bacteriuria associated with signs and symptoms of infection.
- Catheterised patients
  - Diagnosis of UTI in catheterised patients is problematic
  - Clinical symptoms are the key to diagnosis of infection in catheterised patients.
  - Symptoms indicative of infection in immunocompetent patients include fever and haematuria.

10.3 Management

Urinary colonisation

- This is not an indication for systemic antibiotic treatment, whether the patient is catheterised or not, diabetic, elderly, or presenting with urinary bladder dysfunction due to neurological disorders.
- Nevertheless treatment of urinary colonisation may be necessary in some specific cases:
  - When it poses a risk of morbidity and mortality in neutropenic, immunosuppressed, and pregnant patients.
  - In patients in a preoperative situation: surgery and urological explorations, implanting prostheses.
  - In patients with a joint, vascular, or cardiac prosthesis, when undergoing invasive procedures.

Bacterial NUTIs

All bacterial NUTIs should be treated, irrespective of whether the patient has a urinary catheter or not.

Antibiotic therapy

- In patients who are not severely ill:
  - Amoxicillin/clavulanate
  - Fluoroquinolones (ciprofloxacin, levofloxacin)
  - A 2nd (cefuroxime) or 3rd generation cephalosporin (cefotaxime, ceftriaxone, ceftazidime) which may be preferable in pregnant women
  - Aminoglycoside
  - Patients can be switched to oral therapy with a fluoroquinolone if culture results support the change of regimen
  - The switch to oral therapy can be made when the patient has no nausea or vomiting, no fever and no evidence of sepsis
  - Once culture results are known, antibiotic therapy can be adjusted if required.
- In patients who are severely ill with urosepsis:
  - 3rd generation cephalosporin (cefotaxime, ceftriaxone, ceftazidime)
  - 4th generation cephalosporin (cefepime)
  - Piperacillin/tazobactam
  - Amikacin or another aminoglycoside (monitor levels)
  - Fluoroquinolone (ciprofloxacin, levofloxacin). Avoid in pregnancy and children and rather consider a 3rd or 4th generation cephalosporin
  - If infection with an ESBL-producing micro-organism is suspected, treatment with a carbapenem (e.g. ertapenem) should be initiated. This is particularly likely to occur in elderly residents of long-term care facilities. Carbapenems may also be used as part of directed therapy based on microbiological testing.

10.4 Duration of treatment

- This depends on the site of infection.
- The treatment should be shorter for UTIs without parenchymatous infection or in patients without a urinary catheter, for a minimum of 7 days.
- Pyelonephritis requires a 10 - 14-day treatment regimen.

10.5 Nosocomial candiduria

- There is no indication for systemic antifungal treatment in *Candida* spp. colonisation. Removing or changing the urinary catheter is mandatory in *Candida* spp. colonisation.
- Candiduria may be a marker for disseminated candidiasis in ICU patients presenting with several colonised sites, in which case patients should be treated with systemic antifungals (amphotericin B as continuous infusion or fluconazole).
- An amphotericin B bladder washout may be useful where continued catheterisation is required and there is no evidence of upper urinary tract infection.
- A positive blood culture warrants systemic therapy as above.

10.6 Prevention

- The urinary catheter should be removed as soon as it is no longer necessary, or changed when drainage is mandatory.
- The indications for an indwelling urinary catheter and its duration must be limited and reassessed every day.
- The isolation of infected or colonised catheterised patients is recommended.
- It is strongly recommended that hands be disinfected with a hand sanitiser.
- For catheterised patients:
  - It is mandatory to use closed systems
  - Insertion of a permanent catheter must be performed under strict aseptic technique
  - Urine bags must be kept below the patient for gravity flow.

11. Management of nosocomial intra-abdominal infections

11.1 Definition

Nosocomial intra-abdominal infection (IAI) is defined as an IAI occurring more than 48 hours after hospital admission that was neither present nor incubating at the time of the patient's visit or admission to hospital. It may be postoperative or non-postoperative.

Microbiology of nosocomial intra-abdominal infections

- The most common organisms encountered are Gram-negative bacilli (*E. coli*, *P. aeruginosa*, *A. baumanii*, *Klebsiella* spp.), Gram-positive cocci (enterococci, *S. aureus*), anaerobic bacteria (*Bacteroides* spp.) and fungi (*Candida* spp.)
- Commonly encountered resistant organisms are:
  - ESBL-producing *Klebsiella* and *Enterobacter* spp. including *E. coli*
  - Enterococci, including those that are glycopeptide-resistant although these are infrequent in South Africa
  - *P. aeruginosa*
  - *A. baumanii*
  - *S. aureus*, especially those resistant to cloxacillin (MRSA)
  - Coagulase-negative staphylococci (CoNS)
  - *Candida* spp.
  - Device-associated infections are frequently due to resistant *S. aureus*, CoNS, *E. faecalis* and *E. faecium* (including glycopeptide-resistant species), ESBL producers and fungi.

11.2 Management

- Surgery remains the mainstay of treatment.
- Source control is the cornerstone in treating these infections successfully and failure to achieve this is associated with a very high mortality rate.
- Antibiotic therapy should be commenced empirically based on knowledge of the common causative organisms, surveillance data, and the prevalence and sensitivity of organisms within each unit.
- Where possible, therapy should be culture-driven.
- In this regard cultures should be performed initially and at each re-look laparotomy.
- There is also emerging evidence that antifungal preventive therapy (amphotericin B or fluconazole) may be beneficial especially in cases of necrotising pancreatitis and in patients with complicated IAIs, i.e. those with delayed initial surgery, those with anastomotic dehiscence, those requiring multiple re-look procedures and those who have received multiple courses of antibiotics.
- The Gram-negative fluoroquinolones (ciprofloxacin, levofloxacin) and cephalosporins have inadequate anaerobic activity when used as monotherapy.
- Additional anaerobic cover is unnecessary with the carbapenems or with piperacillin/tazobactam.
- In cases of suspected or confirmed ESBL infections, the carbapenems, and in particular ertapenem, are the agents of choice.
- Monotherapy is adequate for Gram-negative sepsis. Some practitioners may add an aminoglycoside or quinolone in the case of pseudomonal sepsis although the evidence for this practice is lacking.
- A glycopeptide (teicoplanin or vancomycin) should be added empirically, should there be a significant chance of

staphylococcal infection (MRSA or CoNS). De-escalation is essential if the organism is proved to be Gram-negative or if it is sensitive to less broad-spectrum agents.

- In the scenario of nosocomial IAI, where cultures reveal an isolated enterococcal infection, this should be treated according to sensitivity.
- Linezolid should be reserved for VRE and VREF infections, but may be used as second-line therapy for staphylococcal infection, which does not respond to glycopeptide therapy (review source control).

11.3 Duration of therapy

Duration should be guided by clinical response and shorter courses of antibiotics are now advocated, with no evidence having shown that therapy beyond 5 - 7 days is beneficial.

12. Management of nosocomial surgical skin and soft-tissue infections

12.1 Definition

- Surgical site infections (SSIs) may be divided into organ or body cavity infections and skin/skin-related structures/soft-tissue infections.
- SSIs may be further divided into those that are superficial, i.e. involving only skin and subcutaneous tissue, and deep SSIs involving fascia and muscle with or without superficial extension.
- Superficial SSIs occur within 30 days of a surgical operative incision.
- Deep SSIs usually occur within 1 month of the operation, but may present as much as 1 year later with implants or prostheses.

Microbiology of nosocomial surgical skin and soft-tissue infections

- The vast majority of SSIs are caused by skin commensals, usually *S. aureus* and coagulase-negative staphylococci (CoNS).
- Patients who have recently been hospitalised or on antibiotics, those currently in hospital and those from LTCFs are at risk for infection with more resistant organisms such as methicillin-resistant *S. aureus* (MRSA) or resistant Gram-negative organisms, *Klebsiella* spp., *Enterobacter* spp., *Pseudomonas* spp., etc.
- In patients undergoing hollow visceral or mucous membrane surgery, the endogenous flora usually cause subsequent infections. Usual pathogens are Gram-negative aerobic bacilli, enterococci, and occasionally anaerobes. Infections by staphylococci, *Pseudomonas*, *Proteus*, *Clostridia*, streptococci and *Candida* species are also not uncommon.
- In patients who have been in ICU additional pathogens to consider besides MRSA and *Pseudomonas* spp. are *Enterobacter* and *Acinetobacter* spp.

12.2 Management

- Debridement and source control are essential.
- Culture is mandatory for all SSIs.
- If the SSI is superficial and there is no evidence of systemic sepsis, an antibiotic is not necessary. Otherwise the antibiotic choice is determined by sensitivity or the potential for resistance and the site of surgery.
- Organisms cultured from patients who have been hospitalised or on antibiotics recently, those currently in hospital and those from LTCFs are particularly likely to be resistant. If Gram-positive organisms are isolated, a glycopeptide (teicoplanin or vancomycin) or linezolid is reasonable until sensitivities are available. If Gram-negative, a broad-spectrum agent such as a carbapenem, piperacillin/tazobactam, fluoroquinolone (ciprofloxacin, levofloxacin) or cefepime is indicated. De-escalate antibiotic therapy whenever possible.
- In patients who have had hollow visceral surgery or mucous membrane surgery, amoxycillin/clavulanate or a 2nd generation cephalosporin (cefuroxime) or a fluoroquinolone (ciprofloxacin, levofloxacin) is recommended. Metronidazole may be added as indicated. Alternatively ertapenem may be an option.
- If resistance is likely, broad-spectrum agents may be considered before availability of sensitivity.

12.3 Prevention

- Preoperative antiseptic washing has been shown to decrease the skin microbial count, but there is no definitive evidence that this decreases postoperative wound infection.
- Preoperative hair removal should be performed as close to the operating time as possible. Clippers are preferable to razors.
- Proper surgical site preparation with chlorhexidine-based, alcohol-based or iodine-based antiseptic solutions is essential.
- Apply guidelines for theatre and instrument preparation.
- The wearing of scrub suits, surgical caps, shoe covers, gowns, masks and gloves is standard worldwide.
- Meticulous adherence to asepsis is essential.
- The exact choice of agent for preoperative hand washing/scrubbing has not been shown to have a significant impact on SSI; alcohol, iodine and chlorhexidine solutions are all acceptable. Scrubbing itself is only of value under the nails and to remove macroscopic organic matter.
- Preoperative MRSA screening for high-risk elective surgical cases may be necessary including patients transferred from other hospitals and institutions.

Prophylactic antibiotic usage

- The choice of antibiotic depends on the site of surgery and the pathogens likely to be encountered.
- The best time to administer these antibiotics is within 30 minutes of the commencement of the operation.
- A single dose has been shown to be adequate in most cases. This should only be repeated if the duration of the operation exceeds the half-life of the selected antibiotic. Benefit has not been seen in further antibiotic dosing.
- Most clean surgical procedures do not require prophylactic antibiotics.
- For elective surgery, cefazolin (2 g) is usually recommended.
- Clindamycin is a reasonable alternative for penicillin allergy.
- For bone surgery, a 1st generation cephalosporin like cefazolin is sufficient.
- Glycopeptides are only rarely necessary and their use should be discouraged.
- For hollow visceral or mucous membrane surgery, amoxicillin/clavulanate or 2nd generation cephalosporin (cefuroxime) (1.5 g), with the addition of metronidazole or clindamycin to the latter, are the recommended agents.
- In patients who have been hospitalised for prolonged periods of time, piperacillin/tazobactam may be indicated although skin commensals are still the most likely organisms. If a patient is known to be colonised with MRSA or has had MRSA sepsis a glycopeptide (teicoplanin or vancomycin) or linezolid may be used.
- Most patients in ICU are already on antibiotics and do not need additional cover. If the unit has a high incidence of MRSA sepsis a glycopeptide (teicoplanin or vancomycin) or linezolid may be indicated.

13. Tables

Tables I and II have been added to the summarised guideline document and indicate the currently recommended standard antibiotic dosing regimens as well as alternative antibiotic options for the management of nosocomial infections.

Table I. Currently recommended antibiotic dosing regimens*†

- Amikacin, 20 mg/kg daily
- Amoxycillin/clavulanate, 1.2 g 8-hourly
- Amphotericin B, 0.75 - 1 mg/kg daily
- Ampicillin, 1 g 4 - 6-hourly‡
- Caspofungin, 70 mg loading followed by 50 mg daily
- Cefepime, 1 - 2 g 8- or 12-hourly
- Cefotaxime, 1 - 2 g 8- or 12-hourly
- Ceftazidime, 1 - 2 g 8- or 12-hourly
- Ceftriaxone, 1 - 4 g daily
- Cefuroxime, 1.5 g 8-hourly
- Ciprofloxacin, 400 mg 8-hourly
- Clindamycin, 600 mg 6-hourly
- Cloxacillin, 1 g 4- or 6-hourly
- Ertapenem, 1 g daily
- Fluconazole, 800 mg 1st day followed by 400 - 800 mg daily
- Gentamicin, 5 - 7 mg/kg daily
- Imipenem/cilastatin, 500 mg or 1 g 6-hourly
- Levofloxacin, 750 mg daily or 500 mg 12-hourly
- Linezolid, 600 mg 12-hourly
- Liposomal amphotericin, up to 3 mg/kg daily
- Meropenem, 1 g 8-hourly
- Metronidazole, 500 mg 8-hourly IVI
- Piperacillin/tazobactam, 4.5 g 6-hourly
- Teicoplanin, 400 mg 12-hourly loading dose (day 1) followed by 400 mg 12 - 24-hourly thereafter
- Tobramycin, 5 - 7 mg/kg/day
- Vancomycin, 500 mg 6-hourly or 1 g 12-hourly (adjust dose to maintain daily measured levels of 20 µg/ml)
- Voriconazole, 6 mg/kg 12-hourly loading dose (day 1) followed by 3 - 4 mg/kg 12-hourly

*The higher recommended doses of the various antimicrobial agents should be considered for use in seriously ill patients and/or more severe infections.
†Modifications may need to be made for alterations in renal and/or hepatic function.
‡Only as directed therapy in cases of enterococcal infections.

Table II. Alternative antibiotic options for multidrug or pan-resistant bacteria

- Aztreonam, 1 g 8-hourly
- Polymixin B*,†,‡
  - > 60 kg: 1 - 2 million units 8-hourly, maximum 6 million units/day
  - < 60 kg: 50 000 units/kg/day divided in 3 doses, maximum 75 000 units/kg/day
- Tigecycline, 100 mg loading followed by 50 mg 12-hourly‡

* Nebulised polymixin B can also be in used in conjunction with the intravenous administration in cases of NP and VAP. Standard adult dose is 2 million units 12-hourly (dissolved in 2 - 4 ml 0.9% sodium chloride solution). (Doses up to 2 million units 8-hourly have been found to be safe and effective in patients with cystic fibrosis.)
†Dose adjustment in renal impairment:

Creatinine clearance (ml/min)	≥ 60 kg body weight
20 - 50	1 - 2 million units 8-hourly
10 - 20	1 million units every 12 - 18 hours
< 10	1 million units every 18 - 24 hours

‡ As these antibiotics are not currently registered for routine use, requests need to be made to the Medicines Control Council (MCC) on the basis of compassionate grounds (**www.mccza.com**, tel. 012-312 0000). The following has to be faxed: (*i*) application form filled in by the attending doctor; (*ii*) consent form (patient or family, if not possible by the attending doctor); (*iii*) script; and (*iv*) a deposit of R200 in the MCC account.