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# Inflammaging: A Concept Analysis

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**ABSTRACT**

In this report we assess the concept of inflammaging. As the population ages, the prevalence of chronic illness will dramatically increase. Inflammaging describes the chronic inflammatory state associated with aging. Antecedents include immunosenescence, genetics, gonadasenescence, adrenosenescence, somatosenescence, calcium senescence, and lifestyle factors. The defining characteristics are an age-related chronic, systemic, asymptomatic, low-grade inflammation. Frailty, morbidity, and mortality are the consequences. Clinical indicators are serum levels of C-reactive protein, interleukin-6, tumor necrosis factor-α, and interleukin-1β. This concept attempts to unify disparate diseases that affect the elderly by suggesting they have similar etiology. Inflammaging has significant research and clinical implications for nurse practitioners.

**Keywords:** aging, chronic disease, chronic inflammation, concept analysis, inflammaging



## INTRODUCTION

Each year, 7 of every 10 deaths in the United States are due to chronic illnesses. Heart disease, cancer, and stroke have accounted for 50% of these deaths.[1] In 2010, there were 40 million Americans over the age of 65, accounting for about 13% of the population, and 60% of them had 2 or more chronic diseases.[2] In 2011, the first of the "baby boomers" began turning 65. By 2030, it is estimated that there will be 72 million people over the age of 65, accounting for nearly 20% of the population.[3] The prevalence of chronic illnesses will increase dramatically in the upcoming years.

A link between chronic disease and chronic inflammation is developing in the literature. Signs and symptoms of acute inflammation are familiar to many and include pain, redness, swelling, warmth, and loss of function. However, there is less familiarity with chronic inflammation. The concept of inflammaging is evolving to describe the chronic inflammatory state associated with aging. Given the significant burden of chronic disease in the United States among older people, and the predicted growth of this population, a closer look at one of the potential causes of chronic disease is warranted. The purpose of this report is to define the concept of inflammaging as it relates to chronic disease. Agreement on the definition of inflammaging could serve to focus research on the same concept and accelerate knowledge advancement.

## DATA SOURCES

A literature search was conducted using the key words inflammaging, inflamm-aging, and inflamm-ageing in PubMed, CINAHL, Embase, and Web of Science. Duplicate articles, articles in a foreign language, animal studies, and cosmetic treatment studies were excluded. In addition to the search, articles referenced in seminal works were included.

Five hundred sixty-five articles published between 1996 and 2014 were retrieved in the literature search. After the aforementioned criteria were applied, a total of 205 articles remained, of which 39 were original research and 144 were review articles. The articles were mainly in the disciplines of gerontology, immunology, virology, genetics, and nutrition. There were an additional 22 less relevant articles and abstracts from conference proceedings that were not included in this analysis. The review articles are primarily referenced in this report.

## METHOD OF ANALYSIS

In this work, Rodgers's evolutionary view of concept analysis was used to define inflammaging.[4] Inflammaging occurs within the context of aging and its relation to chronic disease. Inflammaging is a dynamic process

with numerous antecedents and consequences that are interrelated; what are initially consequences can later become antecedents through a feedback loop, contributing to amplification of the defining characteristics. Last, there is growing interest in this concept. More than 50% of the literature on this topic was published in the last 5 years. As research continues, the concept is likely to evolve. For these reasons, the evolutionary view of concept analysis is an appropriate method for examining this dynamic concept.

## RESULTS

### Seminal Work

Although literature suggesting an association between aging and chronic inflammation can be traced back to the 1960s, the term "inflammaging" was first coined in 2000 by Franceschi and colleagues. Their work focused on studying centenarians as a model of human longevity. They defined inflammaging as an age-related "global reduction in the capability to cope with a variety of stressors and a concomitant progressive increase in the pro-inflammatory status."[5(p244)] The use of this term signified the conceptualization of chronic inflammation as the underlying etiology to a multitude of chronic diseases occurring in the elderly.

### Antecedents

Antecedents are contributors to the concept or events that occur before or leading up to the concept.[4] There are a number of antecedents to inflammaging, including immunosenescence. Immunosenescence is the change or remodeling of the immune system that takes place with aging.[6] It is thought to be due to continued antigenic stress that is not cleared, which essentially amounts to chronic infection. Chronic infections, such as cytomegalovirus and *Helicobacter pyloris*, are examples of sources of antigen, although there is no general consensus on which agents lead to antigenic stress. Chemical, physical, psychological, or environmental stressors may also be considered antigenic, because the immune system responds similarly to stress and antigen.[5]

As one ages, increasing antigen load leads to changes within the different compartments of the immune system. The T-cell compartment is the most frequently discussed subset of the immune system in relation to inflammaging. It is thought that, due to the antigenic load, there is a shift in the T-cell repertoire to one that contains large clones targeted at those chronic antigens. This leads to the increased proportion of memory T cells. Effector-memory T cells lose CD28, and such cells produce pro-inflammatory cytokines.[6] Aging T cells have a different phenotype and some of these changes add to an inflammatory state.

The increased proportion of memory T cells leads to a decrease in proportion of naive T cells, another hallmark of immunosenescence.[6] Other features of a senescent adaptive immune response include a decreased ability of CD4 cells to help B cells due to a decrease in CD40L expression and decreased expansion and differentiation.[7] These changes are significant contributors to an inflamed state and to an aging immune system ill-equipped to mount an appropriate response to new infections, such as to new strains of influenza.[6]

In addition, in immunosenescence, there are changes in the B-cell compartment. As in the T-cell compartment, the proportion of memory B cells increase with a corresponding decrease in the naive B-cell population. Antibodies made in older age are of lower affinity, making them less efficient.[7]

Immunosenescence also occurs in the innate immune system. Neutrophils make up a large part of the innate immune system and they have been shown to have increased adherence and decreased chemotaxis, phagocytosis efficiency, and antioxidant capacity.[7] There is also evidence that phagocytic cells, such as dendritic cells, have impaired function, including in their ability to stimulate T cells.[7]

Genetics is another major contributor to inflammaging. Interleukin-6 (IL-6) is an important proinflammatory cytokine for acute response of the innate immune system. The polymorphism, -174GG, has been associated with higher plasma IL-6 levels in the elderly.[8] Conversely, IL-10 is an anti-inflammatory cytokine and suppresses T cells of the adaptive immune system. The IL-10 polymorphism, -1082GG, has been associated with higher IL-10 production in some elderly patients, whereas the AA polymorphism has been associated with lower IL-10 production.[8] There are also polymorphisms associated with IL-1, tumor necrosis factor-α (TNF-α), transforming