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8.2.3 Nosocomial infections Ian C.J.W. Bowler and Matthew Scarborough ESSENTIALS Hospital-acquired or nosocomial infections—defined for epidemio- logical purposes as infections manifesting more than 48 hours after hospital admission—are common. They affect 1.4 million people worldwide, involve between 5 and 25% of hospitalized patients
at any one time and are associated with considerable morbidity, mortality, and cost. The most common sites of nosocomial infection are the urinary tract, surgical wounds, and the lower respiratory tract. Most are bacterial in origin, the most common species being Escherichia coli, Staphylococcus aureus (including methicillin-resistant Staphylococcus aureus), enterococci, Pseudomonas aeruginosa, and coagulase- negative staphylococci. The principal risk factors are extremes of age, the severity of underlying acute disease (e.g. neutropenia, organ system failure), and chronic medical conditions (especially diabetes, renal failure, and alcohol abuse). Between 15 and 30% of nosocomial infections are preventable, and hospital practitioners have a duty of care to minimize the risk of infection for their patients. Systematic surveillance to assess the incidence and prevalence of such infections, together with a regu- larly audited organized programme to minimize their impact, should be an important part of every hospital's quality assurance system. All staff should receive regular education to ensure that they recognize that infection control is 'everyone's business' and hospital managers must ensure appropriate staffing and resources to provide: • access to advice from appropriately trained experts in infection control • surveillance of infection with regular feedback of the data to staff • isolation of patients with infections, with appropriate arrange- ments for their nursing and medical management • appropriate arrangements for carrying out procedures likely to in- crease the risk of infection (e.g. insertion of central venous lines) • policies for outbreak management Definitions Nosocomial infections, as distinct from community-acquired in- fections, are defined for epidemiological purposes as infections manifesting more than 48 hours after admission to hospital. More rarely, nosocomial infections can affect hospital staff; in such in- stances they are defined as infections acquired through exposure at work. Some nosocomial infections may not be so easily identified as hospital acquired; for example, hospital-acquired hepatitis B in- fection may not become clinically apparent until months after the patient has been discharged because of the prolonged incubation period. Healthcare-associated infections are those that present in non- hospitalized patients who have had extensive or recent healthcare contact. They include infections in nursing home or long-term care

 facility residents, and infections arising within 90 days of discharge from hospital or 30 days from hospital attendance. Iatrogenic infections are acquired as the direct consequence of a therapeutic intervention (e.g. insertion of a urinary catheter). Opportunistic infections are caused by organisms that do not ordinarily harm healthy people; they occur in people with impaired immune defences. Endogenous (autogenous) infections are produced by the patient's normal flora. Exogenous infections result from transmission of organisms to the patient from elsewhere. Although in practice it may not always be possible to distinguish endogenous from exogenous infections, this differentiation must be attempted because of important implications for infection control. Scale and costs of nosocomial infections Rates of nosocomial infections between 4 and 6.4 per 100 admissions have been reported. The urinary tract, surgical wounds, and the lower respiratory tract are the most common sites (Table 8.2.3.1).

In the United States of America, an estimated 75 000 deaths per year are dir- ectly attributable to nosocomial infection. In 2013 the cost associated with nosocomial infection in the United States was estimated at $9.8 billion, most of which was attributed to delayed discharge from hos- pital. Rapid changes in healthcare provision mean that the frequency and nature of nosocomial infection are changing. The increasing trend towards early discharge, particularly for surgical patients, can lead to an underassessment of the disease burden. New interventions provide new opportunities for infection. For instance, flexible endo- scopes, which have revolutionized the investigation and manage- ment of a wide variety of diseases, can transmit hepatitis B between patients if the endoscopes are not appropriately decontaminated between procedures. In 2015 heater/cooler equipment used during cardio-pulmonary bypass was implicated in the transmission of Mycobacterium chimaera resulting in mediastinitis and endocarditis. Host and environmental factors The principal risk factors are extremes of age and the severity of the underlying disease (e.g. neutropenia, organ system failure). The ageing population in more developed countries has had a major im- pact on the prevalence of hospital-acquired infection. In multivariate analysis, certain medical diagnoses, including diabetes mellitus, renal failure, and alcohol abuse, are strongly associated with risk. Treatment itself lower host defences (e.g. surgical incisions, bladder catheterization, mechanical ventilation, and neutropenia following cancer chemotherapy). The increasing use of prosthetic devices (e.g. intravascular catheters, cardiac valves and pacemakers, vascular grafts, and joint replacements) which facilitate formation of biofilm by certain bacteria, can also subvert normal defence mechanisms. Patients with similar clinical problems, who are likely to share similar risk factors for infection, tend to be nursed together for convenience, so the introduction of a microorganism into such a group can rapidly infect several patients. A good example is the rapid spread of norovirus gastroenteritis in geriatric wards. A poorly maintained hospital envir- onment is a threat to vulnerable patients; for instance, in units caring for patients with solid organ transplants, outbreaks of legionellosis can result from defective air conditioning and hot water systems. Microorganisms and use of antibiotics Bacteria are the most frequently implicated pathogens in nosocomial infections. These include Escherichia coli, Staphylococcus aureus, enterococci, Pseudomonas aeruginosa, Klebsiella spp, coagulase- negative staphylococci, and Clostidium difficile, in decreasing order of frequency. Viruses, fungi, and protozoa play a minor part. Whether endogenous or exogenous, the organisms causing noso- comial infection are usually part of a patient’s normal colonizing flora and it is often difficult to distinguish infection from coloniza- tion using bacteriological tests alone. The organisms are frequently multidrug resistant, since the widespread use of antibiotics in hos- pitals gives these strains a selective advantage. Empirical antibiotic therapy should accommodate the shift towards more resistant col- onizing flora in hospitals, particularly in burns units and intensive care units. Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, methicillin-resistant S. aureus (MRSA), and enterococci are often resistant to multiple antimicrobials, making them difficult and expensive to treat. Increasing international travel means that organisms which were previously geographically restricted (e.g. NDM E. coli and Klebsiella pneumoniae in India) are becoming increasingly common globally. These organisms may be resistant to nearly all antibiotics, including carbapenems, and can spread when patients are transferred between countries and between centres. It is im- portant that such organisms are detected by screening cultures at the time of admission, so that appropriate precautions to prevent their spread can be implemented. Antibiotic resistance in bacteria causing nosocomial infection is a topic of worldwide concern. There is increasing emphasis on im- plementation of ‘stewardship’ programmes to ensure antibiotics are targeted appropriately and indiscriminate use avoided. Table 8.2.3.1 Rates and sites of nosocomial infection in three

regions European Union, Norway, Iceland,
and Croatia (2011) UK (2011) USA (2011) Rates: cases/100 admission sites (% of all infections) 5.7 6.4 4 Lower respiratory tract infection 24 23 22 Surgical wound infection 20 16 22 Urinary tract infection 19 17 13 Other 37 44 47

8.2.3 Nosocomial infections 671 Principles of hospital infection control The principal aim of the hospital infection control programme is to prevent nosocomial infection. The identification and typing of iso- lates causing nosocomial infection allows recognition of organisms that are epidemiologically linked. Invasive multidrug-resistant or- ganisms, such as MRSA, often require infection control measures to prevent their spread and so minimize the use of expensive, some- times toxic, antibiotics required for their prophylaxis and treatment. Epidemic infections account for less than 10% of the nosocomial disease burden but attract professional and media interest because they are unusual. They are amenable to measures that interrupt the spread of infection, such as the use of gowns and gloves, and meticulous hand hygiene. Care of colonized or infected patients in single rooms or an isolation ward is a physical means of preventing spread. Alternatively, patients infected with the same organism can be grouped together (cohorted) and attended to by a group of nurses not involved with un- infected patients. Identification of additional carriers and elimination of colonization may be necessary to control some epidemic outbreaks. There have been no randomized trials demonstrating the efficacy of such measures, but many observational studies support their use. Endemic nosocomial infections are more difficult to control. The size of the problem may not be apparent either because attack rates in individual units may be low or because infection is seen as a normal consequence of certain interventions. It is important that information about endemic infections is collected systematically in a comprehensive surveillance programme, analysed, disseminated, and discussed so that preventive strategies can be improved. Control measures are applied to selected patients according to risk (e.g. cor- rectly timed antimicrobial prophylaxis and meticulous sterile tech- nique in prosthetic joint replacement surgery). Site of nosocomial infections Urinary tract A bacterial count of at least 105 organisms/ml in a freshly voided urine sample indicates infection, although counts as low as 102 or- ganisms/ml are included by some classifications. The presence of any organisms in a sample taken from a urinary catheter at the time of insertion or from a suprapubic aspirate may indicate infection. Indwelling urinary catheters account for 80% of nosocomial urinary tract infections, and 80% of patients catheterized for longer than 7 days develop bacteriuria (bacteria in the urine). Most patients with catheter-related urinary tract infection remain asymptomatic, but 20–30% develop the symptoms of urinary tract infection and about 1 in 100 of these develops bacteraemia. Instrumentation of the urinary tract is also a risk factor for urinary tract infection. The main source of organisms is the periurethral flora, with E. coli reported as the dominant pathogen in all studies. Treatment is with broad- spectrum antimicrobials administered empirically after obtaining appropriate cultures and later adjusted according to the results of bacteriological studies. Asymptomatic patients need not be treated. Since the most important risk factor is the duration of catheteriza- tion, avoiding catheterization (or ensuring their early removal) is the most effective means of preventing nosocomial urinary tract infec- tion. In addition, catheters should be inserted aseptically, attached to a closed sterile drainage system, and placed on uninterrupted gravity drainage. Suprapubic or intermittent urethral catheterization are also sometimes employed to reduce the risk of nosocomial infection. Some practitioners advocate a single prophylactic dose of antibiotic at the time of urinary catheter insertion or exchange in men to prevent bacteraemia. In other settings prophylactic antibiotics have not been shown to prevent infection for more than a

few days. Catheters coated with antimicrobials such as silver have been shown to reduce infection rates in some patient groups, but their cost-effectiveness is disputed. Surgical wound infection The diagnosis of a surgical wound infection usually requires the pres- ence of spreading erythema or purulent discharge from a wound, but rates vary according to the definition used. Internationally agreed diagnostic criteria are used for high-quality clinical and epidemio- logical studies Most wound infections result from direct inoculation of organ- isms into the wound at the time of surgery. The main risk factor is the degree of wound contamination at operation. Operations may be ‘clean’ (e.g. herniorrhaphy), ‘clean–contaminated’ (e.g. appendicec- tomy which requires incision of bowel), or ‘contaminated’ (e.g. gross spillage from the gastrointestinal tract during surgery). S. aureus is the most common pathogen complicating clean surgery, for which rates below 2% are expected. ‘Contaminated’ surgery is often associ- ated with polymicrobial infections, especially with E. coli and mixed anaerobes originating from the patient’s gastrointestinal tract; rates of infection following contaminated surgery are reported to be be- tween 5–25%. Other risk factors include age, obesity, the duration of the operation, and the presence of a remote infection. Wound infections usually present with local symptoms and signs (pain, erythema, pus, dehiscence) and with general features of infec- tion, such as fever. Appropriate cultures, including blood cultures, are taken, pus is drained, and broad-spectrum antimicrobials are given empirically, directed at the likely flora but later adjusted ac- cording to bacteriological results. Prevention is by meticulous aseptic surgical techniques. Prophylactic antimicrobials, given no more than 2 hours before the surgical incision, have been shown to reduce wound infection rates by between two- and fivefold for clean–contaminated and contam- inated procedures, and in clean surgery when a prosthesis is inserted (e.g. joint replacement, vascular graft insertion). Nosocomial pneumonia Pneumonia is defined clinically by the production of purulent sputum, signs of respiratory consolidation, a fall in arterial Po2, and the appearance of new infiltrates on the chest radiograph. Between 0.55 and 1.5% of patients admitted to hospital develop lower respira- tory tract infections. Crude case fatality rates of between 20 and 30% are quoted, but death occurs most commonly as a result of underlying disease. Patients who are intubated and ventilated have a high risk of developing pneumonia as a result of aspiration of bacteria colon- izing the upper respiratory and gastrointestinal tracts. The organisms causing ventilator-associated pneumonia are usually acquired after admission to hospital and the bacteria are often more antibiotic- resistant than community-acquired organisms. Examples of organ- isms causing nosocomial pneumonia are listed in Table 8.2.3.2. Culture of expectorated sputum or tracheal aspirates is poorly predictive of the bacterial cause of nosocomial pneumonia, which

 is best determined by quantitative culture of specimens obtained by sampling the terminal airways (e.g. by bronchoalveolar lavage). Initially, broad-spectrum antimicrobials should be given empiric- ally. Once the susceptibility of the causative pathogen has been de- termined, specific antimicrobial treatment can be instituted. The risks of nosocomial pneumonia can be reduced by a var- iety of strategies, including avoidance of intubation and the use of noninvasive ventilation techniques. For those who are intubated, continuous aspiration of subglottic secretions and nursing in the semi-recumbent position have been shown to be effective. Selective decontamination of the digestive tract by the administration of nonabsorbable antibiotics has shown modest mortality benefit in ventilated patients in countries where resistance rates are low, but very limited advantage in areas where there is a high prevalence of multidrug-resistant organisms. Short courses of antibiotics at the time of intubation have been shown to be effective in certain pa- tient groups. Epidemic nosocomial pneumonia usually results from bacterial contamination of respiratory equipment, such as nebu- lizers,

ventilators, or bronchoscopes. It is best prevented by ensuring single-use respiratory devices, by cleaning and disinfecting equip- ment, and by hand hygiene before and after every patient contact. Intravascular device-associated infections Bacteraemia is the most important intravascular device-associated infection; it varies in prevalence from about 0.04% for subcuta- neous central venous lines to about 0.2% for peripheral intravenous cannulae, and approximately 10% for temporary nontunnelled cen- tral venous haemodialysis catheters. The duration of intravascular access is the most significant risk factor. Bacteria usually gain entry by direct spread from the skin surface incision along the subcutaneous catheter tunnel to its tip in the blood vessel. Less commonly, line infection results from contamination of connecting devices; this is particularly important in catheters with sub- cutaneous cuffs, such as Hickman catheters, where the peri-luminal route of infection is less likely. The organisms that most frequently cause intravenous device-related bacteraemia are coagulase-negative staphylococci, S. aureus, Pseudomonas spp., and Candida spp. Line-related infection most commonly presents with features of bacteraemia. In a minority of cases, there are clear signs of local in- flammation or thrombophlebitis at the insertion site. Management most commonly involves taking blood cultures, removal of the catheter (with culture of the tip), and empirical antimicrobials. Sometimes, long-term intravenous catheters, such as Hickman lines, can be ‘sterilized’ by administering parenteral antibiotics into the line as ‘antibiotic lock’ therapy. Superficial infections which are restricted to the insertion site can sometimes be treated with antibiotics and line retention. Tunnel infections usually require removal of the line. Prevention of line-associated infections is best achieved by using aseptic techniques during insertion, maintaining high standards of line care, and removing catheters as soon as possible. Before insertion, the skin should be prepared with a reliable disinfectant such as an al- coholic solution of chlorhexidine. For insertion of long lines, the op- erators should wash their hands, use a large sterile drape to isolate the insertion site, and wear sterile gloves, gown, face mask, and hat. Central venous catheters are usually removed only if blocked or suspected as a source of sepsis. The skin at the exit site of peripheral intravascular devices should be checked daily and the device removed if infection is suspected. Subcutaneous tunnelling, use of a cuffed device (Hickman line), use of subcutaneous access (e.g. portacaths), and use of antimicro- bial coated lines can all reduce the infection rate significantly. Replacing the entire intravenous delivery set every 72 hours is sufficient to reduce sepsis secondary to intraluminal contamination of ‘giving’ sets. Prosthetic device-related infection Infections of prosthetic devices such as heart valves, vascular grafts, cerebrospinal fluid shunts, artificial lenses, and joint replacements are usually caused by the normal skin flora. The devices become coated with a layer of host-derived macromolecules such as fibronectin and fibrin which have specific adhesion receptors for bacteria, particularly staphylococci. Once attached, these organisms multiply on the sur- face of the coated prosthesis forming a biofilm. Microbes embedded in biofilm are relatively inactive metabolically and far less susceptible to antibiotics as compared to planktonic or free-living bacteria. The formation of biofilm, therefore, confers significant phenotypic resist- ance to medical therapy even if the organisms appear susceptible to antibiotics in vitro. Apart from those involving an intraocular lens, such infections are rarely cured with antimicrobial therapy alone and frequently require removal of the prosthetic device. Bacteria gain access to prosthetic devices by direct inoculation, usu- ally at the time of surgery, or less commonly by settling on the pros- thesis after haematogenous spread. Direct inoculation at surgery can be responsible for prosthetic device infections presenting more than 1 year after insertion since the organisms involved are usually skin commensals of low virulence (e.g. coagulase-negative staphylococci). Prevention is by avoiding contamination of the wound at sur- gery and by using strict aseptic surgical techniques. In ortho- paedic implant surgery, a large randomized controlled trial showed that an ultraclean air supply to the operating theatre is

of benefit. Prophylactic antimicrobials given at the time of surgery have also been shown to reduce the risk of prosthetic joint infections. Antibiotic-associated diarrhoea Up to 30% of patients treated with antibiotics will develop diarrhoea as a result of the disturbance of the complex gut flora. In a few, loss of ‘colonization resistance’ predisposes to acquisition of Clostridium difficile. Colonization by this organism is usually harmless, but in about 3% of patients, particularly older people, the organism may overgrow and produce a cytotoxin resulting in colitis. The clinical picture varies from mild diarrhoea with fever to fulminating colitis with dilatation of the colon (toxic megacolon) requiring colectomy. More severe disease and a greater likelihood of relapse are associated with a quinolone-resistant clone of C. difficile, Table 8.2.3.2 Causative organisms identified in samples obtained at bronchoscopy or tracheal aspiration (percentage
of all pneumonias) USA (2007) Staphylococcus aureus including MRSA 27 Pseudomonas aeruginosa 18 Escherichia coli and other Enterobacteriaceae 15 Acinetobacter spp. 8 Stenotrophomonas maltophilia 7 Streptococci 3 Other species 22

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