

Aging as Risk Factor of Bacterial Skin Infection

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Abstract

In the last decades, the elderly population rise significantly, and estimated that one fifth of global population will be more than 65 years old, by the year 2050. As people get older, they become more susceptible to bacterial skin infections. Bacterial skin infection in elderly has higher mortality and morbidity rate, compared with young adult. Skin changes that occur in the elderly, including thinning of the skin layer and decreased function of the skin, make the elder's skin become sensitive skin. Elderly skin has higher risk to get inflammation or irritation, and become port d'entry of bacteria that may cause bacterial skin infection. Apart from that, immunosenescence in elderly is also a major factor in the occurrence of bacterial skin infection in the elderly.

Keywords: aging; bacterial skin infection; elderly; sensitive skin; human and disease

1. Introduction

In the last few decades, life expectancy has increased significantly, as seen by the growing population of elderly. The World Health Organization (WHO) estimated, that between 2015-2050 there will be 900 million to 2 billion people aged over 60 years. By the year 2050, it is estimated that one fifth of the global population (which is around 2.1 billion) will be more than 65 years old and 434 million elderly will be more than 80 years old [1–4].

Bacterial skin infections or pyoderma are infections of the skin that are pyogenic. It is mostly caused by *Staphylococcus aureus* or *Streptococcus pyogenes*. It causes a broad clinical spectrum of infections, which range from superficial pyodermas to more invasive skin & soft-tissue infections (SSTI). Reported in the United States, the visits for SSTIs is 32.1 to 48.1 per 1,000 population. Review on Antimicrobial Resistance in United Kingdom, states that infections caused by antimicrobial resistance will cause more deaths than cancer, which is around 10 million people per year by 2050 [5–7].

Structural and physiologic changes in the skin produce marked susceptibility to dermatologic disorders, including bacterial skin infection in the elderly. As we age, epidermal and dermal layers are thinner. In the epidermal layer, keratinocyte atrophy occurs. In dermal layer, there is a decrease in the amount of extracellular matrix, including collagen and elastin, which causes the clinical manifestation of wrinkle. In addition, in the subcutaneous layer there is also adipose layer thinning, which may reduce antimicrobial protection against bacterial infections in the skin [8–10].

The incidence of bacterial skin infection is increasing with the growth of elderly population, who are often in critical or immunocompromised condition. In the United States, a 20% increase in outpatient SSTI cases and a 40% increase in SSTI cases in the emergency ward over a 13 year period was reported. SSTI in elderly increases two-fold in more than 65 years old people. Bacterial skin infection may appear atypical, mild or even unspecific. The clinical manifestation in elderly quite common begins with slight fever or without fever, but evolving rapidly to sepsis [7, 11].

Skin bacterial infection in the elderly has several peculiarities. Elderly is the population that has high risk of suffering from skin bacterial infection. It leads to poor outcome and response to therapy of skin bacterial infection [7].

2. Bacterial Skin Infection

Infection of the skin and soft tissue occurs in 10% of hospitalization cases were caused by bacterial infection. Bacterial skin infections are classified into primary and secondary bacterial infections (pyoderma). Meanwhile, secondary pyoderma occur on the non-intact skin, which proliferation and invasion of secondary bacteria at the surrounding area was differ from the causative bacteria, that will worsen the underlying disease. Secondary pyoderma occur as a result of impetiginization of other dermatoses, and the culture examination reveals several organisms, which are often difficult to determine the main causative bacteria [5, 12]

Primary bacterial skin infection is caused by one species of pathogenic bacteria in normal skin. Primary bacterial skin infection is classified into superficial pyoderma and invasive infection. Superficial pyoderma consist of infection in the skin and infection in the hair follicle. Impetigo, bullous impetigo, and ecthyma are pyoderma occurred in the skin, while folliculitis, furuncle, and carbuncle occurred in the hair follicle. Cellulitis, erysipelas, abscess were included in invasive infection [5].

Folliculitis, furuncle, and carbuncle are pyoderma that occurred in the hair follicle. Folliculitis is often found in tropical climates, with the axilla, pubis and thighs as the predilection area. Furuncle is an acute inflammation in the hair follicle and its surroundings, forming a painful nodule, which often originates from folliculitis, which develops into a hard, enlarged and very painful red perifollicular nodule, then after a few days becomes fluctuating and rupture releasing pus and necrotic tissue. Carbuncle is an extensive and deep infiltrating lesion, which develops into suppurative lesion. Furuncles and carbuncles mainly occur in hairy areas, where friction, occlusion and sweating often occur, such as in the neck, axilla and gluteal areas [5, 13, 14].

Cellulitis and erysipelas often cause local pain with clinical manifestations of erythematous rash and systemic symptoms (fever, chills, malaise). Local pain is usually severe. The absence of erythematous rash indicates that the infectious process occurs in the deep layers of the skin. Cellulitis occurs in the dermis and subcutaneous tissue layers, while erysipelas can involve the dermal lymphatic vessels. Erysipelas usually begins on the face or lower extremities, accompanied by pain, superficial erythematous macules and plaque-like edema with firm borders (peau d'orange appearance). Erythematous macules in erysipelas are bright red in color with infiltrates at the edges, and may be accompanied by vesicles or bullae. Cellulitis manifests as erythematous macules with ill-defined borders, accompanied by pain. Cellulitis lesions can manifest as induration or fluctuating lesion, and crepitation is often present on palpation. In some cases of cellulitis, bullae or necrosis can also occur which will leave epidermal detachment and superficial erosion. Cellulitis in the elderly has higher risk to cause complications, such as thrombophlebitis. [5, 15].

The diagnosis of pyoderma is usually clinical. Clinical characteristic, such as erythema, exudate, odor, pain, will show the evolution of the infection. Gram preparation, cultures and antibiotic sensitivity test of the wound help obtain information on the type of bacteria. Global incidence of bacterial skin infection increased marginally from 1990 to 2019 (7.38%). The most common causative bacteria are *Staphylococcus aureus* and *Group A-Streptococcus*, including *Streptococcus pyogenes*. Cultures and antibiotic sensitivity test are important to determine the management of pyoderma, if the empiric antibiotic do not give adequate response [5, 16].

3. Characteristic of Bacterial Skin Infection in Elderly

Skin and soft tissue infections (SSTI) are common in elderly. Mortality and morbidity of SSTI increases twofold to threefold compared with young adult. The incidence of bacterial skin infections is increasing with the increase of elderly population, who are often in critical or immunocompromised condition. In addition, the use of immunosuppression drugs, malignancy therapy, organ transplants, medical interventions, or surgical wound infections are also predisposing factors for bacterial skin infections, especially in the elderly. Pathogenesis of bacterial skin infections is based on the skin barrier function, host defense, and the pathogenic nature of the organism. Normal skin is relatively resistant to bacterial invasion. However, on elderly skin, which has decreased skin barrier function and often has dry skin, it will be easier for bacteria to pass through the skin barrier and cause skin infection [12].

It was reported in 2012, that dermatitis and skin infections were the 2 most common diseases in the field of dermatology in elderly (35.8% and 27.2%). Additionally, there was a 25% increase in the prevalence of cutaneous colonization of *Proteus mirabilis* and *Pseudomonas aeruginosa* in the elderly population [17].

Skin bacterial infection in the elderly has several peculiarities. It may appear atypical, mild or even unspecific. The clinical manifestation in elderly quite common begins with slight fever or even without fever, but evolving rapidly to sepsis. Elderly often present with mental confusion, making anamnesis to find out subjective complaints becomes difficult. Skin bacterial infection can complicate pre-existing chronic cutaneous pathologic condition in elderly, such as xerosis, venous insufficiency, or pruritus senilis [7, 11, 17].

4. Comorbidities Factors of Bacterial Skin Infection in Elderly

The prognosis of bacterial skin infection in the elderly is determined by the presence of multiple comorbid factors that can affect the progression and course of the disease. History of heart failure, diabetes mellitus, peripheral edema is the most common comorbid factor in cellulitis and erysipelas, in patients over 65 years of age. Reports from the United States in 2005-2010 showed that patients with abscesses, cellulitis, and other bacterial skin infections is more frequent having history of diabetes mellitus. Patients with diabetes mellitus have a fourfold risk of developing bacterial skin infections compared to patients without diabetes mellitus [7, 18].

Malnutrition also plays an important role in the occurrence of bacterial skin infection in the elderly. Malnutrition occurs in 30-50% of inpatients, and 12.5-78.9% of elderly in long-term facilities [19, 20].

5. Methicillin Resistant *Staphylococcus aureus* (MRSA) in Elderly

MRSA is becoming an important health problem, especially in the hospital setting. In the last few decades, there have been MRSA outbreaks in the community, named community-acquired-MRSA (CA-MRSA). Skin and soft tissue infection (SSTI) is reported as the most clinical manifestations of CA-MRSA in the worldwide. Risk factors for MRSA include history of hospitalization or nursing home admission within 12 months, recent antibiotic exposure within 1-12 months, chronic illness, injection drug use, and close contact with people with risk factors of having MRSA [20].

Elderly itself is not considered as risk factor of MRSA infection. However, advancing age is linked to MRSA infection, indirectly. Epidemiology of MRSA infection in elderly in Polland, showed that 14.1% of MRSA infection occurred in the age of 60-74 years-old, 19.5% in 75-85 years-old; and 26.7% in more than 85 years-old [20].

Sixty percent of healthy individuals are reported to be carriers of MRSA, which is collected through skin or mucosal swabs. Common sites of colonization are the inguinal region, axillae, perianal skin, nasal, pharynx, or rectal mucous membrane. It was reported that MRSA colonization was found in 37% of patients having clinical manifestations of purulent CA-MRSA infection [5, 20].

6. Skin Structure in Aging

Epidermal layer is thinner in elderly, due to keratinocyte atrophy and reduced epidermal mitotic activity. Epidermal thinning leads to an increased transepidermal water loss (TEWL), which causes dry skin in elderly (**Figure 1**) [8-10, 17].

As a result of aging process, the components of collagen and elastin as the extracellular matrix in dermal layer are change, marked by decreased in the amount of collagen and elastin. This will affect the strength and elasticity of the skin. Increased expression of matrix metalloproteinase (MMP) in elderly causes collagen and elastin fragmentation, which leads to wrinkle as a result of decreased skin elasticity [8-10].

Reduced in size of dermal fibroblasts also contribute to the thinning of dermal layer. Dermal fibroblasts in elderly produce less pro-collagen, and there is an increase in MMP-1 expression which causes collagen fragmentation. As we age, there is also decreased sweat and sebum production. The adipose tissue is thinning, due to decreased white adipose tissue, so that antimicrobial protection against infection also significantly reduced [8-10]. Reduced blood flow also play role in dry skin in the elderly, apart from epidermal and dermal thinning. Alteration due to skin aging usually delay wound healing, including in bacterial skin infection (**Figure 1**) [17].

Skin changes that occur in the elderly, are also influenced by extrinsic factors, such as ultraviolet exposure and lifestyle. Inadequate use of sunscreen, smoking habit, and environmental pollution cause the skin more susceptible to mechanical injury, disrupt the balance of the skin microbiome, and alter the skin barrier immunity [8].

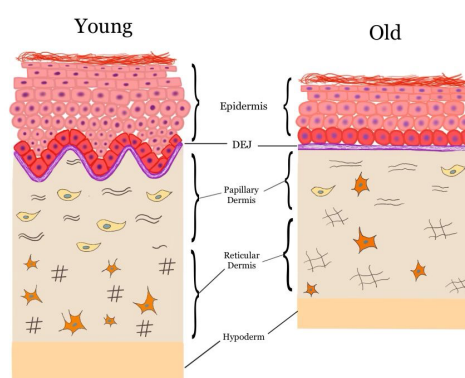


Figure 1. Histopathology differences of Youth and Aging [9]
(DEJ= dermal-epidermal junction)

7. Immunosenescence in Elderly

Elderly is one of the populations that are prone to bacterial skin infections, due to a combination of factors, including age-related thinning of the skin and immunosenescence. Immunosenescence is an "ageing phenotype", which is the result of imbalance between inflammatory and anti-inflammatory mechanisms, as a result of "inflammaging". Inflammaging occurs as a result of chronic antigen stimulation in life and also as a result of oxidative stress which involves the production of free radicals and toxic oxygen products. Both of these factors can cause lymphocyte apoptosis. The component that is primarily involved in the process of longevity and senescence-related disease is the upregulation of proinflammatory cytokines, including interleukin-6 (IL-6) [21–23].

Good health status in the elderly is the result of low proinflammatory mechanisms and efficient network that capable to neutralize anti-inflammatory antigenic attacks received in the course of life. Inflammaging is not only important for immunosenescence mechanisms, but also important for longevity issues. It has been reported that overproduction of several lymphokines, known as geriatric cytokines (including IL-6), causes an inflammatory status, which contributes to fragility in the elderly. Immunity plays an important role in the regulation of aging mechanism and the occurrence of diseases due to aging, such as infectious diseases, autoimmune diseases, cancer, metabolic diseases and degenerative diseases [21, 23].

Immune cellular aging and tissue cellular aging play a role in skin immunosenescence in the elderly. Skin immunosenescence affect the epithelial skin and mucous membrane as the first barrier, innate immunity as the second barrier, and acquired immunity as the third barrier. Skin immunosenescence affects the skin structure, that causes keratinocyte atrophy, fibroblast downsizing, decreased collagen count due to increased matrix metalloproteinase activity and decreased collagen production. Skin immunosenescence also affects innate immunity as a second barrier, in the form of decreased dendritic cells maturation, decreased Langerhans cell and migratory properties, decreased antimicrobial peptides expression, decreased dermal dendritic cells migratory and phagocytic capacity. While in acquired immunity, skin immunosenescence causes decreased T naive lymphocyte hematopoiesis, decreased Th1 cell immunity, increased FOXP3+ Treg cells and Th1/Th2 shifting. Skin immunosenescence in elderly plays an important role in the regulation of aging mechanism and the occurrence of diseases due to aging, including bacterial skin infection (**Figure. 2**) [9, 10, 22].

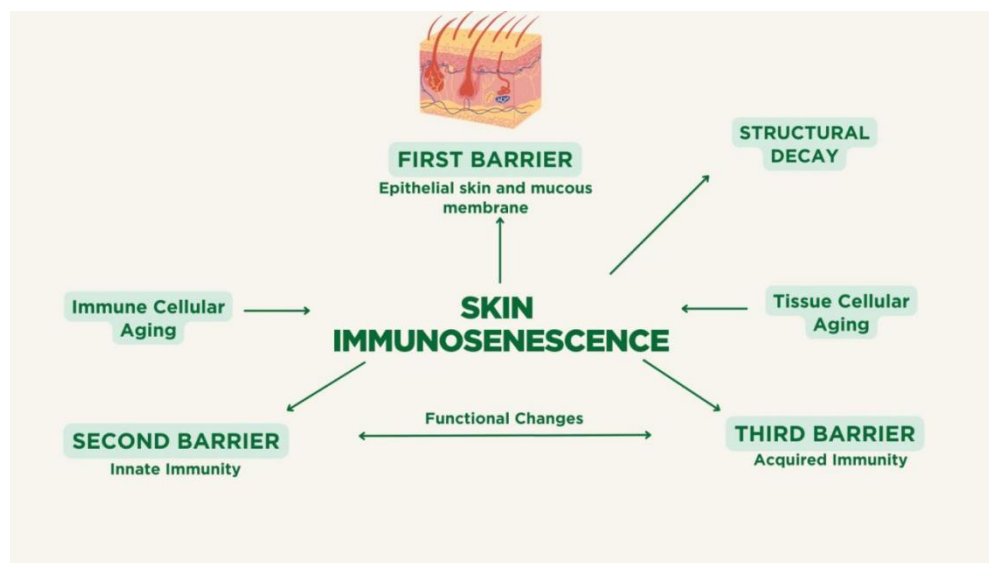


Figure 2. The role of skin immunosenescence.

8. Conclusion

Skin bacterial infection in the elderly has several peculiarities. There is a significant growth in the elderly population, and an increase in deaths due to antimicrobial resistance with elderly as the population that has high risk of suffering from skin bacterial infection. It leads to poor outcome and response to therapy of skin bacterial infection. Various predisposing factors and the existence of polypharmacy which is often found in the elderly, also makes the management very challenging.

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