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Nosocomial Infections in Patients with Human Immunodeficiency Virus (HIV)

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1. Introduction

Human immunodeficiency virus (HIV) results in acquired immune deficiency syndrome (AIDS) and is characterized by a serious disorder of the immune system in which the protective defenses against infection cannot function leaving the individual vulnerable to severe infections and conditions. This results in opportunistic infections causing an unfavourable outcome. Since its discovery in 1981 when the first cases were described, HIV/AIDS continues to affect people globally. According to the UNAIDS (Joint United Nations Programme on HIV/AIDS) and WHO (World Health Organization) 2009 AIDS epidemic update report, the estimated number of people living with HIV worldwide in 2008 was 33.4 million (UNAIDS 2009). Ultimately there is a high prevalence of HIV infection among patients admitted to hospitals as well as a high prevalence of AIDS patients as a result of opportunistic infections related to their HIV status or advanced AIDS (Mbanya, Ateudjieu et al. 2010).

2. Bacterial colonization

A major risk factor for bacterial colonization is immunosuppression subsequently making HIV-infected individuals ideal candidates (Craven, Steger et al. 1996). Bacterial colonization refers to the presence of bacteria in a host but does not cause a specific immune response or infection. However, if the relationship between the host and bacterial agent is changed - such as immunosuppression of the host, this episode can result in infections (Mandell, Bennett et al. 2005). Colonization therefore seems to contribute significantly to the development of nosocomial infections in HIV-positive patients (Petrosillo, Pagani et al. 2003).

Colonization is the first step of microbial infection. It is the establishment of the pathogen at the suitable portal of entry for example, host tissues that are in contact with the external environment. Sites of entry include the conjunctiva, the digestive tract, the respiratory tract and the urogenital tract. Organisms such as *Staphylococcus aureus* have been found to have high rates of nasal colonization in HIV-infected patients (Raviglione, Mariuz et al. 1990; Weinke, Schiller et al. 1992). Additionally other body cavities may also provide productive environments for bacterial colonization. The oral cavity is proximal and contiguous with the trachea and is therefore a portal for respiratory pathogen colonization. The teeth and other

oral mucosal surfaces particularly in ICU patients operate as reservoirs for respiratory pathogen colonization (Raghavendran, Mylotte et al. 2007).

3. HIV and nosocomial infections

A nosocomial (hospital-acquired) infection is one in which there is no evidence that the infection was present or in an incubation period at the time of hospital admission except 48 hours after admission. The condition is classified as an infection when it is manifested as a clinical disease and not a colonization where microorganisms are present but have no harmful effects on the patient's health. However, asymptomatic patients are considered infected if the body fluid or body site that is normally sterile (e.g. blood or cerebrospinal fluid) contains pathogenic microorganisms (Emori and Gaynes 1993). Nosocomial infections constitute a significant public health concern. They contribute to long hospital-stays and additional health care costs and are a significant cause of morbidity and mortality in hospital environments (Petrosillo, Pagani et al. 2003; Singh, Goering et al. 2006). Nosocomial infections are common and not always avoidable because of the large turnover of patients with underlying conditions. Furthermore their immune systems are often in a weakened state. Horizontal transmission from one patient to another creates an opportunity for the spread of hospital pathogens. Various invasive surgical procedures such as indwelling catheters and medical devices bypass the natural body-protective barriers. Prior antimicrobial therapy and inappropriate use of antimicrobial agents resulting in the emergence of resistant strains are traditional risk factors for acquiring infections in the hospitals. Nosocomial infections are therefore a major challenge to the patients' safety in the hospital setting and HIV as an additional factor has led to an increase in morbidity and mortality. This can be explained by the ability of opportunistic pathogens and microorganisms that are normally non-pathogenic to cause disease in immunocompromised individuals (Emori and Gaynes 1993; Craven, Steger et al. 1996; Vandenesch, Naimi et al. 2003; Singh, Goering et al. 2006; Panis, Matsuo et al. 2009). There are several pathogenic processes that are involved in the progression to AIDS in HIV-infected individuals such as: depletion in CD4 lymphocytes, defects in B lymphocytes, neutrophil dysfunction and the breakdown of the integument as a result of AIDS-related dermatological conditions for example bacterial and fungal dermatoses and Kaposi's sarcoma. These individual factors have significant implications regarding host susceptibility to nosocomial infections (Duse 1999). Nosocomial infections appear to be more common in HIV-positive individuals with AIDS as opposed to HIV-negative individuals (Angus and Wax 2001). Studies have suggested that HIV-infected or AIDS patients are at high risk of acquiring nosocomial infections particularly sepsis and bacteraemia due to the implantation of invasive intravascular medical devices (Gobbi, Maggi et al. 1998; Tumbarello, Tacconelli et al. 1998; Laing 1999; Petrosillo, Pagani et al. 2003; Japiassú, Amâncio et al. 2010). Nosocomial urinary tract and respiratory tract infections are also common in HIV-infected AIDS patients following bacterial colonization (Petrosillo, Nicastrì et al. 2005).

3.1 Bacteraemia

Bacteraemia or bloodstream infections are among the most severe of hospital-acquired infections and have been shown to cause significant mortality and prolonged hospital-stays in patients with HIV (Tumbarello, Tacconelli et al. 1998). Previous studies have shown that an increase in these bloodstream infections is associated with HIV infections (Beuheza, Beckelman et al. 1989; Fife, Crane et al. 1990).

3.1.1 Etiological agents

Coagulase-negative staphylococci have been implicated as important causes of nosocomial bloodstream infections particularly in patients that are immunocompromised (Tumbarello, Tacconelli et al. 1995; Pagano, Tacconelli et al. 1997) and in those infected with HIV (Weinke, Schiller et al. 1992; Tumbarello, Tacconelli et al. 1996; Tumbarello, Tacconelli et al. 1998). Globally, *Staphylococcus aureus* is the second most common pathogen that is responsible for causing bloodstream infections (Fluit, Jones et al. 2000; Luzzaro, Viganò et al. 2002) and in European countries it is the leading cause of nosocomial bloodstream infections (Luzzaro, Viganò et al. 2002). *S. aureus* is also the most common pathogen isolated from all bloodstream infections in the US (Shorr, Tabak et al. 2006). Bloodstream infections caused by these organisms are associated with a high frequency of life-threatening complications such as metastatic infections and infective endocarditis (del Rio, Cervera et al. 2009). *S. aureus* has also shown to be responsible for a significant number of in-hospital deaths in patients with long-term catheters, cardiovascular, orthopaedic and other medical devices (Chu, Crosslin et al. 2005). Methicillin-resistant strains of *S. aureus* also pose a major problem in nosocomial bloodstream infections (del Rio, Cervera et al. 2009).

Other studies have suggested an increased risk of nosocomial bloodstream infections due to aerobic gram-negative bacilli such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Escherichia coli* in patients that were HIV-infected particularly in those having invasive devices (Hickey and Shanson 1993; Sanford 1995; Zurlo and Lane 1997; Tumbarello, Tacconelli et al. 1998). Nontyphoidal *Salmonella* species is an infrequent cause of hospital infections (Jaspan 2008).

3.1.2 Clinical manifestations

Bloodstream infections may be defined as the presence of viable bacteria in the blood (bacteraemia) with a documented positive blood culture result and the presence of clinical symptoms of systemic infection (Garner, Jarvis et al. 1988). Primary bloodstream infection is a bloodstream infection without a documented primary source of infection (portal of entry or site of infection) and can be distinguished from a secondary bloodstream infection which is a bloodstream infection secondary to a localised site of infection – wound infection, skin and soft-tissue infection, biliary tract infection and pneumonia (Seifert 2009). Infections usually associated with secondary bloodstream infections include deep-seated abscesses, osteomyelitis and endocarditis (Fowler, Olsen et al. 2003). It has been reported that approximately one third of patients with *S. aureus* bloodstream infections develop local complications or distant septic metastases and affect the epidural space and intervertebral discs, bone and joints particularly when prosthetic material and native and prosthetic cardiac valves are being used (Ringberg, Thoren et al. 2000; Fowler, Olsen et al. 2003). Visceral abscesses in the spleen and kidney may also develop (del Rio, Cervera et al. 2009). Risk factors associated with complicated *S. aureus* bloodstream infections include the presence of persistent bacteraemia which is defined as the presence of positive blood cultures after 72-96 hours of appropriate treatment, the presence of skin lesions suggesting distant metastases, persistent fever and community acquisition (Fowler, Olsen et al. 2003).

Bloodstream infections are a major cause of illness in patients infected with HIV. A high percentage of bloodstream infections, ranging from 10% to 63% were observed in hospitalised HIV-infected individuals presenting with fever in a number of studies conducted in Sub-Saharan Africa (Archibald, den Dulk et al. 1998; Ssali, Kanya et al. 1998;

McDonald, Archibald et al. 1999; Peters, Zijlstra et al. 2004). Another study showed that bloodstream infection was associated with recent HIV diagnosis. Almost half the patients with bloodstream infections presented with a temperature of greater than 38°C. Lower T CD4⁺ counts were also strongly associated with those patients having bloodstream infections. Symptoms of abdominal illness such as nausea, vomiting and loss of appetite were also associated with bloodstream infections caused by pathogens (Varma, McCarthy et al. 2010). HIV-infected patients may be predisposed to bloodstream infections due to several conditions such as defective cell-mediated immunity, altered B-cell function with a consequent lack of serum opsonins against some encapsulated bacteria and qualitative and quantitative deficits of neutrophils leading to an increase in the susceptibility of the patient to bacterial and fungal infections (Mertins, Ortona et al. 1990; Zurlo and Lane 1997).

3.1.3 Management

The clinical microbiology laboratory plays an important part in the management of patients with bloodstream infections. A highly specific indicator of bloodstream infections is the culturing of pathogenic microorganisms from blood. In addition antimicrobial susceptibility testing (AST) may assist in the choice of antimicrobial therapy to be administered (Bohte, van Furth et al. 1995; Chalasani, Valdecanas et al. 1995; Fine, Smith et al. 1996). The early and rapid administration of antimicrobial treatment to infected patients has initially shown to decrease mortality (Leibovici, Konisberger et al. 1992). However, due to the emergence of antibiotic resistance there is a need to develop new antimicrobial agents (Ibrahim, Sherman et al. 2000).

It is recommended that for those patients that are infected with coagulase-negative staphylococci due to the presence of catheters, the catheter should be removed and a short course (5-7 days) of antibiotics administered. If the patient has endovascular hardware present, persistent fever or bacteraemia may be experienced after the catheter has been removed, then a long course of antibiotics may be required (O'Grady and Chertow 2011).

The choice of antibiotics for enterococcal bloodstream infections depends on the susceptibility of the infecting isolate due to antibiotic resistance. Ampicillin is the preferred choice of drug for the treatment of ampicillin-susceptible enterococci. If the pathogen is resistant to ampicillin, vancomycin should be used if the isolate is vancomycin-susceptible. Enterococci resistant to both ampicillin and vancomycin can be treated with new oxazolidinones, linezolid or lipopeptides, daptomycin. However, this depends on susceptibility testing (O'Grady and Chertow 2011). Some studies have shown that combination therapy may be more effective than monotherapy. This was seen in a number of patients with enterococcal bloodstream infections in which the catheter was not removed and a combination of ampicillin and gentamicin was used (Sandoe, Witherden et al. 2002).

For gram-negative bacilli removal of short-term catheters followed by 5-7 days of systemic antibiotic therapy is suggested based on antimicrobial susceptibility test results. Usually fourth generation cephalosporins, carbapenems or a combination of β -lactam and β -lactamase inhibitor may be used (O'Grady and Chertow 2011). However, extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* should not be treated with cephalosporins or piperacilin-tazobactam even if they may be susceptible as treatment with these drugs has been associated with poor clinical outcome (Paterson, Ko et al. 2001; Jacoby and Munoz-Price 2005).

Fluconazole may be used to treat individuals with bloodstream infections as a result of *Candida* species. Alternative therapy includes echinocandins as first-line therapy and lipid formulations of amphotericin B (Mora-Duarte, Betts et al. 2002; Reboli, Roststein et al. 2007).

A confirmed catheter-related bloodstream infection for gram-positive organisms requires at least two positive results drawn from different sites. These infections are difficult to treat unless the infected catheter is removed (Cotton, Gill et al. 1987; Peces, Gago et al. 1997).

3.2 Urinary tract infections

Other common nosocomial infections are associated with the urinary tract. Nosocomial urinary tract infection is a major infection acquired in both hospitals and nursing homes. In most cases these infections are commonly related to catheterization. Bacteriuria is a term referring to bacteria in the urine (Mandell, Bennett et al. 2005). Insertion of a catheter may predispose the bladder to the introduction of organisms that may colonize the site of insertion. Any disconnection of the catheter from the collection tube or breakage of the closed system may result in bacteriuria. The collection bag is drained regularly and if the lumen of the drainage tube is contaminated with bacteria, this provides a portal of entry for bacteria to the drainage bag, collection tube and catheter. A biofilm which secures the bacteria against the catheter or mucosal surface protects the bacteria from the mechanical flow of urine, host defences and antibiotics (Warren 2001). The rate of urinary tract infections particularly related to the use of urinary catheters plays a significant role in nosocomial infection in HIV patients (Gobbi, Maggi et al. 1998).

3.2.1 Etiological agents

Common organisms isolated from urinary tract infections include *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Staphylococcus epidermis*, enterococci and *Candida* species (Warren 2001). Uropathic *E. coli* are responsible for most urinary tract infections. The *E. coli* serogroups most often implicated as the cause of high proportion of infection are O1, O2, O4, O6, O7, O8, O75, O150 and O18ab (Roberts and Phillips 1979; Rosen, Hooton et al. 2007). Hospital environments are a significant determinant of the type of organisms causing urinary tract infections. Staphylococci, enterococci, *Proteus*, *Klebsiella*, *Enterobacter* and *Pseudomonas* species are most often isolated from inpatients whereas *E. coli* infection predominate in the outpatient population (Bronsema, Adams et al. 1993). *Corynebacterium urealyticum* (*Corynebacterium* group D2) has been identified as an important nosocomial pathogen (Soriano, Aguado et al. 1990).

3.2.2 Pathogenesis

Urinary tract infections are as a result of the interaction between bacterial virulence and the biologic and behavioural factors in the host. Bacteria may invade and spread within the urinary tract via three possible routes. These are the ascending, haematogenous and lymphatic pathways. The ascending pathway involves colonization of the urethra with bacteria. Microorganisms in the urine can enter the bladder. Once in the bladder, bacteria can multiply and pass up the ureters to the renal pelvis and parenchyma. The haematogenous pathway involves infection of the renal parenchyma by blood-borne organisms. The organisms most often implicated here are *S. aureus* and *Candida* species. In humans, infection of the kidney via the haematogenous route rarely involves gram-negative bacilli. Lymphatic pathway infection occurs when increased pressure in the bladder can cause lymphatic flow to be directed to the kidneys taking with it microorganisms (Mandell, Bennett et al. 2005).

3.2.3 Clinical manifestations

Urinary tract infection may involve the lower urinary tract or both the upper and lower urinary tracts. Lower urinary tract symptoms as a result from bacteria-producing irritation of the urethral and vesicle mucosa. This may cause frequent and painful urination of small amounts of urine that is turbid, suprapubic heaviness or pain and in some cases blood in the urine. Upper urinary tract infection includes fever, flank pain as well as symptoms such as increased frequency of urine, dysuria and the urgency to urinate. However these symptoms may vary greatly (Mandell, Bennett et al. 2005). Urinary tract infections in HIV-infected individuals include HIV-associated nephropathy, as well as skin and soft tissue infections (Eulalia Valencia, Enriquez et al. 1997).

3.2.4 Management

All symptomatic urinary tract infections should be treated whereas asymptomatic infection should be treated if at least two cultures of clean-voided, midstream urine grow the same organism in significant cell counts.

A high fluid intake is recommended resulting in a dilution of the bacteria in the urine. Rapid hydration may reduce bacterial counts but this usually returns to normal once hydration is stopped. Decreasing the urinary pH results in antibacterial activity e.g. ingesting large volumes of cranberry juice contributes to low pH as high concentrations of hippuric acid (derived from the precursors in the berry) penetrates into the bacterial cell preventing optimal functioning. Hippuric acid is a weakly ionisable organic acid and is therefore able to better penetrate bacterial cells. Analgesics may be administered to patients exhibiting pain.

Antimicrobial therapy is effective and guidelines are based on local antibiotic susceptibility patterns. However, antimicrobial drugs may either cure the infection or may cause bacterial persistence, relapse or re-infection. Bacterial cell counts should be reduced within 48 hours after the initiation of treatment with the antimicrobial drug that the microorganism is sensitive to *in vitro*. Bacteriologic cure is expected when the urine cultures are negative after 48 hours of initial treatment and during the follow-up period of 1-2 weeks. Bacteriologic persistence occurs when bacterial counts are not reduced after 48 hours of treatment initiation or if the infecting organism persists in low numbers in the urine after 48 hours. Bacteriologic relapse occurs within 1-2 weeks after treatment has ended. Re-infection occurs during the administration of the drug or anytime thereafter. This is referred to as superinfection and may be identified by a change in bacterial species.

Individuals that are severely ill with pyelonephritis should be hospitalised and parenteral therapy is required.

For hospitalised immunocompromised patients with infections caused by gram-negative bacteria, third generation cephalosporins, aminopenicillin inhibitor combinations and carbapenems may be used with or without aminoglycosides and fluoroquinolones are recommended.

3.3 Respiratory tract infections

Nosocomial pulmonary infections are more common in patients with AIDS and are related to the extent of immunosuppression, prior use of antibiotics, and the exposure to invasive procedures. Nosocomial *Mycobacterium tuberculosis* and bacterial pneumonia are common in HIV-positive individuals and are associated with significant morbidity and mortality (Petrosillo, Nicastrì et al. 2005). The majority of tuberculosis cases and deaths occur in low

resource areas; however nosocomial transmission to the patients with HIV occurs in both developed and developing countries mainly including multiple-drug resistant tuberculosis.

3.3.1 Pneumonia

Nosocomial pneumonia is the second leading cause of nosocomial infection and the leading cause of infection-related deaths in hospitalised patients (Mandell, Bennett et al. 2005). The morbidity associated with nosocomial pneumonia includes longer hospitalised stays and higher costs for health care (Wenzel 1989). Risk factors associated with nosocomial pneumonia are related to the patient's immune status, infection-control practices and introduction of invasive procedures or other intervention (American Thoracic Society 1996). Patient-related risk factors are: age greater than 70 years, malnutrition, coma, metabolic acidosis, severe underlying disease and the presence of any of a number of co-morbid illnesses such as alcoholism, central nervous system dysfunction, and azotemia. Infection-control-related risk factors are a lack of hand hygiene, a lack of glove-use practices and the use of contaminated respiratory equipment. Intervention-related risk factors include procedures and treatment that may challenge normal host defenses or allow exposure of the host to large inocula of bacteria. Sedatives and narcotics may be aspirated, cytotoxic agents and corticosteroids may inhibit the hosts normal responses to infection and prolonged use of antimicrobials may lead to the development of drug resistance. Surgical procedures associated with the chest and abdomen may predispose the patient to pneumonia as these are associated with changes in host defense. Ventilation is also a major risk factor for the development of pneumonia in intensive care units (Craven and Steger 1995; George 1995). Pneumonia often affects individuals with impaired host defense systems such as defects in antibody production, phagocytosis, ciliary function or decreased CD4+ T-lymphocyte counts as seen in AIDS (Braunwald, Fauci et al. 2004).

3.3.1.1 Etiological agents

Reports of an increased risk of nosocomial respiratory tract infections due to aerobic gram-positive and negative bacteria such as *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, *Haemophilus influenzae* and members of the enterobacteriaceae such as *Klebsiella pneumoniae*, *Escherichia coli*, *Serratia marcescens*, *Enterobacter* species in patients with HIV have been observed most frequently. Mortality rates are especially high in patients that have pneumonia caused by *Pseudomonas aeruginosa* or *Acinetobacter* species (Kollef, Bock et al. 1995; Tumbarello, Tacconelli et al. 1998; Mandell, Bennett et al. 2005). Anaerobic bacteria have been isolated from a number of patients with nosocomial pneumonia but only a small percentage of these cases are thought to be caused by these organisms (A'Court and Garrard 1992). *Legionella* species have also occasionally found to be the cause of nosocomial pneumonia and majority of these cases have been in immunocompromised individuals (Mandell, Bennett et al. 2005).

3.3.1.2 Clinical manifestations

Symptoms may vary and may be non-specific. Initial symptoms include fever, chills and malaise. Progressive anorexia and weight loss is usually indicative of chronic illness. Pulmonary symptoms may initially occur but as the illness progresses, this may become more frequent. Patients presenting with prolonged illness and nonspecific complaints together with pulmonary symptoms including shortness of breath, increased respiratory rate, sputum production, new or persistent cough, hemoptysis, chest pain or dyspnea should be evaluated. Extrapulmonary symptoms may also occur. Chronic pneumonia may present with skin and mucous membrane lesions suggesting histoplasmosis, coccidioidomycosis, blastomycosis and

in some epidemiologic settings paracoccidioidomycosis and may be differential in nosocomial settings. Cryptococcosis, nocardiosis and Kaposi's sarcoma are important considerations in AIDS patients (Mandell, Bennett et al. 2005; Raghavendran, Mylotte et al. 2007).

3.3.1.3 Management

Important considerations for the treatment of nosocomial pneumonia include early administration of the appropriate antibiotic (Iregui, Ward et al. 2002). Delay or inappropriate antibiotic treatment results in increased morbidity and mortality. Timely, accurate and appropriate therapy is therefore of vital importance as overuse or the unnecessary use of broad-spectrum antibiotics may result in drug resistance, superinfection and increased drug toxicity rates resulting in an increase in morbidity and mortality (Raghavendran, Mylotte et al. 2007). Ventilator-associated pneumonia is common. The antibiotic therapy that is employed depends on the use of prior antibiotic treatment at the time of onset of ventilator-associated pneumonia. If there is no prior history of antibiotic usage for early onset ventilator-associated pneumonia, third and fourth generation cephalosporins such as ceftriaxone or cefotaxime are the preferred choices or alternatively fluoroquinolones and or macrolides as part of combination treatment. An antipseudomonad cephalosporin such as ceftazadime or cefipime, an antipseudomonad penicillin such as piperacillin, carbapenem such as imipenem or meropenem or aztreonam combined with an aminoglycoside either in the presence or absence of methicillin-resistant *S. aureus* coverage with vancomycin or linezolid particularly if gram-positive cocci have been identified in the sputum Gram-stain, may be an effective combined regimen for the treatment of late-onset ventilator-associated pneumonia (Ost, Hall et al. 2003).

4. Intensive Care Unit (ICU) – Nosocomial infections in HIV-infected patients

Nosocomial infection rates are highest in patients from intensive care units (ICU) and infection rates in adult and paediatric ICUs are about three fold higher than elsewhere in the hospital. The sites of infection and pathogens involved vary depending on the type of ICU treatment (Fridkin, Welbel et al. 1997; Weinstein 1998). Since the beginning of the AIDS epidemic, admissions in the ICU of hospitals have markedly increased with HIV-infected patients being admitted with concomitant infections such as pneumocystis pneumonia, bacterial pneumonia and tuberculosis – all of which are important infectious causes of respiratory failure resulting in pulmonary disease.

Pseudomonas aeruginosa and *Staphylococcus aureus* as noted previously, are particularly significant causes of nosocomial bacterial pneumonias in ICU in both HIV-infected and HIV-uninfected patients. Therefore the management of hospital-acquired and ventilator-associated pneumonia is similar for both group of patients (American Thoracic Society 2005). However, the presence of methicillin-resistant *S. aureus* is an independent risk factor for death in HIV-infected patients and this should be considered in the initial treatment regimens (Franzetti, Grassini et al. 2006). Urinary tract infections in the ICU are as a result of fungal infections. *Candida* species including *Candida albicans* are the main cause of urinary tract infections in the ICU (Fridkin, Welbel et al. 1997). Another major cause of ICU admissions in HIV-infected patients is sepsis (Huang, Quartin et al. 2006; Japiassu, Amancio et al. 2010). Patients with invasive catheters and monitoring devices are predisposed to bloodstream infections caused by coagulase-negative staphylococci. Reports from one study demonstrated a 50% mortality rate in HIV-infected sepsis patients in ICU. The lung was the most common site of infection in

this study followed by primary bloodstream infections, venous catheter-related bacteraemia and urinary tract infections. Nosocomial infections were source of the sepsis and accounted for 90% of cases in this cohort and were composed mostly of gram-negative rods such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Enterobacter* species, *Escherichia coli*, *Acinetobacter* species, *Serratia marcescens*, *Staphylococcus* species, *Stenotrophomonas maltophilia*, *Clostridium difficile*, *Citrobacter freundii*, *Burkholderia cepacia* and *Candida* species. *Mycobacterium tuberculosis* was the etiologic agent in some cases. The CD4 count of the patients in this cohort was very low. This could be associated with greater use of antibiotics for opportunistic infections or bacterial infections resulting in antibiotic resistance and consequently contributing to the development of nosocomial infections (Japiassú, Amâncio et al. 2010). It is challenging for clinicians practicing in the ICU setting to balance the need for providing adequate antimicrobial treatment to potentially infected individuals with the risks of overuse or unnecessary use of antibiotics. Most intensive care units have adopted the following strategy – to initiate broad-spectrum antibiotics followed by the appropriate antibiotic for the specific organism once identified and antimicrobial susceptibility testing is released (Ibrahim, Sherman et al. 2000). Comparison in characteristics of nosocomial infections between HIV positive versus HIV negative patients is presented in Table 1.

Nosocomial Infections	HIV positive patients		HIV negative patients	
	Rate	Common organisms	Rate	Common organisms
Bacteraemia	Increased in patients with central venous catheter and a high proportion of resistant <i>K. pneumoniae</i>	Coagulase-negative staphylococci <i>Staphylococcus aureus</i> , <i>Klebsiella pneumoniae</i> , <i>Candida</i> species, <i>Salmonella</i> species	Lower mortality in HIV negative patients	<i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i>
Urinary tract infections	Higher in catheterized patients and associated with nephropathy	Staphylococci, enterococci, <i>Proteus</i> , <i>Klebsiella</i> , <i>Enterobacter</i> , <i>Pseudomonas</i> species and <i>Candida</i> species	High in catheterized patients	Staphylococci, enterococci, <i>Proteus</i> , <i>Klebsiella</i> , <i>Enterobacter</i> and <i>Pseudomonas</i> species
Pneumonia	The highest rate among all nosocomial infections and mostly increased in patients with CD4 lymphocyte T count < 200 cell/m ³	<i>Mycobacterium tuberculosis</i> , <i>Pneumocystis jiroveci</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus pneumoniae</i> , <i>Pseudomonas aeruginosa</i> , <i>Haemophilus influenzae</i> and members of the enterobacteriaceae such as <i>Klebsiella pneumoniae</i> , <i>Escherichia coli</i> , <i>Serratia marcescens</i> , <i>Enterobacter</i> species	Higher in the patients with risk factors such as: age >65, malnutrition, severe underlying diseases and patients with alcohol abuse	<i>Staphylococcus aureus</i> , <i>Streptococcus pneumoniae</i> , <i>Pseudomonas aeruginosa</i> , <i>Haemophilus influenzae</i> and members of the enterobacteriaceae such as <i>Klebsiella pneumoniae</i> , <i>Escherichia coli</i> , <i>Serratia marcescens</i> , <i>Enterobacter</i> species
Intensive Care Units (ICUs)	More severe and increased in HIV/AIDS patients	As above	Higher in patients with risk factors and prolonged duration of stay	As above

Table 1. Characteristics of nosocomial infections between HIV positive and negative patients.

5. Hospital infection control

In any society, health is a priority and infections particularly infections acquired in the hospital setting are a significant cause of disease worldwide. It is therefore imperative that the correct measures to control such infections are structured accordingly. These include an individual commitment by healthcare workers ensuring careful hand washing, appropriate isolation and use of gloves and the proper and sterile use of medical devices. System issues also need to be addressed – soap and water need to be available and placed at convenient locations easily accessible to healthcare workers. Surgical patients need to be administered pre-operative antibiotics 1-2 hours prior to incision and patients with communicable diseases need to be isolated. In addition, a good starting point for an infection control programme is basic surveillance thereby allowing for the calculation of the rates of infections. The role of such a programme is to provide local data and can be very effective in tracking the spread of nosocomial infections (Wenzel, Bearman et al. 2008). This would allow infection control personnel to rationally identify potential sources of pathogens and aid infectious disease physicians in the development of treatment regimens to manage patients affected by the related organisms (Singh, Goering et al. 2006).

6. Conclusion

Nosocomial infections are a serious problem that are continually increasing and expanding creating a severe public health threat and exhaust the health budget. In immunocompromised HIV-infected patients this threat is further amplified. However there are publications readily available indicating increased rates of nosocomial infections in HIV-infected patients. There is a enormous array of factors that need to be taken into consideration when confronted with such infections. The importance of knowing the risk factors, etiological agents and antimicrobial susceptibility are essential and should not be underestimated. The lifesaving role of antiretroviral therapy has improved and prolonged the survival outcome but some dilemmas around chronic HIV infections persist. It may be related to the lack of case control studies that directly indicate relationship amongst nosocomial infections and HIV/AIDS. Importantly, in nosocomial settings ongoing infection control measures warrant prompt attention.

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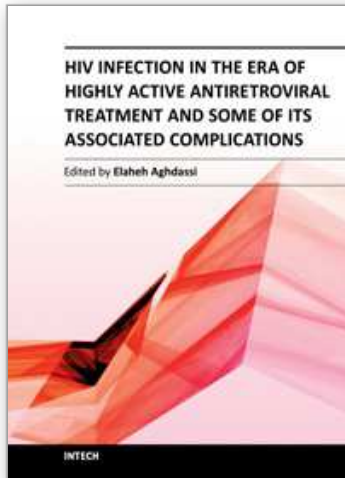
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HIV Infection in the Era of Highly Active Antiretroviral Treatment and Some of Its Associated Complications

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Human immunodeficiency virus (HIV) infection is a complex illness affecting the immune system. Acquired immunodeficiency syndrome (AIDS) is an advanced form of HIV infection in which the patient has developed opportunistic infections or certain types of cancer and/or the CD4+ T cell count has dropped below 200/ μ L. More than 40 million persons around the world are infected with HIV, with approximately 14,000 new infections every day. The disease causes 3 million deaths worldwide each year, 95% of them in developing countries. Optimal management of human immunodeficiency virus requires strict adherence to highly active antiretroviral treatment (HAART) regimens, but the complexity of these regimens (e.g., pill burden, food requirements, drug interactions, and severe adverse effects) limits effective treatment. However, more patients with HIV are surviving longer today because of these drugs. This allows further study of commonly associated adverse effects. These may affect all body systems and range from serious toxicities to uncomfortable but manageable events. This book reviews some of HAART-related metabolic and neurological complications.

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