Nosocomial infections

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Key points

One in ten patients will acquire a nosocomial infection.

A third of nosocomial infections are preventable.

Hand washing is the best preventative measure against the spread of infection; gloves are not a substitute for hand washing.

Inadequate antibiotic therapy is associated with poor outcome and emergence of bacterial resistance.

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Nosocomial infections can be defined as those occurring within 48 hours of hospital admission, 3 days of discharge or 30 days of an operation. They affect 1 in 10 patients admitted to hospital. Annually, this results in 5000 deaths with a cost to the National Health Service of a billion pounds. On average, a patient with hospital acquired infection spent 2.5-times longer in hospital, incurring additional costs of £3000 more than an uninfected patient. Intensive care units (ICU) have the highest prevalence of hospital-acquired infections in the hospital setting. The European Prevalence of Infection in Intensive Care Study (EPIC), involving over 4500 patients, demonstrated that the nosocomial infection prevalence rate in ICU was 20.6%.[1] ICU patients are particularly at risk from nosocomial infections as a result of mechanical ventilation, use of invasive procedures and their immunocompromised status (Table 1).

Gram-positive bacteria are the commonest cause of nosocomial infections with *Staphylococcus aureus* being the predominant pathogen. There has been an increase in the rate of antibiotic resistant bacteria associated with nosocomial infections in ICU. Bacteria develop resistance when they acquire new genetic material. Poor antibiotic prescribing selects for resistant bacteria. The genetic material that encodes resistance is transferred to other strains. Methicillin-resistant *S. aureus* (MRSA) causes up to 60% of nocosomial infection in ICU. A broad-spectrum antibiotic such as vancomycin is usually prescribed for treatment. However, vancomycin-resistant enterococci and isolated cases of vancomycin-resistant *S. aureus* have been reported. This highlights the need for the use of appropriate antibiotics and some centres now discourage the use of vancomycin as first line treatment for *Clostridium difficile* diarrhoea.

Table 1 Factors that predispose to nosocomial infections. *EPIC study risk factors

Factors that predispose to nosocomial infection
Related to underlying health status
Advanced age
Malnutrition
Alcoholism
Heavy smoking
Chronic lung disease
Diabetes
Related to acute disease process
Surgery
Trauma*
Burns
Related to invasive procedures
Endotracheal or nasal intubation*
Central venous catheterisation*
Extracorporeal renal support
Surgical drains
Nasogastric tube
Tracheostomy
Urinary catheter*
Related to treatment
Blood transfusion
Recent antimicrobial therapy
Immunosuppressive treatments
Stress-ulcer prophylaxis*
Recumbent position
Parenteral nutrition
Length of stay*

Infection control

The Study of the Efficacy of Nocosomial Infection Control (SENIC) demonstrated that a third of nocosomial infections might be prevented with appropriate infection control measures.[2] These comprise surveillance methods, prevention strategies and treatment programs. In the UK, Every Trust has infection control teams comprising an infection control doctor (usually a consultant microbiologist), an infection control nurse and a manager. They have responsibility for all aspects of infection prevention and control within a hospital and, since 1995, report directly to the Trust Chief Executive. They organize education for staff, develop local infection control policies and provide advice and guidance as part of a programme of work including surveillance and audit. Effective infection control programs rely on an extensive knowledge of the local epidemiology of pathogens and the provision of a monitoring system that recognizes the emergence of antibiotic-resistant bacteria.

Surveillance

Surveillance is the ongoing, systematic collection, analysis and interpretation of

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information related to health. This is essential for the planning, implementation and evaluation of public health and also the timely dissemination of information. In the UK, the Nosocomial Infection National Surveillance Service[3] was formed in 1996 and is managed by the Health Protection Agency (HPA). This surveillance service aims to collect a database for nationwide comparisons of hospital-acquired infections and to improve patient care by reducing nosocomial infection rates and assisting clinical practice. A total of 102 hospitals participated in the last 2002 survey. At present, two protocols exist: (i) the surveillance of surgical site infections; and (ii) the surveillance of hospital acquired bacteraemia. Further protocols for the urinary tract and lower respiratory tract (second most common cause of nosocomial infections) are yet to be developed. The 2002 survey highlighted the fact that two-thirds of bacteraemias were associated with intravascular devices, with central i.v. catheters being the most common source of hospital-acquired bacteraemia. Bacteraemias were identified in 3.5 patients per 1000 hospital admissions while, in ICU, the figure rose to 9.1 patients per 1000 admissions.

Table 2 shows the common pathogens associated with nosocomial infections and their favourite sites of colonization. These have included MRSA, methicillin-sensitive *S. aureus* (MSSA), vancomycin-resistant enteroccocus (VRE) and multi-drug-resistant *Acintobacter* spp. At a local level, compulsory monitoring of certain pathogens (MRSA and *C. difficile*) has been in place since 2000. Across Europe, a surveillance program was initiated in 1994 called HELICS (Hospitals in Europe Link for Infection Control through Surveillance). Its aim is to create a database for nosocomial infections from public health services in Europe.

Prevention

The European Prevalence of infection in Intensive Care (EPIC) study identified several factors predisposing a patient to nosocomial infections (Table 1). Poor hand hygiene is responsible for 40% of infections transmitted in hospitals. Surveys have shown that the improvement in compliance with hand washing reduces nosocomial infection. Accessibility of the hand washing stations and the use of alcohol gels improves compliance with hand washing. Alcohol gel dries quickly, and is bactericidal, fungicidal and virucidal. Numerous studies have shown that doctors wash their hands less frequently than nurses and backs of hands, tips of fingers, web spaces and thumb are commonly missed areas.[4] The Department of Health has produced guidelines on hand washing on their website (www.doh.gov.uk/hai/epic.doc).

Protective garments are necessary for health providers exposed to body fluids, for example sweat, oropharyngeal fluids, blood or urine. Gloves and aprons should be worn for handling body fluids. High efficiency particulate air (HEPA) filter masks are recommended for sputum smear positive patients with tuberculosis, particularly for cough-inducing procedures.[5] Hands must be washed after glove removal as contamination of the hands can still occur.

The use of invasive procedures increases the risk of nosocomial infections. For venous access, this risk can be reduced by use of specific sites such as subclavian vein rather than internal jugular or femoral veins. Tunnelling the catheter reduces the risk of nosocomial infection. Antimicrobial impregnated catheters can reduce catheter related infections. The use of a strict, aseptic technique is paramount in the insertion of intravascular catheters. By using isolation rooms for patients with MRSA, *C. difficile*, VRE and resistant Gram-negative infections, the spread of infection can be reduced owing to improved awareness of the implementation of appropriate infection control precautions.

Table 2 Common pathogens associated with nosocomial infections in ICU patients. National Nosocomial Infections Surveillance System January 1989–June 1998. BSI = bloodstream infection; PNEUM = pneumonia; UTI = urinary tract infection; SSI = surgical site infection

	Relative percentage by site of infection				
	BSI	PNEUM	UTI	SSI	Others
Coagulase-negative staphylococci	39.3	2.5	3.1	13.5	15.5
Staphylococcus aureus	10.7	16.8	1.6	12.3	13.7
Pseudomonas aeruginosa	3.0	16.1	10.6	9.2	8.7
Enterococci spp.	10.3	1.9	13.8	14.5	5.9
Enterobacter spp.	4.2	10.7	5.7	8.8	6.8
Escherichia coli	2.9	4.4	18.2	7.1	4.0
Candida albicans	4.9	4.0	15.3	4.8	4.3
Klebsiella pneumoniae	2.9	6.5	6.1	3.5	37.7
Others	21.8	37.1	25.6	26	3.5

Antibiotic use

Appropriate use of antibiotics is important. Up to 30% of ventilator associated pneumonias are treated inadequately. There is increasing evidence to suggest that the use of appropriate and early antibiotics improves morbidity and mortality. Appropriate antibiotic use requires a thorough knowledge of their mode of action (Table 3), previous antibiotic history, local bacterial resistance profile and local pathogen prevalence. Antibiotics should be administered at the right dose and for the appropriate duration. The local antibiotic formulary and consultant microbiologist are valuable resources.

Daily ICU ward rounds with the microbiologist can lead to rational use of antibiotics tailored to benefit individual patients. Antibiotic-resistant bacteria prolong hospitalization, increase the risk of death, and require treatment with toxic and expensive antibiotics. Empirical use of antibiotic is often necessary as laboratory results are often not available for 48 h after the samples are sent to the laboratory for culture. Appropriate specimens include blood, urine, sputum, bronchoalveolar lavage, pus and wound swabs. Blood cultures are only positive for pathogens in a third of cases. Once the antibiotic profile is available, a narrow-spectrum antibiotic can be commenced. Indicators of response to treatment include temperature, leucocyte count and C-reactive protein (CRP) levels. Procalcitonin is secreted by macrophages in response to septic shock and is an early

Table 3 Mode of action of common antibiotics

Mode of action	Class of antibiotic	Examples	Clinical uses
Cell wall inhibitors	Penicillin	Penicillin V and G	Gram-positive
	Semi-synthetic penicillin	Ampicillin, Amoxicillin	Gram-positive and -negative bacteria, except penicillinase-producing bacteria, e.g. *S. aureus*
	Cephalosporins	Cefotaxime, cefradine, ceftazidime	Gram-negative organisms with later generation better with Gram-positive
	Monobactams	Aztreonam	Gram-negative organisms
	Carbapenems	Meropenem	Broad-spectrum
	β lactamase inhibitors	Clavulanate	
	Glycopeptides	Vancomycin	Gram-positive organisms (e.g. MRSA and enterococci)
Cell membrane inhibitors	Antifungal		
	Polyenes	Nystatin	Aspergillus, candida
	Imidazoles	Ketonazole	
	Triazoles	Fluconazole	
Protein synthesis inhibitors	Aminoglycoside	Gentamicin	
	Macrolides	Erythromycin	Gram-positive organisms
	Oxaolidinines	Linezolid	*H. influenza*
	Ketolides	Telithomycin	
	Streptogramins	Synercid	
Nucleic acids inhibitors	Fluoroquinonolones	Ciprofloxacin	Broad Gram-negative spectrum
	Nitro imidazoles	Metronidazole	*C. difficile*
	Rifampicin	Sulphonamides	
	Folate inhibitors		

and a more specific marker of bacterial infection than CRP. These parameters must be interpreted in the clinical context. Improvements in the ventilatory and inotrope requirements can provide additional and indirect evidence for response to treatment.

Any antibiotic policy or guideline should aim to limit the use of antibiotics and reduce the selective pressure for resistant micro-organisms. Policies designed to encourage rational antibiotic use in ICU are an important element in quality of care, infection control and cost containment. De-escalation therapy, selective digestive decontamination (SDD), antibiotic rotation (cycling) therapy and restrictive guidelines can address these concerns. Optimizing any antimicrobial therapy includes both shortening the duration of antimicrobial use and appropriate use of combination therapy to reduce the emergence of resistance. Research into these antibiotic management programs is limited and results are controversial.

De-escalation

De-escalation involves early initiation of broad-spectrum antibiotic therapy in patients with suspected sepsis without the availability of microbiology results. The increase in antibiotic resistant pathogens such as MRSA has led some investigators to suggest broader antibiotic coverage by adding a glycopeptide to carbapenem as the initial empirical therapy. This aggressive empirical regimen is continued for 24–48 h by which time laboratory tests have confirmed the causative organisms and sensitivities. This allows for de-escalation of antibiotic therapy.

This regimen should be reserved for selected patients on ICU who are seriously ill, with an extended antibiotic history and evidence of colonization by multi-resistant organisms. Unnecessary continuation of this regime will increase the risk of colonization with resistant bacteria.

Rotational antibiotic therapy

Rotational antibiotic therapy is a strategy to reduce antibiotic resistance by withdrawing an antibiotic, or class of antibiotics, from ICU for a short period, to allow resistance rates to decrease or remain stable. The persistent use of one class of antibiotics leads to the emergence of resistant strains of bacteria; this is known as selective pressure. Rotational regimens are thought to reduce this selective pressure. There is growing support for this regimen. Kollef and colleagues[6] demonstrated a statistical decrease in nosocomial pneumonia in a large ICU after the introduction of an antibiotic rotation policy.

Restrictive antibiotic policies are less flexible and, to a certain extent binding, with respect to prescribing. They require the prescriber to give written justification for any deviation from the policy. Automatic stop orders restrict prolonged antibiotic administration. In the general hospital setting, these measures have had some success with significant reductions in antibiotic resistance. However, the overall survival in ICU was unchanged.

The concept that commensals within the bowel may provide a protective role against more virulent organisms is called colonization resistance. Translocation of Gram-negative bacteria across the intestinal wall is thought to be a major cause of nosocomial infections. SDD aims to eliminate Gram-negative aerobic bacteria by decontamination of the oral cavity and intestinal tract. There are several variations of the SDD regimen. One such regimen is non-absorbable polymyxin E, tobramycin, and amphotericin B for gastrointestinal decontamination and cefotaxime for systemic prophylaxis. Cephalosporins are usually

given as prophylaxis as they act on commensal respiratory flora such as *Streptococcus pneumoniae*, *Haemophilus influenzae* and *S. aureus*. Meta-analysis has demonstrated that SDD regimens decrease the incidence of nosocomial pneumonia but overall survival or duration of intensive care treatment is unchanged. The cost effectiveness of SDD has not been evaluated.

Conclusion

Nosocomial infections are associated with a great deal of morbidity, mortality and increased financial burden. Intensive care is a risk factor for the emergence of antibiotic resistant bacteria. Gram-positive bacteria have overtaken Gram-negative organisms as the predominant cause of nocosomial infections. Inadequate antibiotic therapy is associated with poor outcome and particularly with bacterial resistance. Infection control measures are important for the effective control, prevention and treatment of infection. Knowledge of emerging pathogens and resistance profile is essential for treatment against nocosomial infections. Shorter duration of treatment and correct dosage of antibiotic therapy is recommended to reduce the selection pressure for resistant isolates. Hand washing is the single most important measure to prevent nocosomial infections. Gloves must not be used as a substitute for hand washing; they must be washed on glove removal.

References

1. Louis V, Bihari MB, Suter P, *et al*. The prevalence of nosocomial Infections in intensive care units in Europe. European Prevalence of infection in Intensive care (EPIC) study. *JAMA* 1995; **274**: 639–44
2. Haley RW, White JW, Culver DH, *et al*. The efficacy of infection surveillance and central programs in preventing nosocomial infections in US hospitals (SENIC). *Am J Epidemiol* 1985; **121**: 182–205
3. Nosocomial Infection National Surveillance Service (NINSS). *Surveillance of Hospital Acquired Bacteraemia in English Hospitals 1997–2002*. London: Public Health Laboratory Service, 2002
4. Hospital Infection Working Group of the Department of Health and Public Health Laboratory Service: Hospital Infection Control. Guidance on the control of infection in hospitals. London: Department of Health, 1995
5. Recommendations for the prevention and control of tuberculosis at a local level. Department of Health, 1996
6. Kollef MH, Ward S, Sherman G, *et al*. Inadequate treatment of nosocomial infections is associated with certain empiric antibiotic choices. *Crit Care Med* 2000; **28**: 3456–64

See multiple choice questions 21–23.