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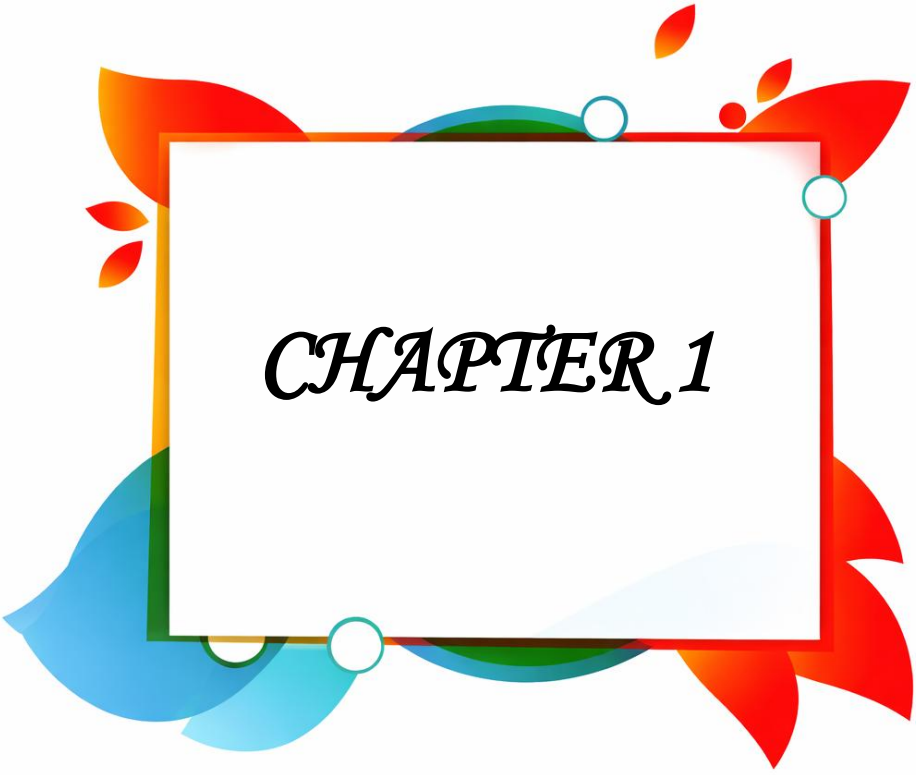
CHAPTER 1

Molecular Foundations of Healthy and Pathological Aging

Ayşe Gülay Şahan[1] & Bediha Köse[2]

Introduction

The World Health Organization (WHO) defines aging as a natural and heterogeneous process resulting from the accumulation of changes in an individual's physical and mental capacity over time. Aging is considered a multidimensional life experience encompassing not only biological changes but also psychological, social, and environmental interactions (WHO, 2021).

Chronological age is the definition of age that refers to the calendar period that has passed since an individual's birth. In contrast, biological age refers to the level of aging assessed according to an individual's cellular, molecular, and physiological functions. Unlike chronological age, biological age reflects the organism's actual physiological state and aging rate (Demirkıran et al., 2014).

In evaluating the aging process, it is necessary to consider the living organism from a holistic perspective. In this context, standardized physiological measurements, functional tests, and increasingly advanced "omics" technologies play an important role in understanding the biological mechanisms of aging. Genomic, epigenomic, transcriptomic, proteomic, and metabolomic analyses contribute to the evaluation of aging processes at the cellular level; It also provides important data for the development of anti-aging strategies. These criteria also allow for the evaluation of the effectiveness of interventions that accelerate or slow down aging (López-Otín et al., 2023).

The common point of the theories and models developed to explain aging is that aging has molecular, cellular and systemic determinants. In this context, the basic biological determinants of aging have been defined within the scope of the "Hallmarks of Aging" approach and explained as the basic mechanisms of the aging process (López-Otín et al., 2023).

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Figure 1. Biological determinants and basic mechanisms of aging.

Although the biological determinants of aging may appear at first glance to be independent processes, they are in reality complex mechanisms that interact with each other. These mechanisms can directly affect the rate of the aging process, the functional capacity of the individual, and the quality of life. Therefore, aging should be considered not only as a process of destruction, but also as a biological process resulting from the accumulation of cellular, molecular, and physiological changes. Understanding the changes occurring at the cellular and molecular level is important for planning protective and developmental approaches that support healthy aging (Miller et al., 2021).

1. Molecular and Cellular Hallmarks of Aging

In modern biology, there are various biological mechanisms that explain the basis of aging. Genomic instability, telomere wear, epigenetic changes, mitochondrial dysfunction, and chronic inflammation are among the fundamental biological determinants of aging. Understanding these mechanisms is important for evaluating the aging process from a gerontological perspective and supporting healthy aging.

1.1. Genomic Instability

Genome integrity; DNA can be damaged by various factors such as oxidative stress, environmental toxins, ultraviolet radiation, replication errors, and metabolic processes. The resulting translocations, mutations, telomere shortening, and deletions cause damage to the genetic structure and accelerate the pathological aging process. To protect itself from this damage, the organism has developed DNA damage repair mechanisms. However, with aging, the decrease in DNA repair capacity leads to an increase in the accumulation of damaged DNA in cells.

Figure 2 Gene expression changes

(A) Endogenous and exogenous factors cause various DNA damages that contribute to normal and pathological aging. (B) Changes in DNA or histone acetylation and methylation, and changes in chromatin-associated proteins and non-coding RNAs lead to epigenetic changes that contribute to the aging process. The red areas in the figure show age-related changes, while the blue areas show strategies to protect against these changes (Lopez et al., 2023). DNA damage accelerates the aging process, especially when it affects stem cells, and prepares the ground for the emergence of age-related pathologies. It has been reported that the DNA damage load in tissues, which can be determined by histological studies, can provide information about the degree of aging (Miller et al., 2022).

The absence of histone proteins in mitochondrial DNA makes it more susceptible to damage. Increased mitochondrial mutations are reported to be observed more frequently, especially in primate oocytes, somatic tissues, and lymphoblasts of individuals with neurodegenerative diseases. It has been stated that reducing mitochondrial DNA mutations can have positive effects on healthy lifespan and life expectancy (Sánchez-Contreras and Kennedy, 2022).

Furthermore, studies conducted on mice have shown that overexpression of the metabolism-related Sirtuin-6 (SIRT6) gene reduces genomic instability, prolongs lifespan, and increases survival (Tian et al., 2019). In line with these findings, it is thought that DNA damage and deficiencies in DNA repair mechanisms may constitute the biological basis of the pathological aging process.

From a gerontological perspective, interventions aimed at preventing genomic instability include regular physical activity, quitting smoking, a diet rich in antioxidants, protection from environmental toxins, and quality sleep. In particular, calorie restriction and regular exercise are reported to support DNA repair mechanisms and reduce oxidative stress (Sen et al., 2016; López-Otín et al., 2023).

1.2. Telomere Shortening

Telomers are repeating nucleotide sequences located at the ends of chromosomes that protect chromosomes from DNA damage and contribute to maintaining genome stability. Telomere shortening during cellular division is considered a natural process. However, factors such as oxidative stress, chronic inflammation, mitochondrial dysfunction, obesity, smoking, and a sedentary lifestyle can accelerate telomere loss. Critical telomere shortening causes cells to lose their proliferation capacity and shift towards a senescent phenotype. In this process, there is an increase in the levels of inflammatory markers such as IL-6, IL-1β, TNF-α, and matrix metalloproteinases (MMPs), and the biological aging process is accelerated (Rossiello et al., 2022). Studies have shown that short telomere length is associated with hypertension, heart failure, endothelial dysfunction, and other cardiovascular diseases (Oeseburg et al., 2010). Furthermore, it has been reported that oxidative damage, which accompanies telomere dysfunction, increases in Alzheimer's and Parkinson's diseases. In metabolic diseases such as diabetes, it is stated that telomere shortening accelerates and, consequently, the cellular aging process is triggered (Chakravarti et al., 2021; Opresko and Shay, 2017).

The enzyme that plays a fundamental role in maintaining telomere integrity is telomerase. It has been reported that an increase in telomerase activity may be associated with slowing down the cellular aging process and extending lifespan. Studies indicate that maintaining telomere length can have positive effects on healthy aging (Berardi et al., 2026). Currently, research on maintaining telomere integrity is increasing. In this context, various approaches such as NAD^+

supplements to support telomerase activation, antioxidant applications, lifestyle changes, and the Mediterranean diet are being considered (Chakravarti et al., 2021).

From a gerontological perspective, interventions aimed at slowing telomere shortening include a Mediterranean diet, regular physical activity, stress management, smoking cessation, and quality sleep. These factors are reported to contribute to the preservation of telomere length. In particular, reducing chronic stress and consuming diets rich in antioxidants are noted to slow telomere loss (Chakravarti et al., 2021; Rossiello et al., 2022).

1.3. Epigenetic Changes

Aging is associated not only with genetic factors but also with epigenetic mechanisms, which refer to the regulation of gene expression without any changes occurring in the DNA sequence. Epigenetic changes pave the way for the disruption of cellular regulation and the development of age-related diseases during the aging process (López-Otín et al., 2013; Sen et al., 2016).

Methylation changes occurring on DNA can lead to dysregulation of gene expression, resulting in the silencing of tumor suppressor genes and increased inflammation processes (Fraga and Esteller, 2007; Horvath, 2013). In addition, dysregulations in histone modifications such as acetylation, methylation, phosphorylation, and ubiquitination are reported to be associated with decreased DNA repair capacity, accelerated neurodegenerative processes, and impaired cellular stress responses (Booth and Brunet, 2016; Pal and Tyler, 2016). Dietary habits, environmental toxins, stress, and lifestyle factors can alter epigenetic patterns. This is associated with decreased tissue function and increased biological age (Li and Tollefsbol, 2010; Vaiserman and Lushchak, 2017). Epigenetic changes are reported to be associated with cardiovascular diseases, diabetes, Alzheimer's disease, and mortality (López-Otín et al., 2013). Therefore, understanding the mechanisms of epigenetic aging is important for elucidating the biological basis of aging and developing interventions to slow down aging. Furthermore, the reversible nature of epigenetic aging constitutes an important area of research for anti-aging studies (Horvath and Raj, 2018).

From a gerontological perspective, interventions aimed at preventing epigenetic changes include healthy lifestyle behaviors such as regular physical activity, balanced nutrition, quality sleep, stress management, and avoiding smoking. It has been reported that these lifestyle practices can contribute to the preservation of epigenetic regulation, slow the rate of biological aging, and support healthy aging (Sen et al., 2016; Vaiserman and Lushchak, 2017).

Figure 3. Factors influencing epigenetic aging.

1.4. Loss of Proteostasis

Proteostasis refers to the cellular control system that ensures the correct synthesis, folding, transport, and, when necessary, degradation of proteins. The disruption of this system, which plays a crucial role in maintaining cellular homeostasis, is defined as "loss of proteostasis." Loss of proteostasis is associated with protein folding errors, the accumulation of misfolded proteins within the cell, and deficiencies in autophagic mechanisms. As a result of this process, cellular stress increases and tissue function deteriorates (Hipp et al., 2019).

With aging, the effectiveness of proteostatic mechanisms decreases, and the accumulation of misfolded proteins within the cell accelerates. This situation has significant effects, particularly on the nervous system and musculoskeletal system. Neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's diseases are reported to be associated with disruptions in protein metabolism. Furthermore, it is stated that conditions such as decreased muscle function, increased fragility, and loss of functional capacity in elderly individuals may be associated with loss of proteostasis (Hipp et al., 2019; Vergani-Junior et al., 2026).

Damaged proteins accumulating within the cell can cause impaired mitochondrial function, increased oxidative stress levels, and accelerated inflammatory processes. As a result, cellular resilience decreases, and the risk of developing age-related diseases increases. In particular, it is reported that misfolded protein aggregates play an important role in the pathogenesis of neurodegenerative diseases (Hipp et al., 2019).

From a gerontological perspective, interventions aimed at maintaining proteostasis include regular physical activity, adequate protein intake, a diet rich in antioxidants, quality sleep, and lifestyle behaviors that support autophagy. It is reported that these interventions can contribute to the maintenance of protein folding mechanisms, the reduction of cellular waste accumulation, and the preservation of proteostatic balance. In particular, regular physical activity is said to support proteostasis and slow the progression of neurodegenerative processes (Hipp et al., 2019; Vergani-Junior et al., 2026).

1.5. Disruption of Nutrient Sensing Pathways

Nutrient sensing pathways are biological mechanisms that play a crucial role in regulating cellular energy balance and metabolic processes. In particular, mTOR (mechanistic target of rapamycin) and insulin/IGF-1 signaling pathways are among the key determinants in the regulation of the aging process.

The mTOR pathway is involved in the regulation of cell growth, protein synthesis, and metabolic activity. While the mTORC1 complex regulates cellular growth and protein synthesis, the mTORC2 complex affects cellular metabolism and cell survival. Over-activation of these pathways can lead to suppression of

autophagic processes, increased accumulation of damaged proteins, and the development of mitochondrial dysfunction. Therefore, chronically high mTOR activity is reported to be associated with aging (Pournajaf et al., 2026).

Insulin/IGF-1 signaling pathways, on the other hand, are involved in regulating glucose metabolism and cellular energy utilization. Disruptions in these pathways can lead to the development of insulin resistance, impaired cellular stress responses, and weakening of the antioxidant defense system. As a result, DNA damage repair mechanisms become insufficient, and the cellular aging process accelerates. These imbalances in nutrient sensing pathways are reported to increase chronic inflammation, decrease autophagy, and be associated with age-related clinical conditions such as type 2 diabetes, cardiovascular diseases, obesity, and neurodegenerative diseases (Pournajaf et al., 2026).

It is stated that overfeeding can accelerate the aging process by increasing mTOR activation; conversely, calorie restriction can extend lifespan by suppressing mTOR activity. Furthermore, maintaining metabolic flexibility is reported to play an important role in slowing down functional aging. In this context, approaches such as calorie restriction, intermittent fasting, regular physical activity, mTOR inhibitors, and metformin are considered among anti-aging strategies (Chen et al., 2026; Li et al., 2026).

From a gerontological perspective, interventions aimed at preventing disruptions in nutrient sensing pathways include calorie restriction, intermittent fasting, regular physical activity, and nutritional models aimed at maintaining metabolic balance. It has been reported that these interventions can contribute to the regulation of mTOR activity, the maintenance of cellular energy balance, and the control of age-related metabolic processes. In particular, calorie restriction and intermittent fasting practices are said to slow down cellular aging and support healthy aging (Pournajaf et al., 2026; Chen et al., 2026).

1.6. Mitochondrial Dysfunction

Mitochondria are organelles found in eukaryotic cells that play a crucial role in ATP production through cellular respiration, regulation of reactive oxygen species (ROS) formation, calcium metabolism, and apoptosis mechanisms. With aging, mitochondrial function deteriorates, leading to various functional losses at the cellular level.

Mitochondrial DNA mutations that develop with aging cause a decrease in ATP production and an increase in ROS production. Increased oxidative stress leads to damage to lipids, proteins, and DNA, causing disruption of cellular functions (Picard and McEwen, 2018). This accelerates the cellular aging process and interacts with other aging mechanisms such as telomere shortening and epigenetic changes (Miwa et al., 2022).

Mitochondrial dysfunction is reported to play a significant role in the development of neurodegenerative diseases such as Alzheimer's and Parkinson's disease. It is also stated that it is associated with impaired myocardial function, vascular aging, and the development of sarcopenia. As a result of this process, problems such as frailty, risk of falls, increased dependency levels, loss of physical performance, and cognitive decline are more frequently observed in elderly individuals. From a gerontological perspective, interventions aimed at preventing mitochondrial dysfunction include regular aerobic exercise, antioxidant supplements, calorie restriction, and healthy eating practices. It is reported that these interventions can contribute to supporting mitochondrial energy production, reducing oxidative stress levels, and maintaining mitochondrial integrity. In particular, it is stated that regular physical activity improves mitochondrial functions and reduces oxidative stress levels (Picard and McEwen, 2018; Stanojevic et al., 2026).

1.7. Cellular Aging

Cellular aging, although initially considered a protective mechanism preventing tumor development, is a biological process characterized by the irreversible loss of proliferation ability in cells over time. This is considered one of the fundamental biological determinants of aging. Even if cells are metabolically active, they permanently lose their capacity for division.

In the cellular aging process, the cell cycle stops, disruptions develop in DNA damage response mechanisms, mitochondrial dysfunction occurs, and oxidative stress levels increase. In addition, resistance to apoptosis develops; particularly the p53/p21, p16INK4a, and retinoblastoma (Rb) pathways are activated. Factors such as oncogene activation, epigenetic changes, telomere shortening, DNA damage, and oxidative stress are reported to trigger cellular aging.

A decrease in telomere length below a critical level leads to cell cycle arrest and the development of an aged cellular phenotype. These cells develop an inflammatory secretory profile called "Senescence-Associated Secretory Phenotype (SASP)" and secrete IL-6, IL-1β, TNF-α, chemokines, and matrix metalloproteinases (Flacco et al., 2026).

SASP development plays a significant role in "inflammaging," a chronic, systemic, and low-level inflammatory state that occurs in the immune system during aging. This leads to increased chronic inflammation and disruption of intercellular communication mechanisms. As a result of cellular aging, atherosclerosis, hypertension, and other cardiovascular diseases can develop; the immune system weakens, and susceptibility to infections increases. In addition, neurodegenerative processes such as Alzheimer's and Parkinson's disease accelerate, sarcopenia develops, and consequently, frailty, increased dependency levels, loss of physical capacity, cognitive decline, and decreased quality of life may occur. From a gerontological perspective, interventions aimed at preventing

cellular aging include regular physical activity, balanced nutrition, stress management, quality sleep, and lifestyle behaviors that reduce oxidative stress. These interventions are reported to contribute to reducing cellular damage, controlling inflammatory processes, and preserving cellular functions. In particular, it is stated that healthy lifestyle habits can slow down the cellular aging process and support healthy aging (Muñoz-Espín and Serrano, 2014).

1.8. Stem Cell Depletion

Stem cells are cells that have the capacity to self-renew, differentiate into different cell types, and maintain tissue homeostasis throughout life. Playing a fundamental role in tissue regeneration and repair processes, the functional capacity of these cells decreases with aging. Mechanisms such as DNA damage, telomere shortening, epigenetic changes, oxidative stress, chronic inflammation, and autophagy disorders that occur during the aging process negatively affect the functional adequacy of stem cells.

This loss of function in stem cells leads to a decrease in tissue regeneration capacity and accelerates the development of age-related diseases. Stem cells that lose their division capacity lead to the deterioration of the tissue microenvironment; consequently, tissue repair processes slow down and biological aging accelerates. Furthermore, the decrease in stem cell function can negatively affect the production of immune system cells, leading to a weakened immune response, delayed wound healing, and increased susceptibility to infections.

As a result of the effects on the musculoskeletal system, muscle strength decreases, fragility increases, and loss of physical performance occurs. A decrease in neural stem cell activity can lead to disruption of neurogenesis processes, cognitive decline, and accelerated neurodegenerative processes (Goya et al., 2018; Papanikolaou et al., 2026).

From a gerontological perspective, interventions aimed at preventing stem cell senescence include regular physical activity, healthy eating, lifestyle practices aimed at reducing oxidative stress and controlling inflammation. It is reported that these interventions can contribute to the preservation of stem cell capacity, the maintenance of tissue integrity, and the support of cellular renewal processes. In particular, it is stated that physical activity and antioxidant-rich diets can have positive effects on stem cell functions (Le Couteur et al., 2017; Papanikolaou et al., 2026).

In addition, it is reported that regular physical activity, calorie restriction, NAD^+ supplementation, stem cell transplantation, and epigenetic reprogramming studies can contribute to the preservation of stem cell functions. In particular, exercise is said to play an important role in improving mitochondrial function by reducing oxidative stress (Le Couteur et al., 2017).

1.9. Altered Intercellular Communication

Intercellular communication refers to the exchange of signals between cells through cytokines, hormones, growth factors, neurotransmitters, and extracellular vesicles. These communication mechanisms play a crucial role in regulating processes such as cellular growth, differentiation, inflammation, immune response, and tissue repair. Maintaining intercellular communication is critical for tissue homeostasis and healthy aging.

With the aging process, disruptions occur in intercellular communication networks, accelerating the systemic aging process. In particular, increased production of inflammatory cytokines, disruption of endocrine signaling, and changes in neuroimmune communication lead to dysregulation of cellular stress responses. As a result, there is a decrease in tissue function and an increase in cellular stress accumulation.

It has been reported that levels of inflammatory markers such as IL-6, TNF-α, CRP, and IL-1β increase with aging. This situation plays a significant role in the development of age-related diseases such as cardiovascular diseases, diabetes, neurodegenerative diseases, and sarcopenia (Fulop et al., 2018). Disruption of intercellular communication mechanisms can lead to endothelial dysfunction, atherosclerosis, vascular aging, synaptic loss, cognitive decline, impaired muscle regeneration, and decreased protein synthesis. This process is associated with chronic inflammation, hormonal imbalances, immune system disorders, frailty, increased dependency levels, and decreased quality of life in older individuals. Therefore, preserving intercellular communication mechanisms is considered an important goal in maintaining healthy aging (Bertoni et al., 2026). From a gerontological perspective, interventions aimed at preventing changes in intercellular communication include anti-inflammatory lifestyle practices, regular physical activity, a Mediterranean diet, and stress management. These interventions are reported to contribute to reducing inflammation levels, supporting immune system functions, and preserving intercellular communication mechanisms. It has been suggested that healthy lifestyle habits, in particular, can have positive effects on reducing chronic inflammation and supporting cellular communication processes (Ayoub et al., 2026; Fulop et al., 2018).

1.10. Chronic Inflammation

Chronic inflammation is one of the fundamental biological markers that arise as a result of the accumulation of cellular damage, the development of dysregulation in immune system functions, and the disruption of tissue homeostasis during the aging process. Under normal conditions, inflammation is a protective response that develops to remove damaged cells and ensure tissue repair. However, the prolonged continuation of the inflammatory process can lead

to cellular damage and impairment of organ functions (Franceschi and Campisi, 2014).

The chronic, systemic, and low-level inflammatory state that develops with aging is defined as "inflammaging". This process is characterized by an increase in the levels of inflammatory markers such as IL-6, TNF-α, C-reactive protein (CRP), and IL-1β in elderly individuals (Franceschi and Campisi, 2014; Cheng et al., 2026). Mitochondrial dysfunction, oxidative stress, senescent cell accumulation, autophagy disorder, and immune system aging are reported to play a significant role in the development of chronic inflammation (Fulop et al., 2018; Salvioli et al., 2013).

The continuous release of inflammatory cytokines as a result of the "Senescence-Associated Secretory Phenotype (SASP)" profile developed by senescent cells contributes to the maintenance of chronic inflammation (Flacco et al., 2026; Fulop et al., 2018). As a result of this process, cardiovascular diseases such as endothelial dysfunction, hypertension, and atherosclerosis may develop; and neurodegenerative processes such as Alzheimer's and Parkinson's disease may be accelerated (Franceschi and Campisi, 2014; Bertoni et al., 2026). Furthermore, increased protein breakdown in muscle tissue leads to the development of sarcopenia, while at the metabolic level, insulin resistance, obesity, and type 2 diabetes may develop (Clegg et al., 2013; Cheng et al., 2026). Due to the effects of chronic inflammation on the immune system, susceptibility to infections increases, vaccine response weakens, and the risk of mortality and morbidity increases (Fulop et al., 2018; Salvioli et al., 2013).

From a gerontological perspective, interventions aimed at preventing chronic inflammation include regular physical activity, a Mediterranean diet, quality sleep, stress management, and a diet rich in antioxidants. It is reported that these interventions can contribute to reducing inflammatory markers, supporting immune system functions, and controlling age-related chronic inflammation (Franceschi and Campisi, 2014; Aitella et al., 2026). It is stated that healthy lifestyle habits, in particular, can support healthy aging by reducing inflammation levels (Fulop et al., 2018; Aitella et al., 2026).

Strategies for reducing chronic inflammation include regular physical activity, calorie restriction, a Mediterranean diet, quality sleep, stress management, antioxidant supplements, and anti-inflammatory treatment approaches. It is reported that these practices can contribute to controlling inflammation and reducing the negative effects associated with aging (Franceschi and Campisi, 2014; Aitella et al., 2026).

1.11. Dysbiosis

Microbiota refers to the complex ecosystem of bacteria, viruses, fungi, and other microorganisms found in the human body. It is reported that approximately

10^{14} microorganisms are present in the human body, and these microorganisms play important roles in immune system, metabolism, inflammation, and neuroendocrine regulatory processes (Claesson et al., 2012; Kaçar, 2021). Disruptions in the structure and diversity of the gut microbiota that occur with aging are defined as "dysbiosis."

A healthy gut microbiota plays an important role in regulating the immune system, maintaining intestinal barrier integrity, controlling inflammation, and maintaining metabolic balance (Claesson et al., 2012). Furthermore, the gut microbiota ferments dietary carbohydrates, enabling the production of short-chain fatty acids such as acetate, propionate, and butyrate. These metabolites are reported to provide an energy source for colon cells, regulate the immune system, and reduce inflammation (Hannan et al., 2026). In addition, the gut microbiota contributes to the synthesis of vitamins B and K, regulates the conversion of bile acids, and affects lipid metabolism (Kaçar, 2021).

Aging, unhealthy eating habits, long-term antibiotic use, and physical inactivity can disrupt the balance of the gut microbiota. As a result of impaired intestinal barrier integrity, endotoxin passage increases and systemic inflammation develops (Kaçar, 2021; Hannan et al., 2026).

Dysbiosis leads to continuous activation of the immune system and an increase in oxidative stress levels. This process can accelerate biological aging by increasing the production of inflammatory cytokines (Claesson et al., 2012; Hannan et al., 2026). Furthermore, dysbiosis is reported to be associated with neurological diseases, obesity, insulin resistance, and metabolic diseases such as type 2 diabetes (Hannan et al., 2026). In addition, it is stated that decreased muscle strength, impaired serotonin metabolism, changes in neurotransmitter production, and consequently problems such as depression, anxiety, and cognitive decline may develop (Claesson et al., 2012; Hannan et al., 2026).

From a gerontological perspective, interventions aimed at preventing dysbiosis include a diet rich in prebiotics and probiotics, increased fiber consumption, regular physical activity, and a Mediterranean-type diet. It is reported that these interventions can contribute to maintaining the diversity of the gut microbiota, supporting the integrity of the intestinal barrier, and reducing inflammatory processes (Claesson et al., 2012; Hannan et al., 2026). It has been suggested that healthy dietary habits, in particular, can have positive effects on regulating the gut microbiota, reducing chronic inflammation, and supporting healthy aging (Claesson et al., 2012; Hannan et al., 2026).

1.12. Impaired Macroautophagy

Macroeutophagy is one of the fundamental cellular mechanisms that enables the breakdown and recycling of damaged organelles, misfolded proteins, and metabolic waste products within the cell via the lysosomal system. This process,

which plays an important role in maintaining cellular homeostasis, loses its effectiveness with age and becomes one of the key biological determinants of aging (López-Otín et al., 2013).

As a result of the disruption of the macroautophagy mechanism, defined as an intracellular cleaning system, toxic protein accumulation increases, mitochondrial functions decrease, and consequently, oxidative stress and inflammatory processes accelerate (Mizushima and Komatsu, 2011). This situation is particularly associated with age-related diseases such as neurodegenerative diseases, type 2 diabetes, cardiovascular diseases, and cancer (Levine and Kroemer, 2019).

The accumulation of abnormal protein aggregates within cells is particularly noteworthy in Alzheimer's and Parkinson's diseases. It has been reported that the failure of autophagic mechanisms prevents these proteins from being removed from the cellular environment, accelerating neurodegenerative processes (Mizushima and Komatsu, 2011; Levine and Kroemer, 2019). Furthermore, it is stated that impaired macroautophagy contributes to disruption of cellular energy balance, increased mitochondrial damage, and accelerated cellular aging (López-Otín et al., 2013).

From a gerontological perspective, interventions aimed at preventing impaired macroautophagy include regular physical activity, intermittent fasting, calorie restriction, quality sleep, and a diet rich in antioxidants. It is reported that these interventions can contribute to reducing cellular waste accumulation, clearing damaged proteins and organelles, and maintaining autophagic mechanisms (Levine and Kroemer, 2019; Mizushima and Komatsu, 2011).

In particular, it is stated that regular physical activity and calorie restriction can activate autophagic processes, contributing to the preservation of cellular functions and supporting healthy aging. It has also been reported that exercise routines that activate AMP-activated protein kinase (AMPK) pathways, as well as the consumption of green tea, turmeric, and various polyphenol-containing foods, can have positive effects on autophagic processes (Levine and Kroemer, 2019).

2. The Impact of Biological Aging on Quality of Life

Cellular and molecular changes occurring during the biological aging process affect not only organ systems but also the individual's physical, cognitive, psychological, and social functioning. Mitochondrial dysfunction, chronic inflammation, sarcopenia, neurodegenerative processes, and changes in the immune system are reported to be associated with fragility, fall risk, increased dependency levels, and decreased quality of life (Clegg et al., 2013; Franceschi and Campisi, 2014).

Functional losses that occur with aging can reduce an individual's capacity to perform daily living activities and negatively affect their independent living skills. In particular, decreased physical performance, loss of muscle strength, cognitive decline, and increased burden of chronic diseases significantly affect the quality of life of elderly individuals (Miwa et al., 2022; Rossiello et al., 2022).

Neurodegenerative processes, chronic inflammation, and cellular aging mechanisms can affect not only physical health but also psychological well-being and the level of social participation. Increased dependency levels in older individuals can be associated with conditions such as social isolation and decreased life satisfaction. Therefore, biological aging should be considered not only as an increase in chronological age, but also as a multidimensional process affecting an individual's functional independence, social participation, and quality of life (WHO, 2021).

Supporting healthy aging is important in terms of preserving functional capacity, maintaining independent living, and improving quality of life. In this regard, understanding the biological mechanisms of aging contributes to the planning of preventive and developmental interventions aimed at improving the quality of life of older individuals (WHO, 2021; López-Otín et al., 2023).

3. Individual Differences and the Biological Basis of the Concept of "Healthy Aging"

Even if every individual is the same chronological age, their biological aging rates can differ. Genetic structure, epigenetic mechanisms, lifestyle habits, diet, physical activity level, stress management, environmental exposures, and social conditions play an important role in the emergence of these differences (Sen et al., 2016; López-Otín et al., 2023). Therefore, aging is considered a heterogeneous process, and different biological outcomes can occur in each individual.

The factors affecting the biological aging process are not limited only to cellular mechanisms. The environmental conditions to which an individual is exposed throughout their life, access to health services, socioeconomic level, and lifestyle habits are also among the important factors determining the rate of aging. In particular, chronic stress, physical inactivity, unhealthy eating habits, and smoking can increase oxidative stress levels and accelerate cellular aging mechanisms (Franceschi and Campisi, 2014; Sen et al., 2016). The concept of "Healthy Aging," as defined by the World Health Organization, is based on an individual's ability to maintain functional capacity, live independently, and preserve quality of life in old age (WHO, 2021). Healthy aging is not only considered the absence of disease, but also the preservation of physical, cognitive, psychological, and social well-being.

There is a strong relationship between the biological determinants of aging and the concept of healthy aging. Reducing cellular damage, controlling inflammation, preserving mitochondrial function, and maintaining epigenetic balance play an important role in slowing down the rate of biological aging (Miwa et al., 2022; Rossiello et al., 2022). It is reported that healthy lifestyle behaviors such as regular physical activity, a Mediterranean diet, quality sleep, and stress management can have positive effects on biological aging processes (Claesson et al., 2012; Sen et al., 2016).

From a gerontological perspective, supporting healthy aging; Maintaining an individual's functional independence is crucial for improving their quality of life and reducing the risk of frailty, dependence, and chronic diseases that may arise in old age. Therefore, understanding the mechanisms of biological aging contributes to the planning of preventive health services for older individuals and the development of multidisciplinary gerontological approaches (WHO, 2021; López-Otín et al., 2023).

4. Recommendations for Healthy Aging

To support healthy aging, it is necessary to adopt protective and developmental approaches that target biological aging mechanisms. Today, aging is considered not only an inevitable biological process but also a life stage whose effects can be managed and maintained in a healthy way with appropriate interventions (López-Otín et al., 2023).

Regular physical activity is one of the most important lifestyle behaviors supporting healthy aging. Physical activity is reported to support mitochondrial functions, reduce oxidative stress levels, suppress inflammation, and contribute to the preservation of musculoskeletal functions (Clegg et al., 2013; Miwa et al., 2022). In particular, aerobic exercises are stated to have positive effects on cardiovascular health, cognitive functions, and muscle strength.

Nutritional habits also play an important role in the biological aging process. The Mediterranean diet is considered one of the important nutritional models supporting healthy aging due to its rich structure of antioxidants, fiber, healthy fatty acids, and plant-based foods. This dietary pattern is reported to reduce chronic inflammation, support gut microbiota, and lower the risk of cardiovascular disease (Claesson et al., 2012; Franceschi and Campisi, 2014).

Quality sleep and stress management also play an important role in controlling biological aging. It is reported that chronic stress and sleep disorders can increase cortisol levels, accelerating oxidative stress and inflammation. In contrast, it is stated that regular sleep habits and stress control practices can contribute to slowing down cellular aging mechanisms (Sen et al., 2016).

Avoiding smoking and alcohol use, undergoing regular health checkups, early diagnosis of chronic diseases, and maintaining social participation are among the

important factors in supporting healthy aging. In addition, it is reported that maintaining cognitive activities and preserving social relationships can contribute to supporting cognitive functions and improving quality of life in older individuals (WHO, 2021).

From a gerontological perspective, supporting healthy aging not only extends lifespan; It aims to protect the individual's independence, maintain their functional capacity, and improve their quality of life. In this regard, the development of multidisciplinary gerontological approaches and the widespread adoption of preventive health practices are of great importance (WHO, 2021; López-Otín et al., 2023).

Conclusion

Aging is a dynamic and multidimensional process resulting from the accumulation of biological, environmental, and behavioral factors that an individual is exposed to throughout their life. Today, it is accepted that aging is not solely dependent on the progression of chronological time; changes occurring at the cellular and molecular levels play a decisive role in the organism's functional capacity. Accordingly, biological mechanisms such as genomic instability, telomere shortening, epigenetic changes, mitochondrial dysfunction, chronic inflammation, cellular senescence, and dysbiosis are among the fundamental determinants of the aging process.

The biological determinants of aging are not independent processes but rather complex mechanisms that progress through mutual interaction. Increased cellular damage, chronic inflammatory processes, impaired energy metabolism, and decreased cellular regeneration capacity pave the way for the development of conditions such as frailty, sarcopenia, cognitive decline, neurodegenerative diseases, and functional dependence in elderly individuals. Therefore, aging should be considered not only as a biological change process but also as a comprehensive public health issue affecting an individual's quality of life, independence, and social participation. However, the biological aging process varies among individuals. Genetic makeup, lifestyle habits, nutritional behaviors, physical activity level, stress management, and environmental conditions can directly influence the rate of aging. In particular, adopting healthy lifestyle behaviors makes significant contributions to reducing cellular damage, controlling inflammation, and preserving functional capacity. This indicates that healthy aging should be supported not only by medical interventions but also by preventive health practices and lifelong healthy behaviors. Consequently, understanding the molecular and cellular mechanisms of aging is crucial for developing multidisciplinary approaches that support healthy aging. Preventive and holistic practices addressed from a gerontological perspective can contribute to maintaining the independence of older individuals, improving their quality of life, and enabling them to maintain their active roles within society. In this regard,

increasing scientific studies that address the biological, psychological, and social dimensions of the aging process together is considered a vital necessity for developing healthy aging policies.

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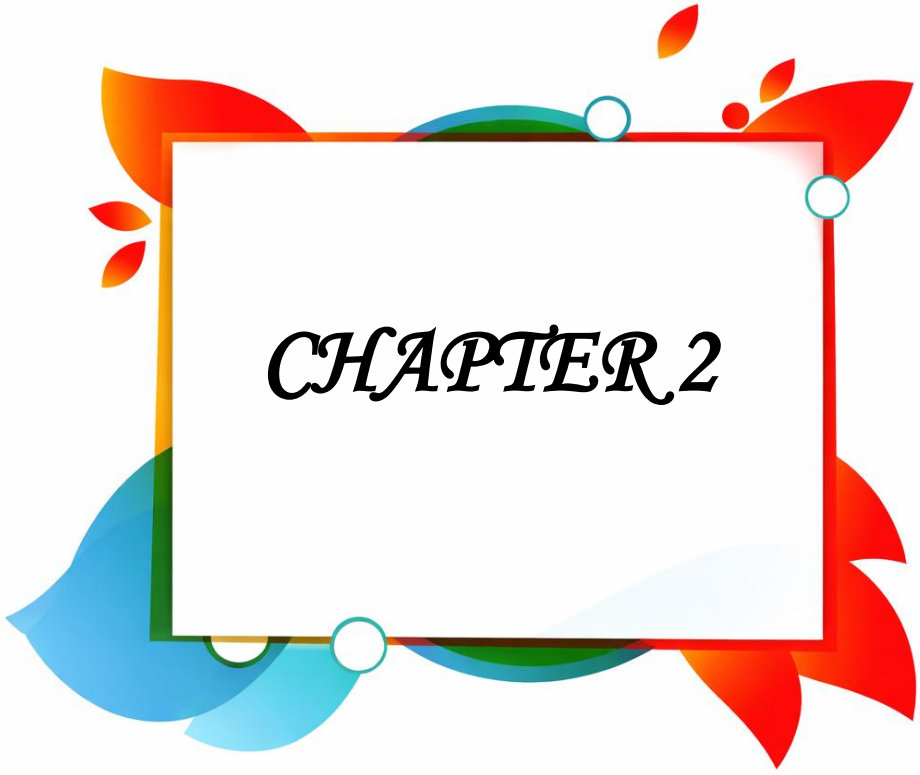
CHAPTER 2

The Importance of Larva (Maggot) Therapy and Multidisciplinary Approach in Wound Management

Nevra Polat[1]

INTRODUCTION

Larval therapy or bio-surgery has established itself in modern medicine as an alternative and effective method in wound care (Sherman, 2014). This treatment method, based on the principle of applying sterile fly larvae (usually *Lucilia sericata*) to chronic and infected wounds, presents complex patient profiles and multifaceted clinical problems (Stadler et al., 2018). Therefore, the successful application of larval therapy necessitates a multidisciplinary approach requiring the coordinated work of professionals from different fields of expertise (Bowling et al., 2007).

Definition and Components of the Multidisciplinary Approach

The multidisciplinary approach involves healthcare professionals from different disciplines working together towards common goals for a patient and each contributing from their area of expertise (Mitchell et al., 2014).

This team typically consists of the following members for larval treatment:

Team Members and Roles

Wound Care Specialists and Nurses: They are responsible for the daily management of larval therapy, dressing changes, and monitoring of the larvae (Nigam et al., 2006). They play a central role in wound assessment, implementation of the treatment protocol, and patient education (Steenvoorde & Jukema, 2004).

Infectious Disease Specialists: They provide guidance on the microbiological management of wound infection, appropriate antibiotic selection, and control of systemic infections (Wolcott et al., 2016). They ensure the integration of maggot therapy with antibiotic treatment (Bexfield et al., 2004).

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Plastic and Reconstructive Surgery Specialists: They plan surgical options for wound closure after debridement, decide on flap or graft applications, and evaluate the role of maggot therapy in preoperative wound bed preparation (Mumcuoglu et al., 2001).

Endocrinology and Metabolism Specialists: They are critical for optimal control of the underlying disease, particularly in wounds associated with metabolic disorders such as diabetic foot ulcers (Armstrong et al., 2020). They provide glycaemic control and metabolic optimisation (Lipsky et al., 2012).

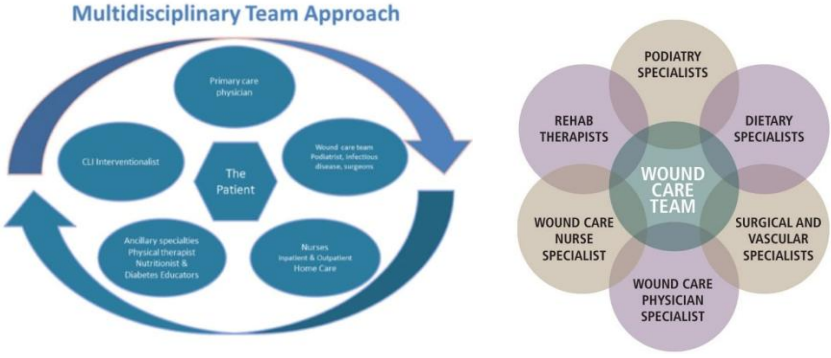
Vascular Surgeons: They offer expertise in assessing the vascular system and performing revascularisation procedures when necessary for chronic venous ulcers and wounds related to arterial insufficiency (O'Meara et al., 2014).

Physical Therapy and Rehabilitation Specialists: They manage functional rehabilitation programmes that support mobilisation, pressure distribution, and wound healing (Gethin et al., 2020).

Psychiatrists and Psychologists: They provide support in managing depression, anxiety, and treatment compliance issues commonly seen in chronic wound patients (Upton et al., 2013). They play an important role in overcoming psychological resistance that may develop towards maggot therapy (Sherman, 2009).

Nutritionists/Dietitians: They ensure the optimisation of the protein, vitamin, and mineral support necessary for wound healing (MacKay & Miller, 2003).

Advantages of a Multidisciplinary Approach



Comprehensive Patient Assessment

Multidisciplinary teams assess the patient holistically (Apelqvist et al., 2008). The wound is not viewed solely as a local problem; underlying systemic diseases, vascular status, nutritional status, psychological factors, and social determinants

are considered together (Lipsky et al., 2012). This comprehensive assessment ensures the creation of optimal conditions that increase the chances of success for larval therapy (Sun et al., 2014). For example, when planning larval application for the treatment of a diabetic foot ulcer, an endocrinologist optimises glycaemic control, a vascular surgeon assesses foot perfusion, an infectious disease specialist investigates the presence of osteomyelitis, and a wound care nurse determines the appropriate larval application technique (Armstrong et al., 2017). This coordination significantly enhances treatment success.

Optimisation of Treatment Protocols

The combined expertise from different specialised fields ensures that larval therapy is administered to the most suitable patients, at the most appropriate time, and in the most effective manner (Dumville et al., 2009). The team jointly determines which wound types will respond best to larval therapy, how long the treatment should last, and which additional therapies should be combined (Opletalová et al., 2012).

Effectiveness in Complication Management

Complications that may arise during larval treatment (e.g. excessive pain, allergic reactions, unexpected bleeding or migration of larvae) can be managed quickly and effectively by a multidisciplinary team (Steenvoorde et al., 2007). Each specialist recognises and intervenes in complications within their own field (Sherman, 2014).

Improving Patient Education and Compliance

A multidisciplinary team can explain the necessity and safety of treatment in a more convincing manner by providing the patient with information from different perspectives (Bowling et al., 2007). Particularly in methods such as larval therapy, which may initially be perceived as uncomfortable by the patient, comprehensive patient education increases treatment compliance (Sherman, 2009).

Objectivity in Clinical Decision-Making

Rather than relying on the biases or limited experience of a single clinician, the collective knowledge and experience of the team enables more objective and evidence-based decisions (Mitchell et al., 2014). This contributes to avoiding unnecessary treatments and increasing cost-effectiveness (Whitaker et al., 2014).

Research and Innovation

Multidisciplinary teams, by bringing together different perspectives, pave the way for the development of new treatment protocols, the design of clinical trials, and innovations that will increase the effectiveness of larval therapy (Sun et al.,

2014). Scientific discussions within the team can make significant contributions to the literature.

Reduced Hospital Stay

Coordinated care accelerates the treatment process and reduces complications (Driver et al., 2010). Studies show that multidisciplinary wound care teams significantly shorten hospital stays and reduce repeat hospital admissions (Apelqvist et al., 2008; Krishnan et al., 2008).

Disadvantages and Challenges of the Multidisciplinary Approach

Coordination Challenges

Bringing together specialists from different departments and organising regular meetings can create significant logistical challenges (Mitchell et al., 2014). It can be particularly difficult to coordinate the schedules of busy clinicians. This can hinder rapid decision-making in emergencies (Santilli & Vogenberg, 2015).

Time and Resource Costs

Multidisciplinary team meetings, consultations, and coordination efforts require significant time (Lemieux-Charles & McGuire, 2006). Each specialist's assessment may be billed separately, which can increase the total cost of treatment. For small healthcare institutions, this additional cost can be a significant burden (Nancarrow et al., 2013).

Communication Issues

Different medical terminologies, perspectives, and priorities can lead to communication problems among team members (Körner et al., 2016). There is a risk of interrupted information flow, the patient receiving conflicting messages from different specialists, or inconsistencies in the treatment plan (Lemieux-Charles & McGuire, 2006).

Uncertainty of Responsibility

In situations involving multiple specialists, it may become unclear who bears primary responsibility for the patient (Nancarrow et al., 2013). This can lead to problems, particularly when complications arise or medico-legal issues emerge. The fact that decisions are made by a ‘committee’ can create the perception of reduced individual accountability.

Slowing Down the Decision-Making Process

Decisions requiring consensus can take longer than those made by a single clinician (Körner et al., 2016). This delay can jeopardise patient safety, particularly in situations requiring urgent intervention.

Hierarchy and Power Dynamics

Hierarchical structures inherent in medical culture may cause some team members (e.g., nurses or junior assistants) to be reluctant to express their opinions (Lemieux-Charles & McGuire, 2006). There is a risk that dominant personalities may unduly influence team decisions.

Feasibility in Resource-Constrained Settings

In developing countries or healthcare facilities in rural areas, there may not be enough specialists to form a multidisciplinary team (Santilli & Vogenberg, 2015). In such cases, the ideal multidisciplinary approach cannot be implemented, and alternative strategies must be developed.

Need for Training and Standardisation

For multidisciplinary teams to work effectively, team members must be trained in teamwork skills, communication competencies, and common protocols (Mitchell et al., 2014). Organising and maintaining these training programmes requires additional resources.

Strategies for Optimising the Multidisciplinary Approach

Certain strategies can be implemented to minimise disadvantages and maximise advantages:

Regular and Structured Meetings: Weekly or biweekly regular team meetings should be planned with a predetermined agenda (Mitchell et al., 2014). Meetings should be managed efficiently and kept within a specific time frame.

Clear Role and Responsibility Definitions: The role and responsibilities of each team member should be clearly defined (Nancarrow et al., 2013). A primary case manager should be designated.

Standard Protocols and Clinical Pathways: Evidence-based standard protocols for larval therapy should be developed and adopted by all team members (Sun et al., 2014).

Electronic Record Systems: Information sharing should be facilitated using shared patient record systems; consultation notes and treatment plans should be accessible to all team members (Körner et al., 2016).

Team Culture and Training: A culture of mutual respect, open communication, and collaborative decision-making should be encouraged, and regular training on teamwork skills should be provided (Lemieux-Charles & McGuire, 2006).

Tele-consultation Opportunities: In resource-constrained settings, access to specialist opinions can be provided through remote consultation and tele-medicine opportunities (Santilli & Vogenberg, 2015).

CONCLUSION

Larval therapy is a complex and multifactorial treatment method (Sherman, 2014). Successful implementation of this treatment requires a holistic approach that goes beyond local wound management and considers the patient's overall medical condition, psychological state, and social factors (Stadler et al., 2018). A multidisciplinary approach provides an ideal framework for meeting these complex requirements (Bowling et al., 2007). Although multidisciplinary teams have disadvantages such as coordination difficulties, time and resource costs (Nancarrow et al., 2013), these challenges can be minimised with appropriate strategies (Mitchell et al., 2014). The advantages, such as comprehensive patient assessment, optimised treatment protocols, effective complication management, and increased patient compliance, significantly outweigh these disadvantages (Apelqvist et al., 2008; Krishnan et al., 2008). With the spread of patient-centred care and value-based medicine in today's healthcare systems, the multidisciplinary approach is becoming increasingly important (Mitchell et al., 2014). In areas requiring specialised expertise and involving complex patient profiles, such as larval therapy, establishing and effectively operating multidisciplinary teams is no longer a luxury but an essential part of quality patient care (Sun et al., 2014). In the future, technological advances and new communication tools will enable multidisciplinary teams to work more efficiently and further reduce the disadvantages of this approach (Körner et al., 2016).

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I. THE MULTIDISCIPLINARY ROLE OF LARVA (MAGGOT) THERAPY AND MICROBIOLOGY IN WOUND MANAGEMENT

INTRODUCTION

Maggot Debridement Therapy (MDT) or biosurgery, performed using *Lucilia sericata* larvae, is a method that has been used for centuries in the treatment of chronic and infected wounds but has recently regained interest in modern medicine. In this treatment modality, the multidisciplinary role of infectious disease specialists and microbiologists is of critical importance.

The Role of Infectious Disease Specialists

Patient Selection and Indication Determination

Infectious disease specialists play a central role in identifying patients suitable for larval therapy. They evaluate the use of MDT particularly in the following situations:

Chronic wounds resistant to conventional treatments

- Wounds infected with multidrug-resistant bacteria (MRSA, VRE, multidrug-resistant Gram-negative bacteria)
- Diabetic foot ulcers
- Venous/arterial insufficiency ulcers
- Pressure ulcers

According to Sherman's 2014 comprehensive review, MDT is recommended as an effective alternative treatment option, particularly for wounds infected with MRSA.

Antimicrobial Treatment Coordination

Infectious disease specialists coordinate the management of systemic antibiotic treatment concurrently with larval treatment. Although the larvae possess antimicrobial activity, systemic antibiotic support is required in some cases. Studies have determined that the excretion/secretion products (ES) of L. sericata larvae exhibit potent antimicrobial activity against Gram-positive bacteria, but have a more limited effect against Gram-negative bacteria.

Biosafety and Infection Control

From an infection control perspective, they are involved in developing protocols to ensure that MDT application does not pose a risk to other patients. The use of sterile, medical-grade larvae is mandatory, and the risk of cross-contamination must be minimised.

Critical Contributions of the Field of Microbiology

Wound Culture and Microbiological Analysis

Microbiology laboratories are essential for analysing wound cultures before and after MDT. Studies have shown that:

Pre-MDT wound cultures determine the existing microbial flora. Post-treatment cultures demonstrate a reduction in bacterial load and compositional changes. In a 2007 study by Bowling and colleagues, MDT was microbiologically proven to significantly reduce the bacterial load in wounds colonised by various pathogens, including MRSA.

Antimicrobial Susceptibility Testing

Microbiology laboratories provide guidance on antibiotic selection, which may be combined with MDT when necessary, by conducting antibiogram studies for wound pathogens. This is particularly critical in the presence of multidrug-resistant organisms.

Investigation of the Antimicrobial Mechanisms of Larval Secretions

Microbiology research has elucidated the mechanisms of the antimicrobial effects of *L. sericata* larvae:

Antimicrobial Peptides: In vitro studies have shown that defensin-like peptides secreted by the larvae exert a bactericidal effect by disrupting bacterial cell walls.

Alkaline pH Effect: The high pH (8-9) of larval secretions inhibits the growth of many bacteria. A 2008 study by Van der Plas et al. demonstrated that this alkaline environment has a bacteriostatic effect, particularly on S. aureus.

Biofilm Degradation: Microbiological studies have demonstrated the capacity of larval secretions to break down established biofilms. Research by Harris et al. in 2009 showed that MDT effectively eliminated *P. aeruginosa* and *S. aureus* biofilms.

Molecular Microbiology and Metagenomic Analyses

The use of modern molecular techniques has enabled detailed examination of the effects of MDT on the wound microbiome: 16S rRNA gene sequencing studies have demonstrated changes in microbial diversity following MDT. Metagenomic analyses have revealed that microorganisms undetectable by culture are also affected by MDT.

Multidisciplinary Collaboration Models Clinical Decision-Making Processes

Regular consultations between infectious disease specialists, microbiologists, wound care nurses, surgeons, and other relevant disciplines are essential for optimal wound treatment. This multidisciplinary approach:

- Optimises patient selection for MDT
- Personalises treatment protocols on a patient-by-patient basis
- Enables early detection of complications
- Evaluates treatment outcomes microbiologically and clinically

Research and Development

Collaboration between the fields of microbiology and infectious diseases is important for developing new approaches to enhance the effectiveness of MDT:

- Purification and characterisation of larval excretion/secretion products (ES)
- Isolation of new antimicrobial agents
- Development of alternative treatment strategies against resistant pathogens

Clinical Evidence and Efficacy

Randomised controlled trials have demonstrated the efficacy of MDT in infection control. Sun and colleagues' 2014 meta-analysis showed that MDT was more effective than conventional treatments in terms of debridement in diabetic foot ulcers, but there was no significant difference in complete healing rates. Dumville et al.'s 2009 Cochrane review stated that MDT is safe in venous leg ulcers but did not show superiority over hydrogel therapy in terms of healing speed.

Safety and Side Effects

The safety profile of MDT should be evaluated under the supervision of infectious disease specialists:

- Migration of larvae outside the wound (rare)
- Local pain (the most common side effect, occurring in 5-30% of patients)
- Allergic reactions (very rare)
- Risk of secondary infection (minimised by the use of sterile larvae)

CONCLUSION

Lucilia sericata larva therapy is an important modality in modern wound care that requires a multidisciplinary approach. Infectious disease specialists play critical roles in patient selection, antimicrobial treatment coordination, and infection control; microbiologists, meanwhile, play critical roles in characterising wound microbiology, elucidating antimicrobial mechanisms, and objectively evaluating treatment efficacy. Effective collaboration between these two disciplines ensures the optimal use of MDT in chronic wound treatment, particularly in today's world where antibiotic-resistant infections are on the rise.

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II. THE ROLE OF THE SURGICAL TEAM IN LARVA (MAGGOT) THERAPY AND WOUND MANAGEMENT

INTRODUCTION

Larva (Maggot) Debridement Therapy (LDT/MDT), which utilises *Lucilia sericata* larvae, has become an important part of surgical practice in the management of chronic and complicated wounds. The role of the surgical team in this treatment modality encompasses a broad spectrum, ranging from patient selection to post-treatment reconstruction.

Surgical Assessment and Patient Selection

The surgical team plays a critical role in identifying candidates for maggot therapy. Sherman (2003) reported that MDT is particularly effective in necrotic wounds where traditional debridement methods have failed (Sherman, 2003). Surgeons formulate the treatment plan by assessing wound depth, amount of necrotic tissue, presence of infection, and underlying anatomical structures.

A Cochrane systematic review by Dumville et al. (2009) evaluated the debridement efficacy of MDT in venous leg ulcers and emphasised the importance of surgical assessment in treatment success (Dumville et al. 2009). Surgeons determine whether larval therapy alone is sufficient or whether it should be combined with surgical debridement.

Preoperative Surgical Preparation

The surgical preparation phase prior to larval application is important. Bowling et al. (2007) demonstrated that limited surgical debridement prior to MDT in diabetic foot ulcers increased larval efficacy by removing loose necrotic tissue (Bowling et al. 2007). The surgical team performs preparatory procedures such as partial removal of thick eschar tissue, abscess drainage, and cleaning of infected foreign bodies. From a vascular surgical perspective, Gottrup and Jørgensen (2011) emphasised that vascular assessment is mandatory prior to larval therapy in ischaemic wounds (Gottrup and Jørgensen 2011). In cases of inadequate perfusion, revascularisation procedures (angioplasty, bypass) should be planned prior to or concurrently with maggot therapy.

Combined Treatment with Surgical Debridement

Sun et al. (2014) evaluated the results of combined use of surgical debridement and MDT in diabetic foot infections involving osteomyelitis and found this combination to be more effective than surgery or larval therapy alone (Sun et al. 2014). The surgical team performs interventions in areas inaccessible to larvae, such as removal of bone sequestrum and cleaning of infected joint

capsules. Steenvoorde et al. (2005) reported that MDT application after aggressive surgical debridement in traumatic wounds accelerated wound bed preparation and increased secondary closure or graft success (Steenvoorde et al. 2005). In this approach, surgery performs macroscopic debridement, while the larvae provide microscopic cleaning.

Surgical Supervision During Larval Therapy

Throughout the treatment process, the surgical team performs regular assessments for early detection and intervention of complications. Whitaker et al. (2007) reported that bleeding complications, seen in 5-10% of patients during MDT, may require surgical intervention (Whitaker et al. 2007). The surgical team plans interventions such as electrocautery, haemostatic agents, or, in rare cases, vessel ligation for bleeding control. Nigam et al. (2006) emphasised the importance of a surgical perspective in managing complications such as maceration and dermatitis, which may be seen at the wound margins during larval treatment (Nigam et al. 2006). Revision of wound margins or surgical protection of surrounding tissue may be necessary when indicated.

Post-Larva Surgical Reconstruction

Wound Bed Assessment

Following larva treatment, the surgical team assesses whether clean granulation tissue has formed. Tantawi et al. (2007) demonstrated that the bacterial load of wounds decreased significantly after MDT and became more suitable for surgical closure (Tantawi et al. 2007). At this stage, the surgical team decides which of the following is appropriate: primary closure, delayed primary closure, or graft/flap procedures.

Graft and Flap Procedures

Parnes and Lagan (2007) evaluated the success rates of split-thickness skin grafts after larval treatment and reported high graft take rates of 85-90%. (Parnes and Lagan 2007). The plastic and reconstructive surgery team determines the appropriate reconstructive option based on the location, size, and depth of the wound:

- **Split-thickness skin grafts (STSG):** Superficial, well-granulated wounds
- **Full-thickness skin grafts (FTSG):** Cosmetically important areas
- **Local flaps**: Medium-sized defects
- **Free flaps:** For large, complex defects and areas with poor vascularisation

Markevich et al. (2000) reported synergistic effects when grafting was combined with vacuum-assisted closure (VAC) therapy after MDT (Markevich et al. 2000).

Orthopaedic Surgical Perspective

In the presence of osteomyelitis, orthopaedic surgical intervention is essential. Cazander et al. (2013) emphasised that, despite demonstrating the antimicrobial properties of Lucilia sericata secretions, bone debridement remains the gold standard in chronic osteomyelitis (Cazander et al. 2013). The orthopaedic surgical team performs the following:

- Excision of the abscess
- Cortical curettage
- Cleaning of the medullary canal
- Placement of antibiotic-impregnated polymethyl methacrylate (PMMA) bead chains
- Application of bone grafting when necessary

Mumcuoglu et al. (1999) demonstrated that while MDT controls soft tissue infection in chronic wounds involving osteomyelitis, surgical intervention remains necessary for bone infection (Mumcuoglu et al. 1999).

Vascular Surgical Approach

Diabetic Foot Ulcers

Armstrong and Lipsky (2004) emphasised the importance of vascular assessment in diabetic foot ulcers and recommended measuring parameters such as the ankle-brachial index (ABI) and transcutaneous oxygen pressure (TcPO2) (Armstrong and Lipsky 2004). Vascular surgeons plan the following procedures in critical ischaemia:

- Angiography and endovascular interventions
- Femoro-popliteal or femoro-distal bypass
- Endarterectomy

Mudge et al. (2014) reported that MDT application after revascularisation reduced major amputation rates in diabetic feet (Mudge et al. 2014).

Venous Insufficiency Ulcers

In venous ulcers, Brem et al. (2004) demonstrated that surgical correction of venous insufficiency (venous ablation, perforator ligation) in conjunction with

MDT improved long-term outcomes (Brem et al. 2004). The surgical team plans venous reconstruction procedures concurrently with or following maggot therapy.

General Surgery and Complication Management

Abdominal Wall Wounds

Grassberger et al. (2007) evaluated the use of MDT in postoperative abdominal wound infections and reported its effectiveness in complicated cases such as mesh infection (Grassberger et al. 2007). The general surgery team performs the following when necessary:

- Partial or complete removal of infected mesh
- Fascial debridement
- Reconstruction with biological mesh
- Component separation techniques after maggot therapy
- Necrotising fasciitis

Naik and Hede (2006) stated that aggressive surgical debridement remains the primary treatment for necrotising soft tissue infections, but that MDT may be beneficial as an adjuvant therapy in wound management following extensive debridement (Naik and Hede 2006).

Trauma Surgery Perspective

War Wounds and Blast Injuries

Sherman and Shimoda (2004) evaluated the use of MDT in traumatic wounds in military settings and demonstrated that it is an effective option, particularly in resource-limited environments (Sherman and Shimoda 2004). Trauma surgeons plan larval treatment for the management of contaminated wounds after primary stabilisation and life-saving interventions.

Thomas et al. (1999) reported that MDT facilitates wound cleansing in metal implant infections in open fractures while allowing for implant preservation (Thomas et al. 1999). In this scenario, orthopaedic trauma surgery combines larval therapy with soft tissue management while evaluating implant stability.

Surgical Technique and Application

BioBag Method

The surgical team selects the appropriate application method based on the anatomy and location of the wound. Sherman (2009) detailed the advantages of the closed BioBag system and recommended its use in areas requiring surgical

precision (Sherman, 2009). This method prevents the escape of larvae and ensures control in the surgical field.

Free-Range Method

The free-range method may be more effective in deep cavities, sinus tracts, or complex anatomical areas. However, the surgical team must carefully restrict the larvae to prevent damage to adjacent healthy tissue.

Anaesthesia and Pain Management

Steenvoorde and Jukema (2004) emphasised that some patients experience pain during MDT and that the surgical team should establish pain management protocols (Steenvoorde and Jukema (2004), Local anaesthetics, hydrogel dressings, and systemic analgesics are planned by the surgical team. In cases of severe pain, a decision is made to terminate the treatment early and switch to alternative surgical debridement.

Long-Term Surgical Follow-Up

Wayman et al. (2000) evaluated long-term wound outcomes following MDT and emphasised the importance of surgical follow-up (Wayman et al. 2000). The surgical team undertakes the following tasks for months and years after treatment:

- Monitoring for wound recurrence
- Assessing the need for scar revision
- Planning functional rehabilitation
- Maintaining control of the underlying disease.

CONCLUSION

Lucilia sericata larva therapy is a valuable modality that complements traditional methods in modern surgical practice. The role of the surgical team is critical at every stage, from patient selection to postoperative reconstruction. Successful outcomes depend on the integration of surgical expertise with the biological advantages of maggot therapy. In the future, more randomised controlled trials are needed on the combination of surgical techniques and maggot therapy.

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III. THE ROLE OF LARVA (MAGGOT) THERAPY IN WOUND MANAGEMENT AND THE DISCIPLINE OF INTERNAL MEDICINE

INTRODUCTION

Maggot debridement therapy (MDT) or biosurgery using *Lucilia sericata* (green bottle fly) larvae is a method known since ancient times but which regained popularity in modern medicine after the 1990s. This treatment has shown remarkable results, particularly in chronic wounds, diabetic foot ulcers, and antibiotic-resistant infections.

Chronic Wounds from an Internal Medicine Perspective

Internal medicine specialists play a central role in managing systemic diseases that predispose patients to chronic wound development. Conditions such as diabetes mellitus, peripheral arterial disease, venous insufficiency, chronic kidney disease, immunosuppression, and nutritional deficiencies directly affect wound healing.

Diabetic Foot Ulcers

Foot ulcers occur in 25% of diabetic patients over their lifetime, and a significant proportion of these patients may require amputation. A study by Sherman et al. (2000) showed that MDT provided faster debridement in diabetic foot ulcers compared to conventional treatment. The role of the internal medicine specialist here is:

- Optimising glycaemic control (HbA1c targets)
- Assessing peripheral neuropathy
- Assessing vascular status (ABI measurement)
- Managing systemic antibiotics in the presence of infection
- Optimising nutritional status

Venous and Arterial Insufficiency Ulcers

In a study conducted by Mumcuoglu and colleagues (2001), it was demonstrated that larval therapy in venous insufficiency ulcers supports effective debridement and granulation tissue formation. Internal medicine specialist:

- Identifies the underlying vascular pathology
- Regulates anticoagulant/antiplatelet therapy
- Manages comorbidities such as heart failure
- Determines indications for compression therapy

Mechanisms of Larval Therapy and Its Relationship to Internal Medicine

Mechanical Debridement

Larvae selectively remove necrotic tissue. A review by Steenvoorde and Jukema (2004) emphasises the capacity of larvae to digest only devitalised tissue through their proteolytic enzymes.

The internal medicine specialist monitors the systemic effects of debridement:

- Assessment of sepsis risk
- Monitoring of acute phase reactants (CRP, procalcitonin)
- Monitoring of systemic infection symptoms

Antimicrobial Effect

The study by Bexfield and colleagues (2004) demonstrated that larval secretions exhibit potent antimicrobial activity against gram-positive bacteria, including MRSA. Bowling and colleagues (2007) demonstrated the efficacy of larval therapy in disrupting biofilm formation.

The role of the internal medicine specialist in antimicrobial management:

- Selection of systemic antibiotics based on culture results
- Assessment of antibiotic resistance patterns
- Treatment strategies for resistant organisms such as MRSA and VRE
- Dose adjustment of nephrotoxic or hepatotoxic antibiotics

Stimulation of Wound Healing

The study by Van der Plas et al. (2008) demonstrated that larval secretions stimulate fibroblast proliferation and migration. They also support granulation tissue by increasing the release of growth factors.

The Role of Internal Medicine in a Multidisciplinary Approach

Patient Selection and Preparation

The internal medicine specialist plays a critical role in identifying suitable patients for larval therapy:

Indications:

- Chronic wound (lasting longer than 4 weeks)
- Presence of necrotic tissue
- Non-response to conventional treatment
- Antibiotic-resistant infections
- Patients unsuitable for surgical debridement

Contraindications and Risk Assessment:

- *Pyoderma gangrenosum* (Sherman, 2003)
- Active vasculitis
- Presence of osteomyelitis in the wound area
- Excessive sensitivity/anxiety
- Assessment of the degree of immunosuppression
- Comorbidity Management

Sun and colleagues' (2014) systematic review demonstrated that larval therapy is effective in diabetic foot ulcers, but success depends on glycaemic control and vascular adequacy.

Management by the internal medicine specialist before and during treatment:

Diabetes Mellitus:

- Target blood sugar: 140-180 mg/dL (ADA guidelines)
- Minimising the risk of hypoglycaemia
- Management of insulin resistance

Renal Insufficiency:

- Maintaining fluid and electrolyte balance
- Effect of uraemic toxins on wound healing
- Dialysis timing

Cardiovascular Diseases:

- Optimisation of tissue perfusion
- Blood pressure control
- Antiplatelet/anticoagulant adjustments

Nutritional Status:

- Albumin, prealbumin levels
- Vitamin and mineral supplementation (zinc, vitamin C)
- Increased protein intake
- Infection Control

Opletalová et al. (2012) demonstrated that larval therapy significantly reduced bacterial load but that systemic antibiotic support was required in some patients.

Internal medicine specialist:

- Monitors sepsis criteria (SOFA, qSOFA scores)
- Assesses the risk of bacteraemia
- Manages empirical and culture-guided antibiotic therapy
- Assesses the possibility of fungal infection

Follow-up and Complication Management

Complications reported in the study by Cerfonteyn et al. (2015):

- Pain (most common, 5-30%)
- Escaped larvae
- Allergic reactions
- Transient bacteraemia

Internal medicine specialist:

- Pain management (assessment of opioid requirement)
- Management of allergic reactions
- Monitoring of systemic toxicity symptoms
- Monitoring of metabolic parameters

Clinical Evidence and Efficacy

Randomised Controlled Trials

Dumville and colleagues' (2009) Cochrane review found that larval therapy is effective in wound debridement but did not show a clear superiority over hydrogel in terms of wound healing speed and amputation rates. However, the study by Mudge et al. (2014) demonstrated the superiority of MDT over conventional treatment in antibiotic-resistant infections and complex wounds.

Cost-Effectiveness

The economic analysis by Wolff et al. (2013) demonstrated that larval therapy is cost-effective, particularly by reducing hospital stay duration and lowering amputation rates. The internal medicine specialist plays a key role in determining the necessity and duration of hospitalisation.

Internal Medicine Outpatient Follow-up

Grassberger and Fleischmann's (2009) study demonstrated that outpatient larval therapy is safe in selected patients. The internal medicine specialist:

Selects suitable patients for outpatient treatment, plans regular outpatient follow-ups, and intervenes early in case of complications.

CONCLUSION

Lucilia sericata larva therapy is a treatment method requiring a multidisciplinary approach. The internal medicine specialist plays the following roles in this process:

- Identifying and optimising underlying systemic diseases
- Patient selection and risk assessment
- Comorbidity management
- Infection control and antimicrobial management
- Nutritional and metabolic optimisation
- Monitoring and managing complications
- Long-term follow-up and secondary prevention strategies.

As Sherman (2014) noted, the success of larval therapy depends not only on the activity of the larvae, but also on optimising the patient's overall health and multidisciplinary teamwork. The internal medicine specialist plays a central role in coordinating this holistic approach and protecting the patient's systemic health.

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IV. THE ROLE OF LARVA (MAGGOT) THERAPY AND RADIOLOGICAL EXAMINATIONS IN WOUND MANAGEMENT

INTRODUCTION

Maggot debridement therapy (MDT) using *Lucilia sericata* (green bottle fly) larvae is a biosurgical method that has been used for centuries, particularly in chronic and infected wounds. In modern medicine, multidisciplinary approaches are critical to enhance the effectiveness of this treatment and prevent complications. Radiological imaging methods play important roles in the planning, monitoring, and evaluation of the results of maggot therapy.

Basic Principles of Larval Therapy

Lucilia sericata larvae support wound healing through three fundamental mechanisms: selective debridement (cleaning of necrotic tissue), antimicrobial activity, and stimulation of tissue regeneration through the secretion of growth factors. A study by Sherman and colleagues in 2000 demonstrated that larval therapy provides faster and more selective removal of necrotic tissue compared to traditional debridement methods (Sherman et al. 2003).

The Importance of Radiological Investigations

Pre-Treatment Assessment

A comprehensive radiological assessment is critical before initiating larva treatment:

Conventional Radiography: This is the primary imaging method for investigating the presence of osteomyelitis, detecting foreign bodies, and assessing bone destruction. Lipsky and colleagues' 2012 guidelines state that radiography is recommended as the first-line imaging modality for diabetic foot infections (Lipsky et al. 2012).

Magnetic Resonance Imaging (MRI): This is the gold standard for assessing the depth of soft tissue infection, bone marrow oedema, abscess formation, and vascular compromise. MRI has been shown to have over 90% sensitivity and specificity in the diagnosis of osteomyelitis (Kapoor et al. 2000).

Computed Tomography (CT): It is superior to MRI in showing bone details, especially in complex anatomical regions, and in detecting gas formations. CT angiography provides critical information in the assessment of vascular insufficiency.

Doppler Ultrasonography: It is a non-invasive method for evaluating peripheral arterial disease, detecting blood flow in the wound area, and monitoring response to treatment. Kalani and colleagues emphasised the importance of Doppler in determining critical perfusion thresholds for wound healing (Kalani et al. 1999).

Monitoring During Treatment

Larval treatment generally lasts 2-4 days, and radiological follow-up is important during this period:

Serial Ultrasonography: Bedside ultrasound can be used for the early detection of soft tissue oedema, abscess formation, and vascular complications. A 2018 study by Paul et al. demonstrated that ultrasonographic monitoring during wound treatment enabled early detection of infection complications (Paul et al. 2018).

MRI Scans: In cases of deep infection or osteomyelitis, periodic MRI examinations may be necessary to assess the response to treatment.

Post-Treatment Assessment

Wound Healing Follow-Up: Serial imaging can be used to assess granulation tissue development, oedema regression, and increased vascularisation. Dumville and colleagues' Cochrane review emphasised the importance of objective treatment response assessment in chronic wounds (Dumville et al. 2009).

Multidisciplinary Approach Modelling Integrated Assessment Protocol

A 2014 study by Sun et al. demonstrated that multidisciplinary wound centres reduced amputation rates by more than 50% in diabetic foot ulcers (Sun et al. 2014).

In this approach, radiological assessment is integrated as follows:

At Presentation: Conventional radiography and Doppler ultrasonography

In Complex Cases: Detailed assessment with MRI or CT angiography

Treatment Follow-up: Weekly ultrasonographic evaluations

Post-Treatment: Follow-up imaging after 4-6 weeks

Radiology-Wound Care Team Collaboration

A 2020 study by Armstrong and colleagues demonstrated that regular communication between radiologists and wound care specialists improves treatment success (Armstrong et al. 2020).

Special Cases and Complications

Larval Therapy in the Presence of Osteomyelitis

The role of maggot therapy in bone infection is controversial. Although Baer demonstrated the efficacy of maggot therapy in osteomyelitis in his classic 1931 study (Baer 1931), the modern approach involves MRI assessment of bone marrow oedema and cortical destruction to guide treatment planning.

Vascular Insufficiency

In cases of critical ischaemia detected by CT angiography or MR angiography, the efficacy of maggot therapy is limited. Gottrup's 2004 study emphasised that wound healing cannot occur without adequate perfusion (Gottrup 2004).

Abscesses and Deep Pocket Formations

Abscess formations detected by ultrasonography and MRI require drainage prior to maggot therapy. A 2001 study by Bowler and colleagues demonstrated that maggot therapy may fail without appropriate surgical drainage (Bowler et al. 2001).

Evidence-Based Imaging Protocols

Minimal Protocol (Uncomplicated Wounds)

- Initial: Conventional radiography + Doppler US
- Follow-up: Clinical assessment + US if necessary

Intermediate Protocol (Deep Wounds, Suspected Infection)

- Initial: Radiography + Doppler US + soft tissue US
- 1 week: Control US
- 4 weeks: MRI (response assessment)

Advanced Protocol (Suspected Osteomyelitis, Critical Ischemia)

- Initial: Full radiological panel (radiography, MRI, CT/MR angiography)
- Weekly: Doppler ultrasound + soft tissue ultrasound
- 2 weeks: MRI follow-up
- 6 weeks: Comprehensive reassessment

Blume and colleagues' 2008 systematic review demonstrated that such protocolised approaches improve treatment success (Blume et al. 2008).

Cost-Effectiveness and Outcomes

Although radiological imaging is costly, it is cost-effective in terms of preventing unnecessary treatments and reducing complications through early and accurate diagnosis. Harding and colleagues' 2013 study demonstrated that larva treatment supported by appropriate imaging reduced amputation rates and decreased long-term costs (Harding et al. 2013).

Future Perspectives

The integration of artificial intelligence-assisted image analysis, 3D imaging techniques, and molecular imaging methods offers new possibilities in the management of maggot therapy. A 2019 study by Wang et al. demonstrated the success of machine learning algorithms in predicting wound healing processes (Wang et al. 2019).

CONCLUSION

A multidisciplinary radiological approach in the treatment of *Lucilia sericata* larvae is a critical component that increases treatment success, reduces complications, and improves patient outcomes. The selection of appropriate imaging modalities, timely follow-up protocols, and radiology-clinical collaboration are indispensable elements of modern wound management. The development and standardisation of evidence-based protocols will further enhance the effectiveness of this treatment modality.

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V. THE ROLE OF LARVA (MAGGOT) THERAPY AND NUTRITION IN WOUND MANAGEMENT

INTRODUCTION

Chronic wound treatment is a significant source of morbidity and cost in today's healthcare system. The medical use of Lucilia sericata (green bottle fly) larvae, known as Larva Debridement Therapy (LDT) or maggot therapy, is an effective biological treatment method, particularly for antibiotic-resistant infections and chronic wounds that do not respond to conventional treatments. However, the success of wound healing depends not only on local treatment methods but also on the patient's overall metabolic status and nutritional condition.

The Relationship Between Nutrition and Wound Healing

Wound healing is a complex process that requires intense metabolic activity. Malnutrition is one of the most important factors delaying wound healing.

Critical Nutrients

Protein and Amino Acids:

Protein requirements during wound healing can increase to 1.2-2.0 g/kg/day (Wild et al., 2010). Specific amino acids such as arginine and glutamine support immune function and collagen synthesis (Stechmiller et al., 2005).

Vitamin C (Ascorbic Acid):

It is essential for collagen synthesis. Its deficiency significantly impairs wound healing. A supplement of 500-1000 mg/day is recommended for patients with chronic wounds (MacKay & Miller, 2003).

Vitamin A:

Critical for epithelialisation, collagen synthesis, and immune function. A daily supplement of 10,000–25,000 IU may accelerate wound healing (Barbul et al., 1987).

Zinc:

Essential for DNA synthesis, cell proliferation, and protein synthesis. Zinc deficiency is common in chronic wound patients (Lansdown et al., 2007).

Omega-3 Fatty Acids:

Support wound healing through their anti-inflammatory effects (McDaniel et al., 2008).

Nutritional Assessment in Patients Receiving Larval Therapy

Patients receiving larval therapy generally fall into the following chronic wound categories:

- Diabetic foot ulcers
- Pressure sores
- Venous/arterial ulcers
- Traumatic wounds etc. The prevalence of malnutrition in these patient groups is between 20-50% (Iizaka et al., 2010).

Nutritional Status Assessment Tools

- MNA (Mini Nutritional Assessment): For nutritional risk screening in elderly patients
- Albumin and Prealbumin Levels: Biochemical indicators of protein-energy malnutrition (albumin <3.5 g/dL indicates poor nutritional status)
- NRS-2002: Nutritional risk screening in hospitalised patients (Kondrup et al., 2003).

Nutrition Intervention Strategies

Oral Nutrition Support:

- High-protein, high-calorie diets
- Immune-supporting formulations (containing arginine, glutamine, omega-3, antioxidants)
- Special commercial formulations for wound healing (Arnold & Barbul, 2006)

Enteral/Parenteral Nutrition:

When the oral route is inadequate, enteral nutrition is preferred. Total parenteral nutrition (TPN) is the last resort (Schols et al., 2009).

Hydration:

Adequate fluid intake (30 ml/kg/day) is critical for wound healing.

Clinical Evidence and Studies

Numerous studies support the synergistic effect of optimal nutrition and maggot therapy:

A systematic review by Sherman (2014) demonstrated that maggot therapy is more effective than surgical debridement in chronic wounds, but treatment success is related to the patient's general health and nutritional status. A meta-analysis by Cereda et al. (2015) found that oral nutritional support containing arginine, zinc, and antioxidants significantly shortened the healing time of pressure ulcers. Demidova-Rice et al. (2012) emphasised the critical importance of adequate nutrition in every phase of wound healing (inflammation, proliferation, remodelling).

Practical Recommendations

Before Larva Treatment

- A detailed nutritional assessment should be performed
- If malnutrition is detected, nutritional support should be initiated before starting treatment
- Serum albumin, prealbumin, transferrin, vitamin, and mineral levels should be monitored

During Larva Treatment

- Protein intake should be optimised (1.5-2.0 g/kg/day)

- Daily calorie requirements should be met (30-35 kcal/kg/day)
- Specific vitamin-mineral supplementation should be provided
- Hydration should be monitored
- Glycaemic control should be ensured

After Larva Treatment

- Nutritional support should be continued
- Regular re-evaluation of nutritional status should be performed
- Nutritional support should be maintained until wound healing is complete

Considerations for Special Patient Groups

Diabetic Patients:

- Low glycaemic index carbohydrate selection
- Regular meal times
- HbA1c monitoring

Elderly Patients:

Higher protein requirement (1.2-1.5 g/kg/day)

High risk of sarcopenia and malnutrition

Possibility of swallowing difficulties

Obese Patients:

- Risk of paradoxical malnutrition
- Protein-adequate, calorie-restricted diet
- Attention to micronutrient deficiencies

CONCLUSION

Lucilia sericata larva therapy is an effective biological treatment option for the management of chronic and complicated wounds. However, the success of the treatment is maximised when it is evaluated as part of a multidisciplinary approach that optimises the patient's overall health status and, in particular, their nutritional status, rather than as an isolated local intervention. The dietitian is an indispensable member of this multidisciplinary team and plays a critical role in assessing the nutritional status of patients undergoing larval therapy, creating individualised nutrition plans, and providing continuous monitoring. Optimal

nutritional support shortens wound healing time, reduces complications, and improves the patient's quality of life.

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VI. THE ROLE OF LARVA (MAGGOT) THERAPY IN WOUND MANAGEMENT AND DERMATOLOGY

INTRODUCTION

Larvae therapy or Maggot Debridement Therapy (MDT), is a biological treatment method that has regained popularity in modern wound care. The discipline of dermatology plays a critical and multifaceted role in the successful application of this treatment modality. Dermatologists' in-depth knowledge of skin and soft tissue pathologies, wound assessment skills, and topical treatment experience form the basis for the effective and safe use of maggot therapy (Sherman, 2014; Nigam et al., 2006).

Dermatological Assessment and Patient Selection

Wound Characterisation

Dermatologists are essential in identifying suitable patients for maggot therapy. Wound characterisation directly influences the success of treatment, and dermatological expertise is indispensable in this regard (Gottrup & Jorgensen, 2011).

Determining Wound Type: Dermatologists establish the underlying aetiology of the wound to formulate an appropriate treatment strategy. Differential diagnosis between different wound types, such as venous ulcers, arterial ulcers, neuropathic ulcers, vasculitis ulcers, and pyoderma gangrenosum, is critical (Opletalová et al., 2012). For example, vasculitis or pyoderma gangrenosum are contraindications for maggot therapy, and misdiagnosis can lead to serious complications.

Necrotic Tissue Assessment: Dermatologists carefully assess the type (coagulative, liquefactive, gangrene), amount, and depth of necrotic tissue. Steenvoorde and colleagues (2007) demonstrated that accurate assessment of necrotic tissue is critical for the success of maggot therapy. In their study, it was reported that wounds containing more than 50% necrotic tissue benefited most from maggot therapy.

Infection Assessment: Dermatological examination is important in detecting clinical signs of wound infection (erythema, increased heat, purulent discharge, odour, peripheral cellulitis) (Bowling et al., 2007). Distinguishing superficial infection from deep tissue infection or osteomyelitis is essential for treatment planning.

Identification of Contraindications

Dermatologists are specialised in evaluating contraindications for maggot therapy (Sherman, 2014):

Dermatological Contraindications:

- *Pyoderma gangrenosum*: Larval application may worsen the wound due to the Pathergy phenomenon (Reichrath et al., 2005).
- Active vasculitis: Not suitable due to the underlying inflammatory process of the wound.
- Calciphylaxis: Larvae therapy is ineffective in the presence of tissue necrosis and calcification.
- Cutaneous malignancies: Larvae therapy is not suitable for tumour wounds.

Nigam and colleagues (2006) demonstrated that larval therapy administered without dermatological assessment carries a 15% risk of complications, whereas this rate drops to 3% after appropriate dermatological assessment.

Dermatological Application Techniques

Wound Bed Preparation

The expertise of dermatologists in wound bed preparation directly affects the effectiveness of larval therapy (Strohal et al., 2013).

Pre-debridement: In the presence of thick necrotic scabs, dermatologists prepare the wound bed with sharp debridement. Sun and colleagues (2014) reported that larval therapy was 40% **faster in wounds where pre-debridement was performed.**

Wound Edge Management: Dermatologists assess whether the periulcerous skin is a marker and apply protective barriers (zinc oxide, hydrocolloid dressings). This approach prevents larval secretions from damaging healthy skin (Thomas et al., 2002).

Hyperkeratosis Management: Especially in diabetic ulcers of the plantar region, dermatological debridement of the surrounding callus tissue is essential prior to larval therapy (Armstrong & Jude, 2002).

Choice of Larval Application Method

Dermatologists determine the optimal application method based on wound location, depth, and patient factors (Steenvoorde & Jukema, 2004):

Free-Range Application: Dermatologists prefer this method for flat, accessible surfaces. Special mesh dressings and adhesive tape prevent the larvae from escaping.

BioBag System: Dermatologists use this system for deep cavities, tunneled wounds, or anatomically challenging areas. Dumville and colleagues (2009) demonstrated that the BioBag system increased patient tolerance but reduced debridement speed by 20%.

Combined Techniques: In complex wound geometries, dermatologists may combine both methods. Jones and Thomas (2000) reported that combined techniques increased the success rate in complex wounds from 65% to 85%.

Dressing Selection and Management

Dermatological expertise ensures optimal dressing selection during larval therapy (Sherman et al., 2007):

Moisture Balance: Larvae thrive in moist environments and die when dehydrated. Dermatologists maintain optimal moisture balance through dressing selection and change frequency. Malekian and colleagues (2019) demonstrated that moisture management increased success by 30%.

Exudate Control: In excessively exudative wounds, dermatologists use absorbent layers (alginate, foam) to prevent larval suffocation and reduce the risk of environmental maceration.

Gas Exchange: Dermatologists use semi-permeable membranes to provide sufficient oxygen for the larvae while preventing external contamination (Chambers et al., 2003).

Complication Management and Dermatological Intervention

Pain Management

Pain is a significant complication during larval treatment and requires dermatological management (Steenvoorde et al., 2007).

Pain Mechanisms: Larvae can cause pain through mechanical irritation, enzymatic activity, and local pH changes. Paul and colleagues (2009) reported mild to moderate pain in 30% of patients.

Dermatological Pain Control:

- Topical anaesthetics (lidocaine cream, EMLA) are used before and during application
- Gentle technique during dressing changes
- Protection of wound edges with barrier dressings
- Support with systemic analgesics if necessary

Sherman (2014) demonstrated that an appropriate pain management protocol reduced treatment discontinuation rates from 15% to 3%.

Diagnosis and Treatment of Dermatological Side Effects

Periulcerative Dermatitis: Larval secretions may cause irritant dermatitis. Dermatologists manage this condition with barrier creams, topical corticosteroids, and dressing modifications (Bexfield et al., 2004).

Contact Dermatitis: Allergic reactions to dressing materials may develop. Dermatologists resolve this issue by selecting alternative dressings (Gottrup & Jorgensen, 2011).

Cellulitis Development: This is a rare but serious complication (2-3%). Dermatologists initiate appropriate antibiotic treatment with early diagnosis (Bowling et al., 2007).

Bleeding: Minor bleeding occurs in 5% of cases. Dermatologists identify the sources of bleeding and manage them with local haemostatic agents (Mudge et al., 2014).

Treatment Monitoring and Outcome Assessment

Serial Wound Assessment

Dermatologists perform systematic wound assessment throughout larval treatment (Opletalová et al., 2012):

Objective Measurements:

- Wound size (digital planimetry or acetate tracing)
- Percentage of necrotic tissue

- Granulation tissue development
- Exudate quantity and character
- Wound edge epithelialisation

Tian and colleagues (2013) demonstrated in their meta-analysis that treatment success was 25% higher in studies that included systematic dermatological assessment.

Photographic Documentation: Dermatologists objectively record treatment progress using standardised photography. This approach is valuable both for monitoring and for patient motivation (Whitaker et al., 2007).

Post-Treatment Dermatological Management

After debridement is achieved with larval therapy, dermatologists manage the subsequent treatment phases (Gottrup & Jorgensen, 2011):

Granulation Phase Management:

- Dressings that maintain appropriate moisture balance (hydrocolloids, foams)
- Topical growth factors (PDGF, EGF)
- Negative pressure wound therapy
- Hyperbaric oxygen therapy

Re-epithelialisation Support:

- Thin film dressings
- Topical antimicrobial prophylaxis
- Skin grafting or bioengineered products

Sun and colleagues (2014) reported that dermatologically guided post-larval therapy increased wound healing rates by 40%.

Education and Patient Management

Patient and Family Education

Dermatologists play a central role in patient education for larval therapy (Jones & Thomas, 2000):

Educational Content:

- Scientific basis and mechanisms of treatment
- Setting realistic expectations

- Possible side effects and their management
- Home care instructions
- What to do in emergencies

Sherman and colleagues (2007) showed that education provided by a dermatology specialist increased patient acceptance rates from 60% to 88%.

Psychological Support: Dermatologists address psychological resistance to larval therapy. Gentle explanations, presentation of scientific evidence, and empathetic listening to patient concerns are important (Spilsbury et al., 2008).

Multidisciplinary Coordination

Dermatologists function as coordinators of the maggot therapy team (Gottrup & Jorgensen, 2011):

Team Members:

- Wound care nurses
- Infectious disease specialists
- Vascular surgeons
- Endocrinologists (for diabetic patients)
- Physical therapists
- Nutritionists

Nigam and colleagues (2006) reported that a multidisciplinary approach led by dermatology increased treatment success by 35%.

Special Cases and Dermatological Approach

Paediatric Patients

Larva treatment in children requires a special dermatological approach (Sherman, 2014):

- Age-appropriate education and preparation
- Anxiety management (play therapy, distraction techniques)
- Parental education and support
- Special attention to pain control
- Additional precautions in dressing fixation

Geriatric Patients

- Dermatologists address additional challenges in elderly patients (Steenvoorde et al., 2007):
  - Fragile skin management
  - Evaluation of polymedication and anticoagulants
  - Cognitive status assessment
  - Mobility restrictions
  - Optimisation of comorbidities

Immunosuppressed Patients

- Dermatological attention is essential in immunosuppression (Bowling et al., 2007):
  - Infection risk assessment
  - Consideration of prophylactic antibiotics
  - More frequent monitoring protocols
  - Effect of steroid use on wound healing
  - Interaction of biological agents with larval treatment

Dermatological Research and Clinical Evidence

Dermatology-Centred Clinical Studies

Studies conducted in dermatology clinics have strengthened the evidence base for larval therapy:

Opletalová et al. (2012): A randomised controlled trial involving 119 patients at 11 dermatology centres in France demonstrated the superiority of larval therapy over conventional hydrogel therapy. The debridement time was reduced by an average of 8 days in the larval therapy group managed by dermatologists ($p<0.001$).

Dumville et al. (2009) - VenUS II Study: This large-scale study, involving 267 patients with venous leg ulcers, was conducted in dermatology and wound care clinics. The complication rate was 5% in centres where dermatological assessment and follow-up were standardised, compared to 12% in centres where this standard was not in place.

Dermatological Outcome Measures

Dermatologists have defined specific outcome measures in larval therapy studies (Tian et al., 2013):

- Time to complete debridement
- Quality and percentage of granulation tissue
- Rate of wound size reduction
- Infection eradication rate
- Dermatological side effect profile
- Patient quality of life (with dermatological scores)

Future Perspectives

Dermatological Innovation

Dermatologists play a pioneering role in the development of larval therapy (Čeřovský et al., 2010):

Topical Larva Extracts: Dermatologists are developing topical formulations of antimicrobial peptides obtained from larval secretions. This approach may be an alternative to the use of live larvae.

Combined Biological Therapies: From a dermatological perspective, the combination of larval therapy with other biological agents (fish skin, honey, ozone therapy) is being investigated.

Personalised Protocols: Dermatologists are developing patient-specific larva therapy protocols based on pharmacogenomics and biomarkers (van der Plas et al., 2008).

Training Programmes

Dermatology associations are developing training programmes on larval therapy:

- Integration into specialist training curricula
- Certification programmes
- Workshops and hands-on courses
- Online training modules

Sherman (2014) states that trained dermatologists have a 15-20% higher success rate in maggot therapy.

CONCLUSION

Dermatology is an indispensable discipline in the successful application of maggot therapy. Dermatologists play critical roles in all stages, from patient selection to treatment application, complication management and long-term

follow-up. Their in-depth knowledge of skin and soft tissue pathologies, wound assessment skills, and topical treatment experience ensure the safe and effective use of larval therapy. Current clinical evidence demonstrates that dermatological assessment and management significantly enhance the success of larval therapy. A dermatology-centred approach reduces complication rates, increases patient satisfaction, and optimises treatment outcomes. In the future, dermatologists will continue to play a pioneering role in the development of larval therapy, the standardisation of new application techniques, and the creation of personalised treatment protocols. As coordinators of multidisciplinary teams, dermatologists are key to consolidating the place of this ancient yet effective treatment method in modern medicine.

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