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# Noscocomial Infections: A brief Review

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## *Abstract*

Many patients around the world suffer harm due to infections caused by viruses, bacteria, fungi, protozoa or helminthes that are no longer susceptible to the common medicines used to treat them. Reports are most often generated on the basis of laboratory results on microbes obtained from human patients. Nosocomial is one such common infection through-out the world. It is an infection whose growth and development is favored by hospital environment. This review elaborates the details of this infections in brief. The review presents its various types, bio-medical classification, pathogen responsible, effective antibiotics against this infection, antibiotic resistance in patients and general guidelines. This concise information could be useful for further research, bio-medical applications, disease management, pharmacy practice, drug administration and exploring the efficacious drug to treat the patient.

***Keywords:*** Nosocomial, Antibiotics, Microbes



## *1.Introduction*

Bacteria that cause disease react to the antibiotics used as treatment by becoming resistant to them, sooner or later. This natural process of adaptation, antimicrobial resistance, means that the effective lifespan of antibiotics is limited. Unnecessary use and inappropriate use of antibiotics favours the emergence and spread of resistant bacteria. A crisis has been building up over decades, so that today many common and life-threatening infections are becoming difficult or even impossible to treat, sometimes turning a common infection into a life-threatening one. It is time to take much stronger action worldwide to avert a situation that entails an ever increasing health and economic burden[1]. Many patients around the world suffer harm due to AMR because infections – caused by viruses, bacteria, fungi, protozoa or helminthes – are no longer susceptible to the common medicines used to treat them. Reports on AMR are most often generated on the basis of laboratory results on microbes obtained from human patients. These reports are used to inform decisions on the treatment of individual patients, and also as evidence for policies at local, national, and international levels. Data from around the world confirm that AMR, including multidrug resistance, is increasing among many pathogens responsible for infections in health-care facilities and in the community[2].

### 1.1. Nosocomial infection

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.

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 nocosomialinfection in ICU. Hospital-acquired infection or HAI, infections include fungal and bacterial infections and are aggravated by the reduced resistance of individual patients [3,4].

Hospital-acquired bacterial species, such as *K. pneumonia*, but also in the typical community-acquired species, *Escherichia coli*. This gene has been identified in strains that possess other resistance mechanisms contributing to their multidrug resistance patterns. It has been recently extensively reported from the United Kingdom, India, Pakistan and albeit to a lesser extent, from a number of other countries worldwide[5]. The Centers for Disease Control and Prevention (USA), 13,300 patients died of antibiotic-resistant bacterial infection in the US during 1992. An incredible 150% increase in the occurrence of drug-resistant *Pneumococcal* was noted between 1987 and 1994. The frequency of methicillin-resistant *Staphylococcus* rose from 2% in 1975 to 32% in 1992[6].

### 1.2 Present status of nosocomial infections in various countries

To take up the detailed studied of nosocomial infections it is important to take up the a brief look at the status of the infection in India and other countries. In India, a number of cases are increasing day by day and the status in other countries is given in **table I**.

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## 2. Common nosocomial infections

**a. Hospital-acquired pneumonia (HAP)**

HAP is defined as pneumonia that occurs 48 hours or more after admission, which was not incubating at the time of admission [7,8]. HAP may be managed in a hospital ward or in the intensive care unit (ICU) when the illness is more severe. Rates of HAP due to MDR pathogens have increased dramatically in hospitalized patients, especially in intensive care and transplant patients[9].

**b. Ventilator associated pneumonia (VAP)**

VAP refers to pneumonia that arises more than 48–72 hours after end tracheal incubation[7,10]. Although not included in this definition, some patients may require intubation after developing severe.

**c. Methicillin resistant *Staphylococcus aureus* (MRSA)**

Infections due to gram-positive cocci, such as *Staphylococcus aureus*, particularly Methicillin resistant *S. aureus* (MRSA), have been rapidly emerging in the United States[11,12]. Pneumonia due to *S. aureus* is more common in patients with diabetes mellitus, head trauma, and those hospitalized in ICUs. MRSA produces a penicillin-binding protein with reduced affinity for β-lactam antibiotics that is encoded by the mec A gene, which is carried by one of a family of four mobile genetic elements[13-15].

**d. Fungal pathogens**

Nosocomial pneumonia due to fungi, such as Candida species and *Aspergillus fumigatus*, may occur in organ transplant or immunocompromised, neutropenic patients, but is uncommon in immunocompetent patients. Nosocomial Aspergillus species infections suggest possible airborne transmission by spores, and may be associated with an environmental source such as contaminated air ducts or hospital construction. By comparison, isolation of *Candida albicans* and other Candida species from endotracheal aspirates is common, but usually represents colonization of the airways, rather than pneumonia in immunocompetent patients, and rarely requires treatment with antifungal therapy[16-20].

***e. Pseudomonas aeruginosa***

*P. aeruginosa*, the most common MDR gram-negative bacterial pathogen causing HAP/VAP, has intrinsic resistance to many antimicrobial agents. This resistance is mediated by multiple efflux pumps, which may be expressed all the time or may be transformed by mutation. Resistance to piperacillin, ceftazidime, cefepime, other oxy imino-β-lactams, imipenem and meropenem, aminoglycosides or fluoroquinolones is increasing in the United States[11, 21-24].

***f. Acinetobacter species***

Acinetobacter species have nonetheless become problem pathogens because of increasing resistance to commonly used antimicrobial agents. More than 85% of isolates are susceptible to carbapenems, but resistance is increasing due either to IMP-type metalloenzymes or carbapenemases of the OXA type. An alternative for therapy is sulbactam, usually employed as an enzyme inhibitor, but with direct antibacterial activity against Acinetobacter species[5,25].

***g. Stenotrophomonas maltophilia***

*S. maltophilia*, which shares with *B. cepacia* a tendency to colonize the respiratory tract rather than cause invasive disease, is uniformly resistant to carbapenems, because of a ubiquitous metallo-β_-lactamase. *S. maltophilia* and *B. cepacia* are most likely to be susceptible to trimethoprim–sulfamethoxazole, ticarcillin–clavulanate, or a fluoroquinolone. *B. cepacia* is also usually susceptible to ceftazidime and carbapenems[14].

**h. Urinary tract infection**

*Enterococcus fecalis* is a normal commensal in the human and animal gastrointestinal tract but it has become increasingly recognised as one of the leading cause of nosocomial infections. Urinary tract infections (UTI) are the most frequent, although more serious infections, such as bacteremia, endocarditis and neonatal infections also occur. One of the main reasons why enterococci can survive in the hospital environment is their resistance to a variety of antimicrobials. In fact, in addition to their intrinsic resistance to low levels of aminoglycosides, cephalosporins, lincosamydes and many β-lactams, enterococci are also able to acquire resistance to many antibiotics, either by mutation of existing chromosomal genes or by transfer of resistance determinants. The past two decades have therefore witnessed the rapid emergence of multidrug resistant enterococci[26-28].

**i. Legionnaires' disease**

**Table 1. Present status of nosocomial infections in other countries**

| | |
|---|---|
| United States: The Centers for Disease Control and Prevention (CDC) | 1.7 million hospital-associated infections, urinary tract infection (36%), followed by surgical site infection (20%), bloodstream infection (BSI), and pneumonia (both 11%) |
| France: at national level, prevalence among patients in health care facilities was | Estimates 6.7% in 1990 to 7.4%6.7% in 1996, 5.9% in 2001 and 5.0% in 2006. The rates for nosocomial infections were 7.6% in 1996, 6.4% in 2001 and 5.4% in 2006. |
| Italy: A survey in Lombardy gave a rate of 4.9% of patients in 2000. | Since 2000, estimates show that about 6.7% infection rates, i.e. between 450,000 and 700,000 patients, which caused between 4,500 and 7,000 deaths. |
| United Kingdom: | Estimates of 10% infection rate, with 8.2% estimated in 2006. |
| Switzerland: | Range between 2 and 14%. A national survey gave a rate of 7.2% in 2004. |
| Finland: | Estimated at 8.5% of patients in 2005 |

*Legionella pneumophila* as a cause of HAP is variable, but is increased in immune compromised. Patients, such as organ transplant recipients or patients with HIV disease, as well as those with diabetes mellitus, underlying lung disease, or end-stage renal disease. HAP due to *Legionella* species is more common in hospitals where the organism is present in the hospital water supply or where there is ongoing construction. Because detection is based on the widespread use of *Legionella* urinary antigen, rather than culture for *Legionella*, disease due to serogroups other than serogroups 1 may be under diagnosed. Detailed strategies for prevention of *Legionella* infections and eradication procedures for *Legionella* species in cooling towers and the hospital water supply are outlined in the CDC/HICPAC Guidelines for Preventing Health-care–associated Pneumonia[8,16,29-31].

**5. Antibiotic resistance**

Trends in antibiotic resistance and their consequences for health, welfare and the economy are rapidly changing. Antibiotic resistance threatens the success of medical interventions at all levels of health care and creates a set of specific challenges for clinical, therapeutic and public health interventions with local, national, and global dimensions. Bacteria that belong to the normal flora in humans become indiscriminately exposed to antibiotic compounds every time antibiotics are used. Therefore, the most significant resistance has been emerging among these microorganisms. Since most of them are truly opportunistic pathogens, the most vulnerable segment of societies i.e. the

**Table 2. Common Antibiotics and their mode of action.**

| 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* |
| | Sulphonamides | Sulphonamides | |

allow Genetic changes reflect phenotypic alleles, and enable the bacteria to deal with the antibiotic. These mechanisms can be summarized as follows[36,37]:

•*Antibiotic inactivating enzymes* e.g. *β-lactamases, aminoglycoside* modifying enzymes, chloramphenicol *acetyl transferase* etc.

• *Impaired uptake of antibiotics* which can be natural due to cell envelope characteristics. In the case of acquired resistance changes in porins may interfere with antibiotic transport.

the bacteria to grow in the presence of the antibiotic. This mechanism is seen in glycopeptide, aminoglycoside, macrolide, sulpha/trimethoprim resistance amongst others.

In essence all strategies aim at optimizing the antibiotic stress in the environment, decrease unintended interaction between antibiotics and pathogens, restrict the spread of resistant organisms and treat infections with the minimum amount of antibiotic necessary to effect cure. Towards this end a number of countries have evolved national programmes that tackle the complex issue. The common methods being focused on are [37,38]:

- Surveillance of antibiotic use and resistance rates.
- Optimizing antibiotic use with treatment guidelines.
- Education of professionals and the public.
- Prevention with infection control measures and immunization.

## 7. Control of antimicrobial resistance

**Table 3. List of infection causing agents and their resistance against antibiotics.**

| S. no. | Causative agent | Cause | Resistant against antibiotics |
|---|---|---|---|
| 1. | *E coli* | urinary tract infections and bacteremia in humans | Aminopenicillins, such as amoxicillin or ampicillin, and narrowspectrum cephalosporins. |
| 2. | *S Aureus(*MRSA) | infection among hospitalized patients | Vancomycin, Methicillin |
| 3. | *P aeruginosa* | opportunistic infections among immune compromised individuals | Multidrug resistance |
| 4. | *Vibrio cholerae* | Watery diarrhea. | furazolidone, cotrimoxazole, nalidixic acid, tetracycline |
| 5 | *Klebsiellae* | pneumonia, bacteremia, thrombophlebitis, urinary tract infection (UTI), cholecystitis, diarrhea, upper respiratory tract infection, wound infection, osteomyelitis, and meningitis | *β*-lactam, multidrug resistant |
| 6. | *Acinetobacter* sp. | nosocomial pneumonia, ventilator associated pneumonia | Penicillin, chloramphenicol, amino glycosides, fluoroquinolones |
| 7. | *Stenotrophomonas maltophilia* | pneumonia, urinary tract infection, or blood stream infection; in immunocompromised | Multidrug resistant |
| 8. | *Serratia sp.* | Nosocomial infections of the bloodstream, lower respiratory tract, urinary tract, surgical wounds, and skin and soft tissues in adult patients | Multidrug resistant |
| 9. | *S. typhi* | typhoid, or enteric fever | Fluroquinolones, chloramphenicol, |
| 10. | *S. paratyphi* | Paratyphoid fevers | Fluroquinolones, chloramphenicol, |
| 11. | *Neisseria gonorrhea* | sexually transmitted diseases | Penicillin, fluoroquinolone |
| 12. | *Neisseria meningitides* | sporadic and epidemic meningitis | Penicillin |
| 13. | *Streptococci sp.* | meningitis, bacterial pneumonia, endocarditis, erysipelas and necrotizing fasciitis | tetracycline's and Macrolides |
| 14. | *Enterococcus fecalis* | Urinary tract infections (UTI), bacteremia, endocarditis and neonatal infections | Ampicillin, trimethoprim, sulphonamides, ciprofloxacin. |

young, elderly and immune-compromised are likely to face infections and the consequences of failing antibiotic effectiveness. The WHO Global Strategy for Containment of Antibiotic Resistance[2,32-34] .

**6. Causes of antibiotic resistance**

Development of an alternate metabolic pathway would would

- Industry involvement, financial resource mobilization and drug development.
- Regulatory issues with central prescribing restrictions and advertising restrictions.
- Audit with evaluation of interventions, audit of compliance and physician feed back.

**7. Guidelines**

The 2001 WHO global strategy1 for the containment of AMR addresses *what to do* and *how to do it* and provides a framework of interventions to slow the emergence and reduce the spread of antimicrobial resistant microorganisms wherever anti-infective medicines are used, through:

- reducing the disease burden and spread of infection;
- improving access to appropriate antimicrobials;
- improving the use of antimicrobials;
- strengthening health systems and their surveillance capabilities;
- enforcing regulation and legislation;
- encouraging the development of appropriate new drugs and vaccines.

WHO is engaged in guiding the response to AMR through:

- policy guidance, support for surveillance, technical assistance, knowledge generation and partnerships, including through disease prevention and control programmes;
- essential medicines quality, supply and rational use;
- infection prevention and control;
- patient safety; Laboratory quality assurance.

**Conclusion**

Hospital acquired infection in medical terms is known as nosocomial infection. It is an infection whose growth and development is favored by hospital environment. It easily spreads to the regular visitors in the hospital and the hospital staff. It includes fungal and bacterial infections that are aggravated by the low immunity. The most effective technique for controlling nosocomial infection is to strategically implement quality assurance, quality control, good laboratory practices measures to the health care sectors and evidence-based management. For those with ventilator associated or hospital acquired pneumonia, controlling and monitoring hospital indoor air quality needs to be on agenda in management, whereas for nosocomial rotavirus infection, a hygiene protocol has to be enforced along with the well defined management for ambulance transport.

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