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THE EFFECT OF CHEMOTHERAPY ON THE CONDITION OF THE ORAL CAVITY

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Abstract. *Chemotherapy remains one of the leading methods of cancer treatment, but its systemic cytotoxic effects often lead to a wide range of side effects, including significant damage to the oral cavity. The oral mucosa is particularly vulnerable to chemotherapy due to its high rate of cell turnover and active metabolic processes. The aim of this study was to determine the specific effects of chemotherapy on the oral cavity.*

Analysis of recent literature data shows that complications in the oral cavity caused by chemotherapy are multifactorial and include direct cytotoxic damage to epithelial cells, activation of inflammatory signaling pathways, oxidative stress, and impaired local immune defense. Oral mucositis has been shown to be the most common and clinically significant manifestation, often accompanied by xerostomia, oral microbiome dysbiosis, and secondary infectious complications. Elevated levels of pro-inflammatory cytokines, such as tumor necrosis factor alpha and interleukin-6, play a central role in the onset and exacerbation of mucosal damage, while decreased salivary secretion and secretory immunoglobulin A contribute to barrier function impairment.

The results of the study emphasize the dynamic nature of oral mucosal damage during chemotherapy and the importance of early detection of molecular and clinical markers of damage. A comprehensive assessment of the oral cavity should be considered an integral part of multidisciplinary care for cancer patients in order to reduce the severity of complications and improve treatment outcomes.

Keywords: *chemotherapy, oral mucositis, oral cavity, inflammatory markers, oral microbiome, cytotoxic toxicity.*

Introduction

Cancer is a serious threat to the health of modern humanity. In recent years, there has been an increase in the incidence of cancer. The global burden of this disease is predicted to increase in the coming years, mostly due to demographic shifts such as population growth and aging in various regions [1]. With the increase in cancer incidence, effective treatment of the disease and its complications has become a major challenge for both patients and healthcare professionals. The three most common methods of cancer treatment are surgery, chemotherapy, and radiation therapy [2, 3]. Chemotherapy is one of the main components of treatment, but along with its therapeutic effectiveness, it is accompanied by the development of side effects that affect various organs and systems. The oral mucosa is particularly vulnerable to cytostatic effects. It is characterized by a high rate of cell renewal, intense blood supply,

and constant interaction with the microbiota [4, 5, 6]. Damage to the oral cavity during chemotherapy not only worsens the quality of life of patients, but can also lead to interruption or reduction in the intensity of antitumor treatment.

One of the most common and clinically significant complications of chemotherapy is oral mucositis, which manifests itself as erythema, erosions, ulcers, pain syndrome, and an increased risk of secondary infections [7, 8]. According to recent studies, the incidence of mucositis in patients receiving chemotherapy can reach 40–80% depending on the type of malignancy, treatment regimen, and individual characteristics of the patient [9, 10, 11]. The pathogenesis of this condition is associated with a complex cascade of molecular events, including direct cytotoxic damage to epithelial cells, activation of pro-inflammatory cytokines, oxidative stress, and disruption of mucosal regeneration processes [12, 13, 14].

In addition to mucositis, chemotherapy is associated with the development of xerostomia, salivation disorders, changes in taste sensitivity, and pigmentation of the oral mucosa [15]. Decreased saliva secretion negatively affects natural defense mechanisms, contributes to changes in the microbial composition of the oral cavity, and increases the risk of candidiasis and bacterial complications [16]. In recent studies by Brnić, et al. (2025) [17], it is emphasized that dysbiosis of the oral microbiome plays an important role in the progression of mucosal lesions and may exacerbate chemotherapy-induced inflammatory processes.

In recent years, scientific literature has also shown considerable interest in studying functional and morphological changes in the oral cavity as markers of the systemic toxic effects of anticancer therapy. Yamada et al. (2023) [18] found that oral mucosal lesions may correlate with the severity of overall treatment toxicity and serve as predictors of other complications. This necessitates a comprehensive approach to assessing the condition of the oral cavity in patients receiving chemotherapy, with the involvement of dentists in a multidisciplinary team.

The aim of the study is to determine the specific effects of chemotherapy on the oral cavity.

Research results A summary of current scientific data shows that chemotherapy has a systemic and multilevel effect on the oral cavity, which is formed as a result of a combination of direct cytotoxic effects, impaired cell regeneration, immune shifts, and changes in microbiological homeostasis. The oral mucosa is one of the tissues most sensitive to the effects of cytostatic drugs, due to the high rate of epithelial cell proliferation, intense metabolic processes, and constant exposure to mechanical, chemical, and microbial factors [6, 19]. In this context, oral lesions are considered not as isolated local manifestations, but as an important component of the overall toxicity of antitumor therapy.

One of the leading and most studied manifestations of the effects of chemotherapy on the oral cavity is oral mucositis. According to the results of systematic reviews and clinical studies, mucositis occurs in a significant proportion of patients receiving chemotherapy, with its frequency and severity depending on the type of malignant neoplasm, treatment regimen, and individual characteristics of the body [3, 9, 10, 11]. The development of mucositis is caused by a disruption in the normal cycle of mucosal epithelial renewal, leading to thinning, loss of barrier function, and increased susceptibility to damage [13].

The pathogenesis of chemotherapy-induced oral mucositis is complex and multifaceted. In the initial stage, cytostatic drugs cause the formation of active oxygen species and direct damage to the DNA of mucosal cells, triggering a cascade of molecular reactions [11, 20]. Further activation of pro-inflammatory signaling pathways is accompanied by increased levels of cytokines such as tumor necrosis factor alpha (TNF-α), interleukin (IL)-1β, and IL-6, which enhance the inflammatory response and contribute to the progression of tissue damage. These processes lead to the formation of erosive-ulcerative defects, which clinically manifest as pain, bleeding, and an increased risk of secondary infections [8, 21, 22].

The pathophysiological mechanisms of oral mucosal damage during chemotherapy are multifaceted and include cytotoxic damage to the epithelium, activation of pro-inflammatory signaling pathways, and disruption of microbiological homeostasis [8, 11].

There are five stages of mucositis pathogenesis: initiation, intensification/activation, signal amplification, ulcer formation, and healing (Fig. 1) [13].

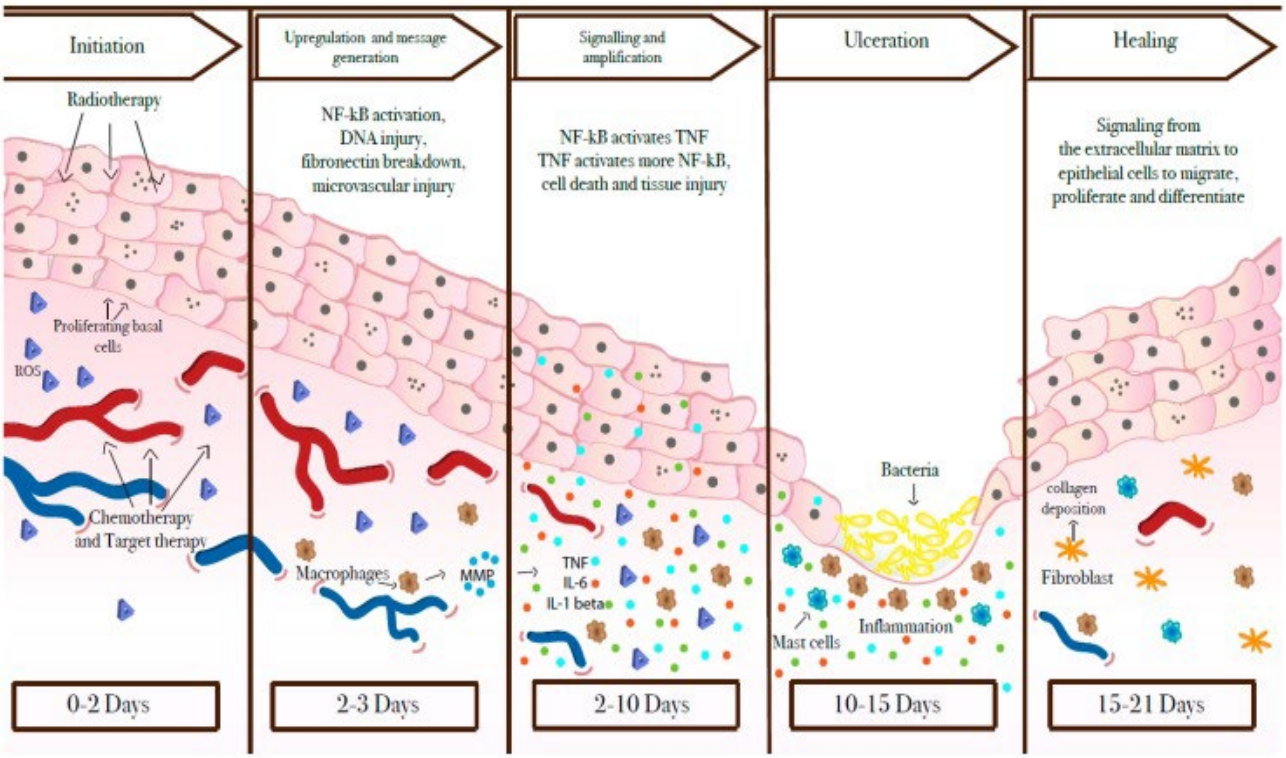

Figure 1 - Main stages of the pathogenesis of mucositis caused by chemotherapy [13]

The multiphase model of oral mucosal damage during chemotherapy presented in Figure 1 allows us to clearly trace the relationship between the molecular mechanisms of damage and the clinical manifestations of the pathological process. The initial phases of initiation and primary signaling are characterized by the predominance of subclinical molecular changes, in particular the formation of active oxygen species and the activation of transcription factors, which corresponds to an increase in the levels of proinflammatory cytokines without pronounced clinical symptoms. The subsequent phase of signal amplification is associated with the progression of the inflammatory response and the formation of clinically significant lesions of the mucous membrane, including erythema, pain, and disruption of epithelial integrity.

The next phase of ulcer formation is clinically significant. Scientists Basile, et al.

(2019) [13], Pulito, et al. (2020) [11], Salmaninejad, et al. (2025) [4] note that it is characterized by a high degree of mucosal damage, bacterial colonization, and the risk of infectious complications. The last phase of healing reflects the mucous membrane's ability to regenerate. Restoration of the normal barrier function of the oral cavity is possible with a reduction in cytotoxic load and inflammatory processes.

The clinical significance of oral mucositis is determined not only by the severity of local manifestations, but also by its impact on the general condition of patients. Intense pain in the oral cavity significantly complicates the intake of food and liquids, which can contribute to the development of nutritional deficiency and deterioration of general well-being. In severe cases, mucositis causes dose adjustments or temporary discontinuation of chemotherapy, which negatively affects the effectiveness of cancer treatment [19, 23, 24].

Along with structural damage to the mucous membrane, chemotherapy causes significant functional disorders of the oral cavity. One of the most common functional disorders is xerostomia, which occurs as a result of decreased secretory activity of the salivary glands or changes in the neurohumoral regulation of salivation [23]. A decrease in the amount and change in the composition of saliva leads to a disruption of its buffering, antibacterial, and remineralizing properties, which negatively affects the protective mechanisms of the oral cavity.

Decreased salivation is closely related to the development of inflammatory processes and infectious complications. In conditions of xerostomia, the adhesion of microorganisms to the surface of the mucous membrane increases, which contributes to the colonization of conditionally pathogenic microflora and the formation of dysbiotic changes [16]. It is the disturbance of the microbiological balance of the oral cavity that is an important factor that not only accompanies mucositis but can also exacerbate its course and slow down healing processes [8, 17].

Changes in the oral microbiome during chemotherapy are considered to be the result of a combination of several mechanisms, including immunosuppression, damage to the mucous membrane, and changes in the chemical composition of saliva. An increase in the number of Candida fungi and Gram-negative bacteria is associated with

an increased risk of developing candidal stomatitis and bacterial complications, especially in patients with neutropenia [11]. It is microbiological changes that play a key role in the formation of the clinical picture of oral lesions during chemotherapy.

In addition to inflammatory and functional disorders, patients receiving chemotherapy may experience morphological and pigment changes in the oral mucosa. In particular, there have been reports of hyperpigmentation of the mucous membrane associated with the activation of melanocytes or the accumulation of drug metabolites in tissues [18]. Although such changes do not usually have malignant potential, they can cause psychological discomfort and require differential diagnosis with other pathological conditions.

Structural, functional, and microbiological disorders of the oral cavity during chemotherapy are of great clinical importance. They can be a gateway for systemic infections, which negatively affects the course of cancer. Patients with severe forms of mucositis and pronounced xerostomia require special attention. They are at high risk of developing complications. This indicates the need for early detection of oral lesions and preventive and therapeutic measures at all stages of chemotherapy [24, 25, 26].

The results of modern scientific studies on the main disorders of the oral cavity associated with chemotherapy, their clinical manifestations, and pathophysiological markers are presented in Table 1, which allows systematizing the available data and assessing their clinical significance.

Table 1. Major oral cavity disorders associated with chemotherapy

Disorder	Clinical manifestations	Pathophysiological markers
Oral mucositis	Erythema, erosions, ulcers, pain syndrome	Increased expression of proinflammatory cytokines (TNF-α, IL-6), oxidative stress
Xerostomia	Dryness, dysphagia, speech impairment	Decreased salivation and secretory IgA levels
Dysbiosis	Candidiasis, bacterial infections	Increased content of conditionally pathogenic microflora
Pigmentation of the mucous membrane	Local or diffuse hyperpigmentation	Activation of melanocytes

Source: compiled by the author based on [6], [8], [11], [13], [16], [17], [18], [23]

Analysis of the data presented in Table 1 allows us to identify a hierarchy of markers of oral mucosal damage during chemotherapy. Proinflammatory cytokines, in particular TNF-α and IL-6, can be considered as primary markers of toxic damage, directly reflecting the activation of the inflammatory cascade and the degree of cytotoxic effect of antineoplastic drugs [8, 11]. Changes in the level of secretory IgA and the development of oral dysbiosis should be interpreted as secondary markers that form against the background of a violation of the barrier function of the mucous membrane and a decrease in local immune protection [16, 17]. Pigment changes in the mucous membrane, in turn, have a different pathogenetic nature and are not directly associated with the intensity of the inflammatory response, which allows them to be considered as an epiphenomenon of the general toxicity of chemotherapy, rather than as a marker of active damage to the mucous membrane [18].

Lesions of the oral cavity during chemotherapy are systemic in nature and are formed as a result of interrelated pathophysiological processes. Oral mucositis occupies a leading place among them, characterized by the most pronounced clinical manifestations and associated with the activation of pro-inflammatory cytokines and the development of oxidative stress [6, 8, 11]. Elevated levels of TNF-α and IL-6 reflect the intensity of the inflammatory response of the mucous membrane and correlate with the severity of erosive and ulcerative lesions, confirming the key role of the inflammatory cascade in the pathogenesis of mucositis.

An important component of the lesions is changes in the oral microbiome, which are reflected in an increase in the number of conditionally pathogenic microflora and the development of candidal and bacterial complications [16, 17]. Dysbiosis is not an isolated phenomenon, but acts as a pathogenetic factor that maintains inflammation of the mucous membrane and can slow down its repair processes. Microbiological changes should be considered an important link in the formation of chronic oral lesions during chemotherapy.

Thus, disturbances in the normal state of the oral cavity during chemotherapy are a multifactorial process. Inflammatory, functional, and microbiological disorders contribute to the development of these disorders. This requires a comprehensive

approach to the assessment and management of patients. The generalized data obtained emphasize the advisability of early detection of changes in the oral cavity and the implementation of preventive measures to reduce the severity of chemotherapy complications. The results of the review analysis indicate that oral cavity lesions during chemotherapy are complex and multifactorial in nature and are formed as a result of a combination of direct cytotoxic effects of antineoplastic drugs, inflammatory reactions, disorders of mucosal regeneration, and changes in microbiological homeostasis. A summary of current data confirms that the oral mucosa is one of the most vulnerable targets of chemotherapy, which is consistent with the results of previously published systematic reviews and clinical observations [6, 11].

Oral mucositis occupies a leading place among oral cavity lesions and is considered a key clinical manifestation of chemotherapy toxicity. The literature suggests that the development of mucositis is caused by a disruption of the cellular homeostasis of the mucosal epithelium, activation of pro-inflammatory signaling pathways, and increased oxidative stress [8, 11, 14]. In this context, elevated levels of cytokines such as TNF-α and IL-6 can be considered not only as a marker of inflammatory response, but also as a potential indicator of the severity of lesions. Similar mechanisms of mucositis pathogenesis are confirmed by the results of other studies, which emphasizes the universality of the inflammatory cascade in different chemotherapy regimens [7].

Changes in the oral microbiome observed in patients receiving chemotherapy play a significant role in maintaining and exacerbating oral lesions. Dysbiotic shifts, in particular an increase in the proportion of opportunistic bacteria and fungi, are associated with an increased risk of developing candidiasis and secondary bacterial complications [16, 17]. The generalized data obtained are consistent with the modern concept that the oral microbiome is not a passive participant in the pathological process, but actively influences the course of inflammation and the rate of reparative processes in the mucous membrane.

Special attention should be paid to morphological and pigmentary changes in the oral mucosa, which, although not accompanied by a pronounced inflammatory

reaction, are clinically and psychologically significant [18]. Hyperpigmentation of the mucous membrane can cause anxiety in patients and requires differential diagnosis with precancerous and pigmented lesions of other etiologies. This emphasizes the need for a thorough dental examination of patients at all stages of antitumor treatment.

From a clinical point of view, oral lesions during chemotherapy have a significant impact on the course of the underlying disease and treatment outcomes. Severe inflammatory changes, pain, and infectious complications can limit the ability to perform full chemotherapy, forcing doctors to adjust doses or temporarily suspend treatment. In this context, early detection and prevention of oral complications are important components of a multidisciplinary approach to the management of cancer patients.

Conclusions

Current scientific data show that chemotherapy has a complex negative effect on the oral cavity. This effect is manifested through a combination of cytotoxic damage to the mucous membrane, activation of inflammatory mechanisms, and disruption of local protective factors. The main clinical manifestations of chemotherapy are induced oral lesions, such as oral mucositis, xerostomia, and infectious complications, which significantly reduce the quality of life of patients and can affect the course of antitumor treatment. The main pathogenetic links in these changes are the activation of pro-inflammatory cytokines, the development of oxidative stress, and dysbiotic disorders of the oral microbiome. The data obtained indicate the need for a comprehensive assessment of the oral cavity and early detection of markers of damage. This may help reduce the severity of chemotherapy complications.

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