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Antibiotic Resistance in Nursing Homes

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1. Introduction

Until early 20th century, infectious diseases were primarily responsible for mortality in the United States; the average life expectancy were 47 years (US Department of Health and Human Services [DHHS], 1985).

The advent of antiseptic techniques, vaccinations, antibiotics and other public health measures, raised life expectancy. In the early 21st century life expectancy has risen to 76 to 80 years in most developed nations (Center for Diseases Control and Prevention, 2003). Therefore, it is estimated that, by the year 2030, in the United States, 70 million persons will be over 65 years old. (National Nursing Home Week, 2005)

This epidemiologic transition has shifted the burden of morbidity from infections and acute illness to chronic diseases and degenerative illness. (Centers for Diseases Control and Prevention, 2003)

Therefore, with multiple comorbid diseases, many older persons develop functional decline and dependency requiring institutionalization in nursing homes (Juthani-Mehta & Quagliariello, 2010). Nowadays there are over 16000 nursing homes in United States and approximately 1.5 million Americans reside in nursing homes. By 2050 the number of Americans requiring long-term care is expected to double, and this trend is expected in all developed nations (Jones AL & Al, 2009).

The patient population and environment of the nursing home, provide a milieu that permits the development of infections and promote transmission of infectious agents (Nicolle LE & Al, 2001; Juthani-Mehta M & Quagliariello VJ, 2010). This is because nursing home residents have a number of risk factors, including age-associated immunological changes (High K, 2007; van Duin D 2007a, 2007b), organ systems changes, multiple comorbid diseases (e.g dementias, diabetes mellitus, cardio-vascular diseases, chronic obstructive pulmonary disease, impaired dentition) (Bettelli G, 2011), and degenerative disease requiring the insertion of prosthetic devices (e.g. joint prostheses, implantable cardiac devices) that lead to frailty and disability with a high impact on development of infections (Jackson ML & Al, 2004; Curns AT & Al, 2005; Fry AM & Al, 2005).

1.1 Immunosenescence

A functional immune system is considered vital for the host's continued survival against onslaught of pathogens. In humans, as well as in many other species, it is becoming recognized that the immune system declines with age (immunosenescence), which leads to a higher incidence of infections, cancers and autoimmune diseases (Pawelec G, 1999). Immunosenescence involves both the host's capacity to respond to infections and the development of long-term immune memory, especially by vaccination (Muszkat M & Al, 2003; Aspinall R & Al, 2007; Jackson MI & Al, 2008; Boog CJP, 2009), therefore it is considered a major contributory factor to the increased frequency of morbidity and mortality among the elderly (Ginaldi, L & Al, 2001)

Immunosenescence is a multifactorial condition leading to many pathologically significant health problems in the aged population. Some of the age-dependent biological changes that contribute to the onset of immunosenescence are listed in Table 1.

Cells	Biological Changes	References
Hematopoietic stem cells	↓ Self-renewal capacity	Ito K & Al, 2004
Phagocytes	↓ Total number, ↓ Bactericidal activity	Lord JM & Al, 2001; Strout, R.D & Suttles J, 2005
Natural Killer (NK)	↓ Cytotoxicity	Bruunsgaard H & Al, 2001; Mocchegiani E & Malavolta M, 2004
Dendritic Cells	↓ Antigen-Presenting function	Uyemura K, 2002
B- lymphocytes	↓ Antibodies production ↑ AutoAntibodies	Han S & Al, 2003
Naïve lymphocytes	↓ Production	Hakim FT & Gress RE, 2007
Memory cells	↓ Functional competence	Ginaldi L & Al, 2001
Macrophages	Disregulation	Cambier J, 2005
Thymus	↓ Epithelial volume	Aspinall R & Andrew D, 2000
Thymocytes (i.e. premature T-cells)	Reduction/Exhausion on the number	Min H & Al, 2004
Lymphokines	↓ Production (e.g. IL-2)	Murciano C & Al, 2006; Voehringer D & Al, 2002; Ouyang Q & Al, 2003
T-cell receptor (TcR)	Shrinkage of antigen-recognition repertoire diversity	Naylor K & Al, 2005; Weng NP, 2006
Response to Antigenic stimulation	Impaired proliferation of T-cells	Murciano C & Al, 2006; Naylor K & Al, 2005; Weng NP, 2006; Voehringer DM & Al, 2006
Memory & Effector T-cells	Accumulation and Clonal expansion	Franceschi C & Al, 1999; Voehringer DM & Al, 2006
Changes in cytokine profile	e.g. ↑ Pro-inflammatory cytokines milieu	Suderkotter C & Kalden H, 1997

Table 1. Age-dependent biological changes of immunosenescence

At a glance, Hematopoietic stem cells (HSC), which provide the regulated lifelong supply of leukocyte progenitors that are in turn able to differentiate into a diversity of specialized immune cells (including lymphocytes, antigen-presenting dendritic cells and phagocytes) diminish in their self-renewal capacity. This is due to the accumulation of oxidative damage to DNA by aging and cellular metabolic activity and the shortening of telomeric terminals of chromosomes (Ito K & Al, 2004). There is a decline in the total number of phagocytes in aged hosts, coupled with an intrinsic reduction of their bactericidal activity (Lord JM & Al, 2001; Strout, R.D & Suttles J, 2005).

The cytotoxicity of Natural Killer (NK) cells and the antigen-presenting function of dendritic cells is known to diminish with old age (Bruunsgaard H & Al, 2001; Mocchegiani E & Malavolta M, 2004); the age-associated impairment of dendritic Antigen Presenting Cells (APCs) has profound implications as this translates into a deficiency in cell-mediated immunity and thus, the inability for effector T-lymphocytes to modulate an adaptive immune response (Uyemura K, 2002). There is a decline in humoral immunity caused by a reduction in the population of antibody producing B-cells along with a smaller immunoglobulin diversity and affinity (Han S & Al, 2003)

As age advances, there is a decline in both the production of new naive lymphocytes (Hakim FT & Gress RE, 2007), and the functional competence of memory cell populations, with increased frequency and severity of diseases such as cancer, chronic inflammatory disorders and autoimmunity (Ginaldi L & Al, 2001) .

A problem of infections in the elderly is that they frequently present with non-specific signs and symptoms, and clues of focal infection are often absent or obscured by underlying chronic conditions (Ginaldi L & Al, 2001). Ultimately, this provides problems in diagnosis and subsequently, treatment. In addition to changes in immune responses, the beneficial effects of inflammation devoted to the neutralisation of dangerous and harmful agents, early in life and in adulthood, become detrimental late in life in a period largely not foreseen by evolution, according to the antagonistic pleiotropy theory of aging (Franceschi C & Al, 2000a). It should be further noted that changes in the lymphoid compartment is not solely responsible for the malfunctioning of the immune system in the elderly. Although myeloid cell production does not seem to decline with age, macrophages become dysregulated as a consequence of environmental changes (Cambier J, 2005). The functional capacity of T-cells is most influenced by the effects of aging: the age-related alterations are evident in all stages of T-cell development, making them a significant factor in the development of immunosenescence (Linton P & Al, 2006). After birth, the decline of T-cell function begins with the progressive involution of the thymus, which is the organ essential for T-cell maturation following the migration of precursor cells from the bone marrow. This age-associated decrease of thymic epithelial volume results in a reduction/exhausion on the number of thymocytes (i.e. pre-mature T-cells), thus reducing output of peripheral naïve T-cells (Aspinall R & Andrew D, 2000; Min H & Al, 2004).

Once matured and circulating throughout the peripheral system, T-cells still undergo deleterious age-dependent changes. Together with the age-related thymic involution and the consequent age-related decrease of thymic output of new T cells, this situation leaves the body practically devoid of virgin T cells, which makes the body more prone to a variety of infectious and non-infectious diseases. (Franceschi C & Al 2000b)

T-cell components associated with immunosenescence include: deregulation of intracellular signal transduction capabilities (Fulop T & Al, 1999), diminished capacity to produce

effector lymphokines (Murciano C & Al, 2006; Voehringer D & Al, 2002; Ouyang Q & Al, 2003), shrinkage of antigen-recognition repertoire of T-cell receptor (TcR) diversity (Naylor K & Al, 2005; Weng NP, 2006), cytotoxic activity of Natural Killer T-cells (NKTs) decreases (Mocchegiani E & Malavolta M, 2004), impaired proliferation in response to antigenic stimulation (Murciano C & Al, 2006; Naylor K & Al, 2005; Weng NP, 2006; Voehringer DM & Al, 2006), the accumulation and the clonal expansion of memory and effector T-cells (Franceschi C & Al, 1999; Voehringer DM & Al, 2006), hampered immune defenses against viral pathogens, especially by cytotoxic CD8+ T cells (Ouyang, Q & Al, 2003) and changes in cytokine profile e.g. increased pro-inflammatory cytokines milieu present in the elderly (Suderkotter C & Kalden H, 1997).

1.2 Organ system and aging

Alterations in organ systems occur with normal aging, and many of these physiologic alterations contribute to the development of infections (Vergese A & Berk S, 1990; Smith PW, 1994) (Table 2)

System	Aging changes
Skin	Epidermal thinning (Ghadially R & Al, 1995), ↓ elasticity, ↓ subcutaneous tissue, ↓ vascularity (Norman RA, 2003; Gilchrest BA, 1999)
Respiratory	↓ cough reflex, ↓ mucociliary transport, ↓ elastic tissue (Mittman C & Al, 1965), ↑ IgA/IgM in bronchoalveolar lavage and ↑ CD4+/CD8* lymphocytes (Meyer KC & Al, 1996) , ↓ antioxidant levels in epithelial lining fluid (Kelly FJ & Al, 2003)
Gastrointestinal	↓ motility, ↓ gastric acidity (Hall KE & Wiley JW, 1998)
Urinary	↓ urine osmolarity, ↑ perineal-vaginal colonization (women) (Farage MA & Maibach HI, 2011) ↑ prostate size and ↓ prostate secretion (men) (Nickel JC, 2003)

Table 2. Physiologic organ systems changes in the elderly

Although generally efficient defenses against infections are associated with the immune systems, many other elements have an important role.

Epithelia from skin, bladder, the bronchial and the digestive system, for a physical barrier and thereby play a key part in preventing bacteria from invading the human body (Ben-Yehuda A & Weksler ME, 1992). In particular, the skin changes, associated with aging lead to delayed wound healing (Ghadially R & Al, 1995).

Changes in respiratory tract function increase the likehood of aspiration and pneumonia. Apart for a decrease in immune function, various mechanisms are likely to contribute to the pneumonia risk of the elderly: blunting of protective reflexes in the airway, seen after stroke but also a part of normal ageing (Yamaya M & Al, 1991), decreased in mucociliary clearance (Incalzi RA & Al, 1989), loss of local immunity (decreased T-cell subsets and immunoglobulin in respiratory secretions) (Meyer KC, 2001).

Alterations in gastrointestinal tract physiology (e.g. decreased mobility and gastric acidity, decreased intestinal mobility, modifications of resident intestinal flora and intestinal mucus) increase the likelihood of infection after ingestion of a potential pathogen (Ben-Yehuda A & Weksler ME, 1992; Klontz KC & Al, 1997)

Moreover, the urinary tract is more vulnerable to infections in both elderly men and women even in absence of other diseases. Factors contributing to this vulnerability include mechanical changes (reduction in bladder capacity, uninhibited contractions, decreased

urinary flow rate and post-void residual urine), urothelial change (enhanced bacterial adherence), prostatic hypertrophy in men (Ben-Yehuda A & Weksler ME, 1992) and hormonal changes (lack of estrogen in post menopausal women) (Yoshikawa TT & Al, 1996)

1.3 Chronic diseases and comorbility

The nursing home population has a high frequency if chronic diseases, many of which increase the likelihood of infections. These chronic diseases are often the major factor necessitating institutional care (Ouslander J, 1989; Hing F & Bloom B, 1990; Van Rensbergen G & Nawrot T, 2010). The most frequent diagnosed underlying chronic diseases include

dementia and neurologic diseases (Banaszak-Koll & Al, 2004; Bowman C & Al, 2004; Van Rensbergen G & Nawrot T, 2010), peripheral diseases (Chong WF & Al, 2011), cerebrovascular diseases (Bowman C & Al, 2004; Van Rensbergen G & Nawrot T, 2010; Chong WF & Al, 2011), chronic pulmonary conditions (Mc Nabney MK & Al, 2007; Van Rensbergen G & Nawrot T, 2010), hearth diseases (Chan KM & Al, 1998; Van Rensbergen G & Nawrot T, 2010; Chong WF & Al, 2011). The prevalence of diabetes mellitus varies from 10 to 30 per cent in the nursing home population (Garibaldi RA & Al, 1981; Nicolle LE & Al, 1984; Ahmed A & Al, 2003; Valiyeva E & Al, 2006; Mc Nabney MK & Al, 2007; IKED Report, 2007; Van Rensbergen G & Nawrot T, 2010).

Comorbidities contribute to the high frequency of infections in nursing homes because the high risk profile of nursing homes residents (Jette AM & Al, 1992): demented residents often have neurogenic bladder and inability to empty the bladder that results in an increased frequency of urinary tract infections (Nicolle LE, 2000; 2002). Patients with peripheral vascular disease have an high risk for skin and soft tissue infections because the impaired vascular supply to extremities and peripheral edema (Sieggreen MY & Kline RA, 2004; Ely JW & Al; 2006). Patients with chronic obstructive pulmonary disease are likely to have bacterial colonization of tracheobronchial tree and recurrent bronchopulmonary infections (Marin A & Al, 2010). Moreover, patients with diabetes mellitus, have increased prevalence of infections (Shah BR & Hux JE, 2003; Bertoni AG & Al, 2001): pneumonia (Valdez R & Al, 1999; Tan JS, 2000), lower urinary tract infections and pyelonephritis (Zhanel GG & Al, 1995; Stamm WE & Hooton TM, 1993), soft tissue infections, including the "diabetic foot", necrotizing fasciitis and mucocutaneous Candida infections (Votey SR & Peters Al, 2005; Fridkin SK & Al, 2005; Miller LG & Al, 2005). Others infections such as invasive (malignant) otitis externa, rhinocerebral mucormycosis (Durand M & Joseph M, 2005; Earhart KC, Baugh WP, 2005) and emphysematous infections (cholecystitis and pyelonephritis) (Votey SR & Al, 2005) occur almost exclusively in diabetics. The optimal management of infections in nursing homes residents includes ensuring optimal therapy of these associated diseases.

1.4 Functional impairment

Disability, functional dependence and deteriorating cognitive performance are strong predictors of nursing home admission among older adults (Jette AM & Al, 1992; Pourat N, 1995; Krauss NA & Altmann, 2004; Miller SC & Al, 1998; Gaugler JE & Al, 2007). On the other hand the chronic diseases affecting the elderly nursing home residents, lead to functional impairment and dependency in activity of daily living (Bajekal M , 2002; Flacker JM & Kiely DK, 2003; Sutcliffe C & Al, 2007; Andresen M & Puggaard L, 2009; Jones AL & Al, 2009).

Poor functional status in nursing home residents has been reported to be associated with increased occurrence of infections and high mortality rate (Curns AT & Al 2005; Jackson ML & Al, 2008; Juthani-Mehta M & Quagliariello VJ, 2010). Chair and bed-bound residents are at risk of pressure ulcers (Galvin J, 2002; Henoch I & Gustaffson M, 2003; Pressure Ulcer Advisory Panel/European Pressure Ulcer Advisory Panel Pressure Ulcer Prevention and Treatment Clinical Practice Guideline, 2009; Jankowski IM; 2010). Urinary incontinence is common, affecting as many as 50% of residents in nursing home and approaches to the management of incontinence (including indwelling bladder catheters and external collecting devices for elderly men), increase the incidence of urinary infections (Gammack JK, 2003; Richards CL. 2004; Eriksen HM & Al, 2007; Ricci G & Al, 2010). Fecal incontinence is also associated with an higher risk of urinary infection (Topinkovà E & Al, 1997;) and both urinary and fecal incontinence may contribute to extensive environmental contamination with pathogens and antimicrobial agent-resistant bacteria (Schnelle JF & Al, 1997; Leung FW & Schnelle JF, 2008; Pagliari P & Al, 2011).

1.5 Nutrition and malnutrition

There are a number of studies that document that 10 to 50% of nursing home residents are malnourished (Donini LM & Al, 2000; Saletti A & Al, 2000; Omran ML & Morley JE, 2000; Nakamura H & Al, 2006; Pauly L & Al, 2007). Over 50% of nursing home residents have reported to suffer from protein caloric malnutrition (Nakamura H & Al, 2006; Ordòňez J & Al, 2010). Vitamin, zinc and micronutrients deficiencies are also reported (Mandal SK & Ray AK, 1987; Girodon F & Al, 1997; Bates CJ & Al, 1999a; 1999b; Gosney MA & Al, 2008). The reasons for this high frequency of malnutrition might be comorbidities (Bostrőm AM & Al, 2011; Shahin ES & Al, 2010), feeding difficulties (Hildebrandt GH & Al, 1997; Lamy M & Al, 1999; Lelovics Z, 2009; Chang CC & Roberts BL, 2011), impaired cognition (Blandford G & Al, 1998; Magri et Al, 2003; Bartholomeyczik S & Al, 2010; Bostrőm AM & Al, 2011), bacterial overgrowth of the small bowel (e.g. Escherichia coli or anaerobic organisms) leading to malabsorption (Mc Evoy AJ & Al, 1983; Elphick HL & Al, 2006; Ziegler TR & Cole R, 2011) and poorer clinical outcomes (Kaganski N & Al, 2005; Stratton RJ & Al, 2006) .

1.6 Invasive devices

Because of multiple comorbidities and disabilities, nursing home residents are more likely to require invasive medical devices (e.g. indwelling urinary catheter, percutaneous and naso-gastric feeding tube, tracheostomy, intravenous catheter and cardiac device). Feeding tubes are present from 7 to 41% of cognitive impaired nursing homes residents and urinary catheterization rate range from 11 to 12%. (Warren JI & Al, 1989; Juthani-Mehta M & Quagliariello VJ, 2010)

Moreover the use of some devices, including tracheostomies and intravenous catheters, is increasing in the nursing homes, reflecting the increasing level of impairment among elderly patients admitted to these facilities.

Device use has been associated with both colonization and infection with antibiotic resistant organisms in nursing home residents (Mody L & Al, 2007; 2008; Rogers MA & Al, 2008; L, & Al, 2008; 2010): from 5 to 10% of nursing home residents have long-term indwelling urinary catheters with associated persistent polymicrobial bacteriuria, urinary tract infections (Warren JW & Al, 1982; Beck-Sague C & Al, 1993; Garibaldi RA, 1999; Ha US & Cho YH,

2006; Regal RE & Al, 2006;) and their complications (Ouslander J & Al, 1987; Warren JW & Al 1987; 1988), while enteral feeding solution given to patients with nasogastric and percutaneous feeding tubes, may be contaminated with bacteria of the family of Enterobacteriaceae, including Serratia spp and Enterobacter spp. (Freedland CP & Al, 1989; Greenow JE & Al, 1989). Moreover, nasogastric tubes have been reported to be associated with a greater occurrence of aspiration pneumonia (Fay DE & Al, 1991) which is one of factor promoting the use of percutaneous gastric or jejunal feeding tubes with subsequent complication of stomal site infections, peritonitis (Luman W & Al, 2001) and risk of developing Clostridium difficile antibiotic-associated diarrhea (AAD) (Asha NJ & Al, 2006).

Finally, intravenous peripheral line, peripherally inserted central catheter, tracheostomy and suprapubic urinary catheter are other commonly used devices in nursing home with an increasingly risk of developing sepsis, pneumonia, skin infections, soft tissue infections (Tsan L & Al, 2008). Device use has therefore associated with repeated courses of antimicrobial therapy foster the emergence of resistant pathogens. (Rogers MA & Al, 2008)

1.7 Drugs use in elderly nursing homes residents

Residents in nursing homes often have a complex and complicated illness profile ranging from simultaneous occurrence of several chronic diseases, depression, pain, sleep problems and dementia with the psychiatric and behavioral symptoms (Selbaek G & Al, 2007; Ricci G & Al, 2009) . Thus "polypharmacy" is the norm in nursing home population. The average nursing home resident receives from 5 to 10 different medications at any time (Beers MH & Al, 1992; Furniss L & Al, 1998; Doshi JA & Al, 2005; Kersten H & Al, 2009). Some of these medications may increase the likelihood of infections: atypical antipsychotics may impair consciousness and increase the frequency of aspiration (Knol W & Al, 2008; Gau JT & Al, 2010); H2 blockers and protonic pump inhibitors (PPI) lead to decreased gastric acidity and may contribute to increased gastrointestinal infections (Laheij RI & Al; 2004; Gulmez SE & Al, 2007;Eom CS & Al 2011; Laria A & Al, 2011). Oral and inhaled glucocorticoid therapy are associated with an increased dose-dependent risk of infections (Ernst P & Al, 2007; Calverley PM & Al, 2007; Kardos P & Al, 2007; Drummond MB & Al, 2008; Singh S & Al, 2009; Smitten AL, & Al 2008; Dixon WG & Al, 2011).

2. Management of infections in nursing homes

Clinical criteria used in the diagnosis and surveillance for infections in nursing homes, have generally been developed from observations in younger population with limited comorbidities. It was not until 2000 that the multifaceted nature of the evaluation of patients in long-term care facilities has led the Society for Healthcare Epidemiology of America and the American Geriatric Society to participation, review and support the Guidelines concerning the multidimensional assessment as part of the infectious disease evaluation in an older adult. (Bentley DW & Al, 2000; Kinsella K & Velkoff, VA , 2001; High KP & Al, 2005; Centre for Diseases Control and Prevention, 2003)

These guidelines are specifically intended to apply to older adult nursing home residents of the potential heterogeneity of conditions present in these facilities residents, suggests that the recommendations are intended to assist with the management of the majority of residents: older adults with multiple comorbidities and functional disabilities.

2.1 Clinical presentation of infections

Presentation of infections in nursing home residents are sometimes atypical (McGeer A & Al, 1991; Norman D & Toledo S, 1992; High K & Al, 2009). Several factors contribute to the difficulty of establishing a clinical diagnosis in these patients. Hearing and cognition are often impaired in nursing home patients: symptoms may not be expressed or correctly interpreted by caregivers. Chronic clinical conditions may obscure the sign of infection leading to misinterpretation or overlooking symptoms. For instance, urinary incontinence may mask symptoms of urinary infection, or congestive heart failure may mask symptoms of pulmonary infection. The presence of coexisting diseases such as chronic bronchitis, which may mask acute pneumonia, or rheumatoid arthritis, which can confound the presence of septic arthritis, may compound difficulties in making the diagnosis of infection. (Cantrell M & Norman DC, 2010)

Altered physiologic responses to infection, or for the manner to any acute illness, are due to man factors including the decremental biologic changes of normal aging, which may be exacerbated by lifestyle. For example, age-related changes in chest wall expansion and lung tissue elasticity, which may be made worse by smoking, contribute to a diminished cough reflex. A weakened cough has the double negative effect of contributing to a decline in pulmonary host defenses and making the diagnosis of respiratory infection more difficult.

Another example of an altered physiologic response to infection in older persons that deserves special mention is the often-observed blunted fever response (Harper C & Newton P, 1989; Wasserman M & Al, 1989; Norman D & Toledo S, 1992; Norman D & Yoshikawa TT, 1996) and increased frequency of afebrile infection (Gleckman B & Hibert D, 1982; Meyers B & Al, 1989)

Although fever is the cardinal sign of infection, the traditional definition of fever (oral temperature of 38° to 38.3°C) may not be sensitive enough to diagnose infection in elderly patients. Castle SC & Al (1991) found that, in a nursing home population, baseline body temperatures are approximately 0.5°C below those of a normal young person and that with infection, despite a rise in temperature comparable to that seen in the young, the maximum temperature may be below the traditional definition of fever. However, a temperature of 37.8°C coupled with a decline in functional status is highly indicative of infection in this population. (Castle SC & Al, 1991)

The presence or absence of fever—aside from facilitating or inhibiting the diagnosis of infection—has other implications. The presence of fever (as defined by an oral temperature of 38.3°C) is highly specific for the presence of a serious, usually bacterial, infection (Keating MJ III, & Al, 1984; Wasserman M & Al, 1989). Moreover, when the syndrome of fever of unknown origin (FUO) occurs in elderly persons, it typically signifies a treatable condition such as intra-abdominal infection, infective endocarditis, temporal arteritis, or other rheumatologic condition. (Knockaert DC & Al, 1993; Berland B & Gleckman RA, 1992).

A blunted fever response to infection frequently portends a poor prognosis (Weinstein MP & Al, 1983).

This may be relevant to the mounting evidence that fever may play an important role in host defenses (Kluger MJ & Al, 1996; Norman D & Yoshikawa TT, 1996). The peripheral leukocyte count in bacterial infection is not as high as that observed for younger population and leukocytosis is often absent. (Werner H & Kuntsche J, 2000). So, the elevation of acute phase protein may be a more reliable marker of infection than elevation of erythrocyte sedimentation rate.

In summary, an acute infection in the elderly may present with either typical clinical manifestations or subtle findings.

Signs and symptoms pointing to a specific organ system infection may be lacking. Thus, an infection should be sought in any elderly person with an unexplained acute to subacute (days to weeks) decline in functional status, falls, delirium, anorexia, weakness, disorientation (Gavazzi G, Krause KH, 2002)

2.2 Antimicrobial agent use in nursing homes

Antimicrobials agents are among the most frequently prescribed pharmaceutical agents in nursing homes; the account for approximately 40% of all systemic drugs used (Crossley K & Al, 1987; Wayne SJ & Al, 1992). It is estimated that two to four million courses of antibiotics are prescribed for residents of US nursing homes annually (Strausbaugh LJ & Joseph CL, 2000) . As a result, from 50 to 70% of residents receive at least one systemic antimicrobial agent during 1 year (Montgomery P & Al, 1995) and the prevalence of systemic antibiotic use is reported to be 8% (Crossley K & Al, 1987; Jacobson C & Strausbaugh LJ, 1990; Warren JW & Al, 1991; Montgomery P & Al, 1995; Lee YL & Al, 1996; Mylotte JM, 1996; Loeb M & Al, 2001a). In a 9-month surveillance study in a nursing home care unit (Jacobson C & Strausbaugh LJ, 1990), 51% of the 321 study patients received antimicrobial agents at some time during their stay. More than one agent was prescribed for 30% of these patients. In addition as many as 30% of nursing home residents receive at least one prescription for a topical antimicrobial agent each year (Yakabowich MR & Al, 1994; Montgomery P & Al, 1995).

A substantial proportion of antimicrobial treatment in nursing homes is considered inappropriate: from 30 to 75% of systemic antimicrobial agents (Zimmer JG & Al, 1986; Crossley K & Al 1987; Jones SR & Al, 1987; Katz PR & Al, 1990; Warren JW & Al, 1991; Yakabowich MR & Al, 1994; Pickering TD & Al, 1994; Montgomery P & Al, 1995) and up to 60% of topical antimicrobial agents (Montgomery P & Al, 1995) are inappropriately used.

The inappropriate use of antibiotics, especially in frail elderly nursing home residents, can be burdensome and harmful (Morrison RR & Al, 1998). From a broader public health perspective, antimicrobial use is the primary factor leading to the emergence of antimicrobial-resistant bacteria. Antibiotic resistance among bacteria implicated in the most common infections is rising exponentially throughout the word (D'Agata E & Mitchell SL, 2008). Infections caused by antimicrobial-resistant bacteria are associated with up to 5 times higher mortality rates and lead to more frequent and prolonged hospitalization compared with infections caused by antimicrobial-susceptible bacteria (Carmeli Y & Al, 2002; Cosgrove SE & Al, 2002; 2005). These issues are relevant for older patients who arbor relatively high of antimicrobial-resistant bacteria, and in nursing homes, where antimicrobials are the most frequently prescribed pharmaceutical agents (Crossley K & Al 1987; Warren JW & Al, 1991; Flamm RK & Al, 2004)

3. Infections in nursing homes

Infections are a frequent occurrence in nursing homes. The most important aspects are represented by endemic infections, epidemics and infections with resistant organisms

3.1 Endemic infections

The most frequent endemic infections are respiratory tract, urinary tract, skin and soft tissue, and gastrointestinal infections (primarily manifesting as diarrhea) (Strausbaugh LJ & Joseph CJ, 1999).

3.1.1 Occurrence of endemic infections

In United States nursing homes, 1.6 to 3,8 million infections occur (Strausbaugh LJ & Al, 2000). These infections are largely endemic and have an overall infection rate that ranges from 1,8 to 13,5 infections per 1000 resident care days (Strausbaugh LJ & Al, 2000). The variability of prevalence (Cohen E & Al, 1979; Garibaldi R & Al, 1981; Standfast SJ & Al, 1984; Setia U & Al, 1985; Scheckler W & Peterson P, 1986; Alvarez S & Al, 1988; Magaziner J & Al, 1991; Steinmiller A & Al, 1991; Eikelenboom-Boskamp A & Al, 2011) and incidence (Magnussen M & Robb S, 1980; Farber BF & Al, 1984; Nicolle LE & Al, 1984; Franson T & Al, 1986; Scheckler W & Peterson P, 1986; Viahov D & Al, 1987; Alvarez S & Al, 1988; Schicker JM & Al, 1988; Hoffman N & Al, 1990; Jacobson C & Strausbaugh LJ, 1990; Darnowsky S & Al, 1991; Jackson M & Al, 1992) rate of infections, reflects differences in patients populations in different study institutions, as well as differing surveillance definitions and methods for case ascertainment .

Many of these reports are from Veteran Administration facilities, where over 90% of the population are male and, thus, non representative of the general nursing home population, in which only 20 to 30% are male. The most frequent infections identified are usually respiratory tract infections, varying in rate from 0.46 to 4.4 per 1000 resident days. In most reports, this includes both upper and lower respiratory infections, because the difficulties in distinguishing the two diagnoses on the basis of clinical criteria alone (Cohen E & Al, 1979; Garibaldi R & Al, 1981; Standfast SJ & Al, 1984; Scheckler W & Peterson P, 1986; Magaziner J & Al, 1991). (Table 3)

The reported incidence of symptomatic urinary infections varies from 0,1 to 2,4 per 1000 resident days. (Nicolle LE, 2000)

The influence of different surveillance definition is notable in reports of incidence of febrile urinary infections. Symptomatic urinary infection may be defined permissively as a positive urine culture in a patient with fever and no other apparent source or, restrictively as a positive urine culture in a patient with fever and acute symptoms referable to the urinary tract (Schaeffer AJ & Schaeffer EM, 2007; High K & Al, 2009). Report using the permissive definition overestimate the occurrence of febrile urinary infection, while those using the restrictive definition certainly underestimate the incidence.

The clinical and economic impact of endemic infections in the nursing home residents is difficult to define, because these patients are highly chronic impaired, and additional morbidity from intercurrent infection is difficult to measure. Moreover, in case of fully dependent, non communicative, demented resident, mortality may not be considered an undesiderable outcome. Similarly, the prolongation of institutionalization may also not be meaningful as a measure of morbidity or cost in these permanently institutionalized elderly residents.

Reference	Incidence per 1000 resident days				
	All infections	Respiratory	Urinary	Skin & soft tissue	Gastrointestinal tract
Magnussen M & Robb S, 1980	3.4	0.46	2.4	0.3	0
Alvarez S & Al, 1988	2.7	0.7	1.2	0.5	Not stated
Nicolle LE & Al, 1984	4.1	1.8	0.1	1.0	0.9
Farber BF & Al, 1984	6.7	3.2	1.8	0.1	0
Franson T & Al, 1986	4.6	1.0	2.3	1.0	Not stated
Scheckler W & Peterson P, 1986	3.6	1.3	1.6	0.5	0.04
Vlahov D & Al, 1987	3.6	1.1	1.2	0.2	0.7
Schicker JM & Al, 1988	5.4	2.0	1.9	0.7	0.24
Jacobson C & Strausbaugh L, 1990	2.6	0.9	1.0	0.45	0.15
Hoffman N & Al, 1990	4.6	1.0	1.9	0.09	0
Darnowski S & Al, 1991	9.5	4.4	1.5	2.1	Not stated
Jackson M & Al, 1992	7.1	3.3	1.3	1.8	0.09
Brusaferro S & Moro ML, 2005	4.8	1.8	1.5	0.7	Not stated

Table 3. Incidence of infections in nursing homes (described in published studies)

Indices that may be used as measures of the impact of endemic infections include the volume of antimicrobial agent use (Warren JW & Al, 1982; Crossley K & Al, 1987; Montgomery P & Al, 1995), frequency of transfer to acute-care facilities for management of infection and infection-related mortality. Reports summarizing antimicrobial agent use consistently identify urinary infection as the most frequent diagnosis for which treatment is prescribed, with respiratory infections second in frequency (Zimmer JG & Al, 1986; Crossley K & Al, 1987; Warren JW & Al, 1991; Waine SJ & Al, 1992; Montgomery P & Al, 1995; Bentley DW & Al, 2000).

From 7 to 30% of elderly residents transferred from nursing homes to acute-care institutions, are transferred for management of infections (Irvine P & Al, 1984; Gordon WZ & Al, 1985; Jacobson C & Strausbaugh LJ, 1990; Kerr H & Byrd J, 1991); respiratory and urinary infections are the diagnoses that most commonly require transfer (Irvine P & Al, 1984; Gordon WZ & Al, 1985). One prospective study reported that 6,3% of all infectious episodes in nursing homes were associated with death, or 10,3 deaths per 100 residents per year (Nicolle LE & Al, 1984). However, overall mortality is reported to be similar in residents with and without infection (Jacobson C & Strausbaugh LJ, 1990). The only common infection with a high case/fatality ratio is pneumonia (Ahlbrecht H & Al, 1999). Autopsy series of elderly nursing home residents consistently fail to identify an infection other than pneumonia as an immediate cause of death (Nicolle LE & Al, 1987a; Gross JS & Al, 1988)

3.1.2 Respiratory tract infections

3.1.2.1 Upper respiratory tract infections

Upper respiratory infections in nursing home patients include sinusitis, otitis media, otitis externa and pharyngitis. Generally, the incidence of upper respiratory tract infections is reported to be less than that of lower respiratory tract infections: Scheckler and Peterson (1986) reported 1,1 upper respiratory tract infections per 100 resident months, compared with 1,9 pneumonia and bronchitis. The different clinical syndromes included as upper respiratory tract infections are usually reported as a single group, and the incidence of infection at each side is not known for nursing home residents. Group A streptococcus may cause pharyngitis, but most reports of streptococcal pharyngitis describe relatively uncommon episodes of epidemic infections (Schwartz B & Ussery X, 1992). Overall, these infections seem to have limited impact in the nursing home population.

3.1.2.2 Lower respiratory tract infections

Lower respiratory tract infections, including both pneumonia and bronchitis, are the most important infections occurring in nursing homes in both frequency and clinical consequences (Jackson M & Al, 1992; Beck-Sague C & Al, 1994). Increased aspiration of oropharyngeal contents and impairment pulmonary clearance mechanism resulting from physiologic aging changes, as well chronic pulmonary, cardiovascular and neurologic disease, contribute to the high incidence of pneumonia.

Pneumonia is the only infection that is an important contributor to mortality, in this population, with a reported case/fatality rate of 6 to 23% (Nicolle LE & Al, 1984; Scheckler W & Peterson P, 1986; Jackson M & Al, 1992; Jacobson C & Strausbaugh LJ, 1990).

Studies of the etiologies of nursing home-acquired pneumonia are generally flawed because they rely on expectorated sputum specimens to define bacteriology, and sputum specimens cannot differentiate oropharyngeal colonization from pulmonary infection.

Invasive methods to estabilish an etiologic cause (transtracheal or transthoracic aspiration, bronchoscopy) are infrequently performed in nursing home population. Bacteriemia occurs in less than 25% of cases, even if it would allow the identification of the causative agent.

With this limitations, streptococcus pneumoniae, remains the most important pathogen (Phair J & Al, 1978; Bentley DW, 1984; Farber BF & Al, 1984; Marrie TJ & Al, 1986; Peterson PK & Al, 1988). (Table 4)

Patients with chronic obstructive pulmonary disease have an increased frequency of bronchopneumonia, associated with Haemophilus influenzae and Moraxella catarrhalis. There is an increased occurrence of Gram-negative organism such Klebsiella pneumonia in the nursing home relative to other populations.

In at least one study in which specimen for culture were obtained through transtracheal aspiration, 37% of episodes were reported to have mixed respiratory flora (Bentley DW, 1984). Atypical pathogens such as Chlamydia pneumonia, Mycoplasma pneumonia and Legionella pneumophila may cause pneumonia in nursing home residents, but appear to be relatively infrequent.

Bacteria (percentage of total isolates)	Garb J & Al, 1978 (n=47)	Marrie TJ & Al, 1986 (n=12)	Peterson PK & Al, 1988 (n=129)	Bentley DW, 1984 (n=115)	Phillips SL & Brahaman-Phillips MA, 1993 (n=92)	Lim WS & Macfarlane JT, 2001 (n=22)	El-Sohl AA & Al, 2002 (n=21)	El-Sohl AA & Al, 2004 (n=93)	Carratala J & Al, 2007 (n=126)	Kothe H & Al, 2008 (n=1349)	Shindo Y & Al , 2009 (n= 141)
Streptococcus pneumoniae	19	17	30	32	34	55	0.04	25	27.8	43.3	13.5
Klebsiella pneumoniae	30	25	7.5	-	2.2	-	0.04	-	-	-	7.1
Hemophilus influentiae	4.3	-	23	5.2	23	-	-	-	11.9	3.4	-
Enterobacter spp	11	8.3	-	-	1.1	-	24	28	-	-	-
Escherichia coli	6.4	17	13	-	6.5	-	-	-	2.4	-	3.5
Serratia marcescens	4.3	-	-	-	-	-	-	-	-	-	-
Pseudomonas aeruginosa	4.3	-	2.5	-	6.5	-	14	-	1.6	-	5.7
Citrobacter spp	2.1	-	2.5	-	2.2	-	-	-	-	-	-
Proteus spp	-	-	2.5	-	2.2	-	-	-	-	-	2.8
Branhamella catarrhalis	-	-	13	-	4.3	-	-	-	-	-	-
Other Gram-	-	-	-	17	6.5	22	-	-	6.4	7.1	2.8
Staphylococcus aureus	19	8.3	7.5	1.7	12	-	33	31	2.4	2.2	9.9
Mixed	-	25	-	43	-	-	38	5	-	20.9	20.3

Table 4. Bacteria reported in published studies as a etiologic agents in subjects with nursing home-acquired pneumonia

3.1.2.3 Tuberculosis

The occurrence of Mycobacterium tuberculosis is variable among different institutions, although it is an important cause of infection in some nursing homes (Stead W, 1981; Stead W & Al, 1985; Brennen C & Al, 1988; Bentley DW, 1990a).

The prevalence of positive tuberculin skin test in nursing home residents has been reported to vary from 21 to 35% (Stead W & Al, 1985; Welty C & Al, 1985; Perez-Stable EJ & Al, 1988).

While active tuberculosis in nursing home residents is usually due to reactivation of latent infection, primary infection or reinfection may occur following exposure to an infectious case (Bentley DW, 1990a). Stead W (1985) reported that residents with negative skin test on admission to nursing homes, had a 5% year conversion rate in a home with a known infectious case, while the rate was 3,5% year in a home without a known case.

About 10% of skin test convertors who did not receive prophylactic isoniazid therapy developed active infection.

When an infectious case occurs, delay in diagnosis due to preexisting chronic pulmonary symptoms, or delay in obtaining a chest radiography, may lead to prolonged, extensive exposure of other residents and staff.

3.1.3 Urinary tract infections

3.1.3.1 Symptomatic urinary infections

In most survey the leading infection in nursing homes and in long-term care facilities is urinary tract infection (Bentley DW & Al, 2000; Philip W & Al, 2008) although with restrictive clinical definitions, symptomatic urinary infection is less frequent than respiratory infection (Stevenson KB & Al, 2005). Bacteriuria is very common in nursing home residents but, by itself, is not associated with adverse outcomes and does not affect survival (Eberle CM & Al 1993; Smith PW, 1985; Nicolle LE & Al, 2005a), therefore practitioners must distinguish symptomatic UTI from asymptomatic bacteriuria in making therapeutic decisions.

Diagnosing urinary tract infection in nursing home residents is problematic. Given the high incidence of asymptomatic bacteriuria and pyuria, a positive urine culture and pyuria on urinalysis are non-diagnostic (Nicolle LE, 2000). Practitioners utilize clinical criteria to differentiate symptomatic urinary tract infection from asymptomatic bacteriuria, but existing clinical criteria were developed by expert consensus (McGeer A & Al, 1991; Philip W & Al, 2008) . The McGeer consensus criteria for urinary tract infection are widely accepted as surveillance and treatment standards (Centers for Medicare and Medicaid (CMS) Manual System, 2005).

For residents without an indwelling catheter, three of the following criteria must be met to identify urinary tract infection : (1) fever ≥38°C; (2) new or increased burning on urination, frequency, or urgency; (3) new flank or suprapubic pain or tenderness; (4) change in character of urine; (5) worsening of mental or functional status (McGeer A & Al, 1991) The Loeb consensus criteria for urinary tract infection are minimum criteria necessary for empiric antibiotic therapy. For residents without an indwelling catheter, criteria include acute dysuria alone or fever (>37.9° or 1.5°C increase above baseline temperature) plus at least one of the following: new or worsening urgency, frequency, supra-pubic pain, gross hematuria, costovertebral angle tenderness, or urinary incontinence. (Loeb M & Al, 2001) The reliability, specifically inter-observer variability, for elements of these consensus criteria has not been determined.

If the typical symptoms of urinary tract infection are dysuria and frequency (cystitis) or fever and flank pain (pyelonephritis), the elderly may present with atypical or non-localizing symptoms. Chronic genitourinary symptoms are also common but are not attributable to bacteriuria (Nicolle LE & Al, 2005a; Ouslander JG & Schnelle JF, 2005). Because the prevalence of bacteriuria is high, a positive urine culture, with or without pyuria, is not sufficient to diagnose urinary infection (Nicolle LE & Al, 2005a). Clinical findings for diagnosis of urinary tract infection in non-catheterized residents must include some localization to the genitourinary tract (Mc Geer & Al, 1991). The diagnosis also requires a positive quantitative urine culture obtained by the clean-catch voided technique, by in and out catheterization, or by aspiration through a catheter system sampling port. A negative test for pyuria or a negative urine culture obtained prior to initiation of

antimicrobial therapy, excludes urinary infection, while a positive urine culture is not helpful in defining a urinary source for symptoms. Given these provisos, rates of symptomatic urinary infection of 0,11 to 0,15 per bacteriuric year have been reported in studies with restrictive clinical definition, that require the presence of localizing genitourinary symptoms or signs (Nicolle LE, 1983; 1987). Moreover, symptomatic urinary infection is reported as the diagnosis necessitating transfer from a nursing home to an acute-care facility in 1 to 8% of such transfers (Irvine P, 1984; Gordon WZ, & Al, 1985). The urinary tract is the most common source of bacteriemia in the institutionalized elderly, contributing to over 50% of episodes (Setia U & Al, 1984; Rudman D & Al, 1988; Muder RR & Al, 1992; Nicolle LE & Al, 1994a) with a case/fatality ratio of 16 to 23% (Setia U & Al, 1985; Muder RR & Al, 1992; Nicolle LE & Al, 1994a). The prevalence of indwelling urethral catheters in the nursing homes is 7 to 10% (Ribeiro BJ & Smith SR, 1985; Warren JW & Al, 1989; Kunin CM & Al, 1992). Catheterization predisposes to clinical urinary tract infection and the catheterized urinary tract is the most common source of bacteriemia in nursing homes (Smith PW, 1985; Nicolle LE & Al, 1996). Bacteriemia occurs significantly more frequently in subjects with indwelling urinary catheters (Rudman D & Al, 1988; Muder RR & Al, 1992). Residents with long-time catheters often present with fever alone.

Nursing home residents with indwelling urinary catheters, are uniformly colonized with bacteria, largely attributable to biofilm on the catheter (Warren JW & Al, 1982). These organisms are often more resistant to oral antibiotics than bacteria isolated from elderly persons in the community (Gambert SR & Al, 1982; Daly PB & Al, 1991). Specimen collected through the catheter present for more than few days, reflect biofilm microbiology. For residents with chronic indwelling catheters and symptomatic infections, changing the catheter immediately prior to instituting antimicrobial therapy, allows collection of a bladder specimen, which is a more accurate reflection of infecting organisms (Raz R & Al, 2000). Catheter replacement immediately prior therapy is also associated with more rapid defervescence and lower risk of early symptomatic relapse post-therapy (Raz R & Al, 2000).

Guidelines for prevention of catheter-associated urinary tract infections in hospitalized patients (Wong ES & Hooden TM, 1981), are generally applicable to catheterized nursing home residents (Philip W & Al, 2008). Recommended measures include limiting use of catheters, insertion of catheters aseptically by trained personnel, use of as small diameter a catheter as possible, handwashing before and after catheter manipulation, maintenance of a closed catheter system, avoiding irrigation unless the catheter is obstructed, keeping the collecting bag below the bladder and maintaining good hydration in residents. Urinary catheters coated with antimicrobial materials have the potential to decrease urinary tract infections, but have not been studied in the nursing home setting (Ha US & Cho YH, 2006; Schumm K & Lam TB, 2008). For some residents with impaired voiding, intermittent catheterization is an option, and clean technique is as safe as sterile technique (Duffy LM & Al, 1995). External catheter are also a risk factor for urinary tract infections in male residents (Smith PW & Al, 1991), but are significantly more comfortable and associated with fewer adverse effects, including symptomatic urinary infection, than indwelling catheter (Saint S & Al, 2006). Local external care is required.

The reported microbiology of symptomatic urinary tract infections in nursing homes shows that E. coli in women, and Proteus Mirabilis in men are the most frequently isolated infecting organisms (Nicolle LE & Al, 1987; 1996; Ricci G & Al, 2010). Gram-negative

organisms of increased antimicrobial resistance, including Klebsiella pneumoniae, Providencia spp, Morganella morganii, Enterobacter spp, Citrobacter spp and Pseudomonas aeruginosa are frequently isolated (Nicolle LE & Al, 1987; 1996; Ricci G & Al, 2010). Gram-positive organisms, including Enterococcus spp, coagulase-negative Staphylococci, and less frequently, Staphylococcus aureus, are also identified (Ricci G & Al, 2010). (Table 5)

Bacteria (percentage of total isolates)	Grude N & Al, 2001	Mathai D & Al, 2001	Nicolle LE, 2005	Das & Al, 2009	Ricci & Al, 2010
Escherichia coli	56.7%	46.9%	15%	53.6%	55,5%
Proteus Mirabilis	72%	5.0%	42%	14.6%	12.4%
Klebsiella pneumoniae	-	11%	8.2%	13.9%	11.8%
Providencia spp	-	-	22%	3.7%	0.26%
Morganella Morganii	-	-	-	1.5%	0.52%
Enterobacter cloacae	0.9%	-	7.1%	-	3.52%
Citrobacter spp	0.2%	-	-	-	0.26%
Pseudomonas aeruginosa	1.3%	7.5%	27%	2.6%	7.64%
Enterococcus faecalis	7.9%	12.8%	-	4.5%	2.35%
Coagulase-negative Staphylococci	12.5%	3.4%	2.4%	-	-
Staphylococcus aureus	2.2%	-	-	4.1%	-

Table 5. Bacteria reported in published studies as etiologic agents in urinary tract infections

Providentia stuartii, is an organism with a unique proclivity for causing infections in nursing homes (Flerer J & Ekstrom M, 1981; Muder RR & Al, 1992). The major site of isolation of the organism is the urinary tract of patients with long-term indwelling urinary catheters or external urine-collecting devices (Flerer J & Ekstrom M, 1981; Warren JW & Al, 1982). The occurrence of Providencia stuartii is highly variable among different facilities. When present, it is often identified in urine cultures from virtually all patients with long-term indwelling urinary catheters: this observation suggest that cross-infection either through the environment or on the hands of staff members is the major determinant of Providencia stuartii urinary infections in the nursing home setting (Nicolle LE & Al, 1983)

3.1.3.2 Asymptomatic bacteriuria

If the prevalence and the incidence of symptomatic urinary infection is high, the prevalence and the incidence of asymptomatic bacteriuria are also high (Table 6). In a male population from whom monthly urine cultures were obtained, the incidence of new episodes of bacteriuria was 45 per 100 patients/years (Nicolle LE & Al, 1983). In a female population, 1,2 infections per resident/year were identified (Nicolle LE & Al, 1987) and in a 58 month follow up of an Italian nursing home population, the rate of positive urine samples in asymptomatic subjects was higher than 45% (Ricci G & Al, 2010).

Early recurrence of bacteriuria following treatment is the norm, with as many as 50% of men or women experiencing recurrence within 6 weeks of therapy (Nicolle LE & Al, 1983; 1988). The 5 to 10% of nursing home residents managed with long-term indwelling catheters, have a 100% prevalence of asymptomatic bacteriuria, usually with three to five organism isolated at any time (Warren JW & Al, 1982). The reported microbiology of asymptomatic infections is summarized in Table 7 and is similar to that of symptomatic infections.

References	Prevalence (%)
Hedin K & Al, 2002	23
Hassanzadeh P & Motamedifar M, 2007	53
Lin YT & Al, 2007	57.8
Aguirre-Avalos G & Al 1999	24.7
Ouslander JG & Al, 1996	43
del Río G & Al, 1992	38.5
Kaye D & Al, 1989	23.5
Boscia JA, 1986	23.5
Rodhe N & Al 2006	14.8
Ricci G & Al, 2010	46,05

Table 6. The prevalence of asymptomatic bacteriuria (reported in published studies)

Bacteria (percentage of total isolates)	Hedding K & Al, 2002	Rahav G & Al, 2003	Lin YT & Al, 2006	Hassanzadeh P & Motamedifar M 2007	Ricci & Al, 2010
Escherichia coli	67.27	49.0	29.7	45.3	59.2
Proteus Mirabilis	9.09	2.0	-	13.2	14.11
Klebsiella pneumoniae	10.90	2.0	21.6	13.2	7.06
Providencia spp	-	-	16.2	-	-
Morganella Morganii	-	-	-	-	0.61
Enterobacter cloacae	1.81	2.0	-	3.8	0.31
Citrobacter spp	-	1.8	-		0.92
Pseudomonas aeruginosa	-	9.0	13.5	5.7	2.15
Enterococcus faecalis	7.27	8.0	-	-	2.15
Coagulase-neg Staphylococci	-	4.0	-	-	-
Staphylococcus aureus	-	6.0	-	5.7	-

Table 7. Bacteria reported in published studies as etiologic agents in asymptomatic bacteriuria

3.1.4 Skin and soft tissue infections in nursing homes

3.1.4.1 Pressure ulcers

The frequency of pressure ulcers (also termed "decubitus ulcers") in nursing homes patients reflects the quality of nursing home care (Shepard M & Al, 1987; Allman R, 1988). The reported prevalence of pressure ulcers, has varied from 1,6 to up of 20% in different institutions (Michocki RJ & Lamy PP, 1976; Spector WD & Al, 1988; Branders GH & Al, 1990; Young JB & Dobrzanski S, 1992; Nicolle LE & Al, 1994a; Berlowitz DR & Al, 1996; Coleman EA & Al, 2002; Zulkowski K & Al, 2005), with an incidence as high as 10 to 30% patient per year (Berlowitz DR & Wilking SVB, 1989; Branders GH & Al, 1990), and as low as 3,4 to 4,8 episodes per 100000 resident days (Nicolle LE & Al, 1994b). Pressure ulcers are associated with increased mortality (Branders GH & Al, 1990; Livesley NJ & Chow A, 2002; Garcia AD

& Thomas DR, 2006). Infected ulcers are reported to occur from 0,1 to 0,3 episodes per 1000 resident days (Farber BF & Al, 1984; Scheckler W & Peterson P, 1986) or 1,4 per 1000 ulcer days (Nicolle LE & Al, 1994b). Infected pressure ulcers often are deep soft tissue and may have underlying osteomyelitis, cellulitis and bacteremia. Muder RR & Al (1992) reported that 36% of bacteremic skin and soft tissue infections was due to infected decubiti with a case/fatality ratio of 14% for all skin infections, and Livesley NJ & Chow AW (2002) reported that secondary bacteremic infections have a 50% mortality.

Medical factors predisposing to pressure ulcers have been delineated (Berlowitz DR & Wilking SVB, 1989; Garcia AD & Thomas DR, 2006) and include immobility, pressure, friction, shear, moisture, steroids, incontinence, sensory impairment, malnutrition and infections; reduced nursing time can also increase the risk of developing pressure ulcers. Several of these factors may be partially preventable (i.e. malnutrition and fecal incontinence). Prevention of pressure ulcers involves developing a plan for turning, positioning, eliminating focal pressure, reducing shearing forces and keeping skin dry. Attention to nutrition, using disposable briefs and identifying residents at a high risk using prediction tools, can also prevent new pressure ulcers (Smith PW & Al, 2008). The goals are to treat infection, promote wound healing and prevent future ulcers. Many physical and chemical products are now available for the purpose of skin protection, debridement and packing, although controlled study are lacking in the area of pressure ulcer prevention and healing (Lyder CH, 2003) and a variety of products may be also used to relieve or distribute pressure, or to protect the skin (Smith PW & Al, 2008).

Because pressure ulcers, like the skin, are frequently colonized with several different bacteria, antibiotic therapy is not appropriate for a surface swab culture without sign and symptoms of infection (Smith PW & Al, 2008). Surface cultures yield a polymicrobial flora of gram positive and gram negative, aerobic and anaerobic species (Allman R, 1988; Nicolle LE & Al, 1994b). Therefore, surface cultures are not considered reliable to identify infection or, when infection is clinically present, in identify infecting organisms. Non intact skin is more likely to be colonized with pathogens; so some authors obtained positive results for 97% of cultures of superficial swab specimens (Rudelsky B & Al, 1992) even if there were a poor concordance between the different bacterial species identified by biopsy and those identified by aspiration (43% of positive specimens) and swab culture (63% of positive specimens). Another study compared deep-tissue biopsy with aspiration of draining pressure ulcers (Ehrenkranz NJ & Al, 1990). Compared with deep-tissue biopsy, this technique had a sensivity of 93% and a specificity of 99% Ehrenkranz NJ & Al, 1990). Similar species were identified by irrigation-aspiration and deep tissue biopsy. However, aspirates samples of clinically non infected ulcers have also been shown to contain bacteria in 30% of cases (Nicolle LE & Al, 1994b). Culture results must be interpreted with caution, because should not be used as the sole criterion for infections, without clinical or histopathological evidence of infection (Hirshberg J & Al, 2000). Despite the aforementioned information, there is agreement on the most frequently isolated bacteria, including Staphylococcus aureus, beta-Hemolytic Streptococci, Gram negative organisms (including Enterobacteriaceae and Pseudomonas spp, and other Gram positive organisms such Enterococcus spp) and Anaerobic organisms (Chow AW & Al, 1977; Sapico FI & Al, 1986; Muder RR & Al, 1992; Nicolle LE & Al, 1994b; Smith DM & Al, 2010; Lund-Nielsen B & Al, 2011). Colonization with Methicillin-Resistant Staphylococcus Aureus occurs frequently in institutions with

Endemic Methicillin-Resistant Staphylococcus Aureus (Bradley SF & Al, 1991; Strausbaugh LJ & Al, 1991)

3.1.4.2 Cellulitis

Cellulitis (infection of the skin and soft tissue) can occur either at the site of a previous skin break (pressure ulcer) or spontaneously. Skin infections generally are caused by group A Streptococci or Staphylococcus Aureus. However, in cases in which cellulitis is a complication of pressure ulcers or chronic foot ulcers in patients with diabetes or peripheral vascular impairment, infections with other agents, including members of the Enterobacteriaceae, anaerobes or polymicrobial flora are common. Outbreaks of group A streptococcal infections have been described, presenting as cellulitis, pharyngitis, pneumonia or septicemia (Auerbach SB & Al, 1992; Schwartz B & Ussery XT, 1992; Green CM & Al, 2005)

3.1.4.3 Conjunctivitis

Conjunctivitis in the adult presents as ocular pain, redness and discharge. Conjunctivitis has been reported frequently as a common infection in nursing home, but the frequency is variable in different institutions. A prevalence of 0.3 to 3.4% has been reported in different surveys (Garibaldi RA & Al, 1981; Schleckler W & Peterson P, 1986 ; Magaziner J & Al, 1991) while, the incidence of conjunctivitis on different units varied from 0.6 to 3.5 per 1,000 patient-days (Boustcha E & Nicolle LE, 1995). Conjunctivitis occurs more frequently in elderly residents with greater functional impairment (Garibaldi RA & Al, 1981; Boustcha E & Nicolle LE, 1995). It is likely that a high proportion of conjunctivitis cases are noninfectious but are due to irritative, viruses or other factors (Boustcha E & Nicolle LE, 1995). In the nursing homes cases may be sporadic or outbreak-associated (Garibaldi RA & Al, 1981). The batteriology of endemic conjunctivitis is not well studied, but Staphylococcus aureus appears to be the most frequent organism isolated (Boustcha E & Nicolle LE, 1995); infections with upper respiratory flora such as Moraxella catharralis and Haemophilus spp are also reported (Boustcha E & Nicolle LE, 1995). These organisms may be isolated, however, from the conjunctivae of patients without clinical conjunctivitis in the nursing home (Boustcha E & Nicolle LE, 1995). Conjunctivitis has been reported as a clinical presentation for some patients in outbreaks caused by group-A beta-Hemolytic Streptococcus and Methicillin-Resistant Staphylococcus aureus (Center for Disease Control, 1990a; Brennen C & Muder R, 1990). Epidemic conjunctivitis may spread rapidly through the nursing home. Transmission may occur by contaminated eye drops or hand cross contamination. Gloves should be worn for contact with eyes or ocular secretions, with hand hygiene performed immediately after removing gloves (Smith PW & Al, 2008)

3.1.5 Gastrointestinal infections

No surveys have identified either the incidence or the prevalence of infectious diarrhea in non epidemic setting. Most episodes of diarrhea in the nursing home patient are probably noninfectious in origin and are related to the patient's underlying disease, medications (including antibiotics) or diet, especially high protein supplements. Toxigenic Clostridium difficile has been reported to be endemic in some nursing homes (Bentley DW, 1990b; Thomas DB & Al, 1990): the prevalence of Clostridium difficile stool carriage has been reported to be 9 to 26%, with higher rates identified after antibiotic therapy. It is uncertain

whether this phenomenon is limited to selected nursing homes or is generalizable. In those nursing homes with a high rates of colonization with endemic Clostridium difficile, most patients are asymptomatic, but carriage may persist for an extended time (Bentley DW, 1990b).

3.1.6 Bacteremia

Bacteremia in the nursing homes, although rarely detected, may be primary or secondary to an infection at another site: the most common source is urinary tract, with Escherichia coli being the culprit in over 50% of cases (Setia U & Al, 1984; Mylotte JM & Al, 2002). The majority of non urinary cases are secondary to skin or soft tissue infections or pneumonia. The incidence of bacteremia is reported to vary widely, from 4 to 39 episodes per 100000 resident days. The reported variation likely reflects differences in patient populations and interventions in different institutions. The case/fatality ratio for bacteremic patients is 21 to 35% (Setia U & Al, 1984; Rudman D & Al, 1988; Muder RR & Al, 1992; Nicolle LE & Al, 1994a) and is consistent with reports of mortality rates in other populations in which similar organisms have been isolated. (Table 8) From 9 to 22% of episodes are polymicrobial, with a soft tissue source most frequently associated with polymicrobial bacteremia.

Bacteria (percentage of total isolates)	Setia U & Al, 1984	Rudman D & Al, 1988	Muder RR & Al, 1992	Nicolle LE & Al, 1994	Siegman-Igra Y & Al, 2002	Mylotte JM & Al, 2002
Staphylococcus aureus	13	9.1	15	10	5	13
Methicillin-resistant S. aureus	-	7	5	-	9	5
Enterococcus spp	3.7	9.1	7.9	3.3	9	9
Coagulase-neg staphylococcus	0.9	-	3.9	-	-	-
ß-hemolitic streptococcus	3.7	-	4.4	6.7	-	-
Streptococcus pneumoniae	0.9	9.1	3.9	13	7	6
Other Gram-positive bacteria	2.8	-	0.5	-	-	-
Escherichia coli	32	15	13	37	24	27
Providencia stuartii	5.6	24	13	-	-	1
Proteus spp	14	18	8.9	10	21	13
Klebsiella pneumoniae	10	-	5.4	6.7	12	3
Pseudomonas aeruginosa	7.4	6.1	3	-	-	3
Morganella morganii	-	-	3.9	-	-	-
Other gram-negative bacteria	1.9	9.1	4.4	3.3	-	-
Anaerobes	3.7	-	-	10	-	-
Mortality (% subjects)	35	21	21	24	35	18

Table 8. Bacteria reported in published studies as etiologic agents in bloodstream infections and mortality rate

In recent years, the acuity of illness in nursing home residents has risen with a most frequent use of central/peripheral venous catheters and an increased of related bacteremic

complications. The CDC Guidelines for prevention of intravascular catheter-related infections is a useful resource and generally applicable to nursing homes (O'Grady NO & Al, 2002). Relevant points include aseptic insertion of the intravascular cannula, daily inspection of the intravascular catheter for complications such as phlebitis, and quality control of intravascular fluids and administration sets.

3.2 Outbreaks of bacterial infections in nursing homes

Most of nursing homes infections are sporadic; many are caused by colonizing organism with relatively low virulence. However the nursing home, provides a milieu that is conductive in outbreaks of infectious diseases due to close proximity of susceptible patients in the institutional setting and subsequent cross-transmission of organisms among patients through contact with staff members or environmental contamination. An outbreak or transmission within facility may occur explosively, with many clinical cases appearing within a few days, or may, for example, involve an unusual clustering of Methicillin-Resistant Staphylococcus Aureus clinical isolates on a single nursing unit over several months. On the other hand, a case of Methicillin-Resistant Staphylococcus Aureus infection may follow a prolonged period of asymptomatic colonization after an aspiration event or development of a necrotic wound (Drinka PJ & Al, 2005). Tissue invasion may also be facilitated by the presence of a urinary catheter or chronic wounds. Outbreaks in nursing homes, accounted for a substantial proportion (15%) of reported epidemics (Centers for Disease Control and Prevention, 1989a). Clustering of urinary tracts infections, diarrhea, skin and soft tissue infection, conjunctivitis, and antibiotic resistant bacteriuria have been noted (Strausbaugh, L.J., & Al, 2003). Major outbreak of bacterial infection have also been ascribed to Clostridium difficile (Bentley DW, 1990b; Simor AE & Al, 2002;), Salmonella spp. (Standaert SM & Al, 1994), Escherichia coli (Ryan CA & Al, 1986; Carter AO & Al, 1987), group A Streptococcus (Center for Disease Control, 1990a; Auerbach SB & Al, 1992; Harkness GA & Al, 1992; Schwartz B & Ussery XT, 1992; Arnold KE & Al, 2006), Chlamydia pneumoniae (Troy CJ & Al, 1997; Nakashima K & Al, 2006), Staphylococcus aureus (Bradley SF & Al, 1991; Hsu CCS, 1991) and other pathogens (Table 9).

Nursing homes accounted for 2% of all foodborne disease outbreaks reported to the Centers for Disease Control (1975-1987) and 19% of outbreak associated death (Levine WJ & Al, 1991). Transmissible gastrointestinal pathogens may be introduced to the facility by contaminated food or water or infected individuals. High rate of fecal incontinence, as well as gastric hypochlorhydria, make the nursing home ideal for secondary fecal-oral transmission, underscoring the vulnerability of elderly to infections, as well as the role of cross infection in residents with devices, open wounds or incontinence. In addition, mobile residents with poor hygiene, may interact directly facilitating the spread of infections (Standaert SM & Al, 1994; Musher DM & Al, 2004)

3.2.1 Gastrointestinal infections

Bacterial gastroenteritis (caused by Clostridium difficile, Bacillus cereus, Escherichia coli, Campylobacter spp, Clostridium perfrigens or Salmonella spp) as well as viral and parasitic gastroenteritis are well-known causes of diarrhea outbreaks in nursing homes (Carter OA & Al, 1987; White KE & Al, 1989; Slotwiner-Nie PK & Brandt LI, 2001; Olsen SJ & Al, 2001; Winquist AG & Al, 2001; Simor AF & Al, 2002).

Bacteria	Reference(s)
Staphylococcus aureus	Johnson ET, 1983; Storch GA & Al, 1987; Thomas JC & Al, 1989; Bradley SF & Al, 1991; Hsu CCS, 1991; Levine WJ & Al, 1991; Muder RR, 1991; Strausbaugh LJ & Al, 1991
Group A Streptococcus	Reid RT & Al, 1983; Ruben FC & Al, 1984; Center for Disease Control, 1990a; Auerbach SB & Al, 1992; Harkness GA & Al, 1992; Schwartz B & Ussery XT, 1992; Arnold KE & Al, 2006
Escherichia coli O157:H7	Ryan CA & Al, 1986; Carter AO & Al, 1987
Salmonella spp.	Baine WE & Al, 1973; Levine WJ & Al, 1991; Jackson M, 1992; Standaert SM & Al, 1994
Shigella spp.	Levine WJ & Al, 1991
Bordetella pertussis	Addis DG & Al, 1991
Haemophilus influenzae	Smith PF & Al, 1988
Campylobacter jejuni	Levine WJ & Al, 1991
Aeromonas hydrophila	Bloom H & Bottone E, 1990
Antimicrobial agent-resistant gram-negative bacilli	Shlaes DM & Al, 1986; Rice LB, 1990; John JE & Ribner B 1991; Wingard F & Al, 1993
Clostridium perfrigens	Levine WJ & Al, 1991
Clostridium difficile	Bentley DW, 1984; 1990b; Simor AE & Al, 2002
Bacillus cereus	Levine WJ & Al, 1991
Mycobacterium tuberculosis	Stead W, 1981; Narain JJ & Al, 1985; Bentley D, 1990a; Stead W & Al, 1985
Chlamydia pneumoniae	Troy CJ & Al, 1997; Nakashima K & Al, 2006
Legionella spp	Seenivasan MH & Al, 2005

Table 9. Bacteria reported to have caused outbreaks in nursing homes (published studies)

The elderly are at increased risk of infectious gastroenteritis due to age-related decrease in gastric acid. In fact, while food products are usually the vehicle for introduction of the organism, subsequent person to person spread often occurs, prolonging the duration of the outbreak.

In a population with high prevalence of incontinence, the risk of cross infections is substantial, particularly due to shared bathroom, dining and rehabilitation facilities (Bennet RG, 1993). Foodborne disease outbreaks are very common in this setting, most often caused by Salmonella spp or Staphylococcus aureus (Levine W & Al, 1991; Centre for Diseases Control and Prevention, 2004).

E coli 0157:H7 and Giardia also may cause foodborne outbreaks, underscoring the importance of proper food preparation and storage. Some gastroenteritis outbreaks due to Salmonella spp and enterohemorragic E coli, have had a reported case/fatality ratios up to 12% (Levine W & Al, 1991); by contrast, the case/fatality ratio for most other pathogens is low.

3.2.2 Group-A Streptococcus

Outbreak of Group-A Streptococcal infection (Streptococcus pyogenes) have been frequently reported in nursing homes (Center for Disease Control, 1990a; Reid RT & Al, 1983; Ruben FC & Al, 1984; Auerbach SB & Al, 1992; Schwartz B & Ussery XT, 1992). Infected patients may present with bacteremia, pneumonia, cellulitis, wound infection, pharyngitis or conjunctivitis (Schwartz B & Ussery XT, 1992). Rarely, a toxic shock-like syndrome occurs.

Residents with skin ulcers and wounds are at greater risk of invasive infection. In most outbreaks, geographic localization to a floor or wing of the nursing home occurs (Schwartz B & Ussery XT, 1992).

3.2.3 Others outbreaks

A recent paper by Utsumi and co-workers (2010) identified between 1966 and 2008, six hundred and one articles or reports in English, dealing with outbreaks in nursing homes.

Thirty-seven pathogens (21 types of bacteria) were associated with 206 outbreaks. In addition to the above mentioned bacteria, were involved Chlamydia Pneumoniae , Haemophilus Influentiae, Bordetella Pertussis, Neisseria Meningitidis, Aeromonas Hydrophila, and Bacillus Cereus.

The reported median attack rate (proportion of persons who developed infection among those exposed) and their reference lists were reported in Table 10.

Bacteria	Attack rate	References
Chlamydia Pneumoniae	46%	Rice LB & Al, 1990; Miyashita N & Al, 2005; Nakashima K & Al, 2006
Haemophilus Influentiae	11%	Smith PF & Al, 1988
Bordetella Pertussis	36%	Addis DG & Al, (1991)
Neisseria Meningitidis	3%	Anonymus, 1998
Aeromonas Hydrophila	17%	McAnulty JM & Al, 2000
Bacillus Cereus	24%	Halvorsrud J & Orstavik I , 1980

Table 10. Attack rate of outbreaks as reported in published studies

Mycobacterium tuberculosis is responsible for outbreaks spreading from one facility to another (Ijaz, K & Al, 2002). The high frequency of prior infection with Mycobacterium tuberculosis in the elderly population, coupled with the immunological decline, characteristic of elderly persons, foments higher rates of tuberculosis in the nursing home setting. A survey of 15379 reported cases in 29 state indicated that the incidence of tuberculosis among nursing home residents was 39,2 cases per 100000 population, compared with 21,5 cases per 100000 population among elderly persons living in community (Center for Disease Control, 1990b). Residents who develop reactivated disease

and residents who develop active tuberculosis after exposure to those with reactivated disease, constitute the source for facility-wide outbreaks. Because many infected older residents do not present with the classic features of tuberculosis (Rajagopalan S & Yoshikawa TT, 2000), infection in residents may remain unrecognized for prolonged period of time, which sustains transmission. Accordingly, a number of tuberculosis outbreaks involving both residents and staff have been reported (Centers for Disease Control, 1990b; Rajagopalan S & Yoshikawa TT, 2000; Kashef I & Al, 2002). The Centers for Disease Control (1990b) has published specific guidelines for the prevention of tuberculosis in nursing homes.

Since 1990, ten reports have described outbreaks of Streptococcus pneumoniae in nursing homes (Gleinch S & Al, 2000). These have frequently occurred in facilities with low pneumococcal vaccination rates. Multidrug-resistant strains of Streptococcus pneumonia accounted for 4 of these outbreaks. The largest, involved a 100-bed nursing home in Oklahoma (Nuorti JP, 1998). Eleven of 84 residents (13%) developed pneumonia, and 3 residents died. The outbreak strain, serotype "23F", exhibited resistance to penicillin, other ß-lactam antibiotics, trimethoprim-sulfamethoxazole, erythromycin, clindamycin and tetracycline.

Additional reports besides that of Loeb and colleagues (2000) document the occurrence of outbreaks caused by Chlamydia pneumoniae. The attack rate for 3 outbreaks caused by Chlamydia pneumoniae in Ontario nursing homes ranged from 44% to 68% among residents and it was 34% among the staff of one nursing home (Troy CJ & Al, 1997). Of the 302 residents affected, 16 developed pneumonia and 6 died.

Single report identify 5 other respiratory tract pathogens that have caused outbreak in nursing home residents: Chlamydia psittaci (Smith PW, 1994), Legionella pneumophila (Stout JE & Al, 2000), Haemophilus influenza type B (Smith PF, 1988) and Bordetella pertussis (Addis DG & Al, 1991).

4. Antibiotic resistance

Because infections occur frequently in nursing homes, residents are exposed to antimicrobial agents (Nicolle LE & Al, 1984, 1996; Finnegan TP & Al, 1985; Magaziner J & Al, 1991; Jackson M & Al, 1992). With mostly broad-spectrum antibiotics available and in wide use, resistance problems has been repeatedly documented since the early 1970s.

Indeed, numerous studies based on routine surveillance data, indicate a strong relationship between use and resistance (van de Sande-Bruinsma N & Al, 2008) but, nowadays, the epidemiology of antimicrobial resistance in nursing homes remains poorly understood (Lautenbach E & Al, 2009).

4.1 Sources of antibiotic resistance

Antimicrobial agent-resistant bacteria may be introduced into nursing homes by two different routes. They may emerge endogenously in patient flora during courses of antimicrobial therapy, or they may enter with new residents who are already colonized or infected (Bradley SF & Al, 1991; Mulhausen PL & Al, 1996; Muder RR & Al, 1999). Emergence may reflect selection of resistant strains or acquisition of genetic determinants

that confer resistance by either spontaneous mutation or gene transfer. Spontaneous mutations that confer resistance are thought to be rare, but two studies have suggested that gene transfer plays a an important role in long-term care facilities. In an outbreak caused by ceftazidime-resistant bacteria in a chronic-care facility in Massachusetts, Rice and colleagues (1990) reported that the outbreak arose from plasmid transmission among different species and genera of Enterobacteriaceae, and not from dissemination of a single resistant isolate. The outbreak, which involved 29 patients, was caused by strains of Klebsiella pneumonia, Enterobacter cloacae, Escherichia coli, Serratia spp., Enterobacter agglomerans and Citrobacter diversus, that produced similar extended-spectrum ß-lactamases whose genes were located on closely related plasmids. The outbreaks had followed the introduction of ceftazidime into the facility, and its widespread empiric use. Similar observation were reported in a study of gentamicin-resistant gram negative bacilli in a Veterans' Administration nursing home care unit (Shlaes DM & Al, 1990). One Escherichia coli plasmid, which conferred resistance to ampicillin, carbenicillin, tetracycline and sulfonamides, proved identical to plasmids from two Citrobacter freundii strains and a Providencia stuartii strain isolated from three different patients. The introduction of resistant strain by colonized or infected patients who are admitted from other facilities has also been documented: one study reported the entry of an Methicillin-Resistant Staphylococcus aureus strain into the nursing home by a patient who was colonized at the referring hospital (Strausbaugh LJ & Al, 1991). Another study, revealed that 8 of 10 patients admitted to an intermediate-care ward were already colonized with strains of members of the Enterobacteriaceae carrying a plasmid encoding a novel ß-lactamase (Shlaes DM & Al, 1988). Regarding of the route of entry for resistant pathogens into the nursing home, antimicrobial use drives selection pressure for new acquisitions. Bjork and colleagues (1984) reported that in 10 patients with chronic indwelling urinary catheters residing in a Veterans' Administration nursing home care unit in North Dakota over 30 months, 70% of 63 antibiotic courses resulted in bacteriuria with organism resistant to the antibiotic that had been administred. As 40% of the positive urine cultures were polymicrobial, it is likely that antimicrobial therapy merely selected out the more resistant strains. The authors identified cross-infection in only one case and a greater percentage of Escherichia coli strains isolated from nursing home residents were resistant to ampicillin, tetracycline and trimethoprim-sulfamethoxazole, than Escherichia coli strains isolated from patients in the adjoining hospital.

4.2 Risk factors for acquisition of antibiotic resistance

Few studies have examined risk factors for infection with antimicrobial pathogens in nursing home patients. Infections with antibiotic resistant bacteria appears to occur most often in nursing home patients with antecedent colonization (Bradley SF & Al, 1991; Muder RR & Al, 1991; Mulhausen PL & Al, 1996). However, risk factors for colonization and infection are not necessarily the same. Overall infection with resistant bacteria was more likely to occur in nursing home residents who had been hospitalized recently or who a substantial decline in functional status (Terpenning MS & Al, 1994). Muder and colleagues (1991) reported risk factors for Methicillin-Resistant Staphylococcus Aureus (MRSA) infection in residents of their intermediated-care ward and nursing home care unit. In a stepwise logistic regression analysis, both persistent Methicillin-Resistant Staphylococcus Aureus colonization and dialysis were independent risk factor for Methicillin-Resistant

Staphylococcus Aureus infection. Terpenning and colleagues (1994) in an Ann Arbor, Michigan, identified risk factors for infection caused by both Methicillin-Resistant Staphylococcus Aureus and resistant Gram negative bacilli. By stepwise logistic regression analysis, diabetes mellitus and peripheral vascular disease were significant independent risk factors for Methicillin-Resistant Staphylococcus Aureus infection. Moreover, the presence of an indwelling urinary catheter or intermittent urinary catheterization, pressure ulcers and prior antibiotic use were significant independent risk factors for infection caused by resistant Gram-negative bacilli (Terpenning MS & Al, 1994; Muder & Al, 1997) . In a cross-sectional survey among 1,215 residents of long-term care facilities in Jerusalem, the Vancomycin-Resistant Enterococci (VRE) carriage rate was 9.6%. Previous hospitalization and antibiotic treatment were associated with elevated Vancomycin-Resistant Enterococci colonization rate. In contrast, moderate and severe levels of dependency and prolonged stay in a nursing home were associated with a decrease in the Vancomycin-Resistant Enterococci colonization rate. (Benenson S & Al, 2009).

In a prospective cohort study a total of 3339 patients with invasive pneumococcal infection were identified between 1995 and 2002. Multivariate modeling revealed that risk factors for infection with penicillin-resistant as opposed to penicillin-susceptible pneumococci were year of infection, absence of chronic organ system disease and previous use of penicillin, trimethoprim-sulfamethoxazole and azithromycin. Infection with trimethoprim-sulfamethoxazole-resistant pneumococci was associated with absence of chronic organ system disease and with previous use of penicillin, trimethoprim-sulfamethoxazole, and azithromycin. Infection with macrolide-resistant isolates was associated with previous use of penicillin, trimethoprim-sulfamethoxazole, clarithromycin, and azithromycin. Infection with fluoroquinolone-resistant pneumococci was associated with previous use of fluoroquinolones, current residence in a nursing home, and nosocomial acquisition of pneumococcal infection (Vanderkooi OG, 2005).

4.3 Risk factors for colonization

Given the high prevalence of colonization with antibiotic-resistant strains in nursing homes, why do some patients never become colonized and others become persistent carriers? When colonized nursing home residents have been compared with non carriers, underlying illness, presence of intravenous, urinary or enteral feeding devices, antibiotic use, presence of wounds, decline in functional status and increased intensity of nursing care have been associated to various degrees with High-level Gentamicin-Resistant Enterococci, Vancomycin-Resistant Enterococci, Drug-Resistant Streptococcus Pneumoniae and Methicillin-Resistant Staphylococcus Aureus (Zervos MJ & Al, 1987; Bradley SF & Al, 1991; Chenoweth CE & Al, 1994; Terpenning MS & Al, 1994; Brennen C & Al, 1998). Similar risk factors for the carriage of resistant Gram Negative Bacilli have been found. Nursing home residents colonized with resistant Gram Negative Bacilli were significantly more likely to have lived in a large skilled nursing facility, have had prior antibiotic treatment, or have had urinary incontinence or a catheter, than non colonized persons in nursing homes or the community (Gaynes RP & Al, 1985). Colonization with Gram Negative Bacilli resistant to Gentamicin, trimethoprim or cefriaxone, has been associated to varying degrees with increased length of stay, increased debility, need for a urinary device, prior pneumonia, presence of wound or chronic disease (Huovinen P, 1984; Shlaes DM, 1986; MacArthur RD

& Al, 1988; Bradley SF & Al, 1991; Wingard E & Al, 1993; Terpenning MS & Al, 1994). Given the overlap in risk factors, it is not surprising to find that many nursing home residents are colonized with more than one antibiotic-resistant pathogen (Chenoweth CE & Al, 1994; Terpenning MS & Al, 1994; Brennen C & Al, 1998)

4.4 Occurrence: organisms and antibiotic resistance

Even though interest in the epidemiology of antibiotic resistance in healthcare setting outside hospital is on the increase, the extend of antibiotic resistance in nursing home is still relatively unknown. Most information is derived from surveillance studies of infections in nursing home residents or outbreak investigations. No studies have defined the overall magnitude of this problem in a systematic manner, but available data suggest that antimicrobial agent resistant pathogens are frequently encountered in this setting. In fact nursing homes residents have an high frequency of colonization with antimicrobial-resistant organisms, including Methicillin-Resistant Staphylococcus Aureus, Vancomycin-Resistant Enterococci, Enterococci with high-level Gentamicin-Resistance, Extended-Spectrum ß-Lactamase-Fluoroquinolone-Resistant Gram-Negative Pathogens, Gram-Negative Uropathogens, , Penicillin-Resistant Pneumococci.

4.4.1 Methicillin-Resistant Staphylococcus Aureus (MRSA)

Methicillin-Resistant Staphylococcus Aureus was first described in 1961, and since then it has become a worldwide problem (Jevons MP, 1961; Tansel & Al, 2003; Diekema DJ & Al, 2004; Corrente M & Al, 2005). The presence of Methicillin-Resistant Staphylococcus Aureus in nursing homes was first reported in 1970 by O'Tool (O'Toole & Al, 1970). Methicillin-Resistant Staphylococcus Aureus is a frequent colonizer of debilitated patients; on this point, Bradley observed that the rate of colonization with Methicillin-Resistant Staphylococcus Aureus was <25% (Bradley SF & Al, 1991). The same Author showed that in two of the most common sites of colonization, nares and wound, colonization rates range from 8 to 53% and from 30 to 82% respectively (Bradley SF, 1999). Lee YL and colleagues (1997) reported a one-year prospective surveillance study of Staphylococcus Aureus colonization and infection. Nasal and stool or rectal screening cultures were done on admission, and all patients underwent screening on at least a quarterly basis for one year. Overall, 35% of patients were colonized at least once with Staphylococcus Aureus (72% Methicillin-Susceptible; 25% Methicillin-Resistant; 3% mixed phenotype). Mendelson evaluated the rate of colonization by Staphylococcus Aureus, especially Methicillin-Resistant Staphylococcus Aureus, in 270 elderly residents of a large long-term care facility. The Authors showed that 23,3% of residents were carriers of Staphylococcus Aureus and 27% of those had Methicillin-Resistant Staphylococcus Aureus (Mendelson G & Al, 2003). It is estimated that residents of nursing homes who are colonized with Methicillin-Resistant Staphylococcus Aureus have a 4 to 6 fold increase in infection rate. In a study by Muder RR and colleagues (1991), 25% of Methicillin-Resistant Staphylococcus Aureus carriers had an episode of staphylococcal infection, versus only 4% of Methicillin-Susceptible Staphylococcus Aureus carriers.

In a retrospective cohort study, Capitano showed that the median infection management cost of a Methicillin-Resistant Staphylococcus Aureus infection was six times greater than that of a Methicillin-Susceptible Staphylococcus Aureus infection, whereas the median

associated nursing care cost was two times greater. The median overall infection cost associated with Methicillin-Resistant Staphylococcus Aureus was 1,95 times greater than that associated with Methicillin-Susceptible Staphylococcus Aureus. Nursing care cost constituted the major portion of the overall infection cost for both groups (Methicillin-Susceptible Staphylococcus Aureus = 51%; Methicillin-Resistant Staphylococcus Aureus = 48%) (Capitano B & Al, 2003).

Risk factors for Methicillin-Resistant Staphylococcus Aureus colonization include: residence in a medical ward or medical intensive care unit or prolonged hospitalization (13 weeks), advanced age and a history of invasive procedures (Asensio A & Al, 1996). In a study by O'Sullivan, the risk factors significantly associated with Methicillin-Resistant Staphylococcus Aureus colonization were male sex, age over 80 years, residence in the nursing home for more than six months, hospitalization during the previous six months, peripheral vascular disease, pressure ulcers, steroid therapy, poor general skin condition, antibiotic therapy during the previous three months and a mental test score of less than 14. Multivariate analysis identified male sex and pressure ulcers as independent variables (O'Sullivan NP & Keane CT, 2000). In a case control study conducted in a community nursing home, Thomas reported that nasogastric intubation and antibiotic therapy in the previous 6 months were the most important factors associated with Methicillin-Resistant Staphylococcus Aureus colonization (Thomas JC & Al, 1989). Other risk factors are indwelling urinary catheters and urinary incontinence (Terpenning MS & Al, 1994).

4.4.2 Vancomycin-Resistant Enterococci (VRE)

First described in 1987 in Europe Vancomycin Resistant Enterococci have recently emerged as important nosomial pathogens and in the last years have become among the most feared pathogens in US hospitals. Studies dealing with the emergence of Vancomycin-Resistant Enterococci in the United States, revealed that most patients with Vancomycin-Resistant Enterococci were in Intensive Care Units (Clark NC & Al, 1993). Colonization with Vancomycin-resistant Enterococcus has been reported from community settings in the United States, including, to a limited extend, long-term care facilities (Coque TM & Al, 1996; Bonten MJ & Al, 1998). Bonilla showed that prevalence of Vancomycin-Resistant Enterococcus colonization among patients in the long-term care facilities at the Ann Arbor Department of Veterans Affairs Medical Center, exceeded the prevalence in the intensive care unit and in the general medical wards (Bonilla HF & Al, 1997). Brennan decribed the epidemiology of Vancomycin-Resistant Enterococcus colonization in a 400 bed long-term care facility for veterans. The author observed that 24 of 36 patients were colonized with Vancomycin-Resistant Enterococcus that persisted for 67 days and were associated with antibiotic administration (Brennan C & Al, 1998). In a prospective cohort study, 45% (45 of 100 patients) were colonized with Vancomycin-Resistant Enterococcus. The risk factors identified by univariate analysis were: hospitalization in the prior 60 days, an admission diagnosis of infection, inability to ambulate, presence of a feeding tube or urinary catheter or decubitus ulcer and documented more probable antibiotic use in the previous 60 days (particularly the use of Vancomycin and third generation cephalosporins). Stepwise logistic regression analysis identified the presence of decubitus ulcer or hospital admission, and documented a probable antibiotic use in the 60 days before admission, as significant risk factors for colonization with Vancomycin-Resistant Enterococcus at the time of admission (Elizaga ML & Al, 2002).

4.4.3 Enterococci with high-level gentamicin resistance

Two studies, both from the Ann Arbor Veterans Administration nursing home care unit have identified risk factors for colonization with Gentamicin-Resistant Strains of Enterococci. In the first study a one-day prevalence survey reported by Zervos and colleagues, the need for advanced nursing care and antibiotic therapy in the prior 3 months were independent risk factors for colonization (Zervos MJ & Al, 1987). In the second study, presence of wounds, renal failure, intermittent catheterization, low Katz functional status and low serum albumin were independent risk factors for colonization with strains possessing high-level resistance to gentamicin (Terpenning MS & Al, 1994).

4.4.4 Extended-spectrum ß-lactamase gram-negative pathogens (ESBLs)

The first report of Extended-Spectrum ß-Lactamase Gram-Negative bacilli, came from Europe and were quickly followed by reports in the United States. This type of antimicrobial resistance is now recognized worldwide. The prevalence of Extended-Spectrum ß-Lactamase Gram-Negative Pathogens in long-term care facilities is becoming alarming. The first reported outbreak of bacteria resistant to ceftazidime in the United States occurred in 1990 among patients in a chronic care facility in Massachusetts (Rice LB & Al, 1990). In a study of ceftazidime-resistant Escherichia coli and Klebsiella pneumonia in Chicago, 31 of 35 patients from 8 nursing facilities harboured an Extended-Spectrum ß-Lactamase producing enteric pathogen. (Weiner J & Al, 1999). Weiner reported that prior exposure to ciprofloxacin or trimethoprim-sulfamethoxazole was an independent predictor of colonization with Escherichia coli resistant to ceftazidime among nursing home residents. Molecular analysis of isolates, showed that a particular resistance-conferring plasmid appeared frequently, thus supporting the growing concern that long-term facilities may act a reservoir for antimicrobial drug-resistant organisms. Several studies have evaluated the risk factors for colonization or infections with Extended-Spectrum ß-Lactamase-producing organisms in the hospitalized patients. Reported risk factors include the presence of intravascular catheters, emergency intra-abdominal surgery, gastrotomy or jejunostomy tube, gastrointestinal colonization, length of hospital or intensive care unit stay, prior antibiotics (including third generation cephalosporins), severity of illness, presence of an urinary catheter, and ventilator assistance (Schiappa DA & Al, 1996). In a case-control study, Sandoval and colleagues (2004) showed that exposure to any cephalosporin and percentage of residents using gastrotomy tubes within the nursing home, were associated with having a clinical isolate resistant to third-generation cephalosporin (Sandoval C & Al, 2004). Nursing home residents would appear to have several additional risk factors for infection with Extended-Spectrum ß-Lactamase- Gram-Negative producing organisms. It has been well documented that hand-washing rates are low among nursing home personnel (Denman SJ & Burton JR, 1992). Urinary catheterization and decubitus ulcers are frequent, and have been associated with colonization of non- Extended-Spectrum ß-Lactamase producing, antibiotic-resistant gram negative bacilli (Muder RR & Al, 1991; SmithPW & Al, 2000).

4.4.5 Fluoroquinolone-resistant gram-negative pathogens

Resistance in fluoroquinolones has been increasing over time in long-term care facilities. In a correlational longitudinal survey study, Viray showed that Escherichia Coli fluoroquinone-resistance rates was high but variable, and were generally increasing over time (Viray M &

Al, 2005). In a case control study, Cohen showed that Fluoroquinone-Resistant Escherichia coli urinary tract infection was more common with prior fluoroquinolone use (Cohen AE & Al, 2006). Maslow conducted a cross-sectional study to determine the prevalence of, and risk factors for colonization with Fluoroquinone-Resistant Escherichia coli in residents of a long-term care facility. Fluoroquinone-Resistant Escherichia coli were identified from rectal swabs for 25 of 49 (51%) partecipants at study entry. On multivariate analyses, prior fluoroquinolone use was the only independent risk factor for Fluoroquinone-Resistant Escherichia coli carriage and was consistent for fluoroquinolone exposures in the previous 3, 6, 9 or 12 months. Pulsed-field gel electrophoresis of Fluoroquinone-Resistant Escherichia coli identified clonal spread of one strain among 16 residents (Maslow JN & Al, 2005).

4.4.6 Gram-negative uropathogens

Shlaes and colleagues identified risk factors for urinary colonization with Gentamicin-Resistant Gram-negative Bacilli in patients of a Veteran Administration nursing home care unit near Cleveland, Ohio, using stepwise logistic regression (Shlaes DM & Al, 1986). Perineal or rectal colonization with Gentamicin-Resistant strains and presence of a urinary catheter were significant independent risk factors. Another study at the same institution by Wingard and colleagues, examined carriage of Trimethoprim-Resistant Gram-negative Bacilli (Wingard E & Al, 1993). Functional status and length of stay were significant independent risk factors for colonization: functional status was the most important risk factor for acquiring Trimethoprim-Resistant strains by cross-colonization. Gaynes, studying colonization with multiply resistant Gram-negative bacilli in patients admitted to the hospital from community nursing homes, reported that bladder dysfunction, residence in large nursing homes, age and prior antibiotic use were independent risk factors (Gaynes RP & Al, 1985). Terpenning identified intermittent catheterization, inflammatory bowel disease, chronic renal disease, presence of wounds and prior pneumonia, to be independent risk factors for colonization with Gentamicin and/or Ceftriaxone-Resistant Gram-negative Bacilli in a stepwise regression analysis (Terpenning MS & Al, 1994).

4.4.7 Penicillin-Resistant Pneumococci

Penicillin resistance is common in Streptococcus Pneumoniae and is a problem all over the world, both in the community and in hospital setting. In 2002, the European Antimicrobial Resistance Surveillance project (http://www.earss.rivm.nl) reported five countries with a prevalence of Penicillin-Resistant Pneumococci of greater than or equal to 30%. Overall, in 2002, the European Antimicrobial Resistance Surveillance Project reported 11% of Streptococcus Pneumoniae strains as non susceptible to penicillin and 17% non susceptible to erythromycin. Two events have occurred since 2000 that may have reduce the selective pressure driving antimicrobial resistance: the more appropriate use of antimicrobial and the pneumococcal conjugate vaccine (Klugman KP, 2004).The earlier study reports by Millar and Denton were among the first to describe Penicillin-Resistant Pneumococcal infection in elderly institutionalized and debilitated patients (Denton M & Al, 1993; Millar MR & Al, 1994). Nuorti reported a significant outbreak of Penicillin-Resistant Pneumococci in a long-term care facility in rural Oklaoma. The Author observed that 13% of the residents developed pneumonia, and that the mortality rate was 23%. Resistant isolates were recovered from 64% of residents with pneumonia and from 23% of non infected residents (Nuorti JP & Al, 1998).

4.4.8 Others organisms

In addition to those listed above, there are other kinds of antimicrobial-resistant pathogens. Smith and colleagues described an outbreak caused by an Ampicillin-Resistant strain of Haemophilus influenzae, involving six patients in a nursing home and adjoining hospital during a 1-month period (Smith PF & Al, 1988). Two patients were bacteremic and one died. All patients had personal contact with at least one other case patient, suggesting person-to-person spread. Sturm and colleagues reported a similar outbreak involving 15 subjects in a pulmonary rehabilitation centre in the Netherlands (Sturm AW & Al, 1990). The outbreak strain of Haemophilus influenza was resistant to amoxicillin, thrimethoprim-sulfamethoxazole, chloramphenicol and tetracycline. Choi described a nursing home outbreak caused by Salmonella Heidelberg serotype, frequently expressing multiple resistance (Choi AT & Al, 1990). Forty-four (22%) of the 199 residents were affected. Patients treated with antibiotics excreted the outbreak strain for a median duration of 14 weeks, prolonging the presence of a potential source for additional cases.

Although Acinetobacter infections in long-term care facilities and nursing homes are not well described, during the last decade, increasingly resistant strains of Acinetobacter, necessitating greater use of broad-spectrum antibiotics, such imipenem and ampicillin-sulbactam (Jain R & Danziger LH, 2004; Bassetti M & Al, 2008).

Sengstock and colleague in a six-year period reported in an increase of Multi-Drug-Resistant Acinetobacter baumannii, a link between increasing antibiotic-resistance, morbidity and mortality, and a transfer between hospital and nursing home and viceversa (Sengstock DM & Al, 2010). The article demonstrated that Acinetobacter baumannii is widespread including hospitals, long-term acute-care and nursing homes, and that the transfer of multidrug-resistant strains among health care facilities is bidirectional. These data confirm previous report (Gould CV & Al, 2006; Saeed S & Al, 2006; Stephens C & Al, 2007; Furuno JP & Al, 2008)

5. Conclusions

In the nursing home setting, antimicrobial use is an important issue, relevant to antimicrobial resistance. Previous study have found relatively high rates of antimicrobial use and substantial inappropriate use of antimicrobial agents in nursing homes and long-term care facilities (Zimmer JG & Al, 1986; Crossley K & Al 1987; Jones SR & Al, 1987; Katz PR & Al, 1990; Warren JW & Al, 1991; Yakabowich MR & Al, 1994; Pickering TD & Al, 1994; Montgomery P & Al, 1995). In addition to increasing the risk of colonization or infection with antimicrobial-resistant organisms, inappropriate antimicrobial use adds cost to resident care and may place the patient at increased risk for drug adverse reactions (Mylotte JM, 1999). Recommendations for improving antimicrobial use have included development of a formulary and continuing review of antimicrobial use and prevalence of antimicrobial resistance in cultures obtained from patients with suspected infections. In the last decades, an increasing number of nursing homes have developed infections control programs with surveillance and control activities (Smith PW, 1999). A major contribution to this development was the publication of guidelines by the Association for Professional in Infection Control and Epidemiology (APIC) – Society for Healthcare Epidemiologists of America (SHEA) in 1997 (Smith PW & Rusnak PG, 1997), revisited in 2008 (Smith PW & Al, 2008).

5.1 Prevention and control of infections in nursing homes

Most nursing homes have infection control programs, even if the components of these programs vary among different institutions and countries. (Garibaldi RA & Al, 1981; Crossley K & Al, 1985; Kabbuz RF & Tenney JH, 1988; Campbell B, 1991). The overall goal of the infection control program is to prevent infections and, when that is not possible, to limit interpatient transmission of potential pathogens (Nicolle LE & Garibaldi RA, 1995). Surveillance for infections in the nursing home is integral to the program (Smith PW, 1987). Valid infection surveillance requires the use of standard definitions, appropriate for the nursing home (McGeer AB & Al, 1991), effective case finding measures, systematic analysis and reporting of data, and an awareness to identify potential outbreaks as easy as possible. The optimal method for surveillance in nursing home is not identified, because it differs depending on the characteristics of each nursing home, staffing and patients populations.

Infection prevention and control is important for continuum of care and their main functions are (a) to obtain and manage clinical data, including surveillance information for endemic and epidemic infections; (b) to develop and recommend policies and procedures; (c) to intervene directly to prevent infections and (d) to educate and train health care workers, patients and caregivers. (Table 11)

An effective infection control program includes a method of surveillance for infections and antimicrobial-resistant pathogens, an outbreak control plan for epidemics, isolation and standard precautions, hand hygiene, staff education, an employee health program, a resident health program, policy formation and periodic review with audits, and a policy to communicate reportable diseases to public health authorities.

Infection surveillance in nursing homes involves collection of data on nursing home-acquired infections (Do AM & Al, 1999). Surveillance can be limited to a particular objective or may be a facility-wide goal. Surveillance often is based on individual patient risk factors, focused on a unit or based on a particular pathogen or infection type.

Surveillance may be either passive or active; in passive surveillance ("routine surveillance"), an infection control professional uses data collected for routine patient care. Although less costly in term of resources, passive surveillance is inherently biased. It may underestimate the magnitude of outcomes measured and delay detection of outbreaks. The feasibility of passive surveillance has been demonstrated and has led to continuing education opportunities.

Active surveillance uses multiple data sources to detect infections and antimicrobial resistance early, but data in nursing homes are lacking. Hospital definitions may not be applicable in nursing home setting; modified nursing home specific criteria were developed by a Canadian Consensus Conference, which took into account the unique limitations of the nursing home setting (McGeer A & Al, 1991). These criteria have been used widely but not uniformly (Danzig LE & Al, 1995). In addition a facility must have clear goals and aims for setting up a surveillance program. These goals, like other elements of an infection control program have to be reviewed periodically to reflect changes in the facility's population, pathogens of interest and changing antimicrobial resistance patterns. In addition, plans to analyse the data and use them to design and implement proven preventive measures, must be made in advance. The analysis and reporting of infection rates in nursing homes must be conducted monthly, quarterly and annually to detect trends. Because the length of stay in

nursing home is long, and each resident is at risk for a prolonged duration, infection rates (infections/1000 resident days) can be calculated by using resident days or average resident census for the surveillance period as the denominator. These data can be used to estabilish endemic baselines rates and recognize variations from the baseline that could represent an outbreak. Feed back to the nursing home staff is critical to the success of the surveillance program, and this information should lead to specific infection control initiatives and follow up surveillance.

The Centers for Disease Control and Prevention's Healthcare Infection Control and Prevention Advisory Committee (HICPAC) proposes use of "Standard Precautions" which have been designed for the care of all patients in hospitals (Garner JS, 1996). "Standard Precautions" apply to blood, all body fluids, secretions and excretions regardless of whether they contain visible blood, skin that is not intact, or mucous membrane material. Designed to reduce the risk of transmission of pathogens from apparent and ambiguous source of infection, these precautions include hand hygiene compliance, glove use, masks, eye protection, gown and avoidance of injuries from sharp materials. Transmission-based precautions are intended for use with patients who may be infected with highly transmissible or epidemiologically significant pathogens. These include airborne precautions, droplet precautions and contact precautions.

Although these guidelines were designed for acute care setting, several of them, especially the universal precautions, apply to nursing home setting as well. However, facilities should evaluate these guidelines and individualize the plan to obtain cultures based on the population they serve.

Healthcare workers may play an important role in the dissemination of antibiotic-resistant bacteria in nursing homes (Thomas JC & Al, 1989): contamination of the hand of healthcare workers has been recognized as playing a role in the transmission of pathogenetic bacteria to patients since the observations of Holmes, Semmelweis and other, more than 100 years ago (Otherson MJ & Otherson HB, 1987). Hand antisepsis remains the most effective and last expansive measure to prevent transmission of nosocomial infections. However, compliance with hand washing recommendations among healthcare workers averages only 30-50% and improves only modestly following educational interventions (Mody L & Al, 2003). Healthcare workers frequently reported poor compliance with hand hygiene measures because of skin irritation from frequent washing, too little time because of a heavy workload, and simply forgetting. Introduction of alcohol-based hand rubs have been shown to enhance compliance with hand hygiene in the nursing home setting, and should be used to complement educational initiatives (Mody L & Al, 2003).

While the cost of introducing alcohol-based hand rubs could be a concern of nursing homes, recent data in acute care have shown that the total costs of a hand hygiene promotion campaign, including alcohol-based hand rubs, corresponded to less than 1% of costs that could be attributed to nosocomial infections (Pittet D & Al, 2004). Introducing the alcohol-based hand rubs must take into account some problems: alcohol-based hand rubs should not be used if hands are visibly soiled, in which case hand hygiene with antimicrobial soup and water is recommended. Alcohol-based hand rubs can cause dry skin; however recent data on rubs containing emollients have shown to cause less skin irritation and dryness (Centers for Disease Control , 2002).

Management strategies	
Infection control program	
Surveillance	• Review microbiology data • Maintain line listing of cases • Prevalence surveys of residents, staff or new admissions • Identify readmission cases
Outbreak investigation	
Policies, isolates, environment	
Staff education	
Antimicrobial utilization program	
Employee health program	
Patient care strategies	
Optimal management of comorbidities	
Optimal nutrition	
Avoidance of invasive devices	
Vaccination	• Influenza • Pneumococcus • Tetanus
Screening	• Hepatitis B and C virus • Tuberculosis (selected cases)
Precautions	• Hand-washing, antimicrobial soaps • Environment decontamination • Private room for colonized/infected residents • Barrier precautions for colonized/infected residents • Strict isolation for colonized/infected residents • Isolation of new admission • Special placement colonized/infected residents • Cohort colonized/infected residents • Cohort colonized personnel • Establish isolation ward
Reduction of reservoir	• Exclusion of colonized/infected residents from facility • Rapid discharge of colonized/infected residents • Decolonization therapy of residents, personnel o new admissions
Outbreak management	
Mechanism for early identification	
Policies for laboratory utilization	
Case finding and analysis	
Isolation and cohorting	
Specific therapy	

Table 11. Recommended approaches to the prevention and minimization of infections and outbreaks in nursing home

Another key point of the infection control program is staff education. Ongoing staff education is critical in health care setting, because of the plethora of literature published every year, advancements in technology and regulatory demands. The infection control program plays a vital role in educating nursing home personnel on various infection control measures, particularly in view of rapid staff turnover. Informal education and quality improvement meeting should be complemented with in-service education on various topics, including hand hygiene compliance, antimicrobial usage and antimicrobial resistance, appropriate and early diagnosis of infections, infection control and prevention measures, isolation precautions and policies.

5.1.2 Patient care practices

Patient-specific strategies to prevent infection are targeted to increase general and specific immunity and, hence, limit susceptibility to infection. These include maintenance of adequate nutrition and optimal management of associated chronic diseases. For example, nursing care practices should attempt to minimize or prevent the occurrence of aspiration in patients with neurologic impairment, avoid trauma to neuropathic feet, and prevent the occurrence of pressure ulcers in patients with limited mobility. Ensuring optimal use of immunizing agents is important, including pneumococcal vaccination (Center for Disease Control, 1989b). Use of invasive devices should be limited to those situations in which they are essential for patient care. When tube feeding is necessary to maintain nutritional status, percutaneous gastrostomy or jejunostomy feeding tubes may be preferred over nasogastric tubes because of a reported decreased occurrence of aspiration pneumonia (Fay DE & Al, 1991), even if other studies have not supported this observation (Clocon JO & Al, 1988; Peak A & Al, 1990). It has been suggested that use of external condom catheters for incontinence in men may be associated with a lower incidence of invasive urinary tract infections compared with long-term indwelling catheters, but this, too, is controversial, because of reported increased incidence of phimosis and skin irritation that predisposes to urinary infections (Flerer J & Ekstrom M, 1981).

5.1.3 Outbreaks management

Outbreaks of infection should be anticipated in the nursing home setting and policies to respond to a suspected or proven outbreak must be developed prior to occurrence. Such policies should include general aspects of outbreak management including identification, communication and authority, as well as specific issues related to the most frequent organisms likely to occur. Adequate management requires ongoing surveillance for infection to ensure early identification, specific criteria to identify a potential outbreak, case finding strategies and laboratory backup to identify the etiologic agent and plan appropriate interventions. Authority within the facility to initiate appropriate measures to control an outbreak should be clearly defined. Early notification and ongoing communication within the institution and with appropriate public health authorities must be outlined clearly prior to the crisis of an epidemic.

The response to the outbreak must include immediate control measures to identify and isolate cases, as appropriate, and limit patient and staff exposure. Control measures will include use of patient isolation, limitations in patient movement and interaction with the facility and, frequently, specific therapy. Compliance with isolation practices leads to special

problems in nursing homes. As patients' room are their permanent residence, transfer within the institution for isolation purposes is disruptive for patients and family. Cognitive impaired residents will not be able to understand the reasons for and practices of isolation and it may be difficult to restrict movement for some of these patients. Policies developed, should acknowledge these potential problems and identify the methods by which they will be addressed. An integral part of outbreak management is a review and analysis of the course of the outbreak, impact and potential problem areas that may be changed to improve management in the future.

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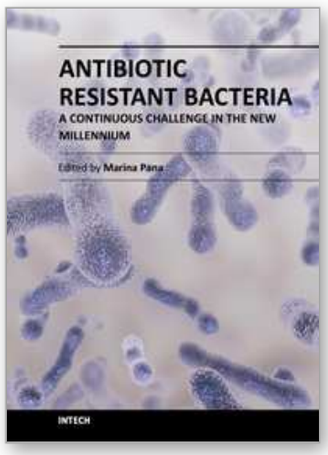

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Antibiotic-resistant bacterial strains remain a major global threat, despite the prevention, diagnosis and antibiotherapy, which have improved considerably. In this thematic issue, the scientists present their results of accomplished studies, in order to provide an updated overview of scientific information and also, to exchange views on new strategies for interventions in antibiotic-resistant bacterial strains cases and outbreaks. As a consequence, the recently developed techniques in this field will contribute to a considerable progress in medical research.

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