

## Review

## Nosocomial infections in adult intensive-care units

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**Nosocomial infections affect about 30% of patients in intensive-care units and are associated with substantial morbidity and mortality. Several risk factors have been identified, including the use of catheters and other invasive equipment, and certain groups of patients—eg, those with trauma or burns—are recognised as being more susceptible to nosocomial infection than others. Awareness of these factors and adherence to simple preventive measures, such as adequate hand hygiene, can limit the burden of disease. Management of nosocomial infection relies on adequate and appropriate antibiotic therapy, which should be selected after discussion with infectious-disease specialists and adapted as microbiological data become available.**

A nosocomial infection (derived from the Greek words *nosos* [disease] and *komein* [to care for], and later the Latin word for hospital nosocomium) is defined as an infection that is not present or incubating when the patient is admitted to hospital or other health-care facility.<sup>1</sup> The time frame for diagnosis of a nosocomial infection will thus clearly be dependent on the incubation period of the specific infection; 48–72 h after admission is generally deemed indicative of nosocomial, rather than community-acquired, infection. Although generally associated with hospital admission (hence the term hospital-acquired infection), nosocomial infections can arise after admission to any health-care facility, and the term health-care-associated infection is increasingly being used. Such infections are common and associated with great morbidity and mortality. Indeed, one provocative headline stated “Hospital acquired infections kill 5000 patients a year in England”.<sup>2</sup> The information for this news piece was taken from a government report on hospital-acquired infection in England, which suggests that there are at least 100 000 cases of hospital-acquired infection every year in England, costing the UK National Health Service some £1 billion each year.<sup>3</sup>

In addition to their association with increased morbidity and mortality, nosocomial infections are frequently associated with drug-resistant micro-organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA) and extended spectrum  $\beta$ -lactamase (ESBL)-producing gram-negative bacteria, which can pose considerable therapeutic problems. Medicolegal issues can also arise, since patients or their families sometimes blame the hospital or staff for the infection, and demand compensation.<sup>3</sup>

Nosocomial infections can affect any part of the body, but respiratory tract infections are most frequent, followed by central line infections, urinary tract infections, and wound infections. In this review, I will briefly describe the pathophysiology and epidemiology of nosocomial infection in general and then concentrate on each of these areas of infection in turn, before assessing means to prevent infection, and suggesting areas for future research

and analysis. There is a vast amount of published work on nosocomial infections, and since very sick patients are more likely to be affected than those who are not as unwell, I will limit this discussion to adult patients in intensive-care units.

### Pathophysiology

The development of nosocomial infection is dependent on two key pathophysiological factors: decreased host defences and colonisation by pathogenic, or potentially pathogenic, bacteria. Although these two factors can arise independently, for infection to result both must be present to some degree.

Decreased host immune defence is common in patients in intensive care, largely because of continuing, concurrent disease processes. Immunosuppression—primarily due to the release of interleukin 10 and other anti-inflammatory mediators, such as interleukin-1-receptor antagonist and tumour necrosis factor (TNF) receptors—creates a state sometimes termed immunoparalysis,<sup>4</sup> which is associated with an increased risk of infectious complications.<sup>5–7</sup> The administration of immunosuppressive drugs, often used in patients in intensive care, can contribute to this state, making such individuals a particularly high-risk group for nosocomial infection. Immune defence also includes local factors; for example, coughing, sneezing, and mucociliary clearance are all important host-defence mechanisms in the prevention of respiratory infection. Endotracheal intubation can reduce these local defences, predisposing to respiratory infection in mechanically ventilated patients.

Bacterial colonisation is strongly associated with hospital stay and is especially common in the critically ill for various reasons, including frequently impaired host defences, the presence of invasive devices that form a nidus for colonisation, and the administration of often long-term or repeated courses of antibiotics. Antibiotics can exert selective pressure on the patient's normal

### Search strategy

We searched MEDLINE, using the following keywords: cross infection, nosocomial infection, hospital-acquired infection, ventilator-associated pneumonia, and healthcare-associated infection. We also searched the bibliographies of all relevant articles. We restricted our search to articles published in English or French, and concerning the adult intensive-care-unit population.

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## 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 transfusions  
Recent antimicrobial therapy  
Immunosuppressive treatments—eg, corticosteroids  
Stress-ulcer prophylaxis  
Recumbent position  
Parenteral nutrition

antimicrobial flora, modifying it to select potential pathogenic colonisers, resulting in so-called endogenous colonisation. This selective pressure will depend not only on how much antibiotic is given but on which antibiotics are used.

Exogenous colonisation arises from cross-transmission via direct contact, droplet, or aerosol spread. Direct contact can include spread from the hands of health-care workers or visitors,<sup>8</sup> but also from contaminated equipment and infusions.<sup>9,10</sup> Microbes transmitted by airborne spread include *Mycobacterium tuberculosis*<sup>11</sup> and some viral infections. The route of transmission will help identify which precautions are most necessary to prevent transfer of infection.

The most common reservoirs for nosocomial colonisers are the oropharynx, the gastrointestinal tract, and the urinary tract, and colonisation with *Klebsiella* spp, *Enterobacter* spp, *Serratia* spp, *Pseudomonas* spp, and candida commonly occurs in these areas. A key feature in the colonisation of the host is the ability of micro-organisms to adhere to host tissue. This function is achieved by microbial adhesions that interact with receptors on mucosal surfaces to bind the bacteria to the host. Adhesin-receptor interactions are important in defining the bacterial population found on any particular surface, with host specificity and tissue tropism—the apparent preference of certain micro-organisms for a particular host tissue—determined (at least in part) by the interaction between adhesins and their complementary receptors on host cell surfaces.<sup>12</sup> Changes in adhesins associated with antimicrobial-resistant micro-organisms, or in the way in which the adhesins interact with host receptors could account for the pathogenicity of certain bacteria commonly involved in nosocomial infection.<sup>13</sup>

## Predisposing factors

The main predisposing factors are associated with either an increased risk of colonisation or with decreased host

defence. There is a plethora of studies detailing the risk factors for various types of nosocomial infection in various groups of patients, but predisposing factors can, essentially, be divided into four key groups: those related to underlying health impairment, those related to the acute disease process, and those related to the use of invasive procedures or to other treatment modalities (panel).

## Underlying health impairment

Certain conditions predispose to bacterial colonisation, and hence nosocomial infection, by impairing host-defence mechanisms. Patients with chronic lung disease are at an increased risk of developing nosocomial infection.<sup>14,15</sup> Immune status can also affect the risk of developing nosocomial infection, with immunocompromised patients, including those with neutropenia, being at greatest risk. Furthermore, older patients are more susceptible than younger ones;<sup>16–18</sup> poor nutrition and chronic debilitation are associated with reduced immune defence, explaining the increased risk of nosocomial infections in such patients.<sup>17</sup>

## The acute disease process

The underlying disease process as well as the severity of disease can affect the risk of developing nosocomial infection. Patients with a primary diagnosis of trauma or burns are at an increased risk.<sup>19–22</sup> In patients with burns, risk might be increased because of the loss of skin, which acts as a physical barrier to micro-organisms, though altered immune status could also play a part.<sup>23</sup> Trauma patients too have altered immune responses,<sup>24</sup> making them more likely to develop infection. In individuals who develop critical illness neuropathy or myopathy, muscle weakness could prolong the duration of mechanical ventilation<sup>25</sup> and hence potentially increase the risk of developing ventilator-associated pneumonia (VAP). Perhaps unsurprisingly, severity of illness as assessed by severity scores has also been associated with the development of nosocomial infection,<sup>26,27</sup> although severity scores cannot be independent predictors of infection<sup>28</sup> but rather associated with other risk factors for infection, such as prolonged length of stay.<sup>29</sup>

## Invasive devices

In a report from the National Nosocomial Infection Surveillance (NNIS) system,<sup>30</sup> involving data from 498 998 patients, 83% of episodes of nosocomial pneumonia were associated with mechanical ventilation, 97% of urinary tract infections arose in patients with a urinary catheter in place, and 87% of primary bloodstream infections were in patients with a central line.

## Treatment methods

Various therapeutic strategies are associated with a raised risk of nosocomial infection. Cook and colleagues<sup>20</sup> noted that the administration of paralytic agents was an independent predictor of nosocomial pneumonia in their study of 1014 mechanically ventilated patients. Sedative drugs,<sup>31</sup> corticotherapy,<sup>32</sup> antacids,<sup>33,34</sup> stress-ulcer prophylaxis,<sup>19,35</sup> previous antibiotic therapy,<sup>16</sup> and multiple blood transfusions<sup>36</sup> have all been identified as risk factors.

## Epidemiology

The quoted incidence of nosocomial infection varies, according to the setting—ie, the type of hospital or intensive-care unit—the population of patients, and the precise definition used (hospital-acquired, intensive-care unit-acquired, nosocomial pneumonia, VAP). One of the

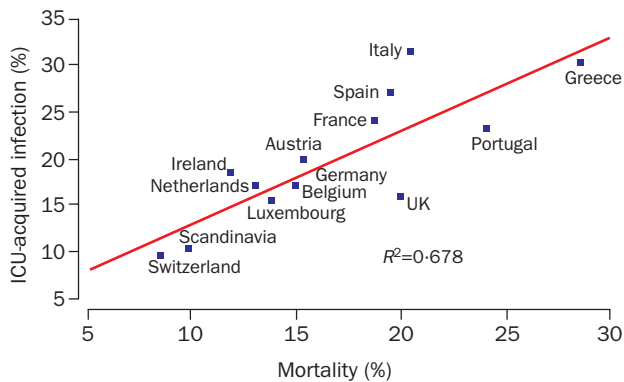


Figure 1: Correlation between prevalence rate of intensive-care-unit-acquired infection and mortality rate by country  
ICU=intensive-care unit.

largest databases related to nosocomial infection in intensive care is the EPIC study.<sup>19</sup> In this 1-day point prevalence study, information was obtained on all patients who occupied a bed in an intensive-care unit over 24 h in 1992: 10 038 patients were recruited from 1417 western European intensive care units. Of these patients, 4501 were infected, and of those 2064 (21% of the total number) had an intensive-care-unit-acquired infection. There was a relation between the prevalence of nosocomial infection and mortality according to country,<sup>19</sup> with greater incidence of infection and higher mortality rates in the southern European countries of Portugal and Greece than in Scandinavia and Switzerland (figure 1). There are many possible reasons for these observed differences, including that, in general, the countries of southern Europe have smaller intensive-care units that treat sicker patients than do the other countries.<sup>37</sup>

Other studies<sup>18,36,38-40</sup> have quoted incidence rates of between 9% and 37%, dependent largely on the populations studied and the definitions used. Differences in surveillance techniques can also affect detection of nosocomial infection and, hence, rates.<sup>41</sup> For example, in a French survey<sup>42</sup> of nosocomial infection surveillance, routine culturing of central venous lines was undertaken in only 55% of intensive-care units, admission urine cultures in 30%, and protected specimen brush for diagnosis of nosocomial pneumonia in 30%. Crude infection rates might not be representative of the overall problem, since they do not take into account patients' intrinsic risk of infection or extrinsic risks associated with exposure to medical interventions, etc.<sup>43</sup>

Is the incidence of these infections changing? One might expect to see an increase in nosocomial infections, since we treat more patients who are at higher risk—eg, elderly, debilitated, and more severely ill individuals—now than we use to. Furthermore, bed shortages in intensive-care units are common and premature discharge, perhaps to free a bed for another patient, can be associated with an increased risk of readmission and infection.<sup>44</sup> However, we are becoming less invasive in our treatment techniques (less aggressive surgical procedures are used, fewer Swan-Ganz catheters are being placed, non-invasive mechanical ventilation is being applied when possible and appropriate), and are more aware of techniques that could prevent nosocomial infection (antibiotic-coated catheters, avoidance of nasotracheal intubation thus limiting sinusitis), which could result in a reduced incidence of infections. Pittet and Wenzel<sup>45</sup> reported an increase in crude nosocomial bloodstream infection rates from 6.7 cases per 1000 discharges in 1980

to 18.4 in 1992. In a study on one intensive-care unit, comparing data over 25 years, the incidence of bacteraemia increased from 1.8% in 1971–75 to 5.5% in 1991–95, with the largest increase seen between 1986–90 and 1991–95.<sup>46</sup> Dagan and co-workers,<sup>40</sup> however, reported a fall in the nosocomial infection ratio from 25.2 in 1987 to 20 in 1992. This decrease was attributed by the researchers to the better management of intravenous and urinary catheters and to a more restricted use of antibiotics. Results from the NNIS for the period 1990–99 lend support to an overall fall in the incidence of respiratory, urinary tract, and bloodstream nosocomial infections across all types of intensive-care unit although the investigators of the report note that there were wide ranges in infection-rate percentiles.<sup>47</sup>

### Effect of nosocomial infection

The effect of nosocomial infection in terms of morbidity, mortality, and increased resource use is substantial. Nosocomial infection is associated with an increased length of stay,<sup>48-51</sup> which results in an additional cost of about US\$3.5 billion per year,<sup>52</sup> without taking into account antibiotic or other therapeutic costs. In a case-control study of 57 patients with catheter-related infection in Spanish intensive-care units, length of stay was increased by about 20 days and infection was associated with excess costs of €3000 (about \$3200) per episode.<sup>50</sup> In a US study of patients with primary nosocomial bloodstream infection, increased costs associated with infection were calculated at an average of \$34 508 per patient.<sup>51</sup>

Crude mortality rates associated with nosocomial infection vary from 12% to 80%, dependent on the population studied and the definitions used. Several researchers have attempted to assess attributable mortality rates<sup>48,53</sup>—ie, the mortality due directly to the presence of nosocomial infection—but this area is a controversial one, since patients who develop nosocomial infection are in general sicker and have a greater risk of death than patients who do not. Indeed, whereas some such studies do claim higher mortality associated with infection,<sup>54</sup> others have shown no increased mortality in infected patients compared with controls,<sup>50,51</sup> emphasising the problems with defining the cause-effect relation in these individuals. Soufir and co-workers<sup>55</sup> showed crude mortality rates of 50% and 21% in patients with and without catheter-related septicaemia, respectively, and infection remained associated with mortality when adjusted for admission prognostic factors. However, when adjusted for severity scores measured during the week before infection, catheter-related septicaemia was no longer associated with mortality.

### Organisms

Any organism can be implicated in nosocomial infection, and many infections are polymicrobial.<sup>19</sup> Recent years have seen a swing in the pattern of infecting organisms towards gram-positive infections.<sup>56</sup> The surveillance and control of pathogens of epidemiologic importance project (SCOPE) data<sup>57</sup> revealed that gram-positive cocci were isolated in 64% of 10 617 episodes of nosocomial bacteraemia, whereas gram-negative bacilli were isolated in only 27% of cases. The EPIC study<sup>19</sup> identified the following as the most commonly reported nosocomial pathogens: *Staphylococcus aureus* (30%), *Pseudomonas aeruginosa* (29%), coagulase-negative staphylococci (19%), yeasts (17%), *Escherichia coli* (13%), enterococci (12%), *Acinetobacter* spp (9%), and *Klebsiella* spp (8%).<sup>58</sup> Other studies have noted similar patterns of causative microorganisms.<sup>30,38,59</sup>

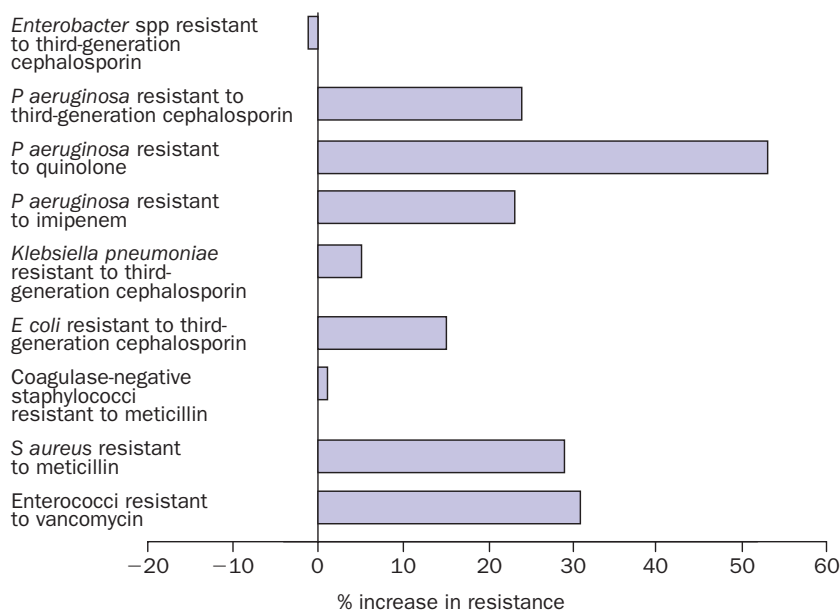


Figure 2: Increases in rates of antibiotic resistance for selected pathogens when comparing resistance rate of January to December, 2000, with mean rate resistance over previous 5 years (1995–99)<sup>65</sup>

Fungal pathogens, especially *Candida* spp, are becoming increasingly common.<sup>45,46</sup> Hospitals involved in the NNIS reported increases of 219–487% for bloodstream infections of *Candida* spp between 1980 and 1990.<sup>60</sup> Although the NNIS reported a decrease in infections due to non-*Candida albicans* between 1980 and 1990,<sup>61</sup> other more recent studies have noted a clear increase in non-*C albicans* isolates. The SCOPE study,<sup>62</sup> undertaken in the USA between 1995 and 1996, reported that 48% of 379 episodes of candidaemia were caused by non-*albicans* species, and the SENTRY study,<sup>63</sup> involving 34 medical centres in the USA, Canada, and South America, revealed that 53% of fungal bloodstream infections were caused by *C albicans*, followed by *Candida parapsilosis* (16%), *Candida glabrata* (15%), *Candida tropicalis* (8%), and *Candida krusei* (2%). Similar distributions have been reported in Italy.<sup>64</sup>

It is noteworthy that the precise pattern of causative organisms, whether bacterial or fungal, varies across countries and even between units, according to patient case mix, site of infection, antibiotic protocols, infection control practices, and local ecology and resistance patterns.

### Antimicrobial resistance

Patients who remain in hospital for long periods can have successive infections, and are more likely to develop nosocomial infections due to resistant pathogens. In the EPIC study,<sup>19</sup> 60% of the *S aureus* for which methicillin resistance patterns were reported were resistant (as high as 80% in Italy, France, and Greece), and 46% of *P aeruginosa* were resistant to gentamicin.<sup>58</sup>

Legras and colleagues<sup>38</sup> similarly reported that 58% of the *S aureus* in their study in French intensive care units were methicillin resistant. The NNIS reports increased rates of resistance for many micro-organisms when comparing data from 2000 with those pooled from the period 1995–99 (figure 2).<sup>65</sup> The increase in resistance of *P aeruginosa* to quinolone antibiotics is especially pronounced and could be related to increased use of these antibiotics as first-line agents both within and outside of

hospital.<sup>66</sup> Additionally, 55% of *S aureus* are now resistant to methicillin and 26% of enterococci are resistant to vancomycin. *Candida* resistance to antimicrobial agents, notably fluconazole, is also on the rise, especially among non-*albicans* species.<sup>67</sup>

Organisms isolated from patients in intensive-care units are more likely to be resistant to antibiotics than those isolated from general-ward patients or outpatients,<sup>68</sup> probably because there is high antimicrobial selection pressure in these individuals. Trouillet and colleagues,<sup>69</sup> in a study of 135 consecutive episodes of VAP, noted that previous antibiotic use and duration of mechanical ventilation were associated with the development of infection due to resistant organisms. The problem, however, is not so much antimicrobials per se, but rather the way in which they are used. Antibiotic treatment should not be started as a reflex to the presence of fever, but, whenever possible, only after identification of a definite

infectious process. Furthermore, narrow-spectrum antibiotics should be preferred. Admittedly, the diagnosis of infection is not always clear-cut in patients with multiple pathologies in intensive-care units, and isolation of organisms can be difficult in individuals often already treated with at least one antibiotic. In such cases, the intensivist or doctor along with infectious disease specialists should institute the most appropriate antimicrobial treatment based on available clinical and bacteriological data, and the range of cover reduced as soon as possible. Indeed, the choice of antibiotic treatment can affect the bacterial spectrum of the entire hospital or community. Even if a patient is responding well to the initial therapy, the spectrum must be narrowed once the infecting organism has been identified and antibiotic sensitivities have been ascertained, to limit the risk of superinfection, of bacterial resistance, and of side-effects, and to limit cost. Computerised systems can help in antibiotic selection and monitoring, by enabling regular input of changes in hospital ecology and protocols, as well as microbiological information as it becomes available for an individual, which could affect prescribing, and by facilitating monitoring of side-effects and doses, costs, and the emergence of resistant organisms. A study that used such a system showed a reduction in excess drug doses, in adverse events caused by anti-infectious agents, in costs, and in length of hospital stay.<sup>70</sup>

One approach to try and reduce the frequency of resistant organisms is to use antibiotic rotation or cycling. Gruson and colleagues<sup>71</sup> noted that antibiotic rotation and restricted use of ceftazidime and ciprofloxacin caused a fall in the number of cases of VAP associated with resistant gram-negative bacilli, and an increase in the numbers of methicillin-sensitive *S aureus*. Raymond and co-workers<sup>72</sup> introduced a quarterly rotation of empirical antibiotics in their intensive-care unit and noted great reductions in the incidence of antibiotic-resistant gram-positive coccal infections (7.8 infections per 100 admissions vs 14.6 infections per 100 admissions,  $p < 0.0001$ ), antibiotic-resistant gram-negative bacillary infections (2.5 infections per 100 admissions vs 7.7 infections per 100 admissions,

$p < 0.0001$ ), and mortality associated with infection (2.9 deaths per 100 admissions *vs* 9.6 deaths per 100 admissions,  $p < 0.0001$ ) during rotation. Other groups have reported similar benefits from such strategies,<sup>73</sup> which require continued input from infectious disease specialists if they are to be employed effectively.

## Specific nosocomial infections

### Respiratory

The respiratory tract is the most common site of nosocomial infection in the intensive care unit. In the EPIC study,<sup>19</sup> pneumonia accounted for 47% of nosocomial infections, the figure rising to 65% if all respiratory infections were included. Data from the NNIS show that nosocomial pneumonia accounts for 31% of all nosocomial infections in intensive care units.<sup>30</sup> In trauma patients, Papia and colleagues<sup>36</sup> reported that lower respiratory tract infection accounted for 28% of infections. Although the development of nosocomial pneumonia is associated with the same risk factors as other nosocomial infections, there are some predisposing factors that are specific to pulmonary infection. These include:

- Endotracheal intubation, which impairs host-defence mechanisms, including cough and mucociliary clearance, and makes nosocomial pneumonia especially common during mechanical ventilation (so-called VAP), especially when long-term.<sup>22,32</sup>
- Mechanical ventilation has been identified as a risk factor per se,<sup>19,22,36</sup> but in other studies it is the duration of mechanical ventilation that seems to be the problem. Artigas and colleagues<sup>32</sup> noted mechanical ventilation for longer than 24 h was a key risk factor in a multivariate analysis of 103 critically ill trauma patients. Cook and co-workers<sup>20</sup> reported a cumulative increased risk of VAP with time, but a decreasing daily risk of VAP, with VAP rates of 3% per day in the first week of mechanical ventilation, 2% per day in the second week, and 1% per day in the third week. These findings lend support to previous work by Langer and colleagues,<sup>74</sup> who similarly showed an increased incidence of pneumonia from 5% in patients who received 1 day of mechanical ventilation to 69% in those who received 30 days of ventilatory support, but when assessed according to date of onset of infection, the highest risk was during the first 8–10 days of mechanical ventilation. The use of non-invasive mechanical ventilation should be encouraged whenever appropriate, since it is associated with lower rates of nosocomial infection.<sup>75–77</sup>
- Microaspiration of oropharyngeal secretions is a common event, but upper airway colonisation by potentially pathogenic organisms is particularly frequent in the critically ill<sup>78</sup>—especially in patients with altered mental status—setting the stage for the development of pneumonia. Various strategies can be used to limit aspiration, including raising the head of the bed to 30–45°,<sup>79</sup> regularly checking the position of any feeding tube, and routinely assessing intestinal motility and adjusting feed volumes accordingly to avoid regurgitation.<sup>80</sup> The use of small-bore tubes or of jejunal rather than gastric tubes has also been suggested, but there is no consistent evidence to support these approaches.<sup>81,82</sup> In terms of reducing gastric colonisation, there has been a continuing debate with respect to the possible advantage of sucralfate over histamine-2-receptor-antagonists, which increase gastric pH and could, therefore, facilitate bacterial growth. However, the differences between these agents are probably small. Moreover, in

a multicenter Canadian study,<sup>83</sup> ranitidine was shown to be more effective than sucralfate at reducing gastrointestinal bleeding, with no differences in the rates of respiratory tract infection.

In addition to non-invasive ventilation and stress-ulcer prophylaxis, various other strategies have been proposed to help prevent nosocomial pneumonia. Selective digestive decontamination (SDD) is supposed to prevent infection by eradicating and preventing carriage of potentially pathogenic aerobic microorganisms from the oropharynx, stomach, and gut. SDD consists of non-absorbable antibiotics (normally polymyxin, tobramycin, and amphotericin B) applied topically to the oropharynx and through a nasogastric tube, plus the use of a systemic antibiotic, most commonly cefotaxime. This technique reduces the frequency of nosocomial pneumonia, especially in trauma patients, and results of meta-analyses have confirmed that SDD with a combination of topical and systemic antibiotics can reduce respiratory infection<sup>84–86</sup> and could have a beneficial effect on mortality.<sup>87</sup> However, SDD is not routinely used in most intensive-care units because of concerns about cost and the risk of increasing bacterial resistance<sup>88</sup> and drug toxicity with this approach.

Continuous subglottic aspiration is another approach that could reduce the incidence of VAP by limiting the quantity of oropharyngeal secretions available for aspiration; pooled secretions also encourage bacterial overgrowth. The technique reduced the onset of VAP in two randomised controlled trials of continuous subglottic aspiration in intensive care units<sup>89</sup> and cardiac surgery patients,<sup>90</sup> and in a randomised study of intermittent subglottic aspiration,<sup>91</sup> the incidence of VAP was reduced in the intervention group with a relative risk of 0.22 (95% CI 0.06–0.81;  $p = 0.014$ ).

### Urinary tract

This is the second most common site of nosocomial infection (accounting for 8–35% of infections<sup>19,22,30,31,38,92</sup>), although the consequences of nosocomial urinary tract infection are usually less severe than for other types of nosocomial infection. Urinary tract infections are generally associated with the presence of a urinary catheter,<sup>30,93</sup> and are most often associated with *Enterococcus* spp, *Candida* spp, *E coli*, *Klebsiella* spp, and *P aeruginosa*.<sup>94,95</sup> Various strategies have been suggested to reduce the incidence of nosocomial urinary tract infection in catheterised patients, including closed drainage systems, but in a prospective trial,<sup>96</sup> a closed drainage system was not shown to be any better than open drainage catheters in patients in intensive care. Silver-hydrogel coated catheters might reduce the incidence of nosocomial urinary tract infection in general hospital patients,<sup>97</sup> although results of several studies,<sup>98,99</sup> including one in patients in intensive care,<sup>100</sup> noted no significant differences. Antibiotic-coated catheters (with nitrofurantoin or ciprofloxacin) have been effective in animals and *in vitro*,<sup>101,102</sup> but no results from clinical tests have been published, and concerns exist as to the effects of such catheters on the development of antimicrobial resistance. Prevention of nosocomial urinary-tract infections should thus aim at avoiding catheter placement whenever possible, but, when necessary, reducing the duration of catheterisation.<sup>103</sup>

### Catheter-related infections

Catheter-related bloodstream infections are associated with pronounced increases in length of time in intensive-care units and hospital costs.<sup>104</sup> The importance of basic

hygiene, clean insertion practices, and regular catheter-site surveillance in the prevention of catheter-related infection cannot be over-emphasised. Sherertz and co-workers<sup>105</sup> documented a fall in catheter-related infections from 4.51 to 2.92 infections per 1000 patient-days ( $p < 0.01$ ) 18 months after a 1-day infection control training course on the use of sterile procedures in the insertion of central venous catheters, and Raad and colleagues<sup>106</sup> noted a much lower rate of infections (4 *vs* 12,  $p = 0.03$ ) when catheters were placed under maximum sterile precautions as opposed to sterile gloves and small drape only.

Other factors can also help reduce the likelihood of catheter-related infection.<sup>107–109</sup> First, for central venous catheters, the subclavian route is less prone to infection than the jugular or femoral routes.<sup>110</sup> Second, tunnelled central-venous catheters are associated with a reduced incidence of catheter-related infection,<sup>111</sup> although the results of a meta-analysis indicated that most evidence in favour of this approach was from one trial that used the jugular site and that there was insufficient evidence to recommend this procedure routinely.<sup>112</sup> Third, antimicrobial-impregnated catheters can reduce catheter-related infections. Findings of a meta-analysis of trials of central-venous catheters impregnated with chlorhexidine-silver-sulfadiazine showed a reduced incidence of catheter colonisation (odds ratio 0.44 [95% CI 0.36–0.54],  $p < 0.01$ ) and of catheter-related bloodstream infection (0.56 [0.37–0.84],  $p = 0.005$ ).<sup>113</sup> Results of a cost-effectiveness study that used a decision analytical model suggest that because of the 2% reduction in catheter-related infections, cost savings in the region of \$68–391 could be made by using impregnated catheters in patients at high risk of catheter-related infection.<sup>114</sup> Other catheters have been developed that are impregnated with minocycline or rifampicin and these too are associated with a reduced incidence of catheter-related bloodstream infection.<sup>115</sup> Indeed, in a comparison of the two types of impregnated catheter, the antibiotic-coated catheters were more effective than the antiseptic-coated catheters at reducing catheter-related infection.<sup>110</sup> However, these catheters are potentially associated with the development of antimicrobial resistance and, until further studies have been done to address this issue, they should be used sparingly. New developments in this specialty that are creating interest include specific polymers and antiadhesion molecules that prevent bacterial adhesion.<sup>109</sup> But, in the meantime, any catheter that could be infected or implicated in an infection, should be removed. The issue of routinely changing catheters has been hotly debated for some years, but regular, routine catheter changing seems to have little effect on the development of infection,<sup>116</sup> and changing central venous catheters over a guidewire could be associated with increased infection.<sup>117</sup> Good practice guidelines and training programmes have been developed for optimum catheter care, and hospitals that use such approaches have shown reduced catheter-related infections.<sup>105,118</sup>

#### Other sites

Nosocomial infections from other sources are generally decreasing in incidence. One good example of how change in practice can affect infection rates is the case of nosocomial sinusitis, a nosocomial infection specific to intensive-care units. Results of studies indicate that nosocomial sinusitis, carrying an increased risk of nosocomial pneumonia,<sup>119</sup> was significantly more common in patients with nasal devices, such as nasogastric or nasotracheal tubes, than in those without.<sup>120</sup> In a randomised trial, Rouby and colleagues<sup>121</sup> reported that

radiological sinusitis developed in 95% of patients intubated with a nasal tube compared with 23% in patients with an oral tube. Use of the orotracheal route for intubation, rather than the nasotracheal route, has reduced the incidence of nosocomial sinusitis.

#### General preventive strategies

Prevention has a key part to play in the limitation of nosocomial infection in intensive care units. Many preventive strategies have been suggested, but the most effective remain basic hygiene and care with catheter insertion and maintenance. The hands of health-care workers have been the subject of considerable research over the years, with several studies reporting high rates of contamination with potentially pathogenic organisms,<sup>122–124</sup> and some linking infection to hand carriage by gel electrophoresis and DNA-typing techniques.<sup>125–127</sup> Clearly, hand-hygiene must be an important part of infectious control procedures,<sup>128</sup> but adherence is generally poor.<sup>129,130</sup> Hospital-wide campaigns that aim to promote hand-hygiene can improve adherence,<sup>131</sup> although this method may not be sustained and such campaigns need to be regularly repeated.<sup>132</sup> Ring wearing can reduce the effectiveness of hand-hygiene<sup>133</sup> and should be discouraged. Hand disinfection, with the use of antiseptic, alcohol-based hand-rub solutions is more effective both at reducing hand contamination and at encouraging compliance than hand-washing with soap and water.<sup>131</sup> Hand rubs involve less time input and in a busy, understaffed unit might facilitate adherence with hand-hygiene protocols.<sup>134</sup> Detailed guidelines with respect to the role of hand-hygiene in infection prevention have been published by the Centers for Disease Control and Prevention (CDC).<sup>135</sup>

#### Future perspectives

I have selected four areas that I see as having a key role if we are to see great and sustained reductions in nosocomial infections in our intensive-care units.

First, the roles of understaffing and staff composition as predisposing factors for nosocomial infection need to be emphasised. Fridkin and colleagues<sup>136</sup> noted that the patient-to-nurse ratio was an independent risk factor for catheter-related bloodstream infection in their population of surgical patients in intensive care. The same group subsequently noted that not only were lower nurse-to-patient ratios associated with higher risks of nosocomial bloodstream infections, but in multivariate analysis, admission during a period of high pool-nurse-to-patient ratio was also associated with an increased risk of infection (odds ratio 3.8).<sup>137</sup> This finding suggests that general organisational measures, involving system modifications at the unit and even hospital level, could effect nosocomial infection rates. No longer can nosocomial infections be blamed on the individual carer or care team; management needs to begin to bear at least some of the responsibility.

Second, infection surveillance can reduce nosocomial infection rates when incorporated with infection prevention programmes,<sup>138</sup> but needs to be improved and implemented and combined with continuing educational programmes to encourage compliance with basic infection control procedures. Infection surveillance is increasingly undertaken, and various surveillance systems have been developed. Perhaps the most widely used system is that of the NNIS (<http://www.cdc.gov/ncidod/hip/NNIS/@nnis.htm>), for which data are collected uniformly by trained infection control personnel, using surveillance protocols that target inpatients at high risk of infection, and are reported routinely to the CDC, where they are aggregated into a database. Participation in the NNIS is voluntary and

involves only acute care general hospitals in the USA. About 315 hospitals across the US are involved in the NNIS. Within Europe, several national surveillance networks for nosocomial infections in the intensive-care unit exist, including the REA-SE in France, the NSIH-ICU in Belgium, KISS-ICU in Germany, PREZIES-ICU in the Netherlands, and ENVIN-UCI in Spain. However, there are considerable discrepancies in the definitions of nosocomial infection used across these networks, and the Hospitals in Europe Link for Infection Control through Surveillance (HELICS) project (<http://helics.univ-lyon1.fr/index.htm>) has been established to try to standardise infection monitoring in intensive care units in Europe. A major goal of infection surveillance programmes is to develop and assess strategies to prevent and control nosocomial infections. The data collected can be used by individual hospitals and national health-care planners to set priorities for their infection control programmes and to assess the effectiveness of their efforts. Data-mining has been suggested as a means of extracting new, unexpected, and interesting patterns in hospital infection control data, allowing hospital infection control programmes to focus their limited resources on issues of probable importance.<sup>139</sup>

Third, continued research is needed into the role of agents and strategies able to affect immune defence, including interferon  $\gamma$ , interleukin 12, and granulocyte-colony stimulating factor; study in this area is exciting and continuing, but clinical trial results are limited. A study<sup>140</sup> that assessed the effects of intensive insulin therapy—ie, maintenance of blood glucose between 4.44–6.11 mmol/L—in patients in intensive care, noted that this approach reduced infections rates and mortality. Further study is needed to confirm these findings and to assess the most effective way of applying them to the general intensive-care-unit population, but this approach could prove a useful and fairly simple means of preventing nosocomial infections.

Finally, the development of nosocomial infection risk indexes<sup>34,141</sup> could be of use in identifying patients at particular risk who might benefit most from available preventive measures, and from techniques to modulate immune defence.

## Conclusion

Nosocomial infection is a cause of increased morbidity, mortality, and resource expenditure throughout the hospital setting, and particularly in the intensive-care unit. A multidisciplinary approach to prevention that involves the whole intensive-care team, including management, is essential if we are to succeed in preventing nosocomial infections. Awareness of risk factors and attention to simple preventive measures such as hand-hygiene can reduce the incidence and effect of these infections. Once present, treatment relies on appropriate, adequate antibiotic treatment, which should be based on microbiological data and ideally managed in association with infectious disease specialists to reduce the risks of antimicrobial resistance. Surveillance of nosocomial infections is increasingly being undertaken and will play an important part in the monitoring of such infections and in the assessment of strategies to prevent their development.

*Conflict of interest statement*  
None declared.

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## Uses of error

### Group practice

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For 15 years we have shared adjacent offices and clinical duties in a University Division of Geriatrics. Years of caring for the frail elderly have fortified a mutual natural distrust of aggressive medical intervention. Our experiences in post-acute settings, where patients must often recover from close contact with acute medical care, have been especially persuasive. When one of us requires a physician to fill out paperwork, or much more rarely when trivial infirmities arise, he has called on the other. This relationship had been the source of some levity, given our nihilism regarding a doctor's value for a healthy patient. Worse, we have both been fortunate to enjoy good health.

During a busy clinic, TEF grabbed WBG mid-flight for advice about a lesion on a woman's arm. WBG examined the patient and, leaving the room, agreed that this needed only careful follow-up. He noted in passing that he wasn't worried about the patient because he himself had something quite similar. He displayed a small lesion on his elbow, but we did not slow down. A few months later,

WBG took his wife to a dermatologist. His wife insisted that the dermatologist examine him as well. After a brief examination the dermatologist biopsied the elbow lesion. Of course it was a melanoma, still in situ thank heavens, but a melanoma nonetheless.

One hundred percent of physicians die, in spite of their medical knowledge. Many diagnose and treat themselves, sometimes successfully, despite the truism that "The physician who treats himself (or herself) hath a fool for a doctor". One lesson from this story is that if you are physician to another physician, you must establish enough discipline, in the face of collegiality, to insist on a proper place and time to provide care. A second is that if a patient's finding is matched exactly by a symptom or finding the physician has, this is not by itself proof the problem is insignificant. Third, sometimes medical intervention is actually a good idea. We, of course, are extremely reluctant to be caught needing medical intervention.

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