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FEATURES OF DIAGNOSIS, TREATMENT AND PREVENTION OF CHEILITIS IN THE FAR NORTH

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CONTENT

INTRODUCTION

Relevance of the study

Cheilitis is a general term describing inflammation of the lips. The disease can manifest itself as an independent nosology or as a symptom of certain systemic acute or chronic diseases (Galchenko V.M., Likhtarnikova E.A., 2021; Sharapkova A.M., Zykova O.S., 2022; Rushworth B., Kanatas A., 2023; Borisova E.G., 2023).

Lips are an aesthetically significant component and the central defining feature of the lower face. The red border differs from the surrounding skin due to its pink hue, the appearance of the lips has a great influence on the aesthetic perception of appearance. Lip diseases cause unpleasant and painful sensations when eating, smiling, talking, can affect the patient's self-esteem, bring not only physical but also psychological discomfort, as well as some inflammatory lip diseases are precancerous and have a risk of malignancy (Gmoshinsky I.V., Nikityuk D.B. 2022, Ponomarev V.V., 2021, Ulyanovskaya S.A., Bazhenov D.V., Shestakova V.G., Kalinkin M.N., 2019)

The region of the Far North, located north of the Arctic Circle, belongs to the Arctic zone of the Russian Federation, which ensures the national security of the country. The relevance of research on improving the quality of life and health of the population of the Far North of the Russian Federation is increasing every year, as the region has important geopolitical and geo-economic importance for the country. The development of the territories of the Far North supports economic stability, protection of state borders, and is a source of natural resources. According to Decree of the President of the Russian Federation No. 645 dated October 26, 2020 "On the Strategy for the Development of the Arctic Zone of the Russian Federation and ensuring national security for the period up to 2035", ensuring the approval of standards and improving the provision of medical care to the population of the Far North is one of the main directions of socio-economic development of the Arctic zone of the Russian

Federation (Bardin M.Yu., Lipka O.N., 2021, Lyshko A.S., Medvedev S.O., Zyryanov M.A., 2021, Guseynova E.D., 2022).

Due to the poor barrier function and low moisture retention capacity, the lips are very sensitive to the effects of adverse environmental factors. Climatic and geographical features of the north negatively affect not only the vitamin status and metabolism, accompanied by processes of free radical oxidation and restructuring of the neuroendocrine link (Ulyanovskaya S.A., Bazhenov D.V., Shestakova V.G., Kalinkin M.N., 2020), but also the condition of the skin, including the most vulnerable – the skin of the lips.

The most common forms of cheilitis in the Far North include primarily meteorological cheilitis and chronic recurrent lip crack, which are facultative precancerous diseases. In the structure of epidemiology, contact, atopic forms of cheilitis are also observed with high frequency (Borisova E.G., 2023, Balashova S.N., Samodova A.V., Belisheva N. K., 2020, Zyryanov B.N., 2021).

The degree of elaboration of the research topic

According to Russian and foreign literature, little attention is paid to the study of methods of diagnosis and treatment of various forms of cheilitis. Basically, the largest number of scientific papers in the literature is devoted to actinic, exfoliative and glandular cheilitis. In addition, there are currently no clinical recommendations for doctors on the diagnosis, treatment and prevention of various forms of cheilitis, despite the fact that some forms are precancerous and have a risk of malignancy. Most often, doctors limit themselves to local symptomatic treatment, not paying attention to general somatic therapy, the study of the immune and vitamin status of the patient, bacterioscopic examination of the affected tissues. There is also practically no data in the literature on meteorological cheilitis, which is most characteristic of a cold climate. The principle of classification of chronic recurrent lip fissure has not been developed, on the basis of which therapeutic and preventive measures would be proposed in accordance with the severity of the course. The problems devoted to the peculiarities of treatment and prevention of various forms of

cheilitis in the conditions of the Far North, including the Arctic zone, have not been previously touched upon in research. Based on the above, the goals and objectives of this study were formed.

The purpose of the study

To identify the clinical and functional features of the course of cheilitis and optimize the treatment and prevention of various forms of this disease in the Arctic zone of the Far North.

Research objectives

1) To analyze the structure of the incidence of various forms of cheilitis in residents of the regions of the Arctic zone of the Far North.

2) On the basis of clinical and laboratory research methods, to evaluate the influence of adverse factors of the Arctic zone of the Far North on the antioxidant and vitamin status of patients with various forms of cheilitis in order to optimize diagnosis.

3) To form an algorithm for the complex treatment of the most common forms of cheilitis in the conditions of the polar region of the Far North.

4) To improve methods of prevention of the most common forms of cheilitis in the conditions of the polar region of the Far North.

Scientific novelty of the dissertation research

• The structure of the incidence of various forms of cheilitis in the population of the polar region of the Far North has been analyzed for the first time.

• A questionnaire of interest in the treatment of patients with chronic lip fissure has been developed.

• A classification of chronic recurrent lip crack by severity has been developed, and an algorithm for the treatment of this nosology has been proposed based on severity.

• The algorithm of etiopathogenetic treatment and prevention of inflammatory lip diseases in the Arctic zone of the Far North is proposed.

Theoretical significance. Based on clinical and laboratory research methods, the dependence of the severity of the course of various forms of cheilitis on adverse environmental factors in residents of the Subarctic climate has been established, and the provocative role of high latitudes in the development and/or course of cheilitis has been determined.

The developed questionnaire of patient interest and the proposed classification in the treatment of chronic lip fissure can determine the treatment tactics of a particular patient, depending on the degree of the clinical picture and its test results. Within the framework of this study, a classification of chronic lip fissure by its localization has been developed.

Practical significance. Based on the conducted research, the need for the use of complex glucocorticoid drugs and photobiomodulation in the treatment of inflammatory lip diseases in the Far North is substantiated. The necessity of using vitamin E, D and antioxidant group preparations in the complex treatment of cheilitis in the Far North is substantiated.

The developed and proposed algorithm for the treatment of the most common forms of inflammatory lip diseases in the Far North helps to reduce the duration of treatment of patients and determine ways to increase the effectiveness of preventive measures in order to increase the duration of remission.

Comprehensive dental rehabilitation of patients with inflammatory lip diseases should take place within the framework of interdisciplinary cooperation between dentists and internists.

Methodology and methods of dissertation research

The methodology of this dissertation is based on the use of empirical and theoretical methods of scientific cognition. The dissertation was carried out in the design of a statistical and randomized open controlled trial using clinical and laboratory methods.

The objects of this study were 117 patients aged 18 to 55 years, living in the Murmansk region for more than three years, with diagnoses: chronic recurrent lip

crack (34 people, 29.6%), meteorological cheilitis (39 people, 33.33%), angular cheilitis (14 people, 11.97%), atopic cheilitis (7 people, 5.98%), exfoliative cheilitis (7 people, 5.98%), 16 people, 13.68%, had a clinical picture of chronic lip crack complicated by meteorological cheilitis. All the subjects were somatically healthy or practically healthy, without signs of acute infectious and non-communicable diseases, and had no history of severe chronic diseases.

Exclusion criteria: age under 18 and over 55 years, endocrine diseases, diseases of the cardiovascular and hematopoietic systems, a psychiatric and narcologically burdened history, type 1 and 2 diabetes mellitus, HIV infection, hepatitis B, C, malignant neoplasms, pregnancy and lactation, the use of drugs: hormonal contraceptives, anabolic steroids, medications or biologically active vitamin D3 supplements. The exclusion criteria were also: patients at risk of hypercalcemia (renal failure, sarcoidosis, etc.), the use of local retinoids, patients participating in other studies. On the basis of Article 20 of Federal Law No. 323-FZ dated November 21, 2011 "On the basics of Public Health protection in the Russian Federation", as well as the order of the Ministry of Health of the Russian Federation dated November 12, 2021. No. 1051n "On approval of the procedure for giving informed voluntary consent to medical intervention and refusal of medical intervention, the form of informed voluntary consent to medical intervention and the form of refusal of medical intervention" before the start of the study, all patients signed a voluntary informed consent to medical intervention, including participation in the study. The subjects were familiarized with all aspects of the study, the purpose and objectives of the study, research methods were explained to them, general and topical medications were described in detail, patients were informed about the treatment regimen, alternative options, and expected risks. The safety criteria and adverse/adverse event reporting reflect all adverse events that may have occurred during the study. All results were documented in the study records, including treatment details, the list of prescribed drugs and their frequency of use, the nature of side effects, the date and time of the onset of an adverse reaction, duration, severity, result and association with

prescribed drugs during the study. Patients were advised to contact researchers immediately about any adverse events requiring medical attention..

Throughout the entire time, there was not a single written or oral refusal of the patient to participate in the dissertation research, no development of adverse events and adverse reactions to treatment was observed, and cases of non-compliance with the inclusion/exclusion criteria were not established during the entire study.

In the course of the dissertation research, the following were conducted: a survey, anamnesis collection, dental examination, patient questioning, examination of medical records, a procedure for taking biological material, a smear from the depth of a lip crack and blood from a vein, laboratory diagnostics and analysis of the vitamin status of patients, indicators of the antioxidant protection system. In patients with chronic recurrent lip fissure, bacteriological and microscopic examination of the smear of the affected lip tissues was additionally performed. General and local treatment has been prescribed, and the tactics of preventive measures have been determined. Clinical research methods were carried out in the polyclinic of the branch No. 3 of FSGI "1469 NCH" of the Ministry of Defense of the Russian Federation (Murmansk)**.**

Main scientific results

1. Inflammatory diseases of the lips in subarctic climates have a high prevalence among the population and require an individual, comprehensive approach in drawing up an etiopathogenetic treatment plan [47, pp. 54]. The results were published in [47]. Personal participation of the author in obtaining these results: collecting literature data, interpreting the results, writing the article.

2. Based on literary sources studying exogenous factors of the Far North, which negatively affect human health, it was established that the effects of not only low temperatures, traumatic aerodynamic conditions, and a deficiency of ultraviolet radiation, but also geomagnetic field stress, microelement shift, fluctuations in atmospheric pressure levels are aggravating factors in the course of inflammatory diseases of the lips [20,49, pp. 30]. The best results in the treatment of cheilitis were

achieved by prescribing combined ointments based on glucocorticoids and antibacterial/antifungal components in combination with physiotherapeutic procedures. The results were published in [20,49]. Personal participation of the author in obtaining these results: collecting literature data, interpreting the results, writing the article.

3. Vitamin D deficiency is a widespread problem among the population of the Arctic zone of the Far North. The study found that in the conditions of the Far North, one of the mandatory components of the prevention and pathogenetic therapy of cheilitis should be vitamin therapy with colecalciferol preparations [17, pp. 58]. The results were published in [17]. Personal participation of the author in obtaining these results: clinical study, interpretation of results, writing the article.

The materials of the dissertation were presented at the All-Russian scientific and practical conference "Theoretical and practical issues of clinical dentistry" (St. Petersburg, 2021), "Theoretical and practical issues of clinical dentistry" (St. Petersburg, 2023), the IV International Scientific and Practical Conference "Actual problems of dentistry" (St. Petersburg, 2023 G.). The main provisions of the dissertation were reported and discussed at a joint meeting of the Departments of General Dentistry, Maxillofacial Surgery and Surgical Dentistry, physical and rehabilitation Medicine of the Military Medical Academy named after S.M. Kirov (St. Petersburg, 2024).

The results of the dissertation research are used in the educational, scientific and therapeutic process of the Department and Clinic of General Dentistry of the Military Kirov Medical Academy, as well as in the medical work of dental departments and offices of branches of FSGI "1469 NCH" of the Ministry of Defense of the Russian Federation.

8 publications have been published on the topic of the dissertation, 5 of them in publications included in the List of Russian peer–reviewed scientific journals recommended by the Higher Attestation Commission, in which the main scientific results of dissertations for the degrees of doctor and candidate of Sciences should be published. Applications for inventions have been submitted: No. 2024107922

"Questionnaire of patients' interest in the treatment of chronic lip fissure (QIT-CLF)", No. 2024107917 "Lip cosmetic, balm "Elabium".

The main results and provisions of the dissertation research are presented in the publications:

1. Borisova, E.G., Isaeva, L.I. Etiopathogenetic aspects of meteorological cheilitis in the conditions of the Far North // Medical and pharmaceutical journal Pulse. 2022. Vol. 24. No. 12. pp. 111-116.

2. Isaeva, L. I., Borisova, E.G. Etiopathogenetic treatment of chronic median fissure of the lower lip in a subarctic climate// Pulse Medical and Pharmaceutical journal. 2023. Vol. 25. No. 1. pp. 5-11.

3. Borisova, E.G., Isaeva, L.I., Khrustaleva, Yu. A. Dependence of the frequency of recurrence of cheilitis on the level of vitamin D // Applied information aspects of medicine. 2023. Vol. 26. No. 3. pp. 60-66.

4. Borisova, E.G., Isaeva, L.I. Methods of diagnosis of contact cheilitis in the population of the Far North // Medical and pharmaceutical journal Pulse. 2023. Vol. 25. No. 9. pp. 4-9.

5. Isaeva, L. I., Borisova, E.G., Khrustaleva, Yu.A. Methodological principles of treatment of cheilitis in the Far North // Problems of dentistry. 2023. Vol. 19. No. 3. pp. 53-57.

6. Nikitenko, V.V., Kovalevsky, A.M., Isaeva, L.I. The effect of oxidative stress on the condition of periodontal tissues in residents of the Far North // Theoretical and practical issues of clinical dentistry: Materials of the All-Russian Scientific and Practical Conference, St. Petersburg, October 07-08, 2021 / edited by V.V. Nikitenko, V.A. Zheleznyak. – St. Petersburg: Military Medical Academy named after S.M. Kirov, 2021. pp. 123-126.

7. Isaeva, L.I., Borisova E.G. Chronic lip cracks: a modern approach to diagnosis and treatment // Actual problems of dentistry: collection of articles of the IV International Scientific and practical Conference, St. Petersburg, November 24, 2023. – St. Petersburg: St. Petersburg State University, 2023.

8. Isaeva, L. I., Borisova, E.G., Pototskaya, A.V. Improvement of diagnostic methods for contact cheilitis // Theoretical and practical issues of clinical dentistry: Proceedings of the All-Russian Scientific and Practical Conference, St. Petersburg, 05-06 October 2023. – St. Petersburg: Military Medical Academy named after S.M. Kirov, 2023. pp. 19-21.

According to the research topic, the dissertation conducted an analysis of foreign and domestic sources of specialized literature. In the course of the work, the author personally conducted a clinical dental examination of 117 patients. The results of laboratory and microbiological studies are analyzed, on the basis of which statistical data processing is performed. An algorithm for the treatment and prevention of patients with inflammatory lip diseases in the subarctic climate of the Far North has been developed. The conclusions of the study are formulated and practical recommendations for dentists are given. In conducting anamnesis collection and statistical research, the share of participation of the dissertation was 100%, in laboratory research, the share of participation of the dissertation was 85%, in clinical research 100%, statistical data processing 95%.

The provisions and conclusions formulated in the dissertation work are reliable, justified and directly follow from the results of research and statistical processing of materials. The theory is based on well-known verifiable data and facts using 195 scientific literature sources, with which the results of the dissertation research are consistent. All data was entered into an Excel spreadsheet and statistical analysis was performed. The data were reflected as the mean ± standard deviation for continuous variables, as the median, as a percentage in determining the proportion of relapses in groups. The Student's t-test was used to statistically test the hypothesis. The value of $p<0.05$ was considered statistically significant. Based on the results obtained, an algorithm was developed for the etiopathogenetic treatment and prevention of various forms of cheilitis in people living in the Arctic zone of the Far North.

Provisions to be defended

1. The developed classification of the severity of chronic recurrent lip crack and the results of the questionnaire of interest determine the choice of treatment algorithm in the subarctic climate of the polar region of the Far North.

2. Etiopathogenetic complex treatment of inflammatory lip diseases in the Far North consists in weakening the effects of adverse environmental factors using agents that affect tissue metabolism and have antihypoxic and membrane protective effects in combination with local therapy, which leads to normalization of clinical, functional and laboratory parameters.

3. The use of vitamin D in the complex therapy and prevention of inflammatory lip diseases in the Arctic zone of the Far North contributes to rapid healing and reduction of cases of recurrence of meteorological cheilitis and chronic recurrent lip fissure.

4. The system of developed preventive measures will help reduce the incidence of such precancerous lip nosologies as chronic lip fissure and meteorological cheilitis.

CHAPTER I. INFLAMMATORY DISEASES OF THE LIPS. FEATURES OF THE CURRENT IN THE CONDITIONS OF THE FAR NORTH (literature review)

1.1. Anatomical and histological structure of the lips

From the point of view of aesthetics, lips are an anatomical component of a smile and the appearance of the face as a whole [61]. If we summarize the information about the structure of the lips, we can conclude that first of all these are two skin-muscle folds, which are a horizontally positioned entrance to the vestibule of the cavity. By musculoskeletal folds, we mean the upper and lower lips connected at the corners of the mouth opening by means of commissures. The basis of the anatomical structure of the lips is formed by the circular muscle of the mouth. The skin of the lips consists of 3 parts, depending on the histological structure of the epithelium. The skin part is a multilayer flat keratinizing epithelium originating from the ectoderm, and characteristic of the skin of the epidermis. The intermediate part (the red border of the lips) is a multi–layered flat non-corneating epithelium. And the mucous part of the lips is the ectodermal epithelium, which is characteristic of the oral mucosa [60,63,164]. Thus, the lips consist of: the skin part, the intermediate part (red border) and the mucous part. Anatomically, the cutaneous part of the upper lip along the median line forms a labial groove that adjoins the tubercle of the upper lip. On the side of the oral cavity, at the junction of the upper or lower lip with the transitional gum, there is a sagittal – median fold – frenulum of the upper or lower lip, cheeks are located laterally to the lips, forming the anterior surface of the horseshoe-shaped mouth vestibule. The vestibule of the oral cavity is limited from behind by the vestibular surface of the teeth and the mucous membrane of the alveolar processes of the upper and lower jaws. From the outside, the lips border on the buccal and chin areas. From the buccal region, the lips are limited by the nasolabial furrow. And from the chin area, the lips are limited by the chin-labial furrow. The shape and mobility of the lips is determined by the striated skeletal

muscle tissue of the circular muscle of the mouth, which is located in the thickness of the lips [21, 44, 88].

The lip of the cutaneous part is similar in structure to the skin of a multilayer flat keratinizing epithelium, containing sebaceous, sweat glands and hair follicles [18]. The muscle bundles of the circular muscle of the mouth are woven into the skin of the commissariat, the fibers of the muscles that lower and raise the corner of the mouth are attached to the right and left to the skin of the commissariat of the lips. Mimic muscle fibers enter the dermis, participating in facial mimic activity [96].

The red border of the lips forms an intermediate part in the anatomical structure of the lip and is the transition of the skin into the mucous membrane. In the structure of the red border of the lips, in the presence of sebaceous glands, there are no sweat glands, hair follicles. On the surface of the multilayer flat keratinizing epithelium of the red border of the lips, the excretory ducts of single sebaceous glands open. The epithelium has a thin stratum corneum, a well-defined granular layer and a large quantity of free and encapsulated receptor nerve endings, as well as mechanoreceptors (Meissner corpuscles, which have the highest sensitivity), Krause flasks (cold receptors) [20].Dermis layer has a transition into its own mucosal plate containing a cell population and fibers of loose connective tissue. The red border of the lips is devoid of a stratum corneum and a network of glands that provide hydration, a vascular network is superficially located on the entire area of the transitional part, which causes a bright color [88,96,150].

On the side of the oral cavity, in the area of the vestibule, the mucous part of the lip is covered with a multi-layered flat non-corneating epithelium, under which there is its own plate of the mucous membrane. In literary sources, the transition zone of the red lip border into the mucous membrane is called Klein [18]. The Klein zone, according to its anatomical structure, passes into the mucous membrane of the gums. In the area of the incisors of the upper and lower jaw there are median vertical folds, frenules. There are muscle bundles and loose connective tissue in the thickness of the lips. Under the multilayer flat non-corneating epithelium, its own connective tissue plate is determined, in which papillae of various sizes are formed. A characteristic

feature of the mucous membrane is the presence of a submucosal layer [47,55,63]. During histological examination, it visualizes: an abundance of blood vessels, adipose tissue with the terminal sections of the labial glands. The histological structure of the labial glands determines two types of secretory departments: complex alveolar-tubular with elongated mucous tubules and rounded mixed-protein, in the cells of which there are many secretory granules. In the area of the terminal sections of the labial glands there is a loose fibrous connective tissue with a neuromuscular network and a characteristic cell population [62,63,96].

1.2. Classification and etiopathogenetic characteristics of various forms of cheilitis

Cheilitis is a general term for various types of inflammatory diseases of all parts of the lip: cutaneous, transitional and mucous. More than a dozen lip diseases of various etiologies, diverse clinical manifestations and pathological features have been studied and described in domestic and foreign literature. Inflammation of the lips can be affected by men and women, all ages, lifestyle, and the nature of work, heredity, and concomitant diseases play a role in the development of some nosologies [20,116]. This nosology presents difficulties in clinical practice, both in differential diagnosis and in treatment, and is one of the most difficult sections of therapeutic dentistry. A feature of the pathology is its polyethologicity, characterized by periods of remission and exacerbation. Inflammatory diseases of the lips include many clinical forms, cheilitis can be both independent diseases of the lips (exfoliative, glandular, actinic, contact and meteorological cheilitis), and can also manifest as one of the symptoms of a systemic disease (eczematous, cheilitis caused by hypovitaminosis, atopic, plasmocellular macroheilitis). This classification is widely used in Russian literature [18].

According to the International Classification of Diseases (ICD-10), lip diseases are assigned the code K13 — other diseases of the lips and oral mucosa [29,180]:

K13.0 — lip diseases

K13.00 — angular cheilitis, cleft lip adhesions (congestion)

K13.01 — granular apostematous cheilitis

K13.02 — exfoliative cheilitis

K13 03 — heilit without additional clarifications

K13.04 — cheylodynia

K13.08 — other specified lip diseases

K13.09 — unspecified lip disease

K13.1 — cheek and lip biting

The classification of cheilitis according to the ICD system is quite abstract, and in the practice of a doctor it is uninformative.

Some forms of cheilitis have a risk of malignancy, the cause of precancerous diseases may be adverse effects of environmental factors or body conditions, lack of treatment for chronically occurring forms of cheilitis. In 1970, A.L. Mashkillayson developed a classification of precancerous diseases of the lips and oral mucosa [16,60,104]. Due to the relevance of the study and the direct connection of cheilitis with precancerous lip diseases, the classification according to the research topic is given below.

Classification of precancerous lip diseases

(Mashkillayson A. L., 1970)

1. Obligate precancerous diseases:

– abrasive precancerous cheilitis of Manganotti,

– limited precancerous hyperkeratosis.

2. Facultative precancerous diseases:

– flat, verrucose and erosive leukoplakia,

– skin horn,

– keratoacanthoma,

– chronic ulcers of the oral mucosa,

– chronic lip cracks,

– post–X-ray cheilitis,

- meteorological and actinic cheilitis.

However, there is a drawback in the above classifications: the classification of cheilitis as an independent disease does not include granulomatous Mischer's cheilitis.

1.3. Territorial boundaries of the Far North region in relation to the research topic

The list of regions of the Far North established by law is fixed in order to provide guarantees and compensations for workers and residents in these territories and is important for the socio-economic development of regions remote from the European part of Russia, ensuring the development of natural resources deposits, improving oil and gas production complexes and mining enterprises, ensuring the security of the country through the basing of military strategic facilities and the organization of border service, living in these territories does not pass without a trace for human health [11,36, 78,110]. Despite the comprehensive impact of adverse environmental factors, the Far North is a strategically important territory of the Russian Federation, where the Northern Sea Route passes, oil producing enterprises and large deposits of natural resources are located. Interdisciplinary studies of the Arctic, based on the concept of coupled human and natural systems, were conducted by Russian authors at different times, but these studies were isolated on a relatively small scale [40,66,68]. With a deeper study of the territorial features of the Far North, according to the List, not only an extremely large spread of territories and a mismatch of geographical localization with the transition to more southern latitudes (up to 50 ° north latitude), but also the heterogeneity of natural and climatic conditions is determined [111]. The problem-oriented approach to understanding the term "Far North" in the field of medicine corresponds to the physical, geographical and climatic criteria of the Arctic region (the Arctic zone of the Russian Federation). From the

point of view of physical geography, landscape, geobotanical criteria, the only logically correct area related to the regions of the Far North are territories in latitudes north of the Arctic Circle or from 66°33'44" north latitude and above [10,31,32,121]. In relation to this study, the term "Far North" has an interpretation exclusively from the field of geography and corresponds to the territories located above the Arctic Circle, namely the strategically important Arctic zone of the Russian Federation.

About a quarter of the territory of the Russian Federation is located beyond the Arctic Circle in the Arctic zone, according to the characteristics of the climate in most of the territory is located in the subarctic zone. In conditions of atmospheric pressure fluctuations [53], oxygen deficiency [90], high humidity, strong winds, extremely low temperatures [54,66], magnetic field instability [114], prolonged frosty winter, desynchronosis due to polar days and nights [91,125], people living in northern latitudes form "polar metabolic type" [82,103,126].

1.4. Clinical manifestations and oncological alertness of dentists in diseases of the lips

In relation to the research topic, exogenous factors include the meteorological conditions of the Far North [35,81,113], endogenous factors are the result of the effects of climatic and geographical features on the human body, in addition to this, endogenous factors include the tendency of the lip skin to hyperkeratosis [16,83].

The lip epithelium is constantly in contact with environmental factors and is exposed to endogenous factors of the body. Cheilitis can be a diagnostic sign or a sign of the manifestation of general and local infectious and allergic diseases [135,156] or a symptom in Melkersson-Rosenthal syndromes [107], Plummer-Vinson, Mischer [187], Meije, HIV infection, tuberculosis [69,162], atopic dermatitis [59,149,192], erythematosis [148], psoriasis [39,69], inflammatory bowel diseases [28,130,160,170], COVID-19 [85,155], autoimmune diseases [183], anemia and hypovitaminosis [132], endocrine [191], neurological and neuropsychiatric diseases [106,108]. Changes in the inflammatory nature of the lip epithelium are often caused

by taking medications (isotretinoin, imiquimod, methotrexate, selumetinib, etc.) [51] and related complications, for example, DRESS syndrome after a course of phenobarbital, lamotrigine, allopurinol, ceftriaxone [134] and other drugs capable of activating T-suppression in some patientslymphocytes followed by a "cytokine storm". Exogenous factors determining the manifestation of cheilitis and chronic recurrent lip cracks include meteorological, chemical, including pharmacological, biological substances that can act both as an allergen [135,156,188] with a cascade of immunological reactions, and as factors that injure the lip epithelium. The effect of certain substances determines the nature of clinical manifestations, possible complications and the outcome of the disease. Low temperatures, severe aerodynamic conditions, increased or decreased humidity or dustiness, excessive insolation contribute to the development of cheilitis and lip cracks [19,20,43,122].

Actinic cheilitis is a precancerous keratosis of the lips caused by chronic exposure to sunlight (ultraviolet radiation). It is most often found in geographical areas with hot and dry climates, prolonged outdoor exposure or in people with phototype I on the Fitzpatrick scale, a significant role is played by the genetic predisposition of susceptibility to damage by ultraviolet radiation. According to statistics, actinic cheilitis occurs in older or middle-aged men, mainly on the lower lip [133,182].

The thin epithelium of the red border of the lips contains a small amount of sebaceous glands and melanin, which mediates the weak protective properties of the lips and high susceptibility to ultraviolet radiation. Excessive insolation damages the tumor suppressor gene p53, a protein that regulates the cell cycle, which leads to uncontrolled replication of damaged epithelial cells, while causing mutation at the gene level. The consequence of this damage is a malignant transformation into squamous cell carcinoma [164,182,194].

Clinical manifestations: the presence of white foci, peeling, ulceration, slight swelling on the red border of the lips, erasure of the boundaries between the red border and the cutaneous part of the lip, actinic cheilitis occurs in dry or exudative form. In this regard, in some cases, erosions or bubbles are observed on stagnant,

hyperemic lip skin [120]. It is necessary to differentiate actinic cheilitis with exfoliative, granulomatous cheilitis, squamous cell cheilitis, glandular cheilitis, abrasive precancerous Manganotti cheilitis [67,133,159]. The disease does not occur in the regions of northern latitudes, even on a polar day, due to the weak activity of ultraviolet radiation in the Far North [24].

Contact cheilitis is an inflammatory reaction of the lips caused by the irritating or allergic effect of various substances directly in contact with the lips: decorative lip cosmetics, oral hygiene products, food products, creams and ointment bases, flavors, preservatives, dyes, dental materials, professional products in contact with the lips, items that are placed daily in the mouth during work or with bad habits, neuroses (for example, nails, needles, pens) [18,48,162,181,188]. Clinically, contact cheilitis is manifested by dryness and burning of the lips, peeling, redness, and cracks form with prolonged course. Contact cheilitis is most often diagnosed on the red border of the lips, spreading to the skin around the red border. The red border of the lips is more prone to the development of contact dermatitis than the mucous membrane of the oral cavity. Allergens that come into contact with both the oral mucosa and the lips often cause only contact cheilitis. This is due to the peculiarities of the histological structure of the mucosa, which ensures rapid absorption and excretion of the allergen, a short period of contact due to dilution of the allergen substance and saliva removal, and the deep location of the basal epithelial layer, in which Langerhans cells are located. The mucous membrane of the oral cavity, including the mucous part of the lip, has a high regenerative ability and is resistant to various mechanical, chemical and thermal stimuli, in the deepest layer of the epithelium there are Langerhans cells that capture antigens that penetrate the epithelium. The pathogenesis of contact cheilitis is based on the mechanism of type IV allergic reaction (delayed type hypersensitivity). Langerhans cells produce interleukins that activate T lymphocytes. The pathophysiological mechanism of contact cheilitis follows the contact form of delayed hypersensitivity for 48-72 hours and is caused only by macrophages and T-lymphocytes, which are responsible for stimulating cellular immunity, activate and trigger an inflammatory reaction at the site of contact with the allergen (induction

phase), which leads to the development of characteristic symptoms and signs of contact cheilitis. At the same time, patients feel burning sensations, unpleasant sensations, hyperemia of varying degrees is clinically determined, in severe cases papules, vesicles, infiltrative processes. In a patient, contact cheilitis must be differentiated from, in fact, cheilitis (dry forms of exfoliative and actinic cheilitis, meteorological), as well as from one of the manifestations of atopic dermatitis - atopic cheilitis [18,48].

Meteorological cheilitis is a traumatic lesion related both to cheilitis proper and to precancerous lip diseases [16,20,60,104]. The disease is associated with adverse meteorological conditions. Exposure to high or low humidity, increased wind and low temperatures, precipitation at subzero temperatures lead to inflammation of the red border of the lips, unpleasant and even painful sensations and aesthetic discomfort. The direct mechanical effect of strong wind and precipitation in winter breaks the epidermal barrier, the cells of the multilayer squamous epithelium trigger the production of cytokines, which have a significant effect on the restoration of the stratum corneum. The thin stratum corneum of the red border of the lips does not have time to recover under prolonged exposure to weather conditions in which people live in the Far North, a cascade of inflammatory reactions is triggered by excessive cytokine production. The production of lipids on the surface of tissues decreases, transepidermal water loss increases resulting xerosis and rejection of the stratum corneum, scales are visualized on the surface of the red border of the lips. Violation of the skin barrier reduces the protective function of the epithelium, conditionally pathogenic microorganisms can join the process, which aggravates the course of the disease. Patients experience discomfort, pain and a burning sensation, to alleviate the condition they unknowingly lick their lips, there is an increase in moisture evaporation, the pathological process is aggravated by the appearance of infiltration and cracks. Leaving the premises to the street, they are again faced with "meteorogenic traumatization" and even greater tissue damage, a vicious circle arises. Symptoms may extend beyond the red border of the lips to the skin part. Meteorological cheilitis must first be differentiated from the dry form of exfoliative

and actinic cheilitis, allergic contact cheilitis, and atopic cheilitis. The disease has a potential malignancy with a prolonged course and can turn into obligate forms of precancerous in the form of limited hyperkeratosis or abrasive precancerous cheilitis of Manganotti [20].

Atopic cheilitis is a chronic inflammatory recurrent lip disease, which is a symptom of atopic dermatitis and refers to additional diagnostic criteria for a genetically determined disease developed by J.M. Hanifin and G. Rajka (1980) [59,76]. According to literature sources, atopic cheilitis occurs in 2-10% of the adult population, the incidence rate has increased 2-3 times over the past 30 years in developed countries. The pathogenesis of this disease has not yet been fully studied, but the leading role is played by a violation of the barrier function of the lip epithelium in combination with immune dysfunction and trigger factors [5,22,192]. Violation of the epithelial barrier leads to loss of transepithelial fluid, increased sensitivity to certain agents [138]. In most cases, atopic cheilitis is characterized by an increase in IgE and a violation of cytokine metabolism and regulation of the Th1/Th2–lymphocyte ratio, immunohistochemical studies determine a deficiency of T-lymphocyte suppressors, as well as a violation of apoptosis processes. Clinical symptoms are caused by allergic inflammation with infiltration of T-lymphocytes and eosinophils. Activation of the immune cell chain in the cascade of interaction between inflammatory infiltrate cells, capillaries and keratinocytes is a key factor in the development of lip epithelial damage [22,76,154,192]. Upon examination, erythematous-squamous inflammation of the red border of the lips and commissures, scales is determined, with prolonged course, lichenification occurs [120,149]. The disease is characterized by autumn-winter seasonality, therefore, atopic cheilitis, in addition to the dry form of exfoliative cheilitis and contact (allergic) cheilitis, should be differentiated from meteorological cheilitis.

Exfoliative cheilitis is a disease most often found in young women with a history of anxiety disorders and previous psychosocial stress [7,93,139]. It manifests itself in the form of a continuous keratinized growth, the formation of crusts and peeling of lips of dry or exudative forms. The disease becomes more severe with the

addition of a secondary infection. In the literature of domestic and foreign authors, the disease is described as a pathology characterized by cyclic and continuous exfoliation of the epithelium of the upper and lower lips due to excess keratin due to chronic trauma of the lips (licking, sucking, biting and picking) [67,97,163]. Histological examination determines hyperkeratosis [120]. Patients have dry and flaky lips, crusts, cracks due to cyclical compulsive actions of a self-injurious nature. Patients usually have concomitant neuropsychiatric diseases: anxiety disorders, depression, attention-seeking behavior, obsessive-compulsive disorder, schizophrenia and schizotypal disorders (delusions, skin-related hallucinations), dissociative disorder, personality disorder, which are either undiagnosed or have no tendency to recover when patients undergo a therapeutic course with a specialist of the appropriate profile. Differential diagnosis with other forms of cheilitis is carried out by removing crusts - with exfoliative cheilitis there are no ulceration sites, the skin of the red border of the lips is pink, without bleeding, erosions and any other pathological elements [7,29,93,139,161].

Glandular cheilitis is a rare inflammatory disease that mainly affects the small salivary glands located in the thickness of the mucous membrane of the lips. According to statistics, the disease is typical for adult men over 40 years old. To date, no specific factor or cause associated with the occurrence of the disease has been identified, some authors highlight the importance of bad habits, chronic injury of the lips in combination with the features of the anatomical structure of the lips [67,128]. The clinical features of the course of glandular cheilitis make it possible to make a diagnosis [55,163]. On the mucous membrane of the lips, there is an expansion of the mouths of the small salivary glands due to hypertphoria, through which there is a separation of thick, mucin-rich saliva due to an inflammatory process inside the glandular parenchyma (a symptom of dew). Dried out over time, the discharge forms yellow crusts (plaques) that cover the surface of the mucous membrane of the lips. These plaques are easily removed, but they form again, mainly at night. Concomitant signs of the disease are swelling of the lips and their deformation (inversion). The red border of the lips, as a rule, is not affected [62,147,190]. When a secondary infection

is attached, glandular cheilitis turns into a purulent form with a corresponding discharge. The histological picture is characterized by focal infiltration of lymphocytes and plasma cells in the interlobular region in the hypertrophied gland. Due to edema, glandular cheilitis must be differentiated from uncomplicated forms of exfoliative cheilitis, contact cheilitis, taking into account the presence of dry lips and scales in this pathology, differential diagnosis with meteorological cheilitis should be performed [29,55,64,123].

Granulomatous inflammation of the lips is a rare form of cheilitis characterized by the presence of edema of one or both lips (looks like angioedema). Two clinical forms are described in the literature: Mischer's cheilitis as a local isolated nosology and a symptom of Melkersson-Rosenthal syndrome in the presence of the classical triad of orofacial granulomatosis, folded tongue and recurrent facial nerve paralysis. The etiology is still unknown [107,187]. Several etiologies of various orders have been proposed, including genetic, inflammatory, allergic, and infectious. A clear etiological factor and pathogenetic mechanism have not yet been determined. The diagnosis is confirmed by laboratory research methods, the characteristic histopathology is determined, in which granulomatous inflammatory cell infiltration occurs in the layers of the dermis. Differential diagnosis should be performed with periostitis, acquired or hereditary angioedema, glandular cheilitis, dermatological manifestations of various granulomatous diseases [161,171,177].

Eczematous cheilitis is usually observed against the background of contact dermatitis caused by a hypersensitivity reaction or atopic dermatitis. Thus, an eczematous lesion on the lips develops due to the complex effects of neuroallergic, endocrine, metabolic and exogenous factors. Most often, the skin part and the red border of the lips are affected (in severe cases with spread to the skin of the face), hyperemia, slight swelling is determined upon examination, scales and cracks form, accompanied by dry lips. Atopic cheilitis is characterized by the predominance of lichenization of the skin of the lip contours and the duration of the course, contact

cheilitis is characterized by a more monomorphic course and stops after the cessation of the allergen [161,163,185].

Plasma cell cheilitis is a benign proliferative disease of plasmocytic and eosinophilic infiltration in the papillary layer of the dermis of unknown etiology, which usually manifests itself on the lip, a characteristic feature of this disease is the absence of remissions [159]. Etiopathogenesis is poorly studied at this stage, however, most authors tend to consider the traumatic factor leading to the occurrence of pathology. Clinically, the disease manifests itself in the form of finely expressed erythema or dark red or brownish spots (plaques) with relatively clear edges, mainly in the lower lip in the elderly. This disease is accompanied by erosion, ulceration, cracks, bleeding or crusts, which can be interpreted as carcinoma. Differentially, the disease can be confirmed by histological examination, including the phenomena of acantholysis, spongiosis, para- and hyperkeratosis without cell atypia [164,173,194,195].

Angular cheilitis is an inflammatory lesion of the lip commissures, which begins on both sides of the mucosal–cutaneous junction and spreads to the skin of the corner of the lips. Angular cheilitis has a relatively high prevalence among all ages and is characterized clinically by fissure(s), erythema, tissue maceration, ulceration and crusting at the corners of the mouth [9,174,175]. According to epidemiological statistics, angular cheilitis is observed in 0.7-3.8% of the population [128]. The difficulty in the treatment of angular cheilitis is the creation by cracks of conditions of a chronic, favorable environment for the growth of microorganisms. Angular cheilitis can be either one-sided or two-sided. Symptomatically, the disease is characterized by a feeling of pain, itching or even burning [61,69,163].

The etiology of angular cheilitis is multifactorial from local causes to systemic disorders. Local factors include anatomical features, mechanical injury and allergic, chemical and infectious effects. Local factors may act independently or combine with each other in the development of this disease. Systemic causes include vitamin deficiency (deficiency of B vitamins, especially cyanocobalamin, folic acid,

riboflavin, mineral deficiency (zinc or iron), general protein deficiency, systemic diseases (inflammatory bowel disease, Sjogren's syndrome, diabetes mellitus) and side effects associated with taking medications, decreased immunity [62]. If we talk about local provoking factors, then anatomical and physical features are relevant in old age: a decrease in the lower calving of the face due to adentia or jaw deformity due to malocclusion, a decrease in elasticity and turgor of skin tissues [92,94,193]. Retrognatic occlusion, increased tooth abrasion - these factors cause accumulation and stagnation of saliva in the corners of the mouth, skin maceration appears [9,174,175]. Mouth breathing and smoking are also local causes. Enzymes present in saliva, such as amylase, maltase, lipase, catalase, sulfatase, hexokinase, carboxylic acid anhydrase and others can cause impaired irritation and inflammation of the tissues of the corners of the mouth [101,146]. A traumatic factor, for example, an orthodontic device, chronic licking or mechanical damage to the lips, thermal burns, aggressive use of dental floss or iatrogenic factors violate the integrity of the tissues of the lip commissures and trigger the inflammatory process. Maceration of the lip commissures plays a leading role in the pathogenesis of the disease due to excessive exposure to saliva, prolonged exposure to which causes a contact and eczematous reaction. Violation of the integrity of the stratum corneum creates conditions for the invasion of microorganisms [21,157,169].

The most dangerous form of lip disease is chronic recurrent lip fissure, which is widespread and affects the quality of human life, presents difficulties in treatment. On examination, the disease is characterized as a linear defect of the red border of the lips in combination with hyperemia and edema, localized mainly in the middle on the lower lip, but according to observations, commissures, lateral sections of both lips may be affected. The disease tends to malignancy in 7-10% of cases, with prolonged course, leukoplakia may occur along the edges of the crack. Quite a lot of etiological factors have been studied in the development of this disease, however, our study examines the importance of the meteorological factor in the subarctic climate, which is a trigger mechanism and sometimes combined with individual anatomical features of the lip structure. The course of chronic lip fissure is often accompanied by

bacterial colonization. Common obligate pathogens cause delayed regeneration. After direct damage to tissues by bacterial toxins, leukocytes are actively involved in the process, which leads to increased production of inflammatory cytokines, proteases and reactive oxygen species (ROS), supporting cascades of inflammatory reactions. Proteases and ROS destroy the extracellular matrix and growth factors, disrupt cell migration and inhibit tissue healing. The bacteria that colonize the chronic lip fissure form polymicrobial biofilms in the secreted polymer matrix, providing an optimal environment for the vital activity of bacteria [19,49]. Chronic lip crack can be combined with all forms of cheilitis with periods of remission [87,117].

According to clinical studies, facultative precancers account for from 6 to 15% of malignancies, obligate - 16%. The processes of malignancy of cheilitis are based on pathological processes of keratinization of the epithelium, including the phenomena of hyper- and parakeratosis, the histological picture is also accompanied by acanthosis, pathomorphologists often diagnose granulosis in the studied samples [43,158,194,195].

Factors of oncological alertness of the doctor are deterioration of the clinical picture, ulceration of pathomorphological elements, hyperkeratosis, increased bleeding, exophytic growth, infiltration and compaction. In order to clarify the diagnosis, the patient is sent for histological and cytological examinations, confirmation of lip cancer is the determination of atypical cells in the test material [16,60,104].

1.5. The influence of climatic and geographical factors of the Far North on the course of the cheilite

D.G. Tikhonov's monograph is devoted to the study of the influence of adverse factors of the Far North on the human body and is described as a concept of a separate branch of medical sciences - Arctic medicine. Russian authors divide the climatic factors of the north into specific and non-specific ones. Specific factors include photoperiodism (phenomena of the polar day and night), sharp variability of

atmospheric pressure, fluctuations in the electromagnetic field. Non-specific influences include the cold factor, severe aerodynamic conditions, and air humidity can be both low and high [25,52,54,98,127]. Due to geomagnetic disturbances in the regions of the Far North, intense electromagnetic fields are recorded, their activity increases as latitudes increase towards the North Pole, permeability to electromagnetic radiation, high-low frequency radio waves, and various charged particles increases [42,56,75,126]. During the period of the polar day, exposure to round-the-clock ultraviolet radiation triggers the release into the atmosphere of charged particles that destroy electron transport chains and proteins of the cellular respiration system, due to disruption of electron transport processes, ATP synthesis is disrupted, this leads to the pathophysiological launch of a cascade of reactions [45,58,131].

The population of the regions included in the Far North zone is under the influence of a complex of adverse environmental factors. Numerous changes in a number of biochemical parameters contribute to the formation of a "polar" type of metabolism [20]. The geomagnetic instability of the Far North negatively affects the daily physiological rhythm of a person, increases hemodynamics, increases the release of cortisol and adrenaline. The human body is stably in a state of hormonal stress [4,27,54,75].

In case of cold exposure, the authors describe the influence of meteorological conditions on the human body, suggesting an increased risk of causing cold injury or the onset of a disturbed thermal state. According to research, prolonged exposure to low temperatures causes activation of free radical mechanisms in tissues. The permeability of the cell membrane increases as a result of lipid peroxidation, this pathogenetic process is accompanied by denaturation and inactivation of proteins, membrane delipidization, disruption of cell division and growth. Pathological processes lead to changes in the mucous membrane and skin of the lips, keratinization processes are disrupted, and histological examination reveals the phenomena of hyperplastic processes in the lip epithelium [20].

The peculiarities of meteorological conditions in the Far North, with the damaging effects of high humidity and low temperatures, reduce the protective properties of the lip epithelium. Prolonged exposure to low temperatures combined with high humidity disrupts the regulation of the keratinocyte differentiation program into corneocytes and leads to a weakening of the mechanical barrier. It has been proven that humidity affects the susceptibility of tissues to mechanical and thermal effects and provokes cellular destruction, elasticity decreases, the organization of protein cellular structures and lipids changes, and hydration of the epidermis occurs. High levels of relative humidity slow down the restoration of the epidermal barrier and reduce the function of natural hydration. The basis of the lipid barrier is the stratum corneum, which contains intercellular lipids. When exposed to extreme environmental factors in the Far North, damage to the stratum corneum occurs, lipid peroxidation is triggered, as a result of loss of tissue elasticity, the integrity of the lip epithelium is disrupted, this causes the appearance of a median linear defect in the form of a chronic lip crack, and meteorological cheilitis. Since the lips are constantly moving, participate in the act of chewing, speech, mimic activity, and are constantly damaged by meteorological factors, such chronic tissue damage blocks the violation of tissue integrity in a prolonged inflammatory state, abundant neutrophil infiltration with associated reactive oxygen species and persistent production of inflammatory mediators that support the cycle, the course of cheilitis is aggravated, regeneration is inhibited [19,49]. The effects of high or low humidity, increased wind and low temperatures, precipitation at subzero temperatures lead to inflammatory phenomena, in the conditions of the Far North, the above factors provoking this pathology are characterized by prolonged exposure due to the duration of winter time in the subarctic climate, and the inflammatory process acquires a chronic form with significant increases in the risk of malignancy [20].

The direct mechanical effect of strong wind and precipitation in winter breaks the epidermal barrier, the cells of the multilayer squamous epithelium trigger the production of cytokines, which have a significant effect on the restoration of the stratum corneum. The thin stratum corneum of the red border of the lips does not

have time to recover under prolonged exposure to weather conditions in which people live in the Far North, a cascade of inflammatory reactions is triggered by excessive cytokine production. The production of lipids on the surface of tissues decreases, transepidermal water loss increases, resulting in xerosis and rejection of the stratum corneum. Violation of the skin barrier reduces the protective function of the epithelium, conditionally pathogenic microorganisms can join the process, which will lead to complications affecting the duration and nature of the course of various forms of cheilitis [20].

The unfavorable climatic conditions of the Far North reduce the adaptive reserves of the body, despite the presence of protective mechanisms: antioxidant protection, sebaceous glands production of protective sebum, morphofunctional features of the multilayer squamous epithelium inflammatory lip diseases in patients are quite common, regardless of gender and age [20].

An important role in the development and course of cheilitis in the Far North is played by the high prevalence of hypovitaminosis. The patronymic authors carried out numerous studies on the vitamin content of residents of the Far North. It was noted that the deficiency of retinol, alpha-tocopherol, 25-hydroxycalferol is approaching 90%, studies of the level of ascorbic acid, thiamine, and essential trace elements also indicate impaired mineral and vitamin metabolism [2,13,35,38,46].

The most difficult situation with hypovitaminosis in the inhabitants of the north is with subclinical vitamin D deficiency [12]. Vitamin D promotes the absorption of calcium and phosphorus, however, the effect of vitamin D is not limited to bone tissue, few foods in the human diet contain sufficient amounts of vitamin D, its main source is the effect of ultraviolet radiation on the skin through insolation. According to hydrometeorological observations, the number of sunny days per year in the regions of the Far North does not exceed 40-50. Lack of sufficient sunlight leads to vitamin D deficiency. The consequences of deficiency are reflected in the severity of the course of various forms of cheilitis, slowing down the regeneration of the lip skin, transition to a chronic form, activation of the processes of transformation of cheilitis into precancerous forms and malignancy. The human skin acts as a site of vitamin D

synthesis, as well as as a target organ for the biologically active form of this vitamin. Vitamin D affects many functions in the skin, ranging from proliferation, differentiation and apoptosis of keratinocytes to barrier maintenance and activation of immunoregulatory processes. In addition, vitamin D is considered as a therapeutic agent for many skin pathologies. The effects of vitamin D are mediated through the Vitamin D Receptor, a nuclear hormone receptor that activates or inhibits the transcription of certain vitamin D target genes. 1,25-dihydroxyvitamin D [1,25(OH)2D3] and its receptor (VDR) are important regulators of epidermal differentiation. The epidermis consists of 90% keratinocytes present in four layers, which have different stages of development. The most important function of the lip epidermis is protection from environmental factors, achieved by the production of keratin by keratinocytes. Keratin in the lip skin maintains the density and elasticity of epithelial tissue. Keratin K5 and K14 are produced in the basal layer, keratins K1 and K10, considered as indicators of more differentiated layers of the epidermis, are produced in the granular layer, keratinocyte differentiation increases, lamellar bodies filled with glycolipid structures that contain collagen are produced, keratogyaline granules accumulate in the cytoplasm, filled with loricrin, involucrin and profilagrin. The filaggrin formed then participates in the process of aggregation of keratin filaments. The nuclei of the granular layer cells are subject to atrophy, followed by the formation of the stratum corneum of the epidermis from densely arranged nuclear-free cells. All layers of the epidermis and their functions within these layers are regulated by VDR and its coactivators. The process of epidermal differentiation is consistent. 1,25(OH) 2 D and VDR regulate all stages from the control of proliferation in the epidermis to the regulation of the production of K1, K10, involucrin and transglutaminase in the thorny layer, the regulation of the production of loricrin and filaggrin in the granular layer, the synthesis of lipids necessary for the permeability barrier in the stratum corneum, and the development of active natural immunity [17].

Vitamin D is involved in wound healing by binding to VDR via calcitriol, regulates transcription in various target cells, stimulating the production of platelet

growth factor (PDGF), epidermal growth factor receptors (EGFR) and keratinocyte growth factor receptor (KGFR). The anti-inflammatory properties of vitamin D have an antiproliferative effect on the regeneration of the skin and mucous membranes with the suppression of monocytes and inflammation mediated by Langerhans cells. It also reduces the expression of keratinocytes by the proinflammatory cytokines IL-1α, IL-6 and IL-8 in response to vitamin D3. Calcitriol directly induces the expression of several pairs of antimicrobial peptides, including cathelicidin and defensin β2, and can recognize microbial toll-like receptor-2 (TLR2) and cofactor CD14. These collective actions provide an immunoprotective effect against colonization by pathogenic organisms. These collective actions provide an immunoprotective effect against colonization by pathogenic organisms [17,137].

Biorhythms change due to desynchronosis provoked by disturbances of astronomical day and night, the antioxidant activity of the body and energy supply decrease. Desynchronoses mediate shifts in the nervous and endocrine systems that perform basic regulatory functions. The body has to turn on adaptive mechanisms through the hypothalamic-pituitary-adrenocortical system, but endocrine-metabolic disorders disrupt humoral regulation factors [3,15,24,31,41]. In the inhabitants of the Far North, the endocrine function of the pituitary gland, adrenal cortex and thyroid gland is activated during the winter period of the polar night, along with this, the endocrine function of the pancreas decreases, triglycerides and atherogenic lipids increase in blood serum, and the concentration of fatty acids decreases [14,57,103]. In the summer, the function of the thyroid gland decreases. Desynchronoses are accompanied not only by disorders of the endocrine system, studies have found that the body's immune defense also decreases, and the risk of cardiovascular, respiratory, and digestive diseases increases [33,58,112,113].

Due to numerous changes in a number of biochemical parameters, the formation of a "polar" type of metabolism, as well as the influence of external natural factors, activation of lipid peroxidation (LPO) occurs under the influence of an excess of free radicals of oxidants [65,82,84,105]. LPO reactions lead to the destruction of the cell membrane, the penetration or exit of substances from it, which leads to their

damage or death. The active processes of lipid peroxidation in the inhabitants of the Far North develop due to the depletion of endogenous antioxidants in the body of an adapting person. Among the reasons for the formation of an insufficiency of the antioxidant protection system, the leading factors are photoperiodicity disorders and geomagnetic shifts. Geomagnetic storms also have a pronounced effect on lipid peroxidation, shifts occur in the oxidant–antioxidant ratio, which leads to increased lipid peroxidation against the background of changes in the electromagnetic homeostasis of the body with the formation of free radicals. Uncontrolled by antioxidants, free radical oxidation of lipids, which occurs under the influence of powerful geomagnetic disturbances characteristic only of high latitudes, is one of the primary mechanisms of cell damage in residents of the Far North. The depletion of the Northerners' own antioxidant defense against the background of metabolic stress leads to damage by free radicals of enzymes that ensure the effectiveness of metabolic processes, inactivation of nitric oxide by free radicals formed during lipid peroxidation occurs, which leads to the development of cellular dysfunction. Activation of free radical oxidation under the influence of an excess of free radicals in the Far North contributes to an increase in the number of underoxidized products in the cell, as a result, a decrease in the hydrogen index of cells, a change in the properties of cell membranes, and the formation of metabolic acidosis [82].

Theoretical and clinical studies indicate shifts in the functioning of the immune, nervous, and endocrine systems, disorders of homeostasis and the work of organs and tissues [2,13,25,46,90,98,103].

Thus, diseases and damage to the lips are quite common in the practice of a dentist. Currently, there is a need to develop modern methods of diagnosis and treatment of these diseases in the Arctic zone. In the conditions of the Far North, this problem becomes relevant due to the rather high incidence and risk of malignancy [43,73,99].

CHAPTER II. MATERIALS AND METHODS OF RESEARCH

2.1. Objects of research

The objects of this study were 117 patients aged 18 to 55 years, living in the region of the Arctic zone of the Far North - Murmansk region for more than three years, with diagnoses: chronic recurrent lip crack (34 people, 29.6%), meteorological cheilitis (39 people, 33.33%), angular cheilitis (14 people, 11.97%), atopic cheilitis (7 people, 5.98%), exfoliative cheilitis (7 people, 5.98%), 16 people, 13.68%, had a clinical picture of chronic lip crack complicated by meteorological cheilitis. All the subjects were somatically healthy or practically healthy, without signs of acute infectious and non-communicable diseases, and had no history of severe chronic diseases. The subjects were selected when contacting the dental office of the polyclinic of the branch No. 3 of FSGI "1469 NCH" of the Ministry of Defense of the Russian Federation (Murmansk), where clinical research methods were conducted.

Exclusion criteria: age under 18 and over 55 years, endocrine diseases, diseases of the cardiovascular and hematopoietic systems, a psychiatric and narcologically burdened history, type 1 and 2 diabetes mellitus, HIV infection, hepatitis B, C, malignant neoplasms, pregnancy and lactation, the use of drugs: hormonal contraceptives, anabolic steroids, medications or biologically active vitamin D3 supplements. The exclusion criteria were also: patients at risk of hypercalcemia (renal failure, sarcoidosis, etc.), the use of local retinoids, patients participating in other studies. On the basis of Article 20 of Federal Law No. 323-FZ dated November 21, 2011 "On the basics of Public Health protection in the Russian Federation", as well as the order of the Ministry of Health of the Russian Federation dated November 12, 2021. No. 1051n "On approval of the procedure for giving informed voluntary consent to medical intervention and refusal of medical intervention, the form of informed voluntary consent to medical intervention and the form of refusal of medical intervention" before the start of the study, all patients signed a voluntary informed consent to medical intervention, including participation in the study. The

subjects were familiarized with all aspects of the study, the purpose and objectives of the study, research methods were explained to them, general and topical medications were described in detail, patients were informed about the treatment regimen, alternative options, and expected risks. The safety criteria and adverse/adverse event reporting reflect all adverse events that may have occurred during the study. All results were documented in the study records, including treatment details, the list of prescribed drugs and their frequency of use, the nature of side effects, the date and time of the onset of an adverse reaction, duration, severity, result and association with prescribed drugs during the study. Patients were advised to contact researchers immediately about any adverse events requiring medical attention.

Throughout the entire time, there was not a single written or oral refusal of the patient to participate in the dissertation research, no development of adverse events and adverse reactions to treatment was observed, and cases of non-compliance with the inclusion/exclusion criteria were not established during the entire study.

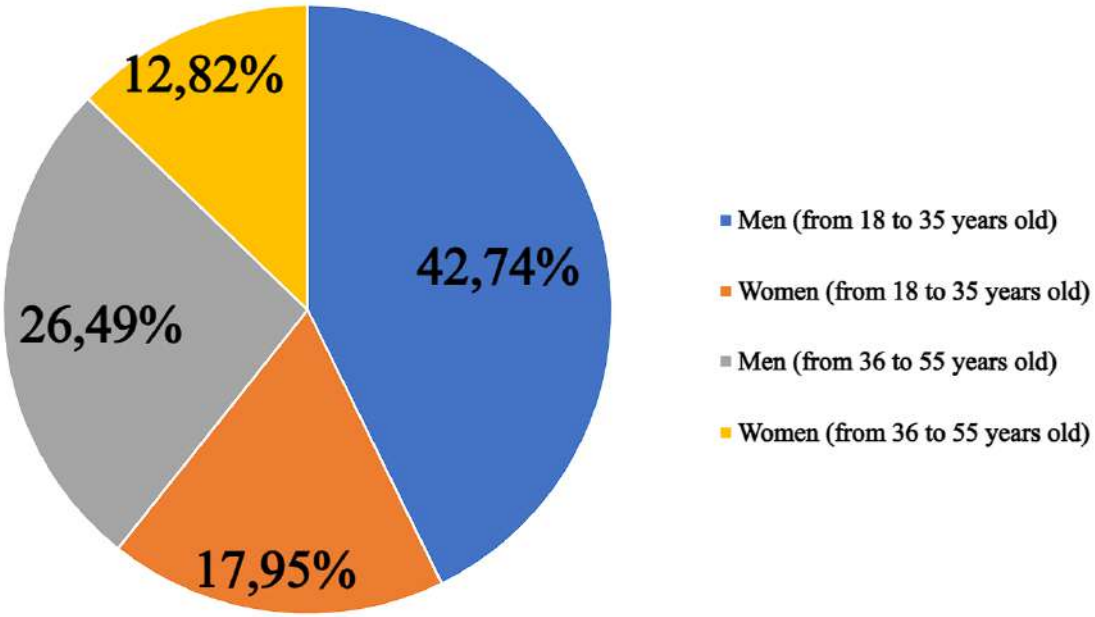

Figure 1. Gender and age distribution of patients who participated in the study

In the course of the dissertation research, the following were conducted: a survey, anamnesis collection, dental examination, patient questioning, examination of medical records, a procedure for taking biological material, a smear from the depth of a lip crack and blood from a vein, laboratory diagnostics and analysis of the vitamin

status of patients, indicators of the antioxidant protection system. In patients with chronic recurrent lip fissure, bacteriological and microscopic examination of the smear of the affected lip tissues was additionally performed.

Of the 117 people who participated in the study, there were: 50 men aged 18 to 35 years, 21 women aged 18 to 35 years, 31 men aged 36 to 55 years and 15 women aged 36 to 55 years (Figure 1).

Among the examined, the most common pathologies were identified: meteorological cheilitis and chronic lip crack. Chronic lip crack was diagnosed in 23.08% (n=27) of men and 5.98% (n=7) of women aged 18 to 55 years (Table 1). Meteorological cheilitis was found to be the second most common in the subjects: 24.78% (n=29) of men, 8.55% (n=10) of women aged 18 to 55 years (Figure 2).

Comorbid nosology was also established – a combination of chronic lip crack with meteorological cheilitis in 5.13% (n=6) women and 8.54% (n=10) men aged 18 to 55 years (Table 1).

The structure of the research work also included patients with angular, exfoliative and atopic cheilitis. Angular cheilitis was 4.27% (n=5) in women and 6.84% (n=8) in men aged 18 to 55 years (Figure 2). The proportion and number of patients with exfoliative cheilitis and atopic cheilitis is equal among both women and men from 18 to 55 years of age was 3.41% (n=4) and 2.56% (n=3), respectively.

Table 1 – Distribution of patients by gender, age and diseases

Clinical diagnosis	Female from 18 to 35 years old	Female from 36 to 55 years old	Male from 18 to 35 years old	Male from 36 to 55 years old
Chronic lip crack complicated by meteorological cheilitis	2,56% (n=3)	2,56% (n=3)	5,12% (n=6)	3,41% (n=4)
Chronic lip crack	2,56% (n=3)	3,41% (n=4)	13,68% (n=16)	9,4% (n=11)
Meteorological cheilitis	4,27% (n=5)	4,27% (n=5)	14,53% (n=17)	10,26% (n=12)
Angular cheilitis	3,41% (n=4)	0,85% (n=1)	5,98% (n=7)	1,71% (n=1)
Exfoliative cheilitis	2,56% (n=3)	0,85% (n=1)	1,71% (n=2)	0,85% (n=1)
Atopic cheilitis	2,56% (n=3)	0,85% (n=1)	1,71% (n=2)	0,85% (n=1)

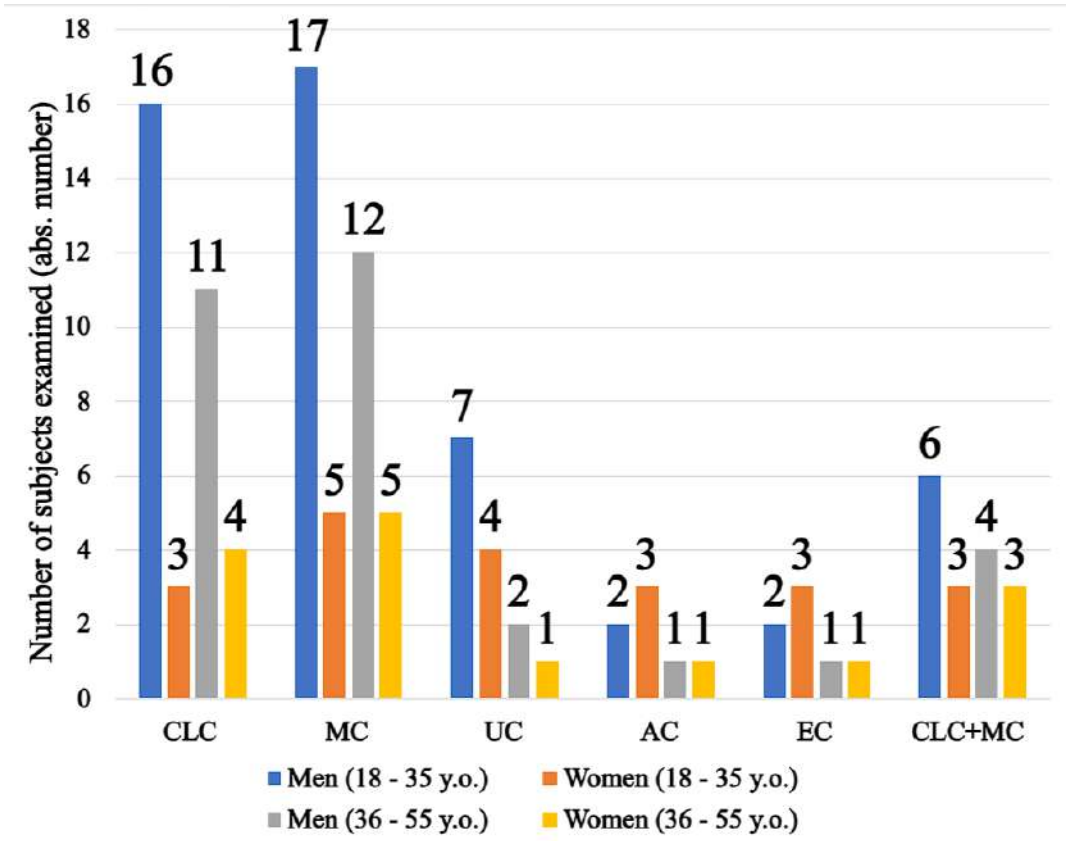

Figure 2. Characteristics of the subjects by nosology according to gender and age characteristics

Patients with actinic cheilitis and macrocheilitis, and other precancerous lip diseases did not apply for an appointment during the entire study period and were not registered during examination as part of a medical examination, therefore these diagnoses were not included in the research work. There were also a few cases of symptomatic forms of cheilitis, as well as granulomatous and contact cheilitis in patients, however, their proportion in the incidence structure was low, so patients with these nosologies were not included in the study area.

2.2. Clinical research methods

2.2.1. Interview, examination, medical history collection

The survey of patients found that all of them are not indigenous peoples of the North and have been living in the Arctic zone of the Far North for more than three

years in the cities of the Murmansk region (Murmansk, Severomorsk). Outpatient patient records do not contain information about concomitant chronic infectious and non-infectious, oncological, autoimmune diseases, there was no pregnancy and lactation stage among women, 5.98% (n=7) of people have a history of atopic dermatitis. The patients did not take medications, and their employment pattern differs from indoor work.

The examination of the patients taking part in the examination took place in a dental chair. Upon examination and anamnesis collection of seven patients under the age of 39 (4 women and 3 men), the diagnosis was made: exfoliative cheilitis (dry form). Patients complained of dissatisfaction with the aesthetics of the face, itching, dryness, peeling and the presence of voluminous crusts that appeared several years ago and the seasonality of the season in the development of the course of this condition did not matter. During the observation, it was noted that the patients were emotionally labile, nervous at the reception, constantly biting their lips. The patients had a slight swelling of the red border of the lips, the crusts had a white (in 5 patients) or yellowish (in 2 patients) color on the upper (57.14%) or lower lip (42.86%). The lesion affected only the red border of the lips, without cracks, erosions and bleeding. When removing the crusts with tweezers, the hyperemic bright red surface of the red lip border was exposed. Taking into account the factor of psychoemotional stress, we recommended that patients consult a neurologist for drug correction of the psychoemotional background and a psychotherapist to eliminate trigger factors.

The examination of patients with meteorological cheilitis (33.33%) revealed the same clinical picture of varying severity. Hyperemic lips, peeling, bleeding, dry lips, slight swelling. Patient complaints: pain when talking, eating, smiling, bleeding, tightness, the subjects noted that the symptoms appeared after moving to the Far North. Meteorological cheilitis in our study was more common in men, this is due to the use of hygienic lipsticks and decorative lip cosmetics by women, which contain emollients that create a "protective film". However, our study included women who were very concerned about the appearance of their lips. According to the patients, the

use of hygienic lipsticks during the appearance of inflammation was almost not effective.

All the subjects with a confirmed diagnosis of meteorological cheilitis noted the seasonality of this disease in the cold season of the subarctic climate. During the summer, the symptoms decreased significantly or disappeared completely.

There were no difficulties in the differential diagnosis of cheilitis in patients with atopic cheilitis. The patients did not complain of pain or discomfort. In patients (n=7) with this diagnosis, the clinical picture is represented by an erythematous red border with dry lips with predominant peeling in the corners of the lips, as inflammatory infiltration develops, small cracks and grooves form. Patients were referred to a dermatologist, where characteristic manifestations of atopy were found in the form of typical skin lesions on other parts of the body (face, elbow bends, areas under the knees). During the survey, the patients confirmed the factor of heredity of the clinical picture in one of the parents and/or siblings, as well as seasonal manifestations of exacerbation in the autumn-winter period.

Patients with angular cheilitis had unilateral or bilateral lesions of the lip commissures in the form of cracks with tissue surrounding hyperkeratosis.

Of the total number of patients in the structure of the incidence of chronic lip crack patients can be statistically divided into two groups: patients with chronic lip crack 29.06% (n=34) and patients with a complication in the form of meteorological cheilitis 15.09% (n=16). Patients with chronic cracked lips complained of pain when talking, eating, smiling, they were also concerned about the deterioration of aesthetics, constant bleeding of cracks. According to the patients, 14 people (28% of the total number of patients with chronic lip fissure) had manifestations of this pathology before moving to the Far North, but the symptoms were not as pronounced. On examination, the disease is characterized as a linear defect, around which hyperemia and edema are determined, localized mainly on the lower lip in 84% of cases in 42 out of 50 patients (Figure 3).

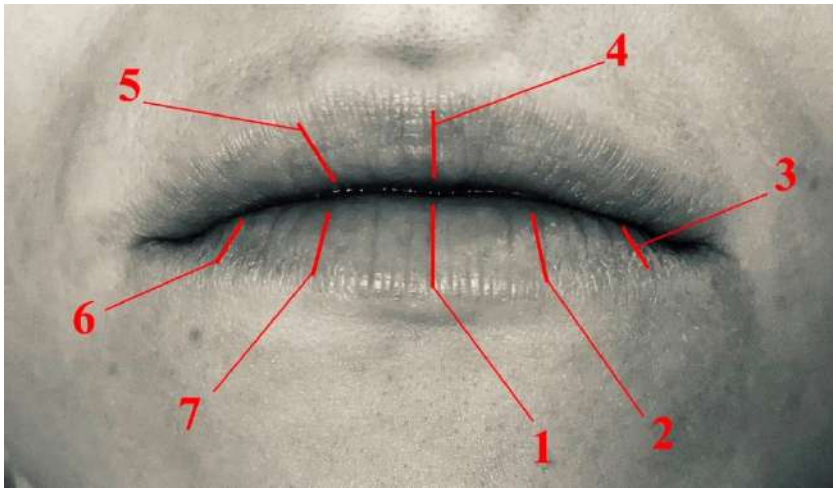

Figure 3. Localization of chronic lip cracks in the subjects

Analyzing the localization of chronic lip cracks, we developed a classification of lip cracks according to the anatomical location on the upper and lower lip: medial (1,4), mediolateral (2,5,7), lateral (3,6) on the right and left. Based on this classification, we were able to make a statistical processing of the anatomical features of the localization of chronic lip fissure of the subjects (Table 2). The table shows data in units of measurement corresponding to the established quantities (cases of identified localizations), patients had a combined location of cracks (several on one lip or on both lips).

Most often, patients had a median fissure of the lower lip in combination with other localizations or in isolation, which accounted for 78% (n=38) of the total number of patients with chronic lip cracks (n=50). An example of a combination of a medial crack of the lower lip with mediolateral cracks on the right and left in a male patient aged 30 years with a complication in the form of meteorological cheilitis. (Figure 3)

Table 2 – Localization of chronic lip cracks detected during examination in the subjects (n=50)*

Localization, № according to the Drawing	Chronic lip crack (established cases)	Chronic lip crack complicated by meteorological cheilitis (established cases)
Medial (upper lip) №4	6	3
Medial (lower lip) №1	27	11
Mediolateral (right, lower lip) №7	4	4

Mediolateral (right, upper lip) №5		1
Mediolateral (left, lower lip) №2	6	5
Lateral (right) №6	5	1
Lateral (left) №3	2	3

Within the framework of this study, a classification of chronic recurrent lip crack by severity has been developed (Table 3). The purpose of clarifying the classification by severity was to develop in terms of complex therapy a special tactic that determines the duration of treatment, prescribing glucocorticoid drugs of a high degree of activity, prescribing a course of physiotherapy procedures, as well as determining the distinctive microflora from smears of crack depth compared with mild degrees of severity.

Figure 3. Patient S. (30 years old) with chronic lip cracks and a complication in the form of meteorological cheilitis

Table 3 – Classification of chronic lip crack by severity of the disease

Degree of severity	Localization	Total remission period (months per year)	Clinical Symptoms
Mild	Upper or lower lip	More than 6	Slight hyperemia of the surrounding tissues, no edema
Moderate	Upper and/or lower lip	2-6	Edema and hyperemia of surrounding tissues
Severe	Upper and/or lower lip	Less than 2	Pronounced edema, hyperemia, hyperkeratosis of the surrounding tissues, sealing around the crack

According to our classification, patients were divided into 3 groups according to severity of the course (Table 4).

Of the total number of patients with chronic lip crack (n=50), the largest proportion of severity in the structure of chronic lip cracks in patients falls on the average and is 40% (n=20), only 25% (n=13) patients were diagnosed with mild degrees of chronic recurrent lip crack, the severe course of the chronic process accounted for 34% of cases (n=17).

Table 4 – Distribution of patients with chronic lip crack by severity (n=50*)

Degree of severity	Chronic lip crack	Chronic lip crack complicated by meteorological cheilitis	Total
Mild	20% (n=10)	6% (n=3)	26% (n=13)
Moderate	30% (n=15)	10% (n=5)	40% (n=20)
Severe	18% (n=9)	16% (n=8)	34% (n=17)

* the selection includes patients with chronic lip crack (n=34) and patients with a complication in the form of meteorological cheilitis (n=16)

2.2.2. Patient survey

In the treatment of chronic recurrent lip fissure, the patient's interest in treatment is of great importance. Unlike many other types of dental care, the treatment of a cracked lip is based on the independent and daily use of external drugs by the patient, since the lips are constantly in motion, they cannot be isolated with an antiseptic bandage. If a decision is made to start a course of therapy for chronic lip fissure, it is necessary to determine the patient's interest in treatment based on passing the QIT-CLF test, which includes 10 questions (Table 5) [19,49].

A total of 34 patients with a diagnosis of chronic lip crack and 16 patients with a complication in the form of meteorological cheilitis participated in the study. After the start of treatment, all patients filled out a questionnaire, the results of treatment and prevention were analyzed and their dependence on the questionnaire responses was established.

Table 5 – Questionnaire of patients' interest in the treatment of chronic lip fissure (QIT-CLF)

№ i/o	Statement of interest	Never 1 point	Rarely 2 points	Sometimes 3 points	Often 4 points	Always 5 points
1	I experience painful sensations when smiling and eating					
2	I'm worried about bleeding cracked lips					
3	I am concerned about the appearance of the lips, because there is a crack on one of them					
4	I am afraid of the long-term consequences of a chronic lip crack (oncology, severe infection)					
5	I observe mimic rest, I do not lick or bite my lipsv					
6	Do you take medicines with you for local and general treatment?					
7	I take the prescribed vitamins every day					
8	Do you follow the sequence and frequency of taking vitamins and other medications throughout the day?					
9	I use medications for topical treatment every day					
10	I use drugs for topical treatment with the regularity recommended by the doctor					

Patients choose answers on a five–point scale, where 1 – never, 2 – rarely, 3 – sometimes, 4 – often, 5 - always (Table 5). The scores for each item were summed up to get a total score: the higher the total score, the higher the patient's interest in treatment. The sum of scores from 10 to 25 indicated a lack of interest in treatment, scores from 26 to 35 were assessed as low interest, from 36 to 50 – high.

2.2.3. Systematization of the sample of the main and control groups of subjects

In the study, patients (n=117) were divided into 2 groups. Patients with chronic lip crack, meteorological, angular, exfoliative and atopic cheilitis were divided as

follows: the main (experimental) group consisted of 64 people, the control group – 53 people. (Table 6).

The largest proportion of the examined patients were patients with meteorological cheilitis, in the control group 33.96% (n=18), in the main group 32.81% (n=21). The next most common nosology was a chronic lip crack of 30.19% (n=16) and 28.13% (n=18) for the control and main groups, respectively. Chronic lip crack with a complication in the form of meteorological cheilitis in the morbidity structure of the main group was 14.06% (n=9), in the control group – 13.21% (n=7). Angular or angular cheilitis in the morbidity structure of the subjects was 12.5% (n=8) for the main group and 11.32% (n=6) for the control group.

Table 6 – Distribution of patients by groups

Diagnosis	The main group (n=64)	The control group (n=53)
Meteorological cheilitis	n=21 (32,81 %)	n=18 (33,96 %)
Exfoliative cheilitis	n=4 (6,25 %)	n=3 (5,66 %)
Atopic cheilitis	n=4 (6,25 %)	n=3 (5,66 %)
Chronic lip crack	n=18 (28,13 %)	n=16 (30,19 %)
Chronic lip crack complicated by meteorological cheilitis	n=9 (14,06 %)	n=7 (13,21 %)
Angular cheilitis	n=8 (12,5 %)	n=6 (11,32 %)

The share of exfoliative and atopic cheilitis of the main group accounts for 6.25% (n=4) of cases, for the control group 5.66% (n=3) for each nosology.

The proportion of men in the main group was 68.75% (n=44), women 31.25% (n=22). When distributed by gender in the main group, the largest percentage of the surveyed was male with meteorological cheilitis 23.44% (n=15), female with the same diagnosis 9.37% (n=6). Among patients with chronic lip crack, males accounted for 20.31% (n=13), females – 7.81% (n=5), male patients with chronic lip crack and a complication in the form of meteorological cheilitis accounted for 7.81% (n=5),

females – 6.25% (n=4). Among patients with angular cheilitis, male patients accounted for 7.81% (n=5), female patients – 4.68% (n=3). In the distribution of patients with exfoliative and atopic cheilitis in the main group, patients by gender were distributed equally as follows: male and female accounted for 3.12% (n=2) for both nosologies separately (Figure 4).

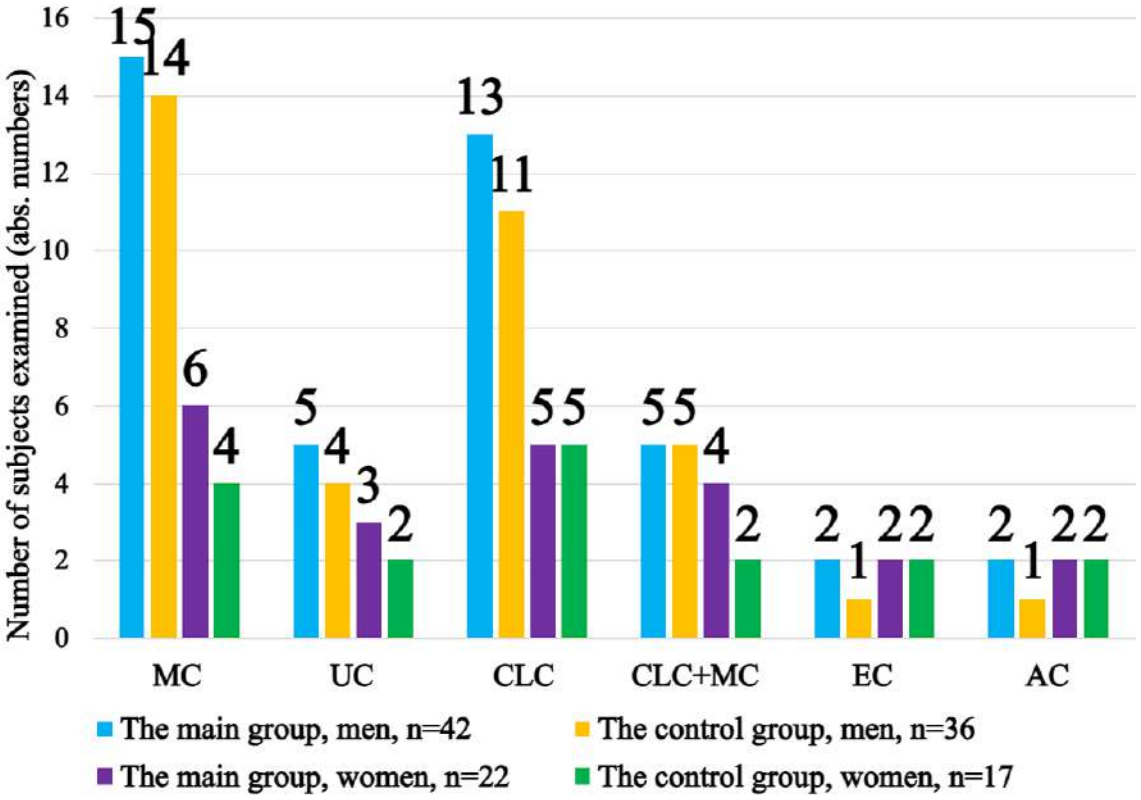

Figure 4. Distribution of patients by age and gender factors

The proportion of men in the control group was 67.91% (n=36), women 32.07% (n=17). When distributed by gender in the main group, the largest percentage of the surveyed was male with meteorological cheilitis 26.42% (n=14), and female with the same diagnosis 7.58% (n=4). Among patients with chronic lip crack, male accounted for 20.75% (n=11), female – 9.43% (n=5), male patients with chronic lip crack and a complication in the form of meteorological cheilitis accounted for 9.43% (n=5), female – 3.77% (n=2). Among patients with angular cheilitis, male patients accounted for 7.55% (n=4), female patients – 3.77% (n=2). In the distribution of patients with exfoliative and atopic cheilitis in the main group, patients by gender

were distributed as follows: the proportion of males with exfoliative and atopic cheilitis accounted for 1.88% (n=1), the proportion of females with exfoliative and atopic cheilitis accounted for 3.77% (n=2) (Figure 4).

2.3. Laboratory research methods

During the study, laboratory blood serum analyses of patients with various forms of cheilitis and lip smear cultures for chronic lip cracks and their complications in the form of meteorological cheilitis were analyzed (Table 7).

Table 7 – Laboratory diagnostic methods used in the study

The indicator of the level in the blood serum	The main group (n=64)			The control group (n=53)		
	Before treatment	After 6 months	After 12 months	Before treatment	After 6 months	After 12 months
Vitamin D	+	+	+	+	-	-
Vitamin E	+	-	-	+	-	-
Malondialdehyde	+	-	-	+	-	-

2.3.1. Determination of the level of vitamins E and D in blood serum, determination of the antioxidant status of patients

The laboratory examination included an assessment of vitamin D and vitamin E availability, and an assessment of oxidative stress. Blood sampling was performed on an empty stomach in the morning at the initial examination, 6 months after the course of treatment and 12 months after the end of the treatment. Venous blood samples were taken from one superficial vein in the elbow fold using a vacuum tube holder with a sterile needle for single-use blood collection Ermines (RU No. RZN 2016/4640 dated November 01, 2018, Russia), into vacuum tubes MiniMed (RU No. RZN 2019/8175 dated December 27, 2019, Russia) with fillers: The coagulation activator and gel (yellow marking) and lithium with heparin (green marking) were delivered to the laboratory. Vitamin D is a fat–soluble vitamin that is synthesized in the skin, the "active" form of vitamin D, 1,25-dihydroxyvitamin D (1,25(OH)2D) is a

form that binds to the vitamin D receptor, but has a relatively short half—life of 1.25(OH)2D after 11-21 hours makes it a poor biomarker for assessing vitamin D status in laboratory studies for statistically significant results in survey groups. Therefore, the circulating total concentration of 25-hydroxyvitamin D (25(OH) is traditionally used to measure vitamin D status) [140,144]. The level of vitamin D was determined by chemiluminescent immunoassay in one of the clinical laboratories of the city of Murmansk, where test tubes with the test material were transported. The results were evaluated in accordance with the Clinical Recommendations "Vitamin D Deficiency" of the Russian Society of Endocrinologists (Table 8) [17].

Oxidative stress plays a key role in the pathogenesis of diseases occurring in the Far North, from the perspective of "Arctic medicine" any nosology in northern latitudes has a more severe form, respectively, it is more difficult to respond to standardized therapy [37,45,57,119].

Table 8 – Interpretation of 25(OH)D concentrations accepted by the Russian Association of Endocrinologists

Classification	Levels 25(OH)D in blood, ng/ml (nmol/l)
Severe vitamin D deficiency	<10 ng/ml (< 25 nmol/l)
Vitamin D deficiency	<20 нг/мл (< 50 nmol/l)
Vitamin D insufficiency	≥20 и <30 ng/ml (≥50 и <75 nmol/l)
Target vitamin D levels	30-60 ng/ml (75-150 nmol/l)
Adequate levels of vitamin D	30-100 ng/ml (75-250 nmol/l)
Levels with possible manifestation of vitamin D toxicity	>100 ng/ml (>250 nmol/l)

To assess oxidative stress in patients, the analysis of the chemically active substance thiobarbituric acid (malondialdehyde) in patients' blood samples using liquid chromatography was used. Lipid peroxidation in the Far North is a process caused by unfavorable conditions of the subarctic climate in which free radicals, such as reactive oxygen species and reactive nitrogen species, break double carbon bonds in lipids with the substitution of a hydrogen molecule for an oxygen molecule in carbon compounds [115,118]. This process leads to the disorganization of organic

compounds, with the formation of lipid peroxyl radicals and hydroperoxides as primary products, as well as malonic dialdehyde (MDA) [77]. The result of lipid peroxidation reactions is the destruction of the cell membrane, an increase in its permeability, followed by damage or death. Malonic dialdehyde is a product of the breakdown of the main chain reactions leading to the oxidation of polyunsaturated fatty acids (PUFA), and thus serves as a reliable marker of oxidative stress. The analysis of malondialdehyde in the blood is widely used in clinical studies as a marker of oxidative stress due to its mild reaction with thiobarbituric acid (TBA) [26]. The reaction leads to the formation of MDA-TBA 2 and gives a red-pink color. For blood sampling with subsequent laboratory tests of the MDA level, MiniMed vacuum tubes (Russia) were used, biological material was taken using a similar technique and delivered to the laboratory.

Oxidative stress is characterized by an imbalance between the production of free radicals and antioxidant protection. One of the most important non-enzymatic antioxidants in the human body is vitamin E, which consists of four different tocopherols and four homologues of tocotrienol (α, β, γ, δ), which have antioxidant activity, with tocopherols being the only antioxidants. The most studied antioxidant mechanism of α-tocopherol, it has the highest biological activity among all vitamin E homologues. Antioxidant activity is determined by blocking lipid peroxidation by binding to free radicals to form oxidized stable tocopherolquinone, etc. The membranotropic effect of α-tocopherol and the anti-inflammatory activity of α- and γ-tocopherols have also been proven, which are directly involved in reducing the expression of cyclooxygenase genes, inflammatory mediators and inhibition of the activity of enzymes involved in the biosynthesis of eicosanoids [1,6,86].

We investigated the antioxidant status of patients by determining the level of a fat-soluble antioxidant, vitamin E (α-tocopherol), in the blood serum. In humans, α-tocopherol is the main form of vitamin E activity found in blood plasma and cells, while β- and γ-tocopherols are minor components, each of which is associated with lipoproteins. At a plasma concentration of 5-15 mg/l-1, α-tocopherol has the highest concentration among all fat-soluble vitamins. Liquid chromatography was performed

in the laboratory to determine the level of α-tocopherol [3]. The biological material was taken by a similar method into vacuum tubes MiniMed (Russia) and delivered to the laboratory.

Laboratory analyses of vitamin status assessment were carried out at the CMD Molecular Diagnostics Center (L041-00110-77/00574836 dated July 01, 2016), malondialdehyde was determined through the Helix laboratory (L041-01126-23/00553381 dated November 10, 2020) in Murmansk according to the relevant reference indicators specified in the laboratory parameters, where biochemical studies of the blood serum of the subjects were carried out (Table 9).

The data obtained were systematized and used to assess the antioxidant status and vitamin D levels in order to prescribe drug treatment in the complex therapy of inflammatory lip diseases.

Table 9 – Reference values of antioxidant status indicators

A marker of antioxidant status	Reference values
Malondialdehyde	0,45 – 1,7 nmol/ml
α-tocopherol	5 – 18 mcg/ml

2.3.2. Bacteriological and microscopic examination of a smear of a chronic lip crack

In this study, microbiological studies were also conducted in a bacteriological laboratory, since bacterial colonization occurs in the chronic course of recurrent lip crack to study the qualitative composition of the microbial flora [19,55]. In accordance with the proposed classification of chronic recurrent lip crack(Table 3), the study was conducted in patients with mild, moderate and severe degrees of the disease – 50 people. The material for the study of the microflora of chronic recurrent lip crack was taken with a sterile probe swab from the surface of the affected lip tissues and the depth of chronic cracks 4 hours after eating, carrying out hygienic procedures and in the native condition of the lips. The collection of material for

bacteriological research was carried out in compliance with the recommendations of the Federal State Budgetary Institution of the Central Research Institute of Epidemiology of Rospotrebnadzor "Collection, transportation, storage of clinical material for PCR diagnostics". To take swabs and transport them to the laboratory, a MiniMed kit was used, Russia (RU No. RZN 2021/14582 dated August 06, 2021), consisting of a polystyrene probe with a viscose swab and a test tube with an Ames transport medium. Material collection technique: opening the package, fixing biological material from the lip surface on the tampon by winding, opening a polypropylene tube with a transport medium, immersing the working part of the tampon with biological material into a tube with an Ames medium, hermetically closing the tube (Figure 5).

Figure 5. Taking a swab from a patient diagnosed with a chronic lip crack

The samples of the material were stored at a temperature in the dental office from + 18 ° C to + 22 ° C and delivered to the bacteriological laboratory during the working day.

To isolate cultures and identify fungi of the genus Candida, a bacteriological method was used to study sowing on a Saburo nutrient medium (RU No. FSR 2011/11416 dated August 06, 2021). To suppress the growth of bacterial coinfection,

antibacterial drugs were added to the nutrient medium in accordance with the protocol of the bacteriological laboratory. In a dry-air thermostat, laboratory TSvL-80 (RU No. FSR 2011/11084 dated June 09, 2011) at a temperature of +22 ° C in the laboratory, fungi were cultured and their subsequent identification after 5 days. Statistically significant results were obtained when obtaining colonies of fungi of the genus Candida in an amount greater than 103 CFU/ml.

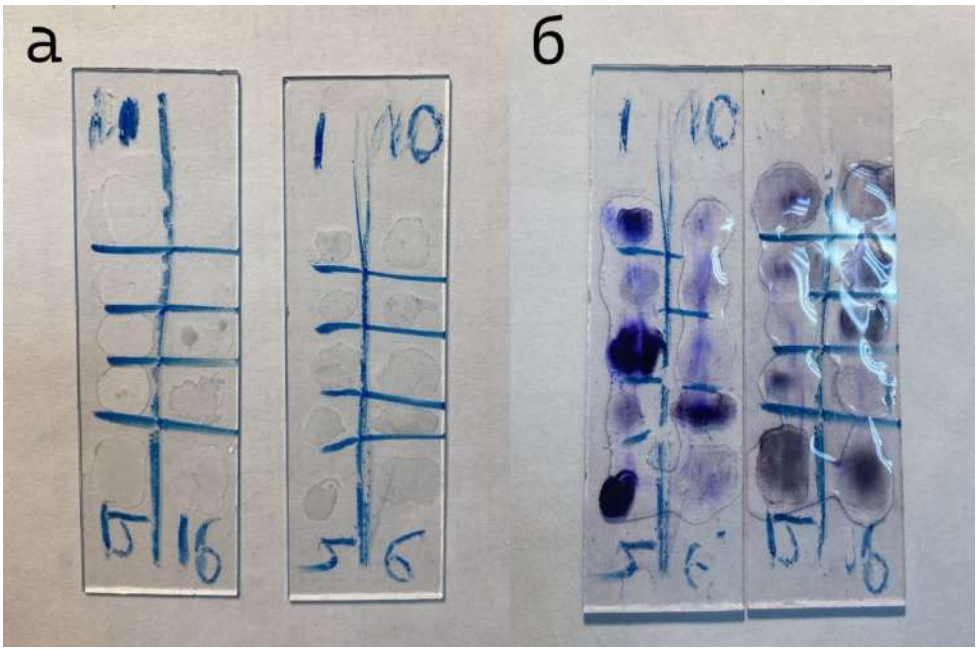

Figure 6. Native smears on a slide (a – fixed samples of microorganisms from colony splinters without staining, b – Gram-stained samples of colony splinters from the nutrient media of the studied samples)

In order to analyze the bacteriological flora, the first stage was seeded with blood agar (RU No. FSR 2012/14082 dated October 11, 2016, Russia), chocolate agar (RU No. FSR 2012/13081 dated December 03, 2020, Russia), UriSelect (RU no. RZN 2019/8613 dated July 16, 2019, France), Levin's Wednesday (RU No.FSR 2008/03063 dated May 26, 2021, Russia), yolk-salt agar (RU No. FSZ 2009/03709 dated December 13, 2012, India). For sowing, the method of scattering homogeneous single colonies and mixtures was used, the growth period of crops was 5 days at a temperature of +37 ° C. The second stage was performed for the identification of bacteria in the grown colonies on blood agar, Kligler medium (RU No. FSR

2007/00968 dated May 26, 2021), yolk-salt agar, medium No. 10 GRM (RU No. FSR 2007/00374 dated August 06, 2021). After the start of growth, all colonies were microscopized with Gram staining (Figure 6) with a set of reagents for staining microorganisms using the Gram method "Micro-GRAM-NITSF" (RU No. FSR 2011/10541 dated October 11, 2016, Russia), having previously made a fence with a sterile loop on a slide with drops of 0.9% sodium chloride solution LLC "MOSFARM" (RU no. LSR – 005263/07 dated December 25, 2007, Russia). The differentiation of the bacterial flora was also carried out by the fermentation reaction of a different spectrum of carbohydrates (Figure 7), a test for plasmocoagulase and lecithinase. To differentiate the bacterial flora, a set of reagents from HiMedia Laboratories (RU No. FSZ 2009/03705 dated 12/21/2012, India), rabbit citrate plasma (ECOlab, No. FSR 2008/03336 dated 09/23/2008, Russia) was used. Microscopic examination was carried out under a biological microscope binocular Micromed (RU No. FSZ 2007/00554 dated 12/26/2007, China).

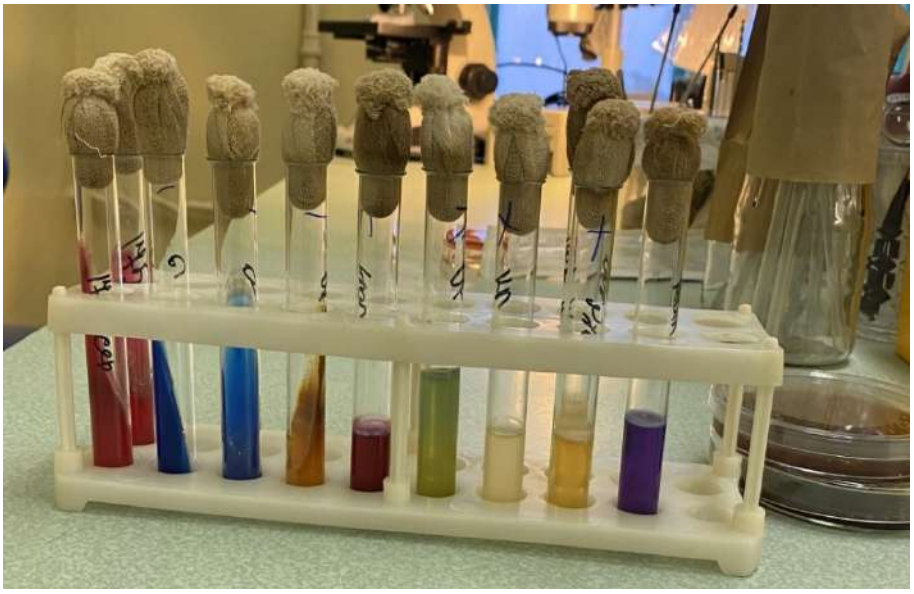

Figure 7. Samples with carbohydrates for biochemical differentiation of the studied bacteria by fermentation of carbohydrates to acid

2.4 Methods of treatment and prevention

The patients of the main (experimental) group were prescribed comprehensive treatment, including topical treatment with a complex ointment, general vitamin and

antioxidant therapy and physiotherapy treatment. Patients in the control group received treatment limited to topical drugs (Table 10). As drugs of choice, depending on the clinical picture, patients were prescribed: Triderm, Pimafucort, Methyluracil, Solcoseryl, sea buckthorn oil, physiotherapy procedures with the Svetozar device (Figure 8), Vitamin D, E, A, Mexidol.

Table 10 – Treatment regimen for patients in the main and control groups

Subjects	Topical treatment	Physiotherapy treatment	Vitamin therapy	Antioxidant Therapy
The main group (n=64)	+	+	+	+
The control group (n=53)	+	-	-	-

Routing to doctors of other specialties was organized for patients with exfoliative and atopic cheilitis of both groups. Patients with exfoliative cheilitis were primarily referred for consultation to a neurologist, patients with atopic cheilitis received a referral to a dermatologist for the treatment of the underlying disease (atopic dermatitis) and relief of other skin manifestations of atopy. Patients with angular cheilitis, depending on the cause and course of the disease, were prescribed appointments by other specialists: a general practitioner, an orthodontist and an orthopedic dentist.

The methodological principles of complex treatment of patients of the main group with various forms of cheilitis, subject to constant exposure to adverse factors of northern latitudes, should include etiopathogenetic therapy aimed at alleviating the effects of adverse factors of the Far North [47].

Dynamic monitoring of patients was conducted continuously for the first 20 days after the start of treatment, followed by follow-up examinations 6 and 12 months after the start of treatment. On day 14, the overall results of treatment were evaluated, after 6 months or earlier, the first cases and the nature of relapses were recorded according to the incidence, after 12 months, methods for the prevention of various forms of cheilitis in the Far North were evaluated.

2.4.1. Drugs used of topical treatment

Patients of the main and control groups, depending on the severity of the manifestation of cheilitis, were prescribed complex Triderm ointments (GRLS Reg. No. N013502/01 dated 07/29/2008, Belgium), composed of antibacterial (gentamicin sulfate), antimycotic (clotrimazole) and glucocorticoid (betamethasone) components or, with a lighter course, Pimafucort (GRLS Reg. No. N012689/01 dated 13.10.2008, Italy), containing neomycin, natamycin and hydrocortisone. Application scheme: applying a thin layer to the affected areas of the lips 2-3 times a day for 5-7 days, depending on the clinical picture (Table 11).

Table 11 – Unified scheme of local treatment with Triderm and Pimafucort drugs in patients of the control and main groups

Nosology	Treatment regimen
Meteorological cheilitis	A thin layer 2-3 times a day for 5 days
Chronic lip crack complicated by meteorological cheilitis	A thin layer on the entire surface of the lips 1-2 times a day for 5 days, spot on the crack 3 times a day until the 7th day of treatment
Chronic lip crack	Spot on the crack 3 times a day until the 7th day of treatment
Exfoliative cheilitis	A thin layer 2-3 times a day for 5 days
Atopic cheilitis	A thin layer 2-3 times a day for 5 days
Angular cheilitis	Spot on the crack in the corners of the mouth 3 times a day within 7 days

After 5-7 days of ointment application, patients of both groups were prescribed therapy aimed at accelerating epithelial regeneration. Patients of the main group were prescribed Methyluracil 10% in the form of ointment ("Industrial Pharmaceutical Company Update", RU LP-No. 001990 dated 03/17/2023, Russia), which patients applied in a thin layer, without rubbing, on the surface of the lips 3 times a day for 7 days. The substance of the pyrimidine derivative of nucleic acids was identified as the main regenerative drug. According to research data, methyluracil has a proven effect of enhancing the growth and mitotic activity of cells, thereby contributing to the activation of regenerative processes in damaged tissues. The mechanism of the

biological properties of methyluracil is based on the enhancement of intracellular biosynthetic processes, the result of which is the stimulation of cell proliferation in tissues. Studies have also established the anti-inflammatory property of the active substance and the stimulation of humoral and cellular immunity factors by methyluracil. An additional drug for patients with exfoliative cheilitis and chronic lip fracture in this study was solcoseryl, which is a deproteinized hemodialysis of young cattle enriched with low molecular weight cellular components [6,23,178]. Due to the active participation of the lips in facial movements, we selected the forms of release of this drug with mandatory fixation on the surface of the lips. The patients of the main group were prescribed the use of Diplen Denta C (Nord Ost, RU No. FSR 2008/02392 dated 06.12.2016, Russia) in the form of a self-adhesive film containing an active substance of 0.05-0.09 mg/cm2. According to our recommendations, patients applied a film with an adhesive surface to the skin of the lips mainly in the Klein zone with exfoliative cheilitis, with chronic lip cracks – to the site of epithelialization of cracks, overlapping them by 2-3 mm 1 time a day at night for 7 days.

Patients of the control group were prescribed the use of sea buckthorn oil oil solution to accelerate regeneration (Altaivitamins, RU R N000245/02 dated 03/11/2022, Russia). The pharmacological properties of sea buckthorn oil determine its ability to stimulate the processes of tissue repair and regeneration. The composition of sea buckthorn oil includes Vitamin A, E, F, flavonoids, carotenoids, Vitamin P, β-sitosterol. The pharmacological effects of sea buckthorn oil are based on the complex effect of all biologically active compounds contained in it and provides damaged tissues with antioxidant, cytoprotective [6,23,], wound healing, anti-inflammatory and regenerating effects. It has also been proven that one of the properties of sea buckthorn oil is its anti-inflammatory and bactericidal activity, including against Staphylococcus aureus and Staphylococcus haemolyticus. Laughter of the use of sea buckthorn oil by patients of the control group: after the end of 5-7 days of application of ointment with a glucocorticoid component, it is prescribed to apply to the surface of the lips 3 times a day and before bedtime for 7 days.

Solcoseryl was selected as drugs to accelerate the regeneration of the lip epithelium in chronic lip cracks and exfoliative cheilitis in the main group due to its multidirectional pharmacological properties, affecting tissues and increasing reparative processes in them, the drug has proven itself in many fields of medicine. The drug has membrane-cytoprotective properties, also having a regenerating effect. In the treatment of chronic lip fissure, the drug may be especially important due to its angioprotective effect. The effect of Solcoserin on improving the transport of oxygen and glucose to cells under hypoxic conditions has been proven in preclinical and clinical studies, the drug increases the synthesis of intracellular adenosine triphosphate and increases the level of aerobic glycolysis and oxidative phosphorylation, stimulates fibroblast proliferation, keratinocyte migration and collagen synthesis [49,64,154].

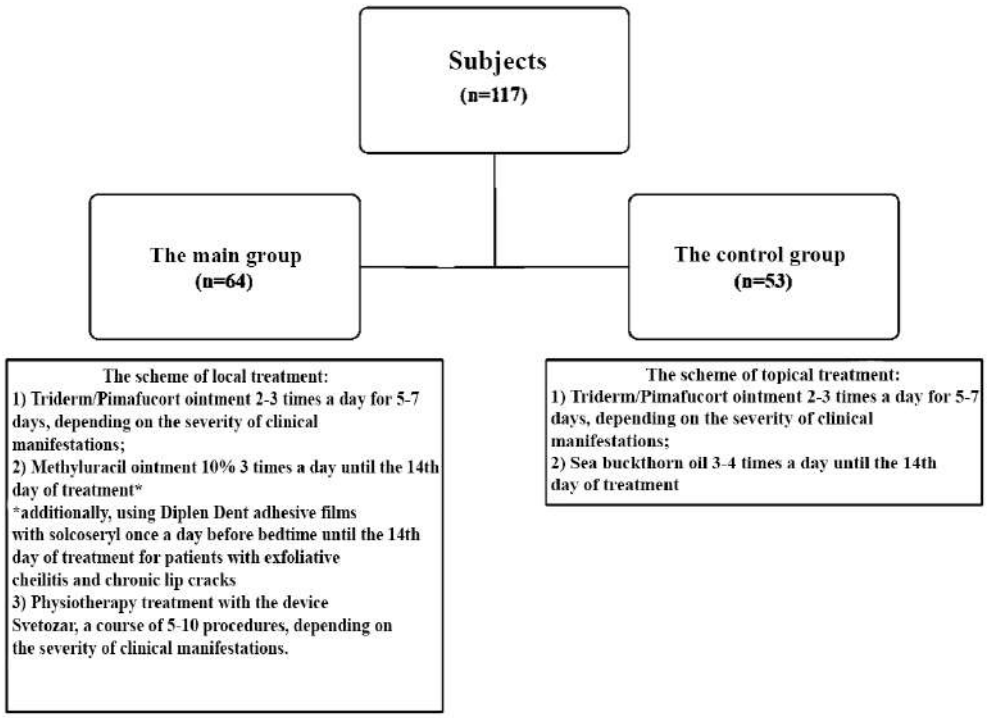

Figure 8. Scheme of local treatment of patients in the main and control groups

The release form in the form of adhesive films contributes to the effective delivery of the active substance in case of lip damage by exfoliative cheilitis in the transition zone of the red border of the lips and the mucous part, which the patient can lick, bite, with chronic lip crack, solcoseryl in the form of a film has the

maximum local effect, at night, thanks to the adhesive film, the long-lasting effect of the active substance on the affected areas will be ensured lip tissues.

2.4.2. Drugs used for general vitamin and antioxidant therapy

Vitamin D is called a "prehormone" by many authors, because it is a key regulator of homeostasis. It is synthesized from the precursor 7-dehydrocholesterol when exposed to ultraviolet rays on the skin and then hydrolyzed in the liver at the position of isomer 25 to finally convert to the active form, 1,25-dihydroxyvitamin D (1,25(OH)2D or calcitriol) in the kidneys [179,184]. Despite the fact that vitamin D is present in foods consumed by humans, the best way of synthesis at the physiological level remains under the influence of ultraviolet rays of type B, the radiation of which is catastrophically low in the regions of the Far North [95]. The biological activity of vitamin D is highest during synthesis induced by ultraviolet radiation, the synthesis process of this substance depends on its binding to the nuclear vitamin D receptor (VDR), followed by the transcription process, the DNA region of the vitamin D response element (VDRE) VDRE interacts with the α-retinoid X receptor [34,71]. The physiological process of vitamin synthesis in the conditions of the Far North is impossible during the polar night, difficult during transitional periods of the year due to low temperatures and the impossibility of sufficient insolation due to closed skin, in the summer the ultraviolet index naturally increases, however, on clear days, insolation during the polar day is about 20%, in products the nutritional content of vitamin D is quite variable, However, this method is not suitable for the treatment of vitamin deficiency or deficiency due to the relatively small amount to compensate for the required level [50,91]. To compensate for vitamin D deficiency in the human body, colecalciferol in the form of a drug was noted in the scientific literature as the most effective proven drug [12,17,71,74,100].

The drug of choice in our study was Vigantol (GRLS Reg. PN011712/01 dated 09/27/2011) manufactured by Lusomedicamenta Sociedade Tecnica Farmaceutica, S.A. (Portugal), product form – oil solution (excipient – triglycerides). 1 drop of the

oil solution corresponds to 500 IU of vitamin. Patients of the main (experimental) group were prescribed colecalciferol according to the clinical recommendation of the Russian Association of Endocrinologists - "Vitamin D deficiency", strictly based on the results of the 25OH vitamin D serum reading. With severe vitamin D deficiency (level 25(OH)D <10 ng/ml) patients were prescribed 6,000 IU per day - 8 weeks orally, with vitamin D deficiency (level 25 (OH)D <20 ng/ml) 6000 IU per day - 6 weeks orally, with a lack of vitamin D (level 25 (OH)D ≥20 and <30 ng/ml) 4000 IU per day – 6 weeks orally, to maintain vitamin D levels ≥30 ng/ml 1000 daily orally. According to the literature, it has been reliably established that the best clinical results from taking vitamin D can be provided by daily doses, rather than weekly or monthly, since daily doses affect serum and tissue concentrations [17,47,136]. Patients were also advised to take Vigantol between 18:00 and 21:00 hours.

In complex vitamin therapy, after the determination of vitamin E in the blood serum, patients were prescribed the drug AEvit (GRLS Reg. LP-005750/08 dated 07/22/2008), containing 55 mg of retinol palmitate and 100 mg of α-tocopherol acetate in a capsule. Vitamin E, including in the form of α-tocopherol acetate, is a powerful antioxidant, since its forms absorb lipid peroxyl radicals, giving off hydrogen from the phenolic group on the chromanol ring, inhibit the synthesis of prostaglandins and leukotrienes in cells. Retinol triggers the proliferative activity of epithelial cells, increases the cell cycle, and stimulates the proliferation of keratinocytes [1,23]. Regimen: 1 capsule 1 time a day in the morning. The duration of treatment for patients will be determined after receiving the results of the vitamin E level in the blood serum.

We categorically did not recommend replacing medicines with biologically active additives with similar names.

As an antioxidant therapy, the drug of choice was ethylmethylhydroxypyridine succinate, release form Mexidol 0.125 g (GRLS RU No. RN002161/01 dated 03/14/2008). The substance belongs to antioxidants and membrane protectors (Figure 9). Antioxidant activity is due to reactions with peroxide radicals by inhibiting free radical oxidation of lipids, increasing the activity of endogenous antioxidant enzymes

(superoxide dismutase), and simultaneously participates in the neutralization of free radical synthesis of eicosanoids. The membrane-protective effect is achieved by the lipid-regulated properties of the drug through an increase in the polar fractions of lipids, membrane-binding enzymes, stabilizing cell membranes. The drug also has a mechanism for regulating lipid levels, exerting a hypolipidemic effect, while lowering low-density lipoproteins and increasing high-density lipoproteins) [6,23,25,89]. The patients were prescribed a course of treatment for 4 weeks, 1 tablet 3 times a day.

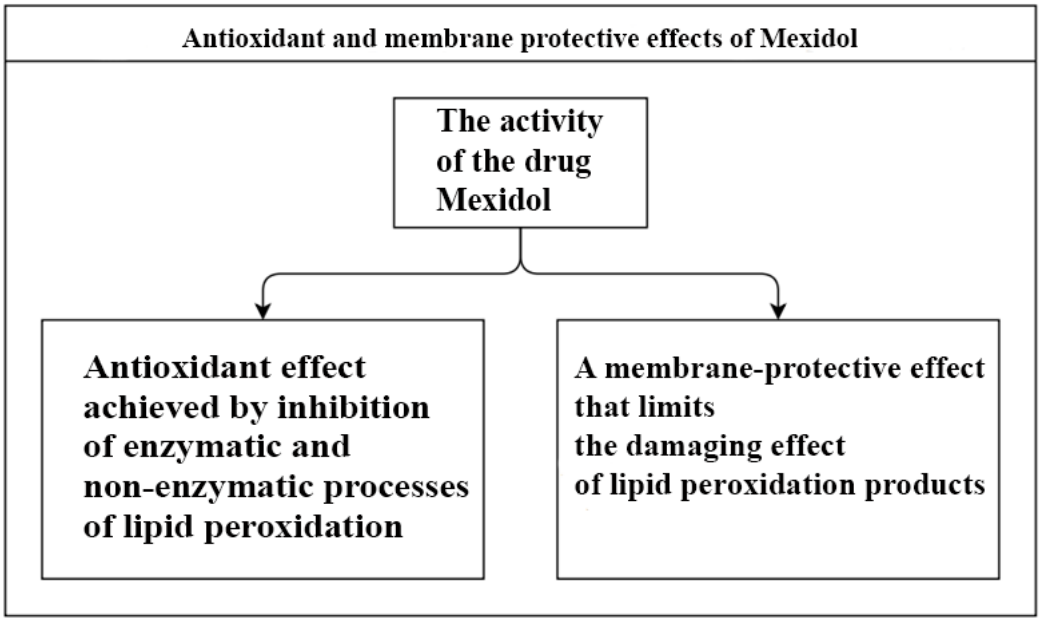

Figure 9. The most important effects of Mexidol used in the study

2.4.3. Physiotherapy treatment

One of the treatment methods used in our study is photobiomodulatory physiotherapy with the Svetozar device. Since the 60s of the XX century, the cellular effect of wavelengths in the red (600-700 nm) and near infrared (770-1200 nm) spectral regions has been studied. Photobiomodulation, also known as non-thermal low-level laser therapy, is the use of red and near-infrared light to stimulate healing, regeneration, pain relief and reduce inflammatory phenomena. The mechanism of physiotherapy is based on the activation of a chromophore by red light, namely

cytochrome c oxidase in the mitochondria of cells and calcium ion channels mediated by light absorption by opsins. Cytochrome c oxidase is the main target of photobiomodulation therapy, the absorption of photons by cytochrome oxidase leads to an increase in the activity of the above-mentioned respiratory chain enzyme in mitochondria, an increase in oxygen consumption and an increase in the production of adenosine triphosphate based on photodissociation of inhibitory nitric oxide. Secondary effects of photon absorption include an increase in synthesis (ATP), a short-term surge in reactive oxygen species, an increase in nitric oxide and regulation of calcium levels [143,145,165]. Tertiary effects include activation of a wide range of transcription factors leading to improved cell viability, increased proliferation and migration, and synthesis of a new protein. The effect of photobiomodulation is two-level: in healthy tissues, ATP is produced by cells, but when exposed to tissues in which pathophysiological processes are present, the level of ATP decreases under oxidative stress. Exposure to red light increases antioxidant protection and reduces the release of free radicals. Changes in the redox state of cells induce the activation of numerous intracellular signaling pathways, regulate the synthesis of transcription factors that directly have a positive effect on the processes of tissue proliferation and regeneration. Molecular studies by foreign authors have established a decrease in inflammation markers when exposed to red light [141,142,153]. Phototherapy with light-emitting diode red light is a safe, non-invasive, inexpensive and portable physiotherapy treatment that can be combined with other treatments. In addition, the visible red spectrum of light has a sufficient penetration depth that allows it to penetrate the epidermis and reach the dermis, red light radiation at the wavelength of the Svetozar device (Figure 10) does not cause DNA damage and does not have a carcinogenic effect. Photobiomodulation using red light sources is being studied more and more every year, it has a wide range of effects at the molecular, cellular and tissue levels, the available published data on phototherapy with light-emitting diodes of red light are used to treat inflammatory diseases of the ENT organs, acne, dermatitis, neuritis, dental diseases of hard dental tissues, periodontal tissues,

alveolitis, burn lesions, trophic ulcers, common surgical and therapeutic diseases, photorejuration in cosmetology-dermatology [133,145,152,185].

Figure 10. The use of the Svetozar device in research. Patient K, 34 years old, chronic lip crack of moderate severity, mediolateral location of a linear defect on the right side of the upper lip

Photons of the Svetozar red light radiation at a wavelength of 665± 15 nm are absorbed by mitochondrial chromophores in lip skin cells. The radiation from the device refers to a coherent light source, a laser [141]. The irradiation time of the lip skin of the subjects is 1.5 minutes, the number of procedures is from 5 to 10 sessions, depending on the clinical picture. The size of the light spot is up to 10 mm with minimal capture of healthy surrounding tissues. The working part of the laser radiation was directed in the sagittal plane directly to irradiate inflamed areas of the lips, if necessary, patients pushed the lip forward and fixed it with their fingers with a sterile gauze cloth.

2.4.4. Methods used for the prevention of cheilitis in the Far North

Patients of the main group, after completing the course of treatment and achieving complete lip epithelization, were prescribed a developed cosmetic product, lip balm "Elabium" (Figure 11), taking a drug containing colecalciferol (Vigantol) 2

drops 1 time a day for 5 consecutive days with a break of 2 days to maintain vitamin D levels in the body.

Each component, which is part of the solid balm "Elabium", is a preventive element in the comprehensive protection of lip tissues from the effects of adverse meteorological conditions. Cocoa butter and sea buckthorn oil were selected as natural oils of the "Elabium" lip product (Table 12).

The basis of our balm is berry wax, a product processed from the fruits of the lacquer tree (Rhus verniciflua), it contains highly structural molecular compounds, esters. First of all, berry wax is present in our product because of its solid-forming function, however, the advantages of berry wax include: high moisture-retaining function and adhesion [168,193].

Most of the balm contains cocoa butter containing saturated fatty acids (palmitic, linoleic, alpha-linolenic, oleic and stearic acids). In addition to fatty acids, the oil is also rich in polyphenolic compounds and minerals. Cocoa butter has the ability to retain moisture on the skin, restore the lipid barrier, and reduce inflammatory phenomena on the skin [109,146,178].

Vaseline is part of a complex balm, it is a fat-soluble ingredient in cosmetics of proven effectiveness in the treatment of xerostomia due to its various properties. However, vaseline is a thick and waxy material, according to studies conducted by Raman microscopy (CRS) to evaluate the effectiveness of moisturizers on skin hydration and penetration, the maximum depth of vaseline diffusion is at least 20 microns [129,168].

Petroleum jelly mainly remains in the stratum corneum of the epithelium and plays an important role in protecting the skin barrier. Vaseline is a ready—made and universal emollient, it forms a film on the surface of the skin, fills the gap between a large number of exfoliating keratinocytes, smoothes the rough surface of the horny layer of the lips with peeling and increases the moisturizing ability of the skin. However, other studies also indicate that vaseline can penetrate the skin and promote the restoration of the skin barrier, starting with the production of intercellular lipids

such as sphingolipids, free sterols and free fatty acids. Vaseline has a low allergenic predisposition [129].

Figure 11. The "Elabium" lip balm developed in the framework of this study in a tube

Vegetable oils make up part of the complex ointment. When exposed to the skin, a small part of the oil is mainly adsorbed in the stratum corneum and reaches deeper layers of the skin. The substance has an anti-inflammatory, antimicrobial, moisturizing and protective effect on the epithelium [6,23].

D-panthenol (as part of D-panthenol 75W) is a precursor of vitamin B5 and has a proven positive effect on the healing of epithelial tissues in general by moisturizing the skin surface and creating a barrier effect. There is evidence of a decrease in inflammatory phenomena of the skin, improvement of skin regeneration and wound healing when using ointments containing D-panthenol, there is an increase in the mobility of the molecular components of the stratum corneum, which performs a barrier function, activation of the expression of genes involved in the healing process. We introduced this component into the structure of the balm for two purposes: to moisturize and restore the skin barrier for preventive purposes and as a factor

contributing to wound healing in case of primary damage to the lips during preventive measures [186,189].

During the development of the balm, we used only purified components, free of impurities and allergens, the ointment does not contain artificial flavors and preservatives that could cause irritation of lip tissues [176]. Cosmetic use of the "Elabium" lip balm is made on the basis of herbal components and oils and does not pose a risk to patients due to the lack of systemic effects.

Table 12 – Composition of the "Elabium" lip balm

№ i/o	Active substance	The content per 5 ± 0.2 grams of balsam (solid form)
1.	Cocoa butter	2,12±0,3
2.	Berry Wax	1,30±0,2
3.	Sea buckthorn oil	0,30±0,05
4.	Vaseline	0,98±0,1
5.	Dimethicone	0,20±0,05
6.	D-Panthenol 75W	0,10±0,03

All the ingredients used in the cosmetic balm Elabium comply with regulatory requirements, most of the ingredients can be used separately from each other. The combined effect of all active substances was combined in consistency, the components were mixed in a separate enameled dish, heated in a water bath to a temperature of 50 °C and mixed evenly until a homogeneous consistency was obtained. Before solidification, the liquid mixture of the components of the "Elabium" lip balm was poured into lipstick tubes with a twisting mechanism.

In addition to vitamin therapy, all patients were given recommendations on compliance with work and rest, proper nutrition, especially in autumn and winter, mandatory inclusion in the diet of foods rich in docosahexaenoic acid [166], oral sanitation. Separately, work has been carried out to teach proper and regular oral hygiene. Patients were warned that if the first signs of lip inflammation reappear, do not resort to a compensatory lip licking measure, which will lead to a more severe

course of cheilitis [151,172]. In case of the first symptoms of the disease, patients had to come to the dentist. The use of hygienic balms was recommended to patients of the control group as a local prophylaxis, without specification, to patients of the main group – the balm "Elabium".

2.5. Statistical research

Based on the analysis of the incidence of various forms of cheilitis, a statistical analysis was compiled based on initial visits to the dental office of the polyclinic of the branch No. 3 of FSGI "1469 NCH" of the Ministry of Defense of the Russian Federation in Murmansk in 2021, 2022, 2023, the proportion of patients with diagnosed forms of cheilitis for 3 years was determined.

The effectiveness of the complex treatment of patients with various forms of cheilitis was assessed by the positive dynamics of the clinical picture (the period of recovery or the period of epithelialization of damaged lip tissues), and the effectiveness of preventive measures was assessed by analyzing the frequency of relapses and the length of remission periods.

In the statistical data of the studies, the coefficient of variation of the indicators indicates their uniformity and weak variation of the data, therefore, the results obtained can be considered reliable. The oscillation coefficient determined for the nosology of each group and the Chi-squared criterion allow us to conclude that the data correspond to the distribution law.

The research results are presented in the form of an arithmetic mean and a quadratic mean deviation (M±SD), as well as a separate data range from the minimum to the maximum value (min↔max).

The study also used the Student's t-test, which is a parametric test used to compare averages from two research groups. Like most statistical tests, the Student's t-test is based on a number of assumptions about the general population and the analyzed sample in the study data. In order to verify the assumptions, we used the t-

criterion to prevent a false interpretation of the study results in the groups of examined patients [72,124].

Thus, statistical data processing was carried out using the Student's t-test, a method of testing hypotheses about the average sample value of the distribution of the data set and the unknown standard deviation of the general population is unknown. The normality of the trait distribution was assessed using the Kolmogorov-Smirnov criterion [8,30] in the computing environment of Medstatistic and STATTECH (Russia).

According to the recommendations of the international committee of Editors of Medical journals (international), all the obtained quantitative assessment data are presented with appropriate measurement error indicators, interval estimates (confidence interval) of the study of the parameters of the distribution of the trait in the general data set are constructed [79,124]. The confidence interval in our study was 95%.

In addition, as a mandatory tool for descriptive statistics of all indicators of our study, point and interval estimates of the following values were determined: arithmetic mean, median, variance, standard error of the arithmetic mean and average absolute error [70,80]. The statistical significance of this study is $p < 0.05$.

Cross-platform software was used to visualize the research: Diagrams.net, Google spreadsheets from Excel.

2.6. Summary of the material and methodological basis of the study

Thus, in the course of our research work, we conducted clinical methods of examination of 117 patients with meteorological cheilitis, chronic lip crack, as well as a complication in the form of meteorological cheilitis, angular, exfoliative and atopic cheilitis of the control and main groups, their gender and age were identified. The laboratory parameters of blood serum were analyzed, data on the vitamin and antioxidant statuses of subjects with various forms of inflammatory lip diseases were obtained, on the basis of which complex therapy was prescribed to patients of the

main group. Biological material was collected and bacterial microflora was evaluated in patients with chronic lip crack and in patients with chronic lip crack in combination with meteorological cheilitis, in order to identify the features of bacterial flora in patients with mild, moderate and severe degrees of severity of chronic lip crack. Similarly, patients in the control and main groups with chronic lip crack and in patients with chronic lip crack in combination with meteorological cheilitis were tested for interest in treatment, which determined whether the doctor could understand the choice of treatment tactics for patients with a low level of interest.

Patients were routed for the purpose of additional diagnostic and, if necessary, therapeutic measures. After the appointment of a course of complex treatment, dynamic monitoring of patients in the control and main groups was carried out for 20 days. Upon completion of treatment, preventive measures were prescribed to patients of the main group.

Based on the obtained diagnostic indicators and the results of complex treatment and prevention, the conclusions of our study were formulated, which are the basis for the algorithm of complex treatment of various forms of inflammatory lip diseases in patients in the Arctic zone of the Far North.

CHAPTER III. RESEARCH RESULTS

3.1. Laboratory test results

During the first appointment, all patients were assigned a laboratory examination of the level of vitamin D and E in the blood serum. According to the results of the analysis, it was found that during the initial examination, 100% of patients had vitamin D levels below the reference values. The average level of vitamin D (M±SD) in serum in patients of both groups is 19.3±3.7 ng/ml, which corresponds to vitamin D deficiency in accordance with the classification of the Russian Association of Endocrinologists.

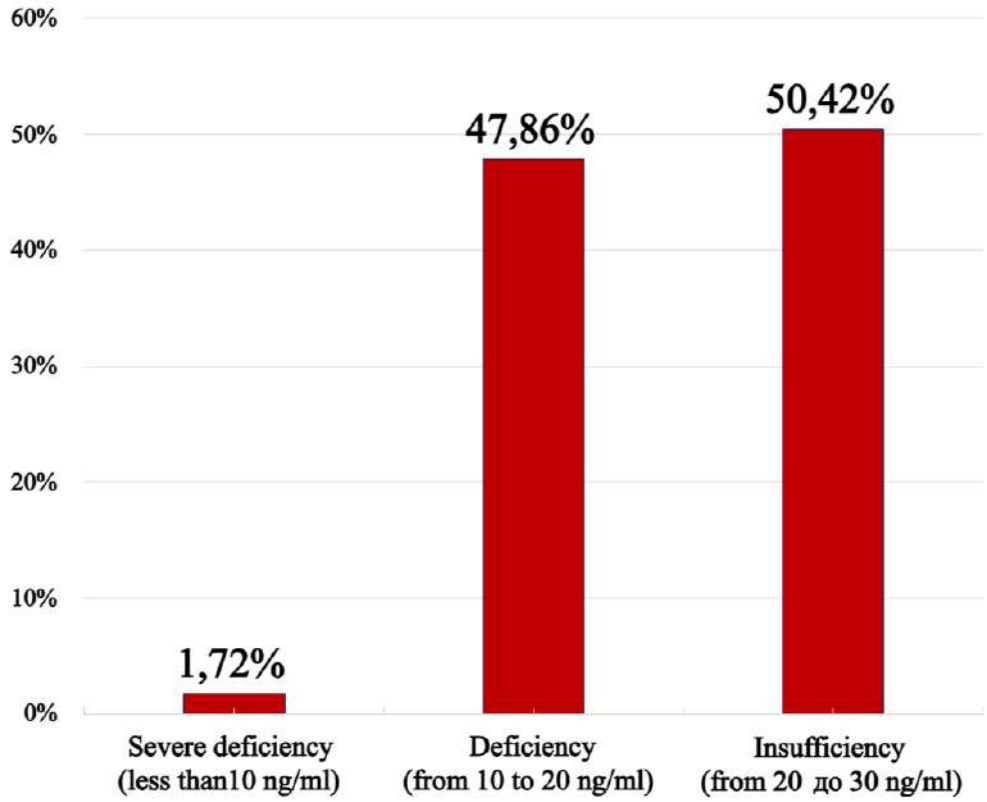

Figure 12. Distribution of subjects (n=117) according to the level of 25 (OH) Vitamin D in blood serum at the beginning of the study

Vitamin D deficiency was detected in 47.86% (n=56), deficiency was detected in 50.42% (n=59), pronounced deficiency was determined in 1.72% (n=2) (Figure 12). Most of the subjects with chronic lip crack, meteorological cheilitis or their

comorbid condition participated in the study in the autumn-winter period, respectively, most of the laboratory studies at the initial admission occurred during the polar night or the state of transition periods and low temperatures.

The distribution of patients into groups was randomized without taking into account their serum vitamin D levels. The average laboratory test values for the control group were 19.85±3.5 ng/ml, the main one was 18.88±3.88 ng/ml (Table 13).

Table 13 – Serum vitamin D level 25(OH) at the initial examination

Group	M±SD (ng/ml)*	min↔max (ng/ml)*
Control (n=53)	19,85±3,5	10,6 – 25,1
CLC (n=16)	19,24±4,18	10,6 – 25,1
MC (n=18)	19,68±3,83	11,8 – 24,7
CLC+MC (n=7)	20,04±2,66	15,3 – 23,2
AC (n=3)	20,36±0,68	19,4 – 20,9
EC (n=3)	22,26±1,53	20,6 – 24,3
UC (n=6)	20,21±1,82	17,7 – 23,1
Main (n=64)	18,88±3,88	9,1 – 27,3
CLC (n=18)	18,27±4,39	9,1 – 27,3
MC (n=21)	17,97±4,45	9,8 – 24,7
CLC+MC (n=9)	20,55±2,18	16,5 – 23,4
AC (n=4)	18,75±2,55	15,4 – 22,3
EC (n=4)	20,82±2,57	16,2 – 23,4
UC (n=8)	19,9±1,97	17,5 – 23,8

*$p < 0,05$ – reliability in comparison between the main and control groups

The graphical display of the results of the initial study of vitamin D levels in patients (Figure 13) clearly demonstrates the problem of low content of this vitamin in the population of the Far North. The highest (27.3 ng/ml) and lowest (9.1 ng/ml) vitamin D levels were recorded in patients with chronic lip crack of the main group.

Examination of patients for the content of 25(OH) vitamin D found a low content of this vitamin in the body of all subjects. In the structure of vitamin D

deficiency and deficiency, the highest average values were recorded in patients with exfoliative cheilitis (n=3) of the control group 22.26±1.53 ng/ml.

The population of the Far North, living in the absence of sunlight beyond the Arctic Circle and not taking regular vitamin therapy with colecalciferol preparations, are at high risk of vitamin D deficiency. The state of vitamin D levels cause alertness in northern geographical regions, since the biological method of vitamin D synthesis by the skin, activated by ultraviolet rays B, is absent for most of the year: from October to April, in the summer months, solar activity is extremely low, synthesis is limited and insufficient.

Since the measurement of the vitamin D level of patients was preceded by the distribution at the initial admission into the main and control groups, we do not use a comparative statistical analysis of vitamin D levels between groups during the primary measurement, but conduct a study within the nosology groups.

The lowest index of the average vitamin D level was recorded in the main group of meteorological cheilitis at 17.97±4.45 ng/ml (n=21). The highest index of the average vitamin D level was recorded in the control group in patients with exfoliative cheilitis of 22.26±1.53 ng/ml (n=3). Conditions of pronounced vitamin D deficiency of less than 10 ng/ml were established in the main group in a patient with meteorological cheilitis (n=1) and in a patient with chronic lip crack (n=1). The optimal level of vitamin D was not recorded in any of the subjects of the main or control groups (Table 13).

The study of vitamin D levels in patients of the main and control groups showed that not only vitamin D deficiency, but also vitamin D deficiency is widespread among the population of the Far North, the problem requires a comprehensive solution at the regional health level, the introduction of preventive measures. In relation to our study, the vitamin D level determined in patients of the main group determined the treatment tactics and dosage of the vitamin D drug, Vigantol, in the complex therapy of diagnosed forms of cheilitis.

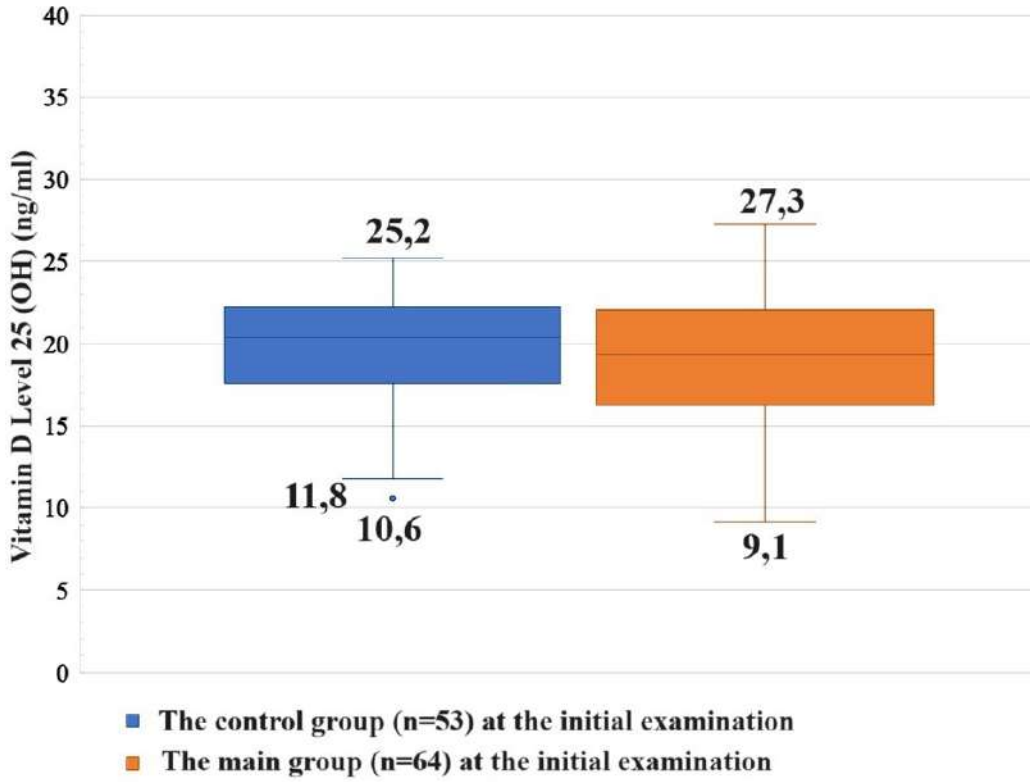

Figure 13. The level of vitamin D in the blood serum of patients of the main and control groups during the initial examination

Due to the fact that prior to the analysis, none of the patients took vitamin D supplements either in the form of biologically active additives or in the form of medicines, the results can be considered a reliable epidemiological indicator of vitamin D availability in the population beyond the Arctic Circle in a subarctic climate. Vitamin D deficiency and deficiency in patients is subclinical in nature.

6 months after the start of taking the drug Vigantol, in accordance with the initial level of vitamin D in the blood serum, a repeat determination was performed in patients of the main group (n=64).

Vitamin D deficiency was not observed in any of the subjects 6 months after the start of treatment. However, it was noted that 10.94% of patients in the main group (n=7) had vitamin levels below normal values, when studying the medical records of patients with an identified level of vitamin D deficiency, it was found that patients with chronic lip fissure and chronic lip fissure complicated by meteorological cheilitis have the results of a questionnaire of interest in treatment "low of interest."

Also, at a follow-up examination 6 months after the start of treatment, relapses of the corresponding forms of cheilitis were recorded, and from the survey it was found that the doctor's recommendations were followed "on a case-by-case basis". The minimum vitamin level was recorded in a patient with a chronic lip fracture (25.1 ng/ml) (Figure 14).

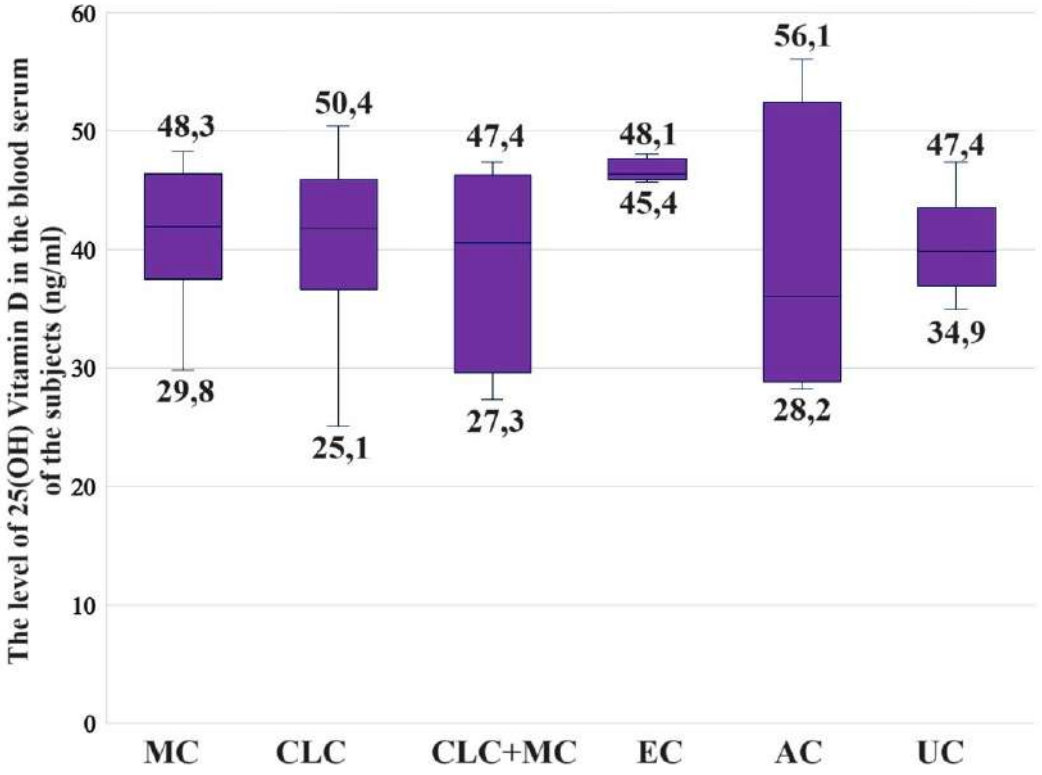

Figure 14. Vitamin D levels in patients of the main group (by nosology) after 6 months

Normal serum vitamin D levels were determined in 89.06% (n=57). The maximum level was recorded in a patient with atopic cheilitis (56.1 ng/ml).

Taking into account the current vitamin D levels, a course of Vigantol was re-prescribed to patients with vitamin deficiency (n=7), the rest of the study participants were given recommendations for maintenance doses of vitamin D.

12 months after the start of treatment, we re-analyzed the results of vitamin D levels. As well as 6 months after the start of the examination of patients, vitamin D deficiency was not observed. Vitamin levels below normal values were recorded in 4.69% (n=3), among them patients with nosologies such as meteorological cheilitis

(n=1), chronic lip crack (n=1), chronic lip crack complicated by meteorological cheilitis (n=1), while patients with chronic lip crack and chronic lip crack complicated by meteorological cheilitis have the results of the questionnaire of interest in treatment "low level of interest". The minimum vitamin level was recorded in a patient with a chronic lip crack (27.8 ng/ml). Also, at a follow-up examination 12 months after the start of treatment, relapses of the corresponding forms of cheilitis were recorded in patients with low vitamin D levels, a survey of patients found that regular compliance with the recommendations was not supported (Figure 15).

95.31% (n=61) had normal serum vitamin D levels. The maximum level was recorded in a patient with atopic cheilitis (51.3 ng/ml).

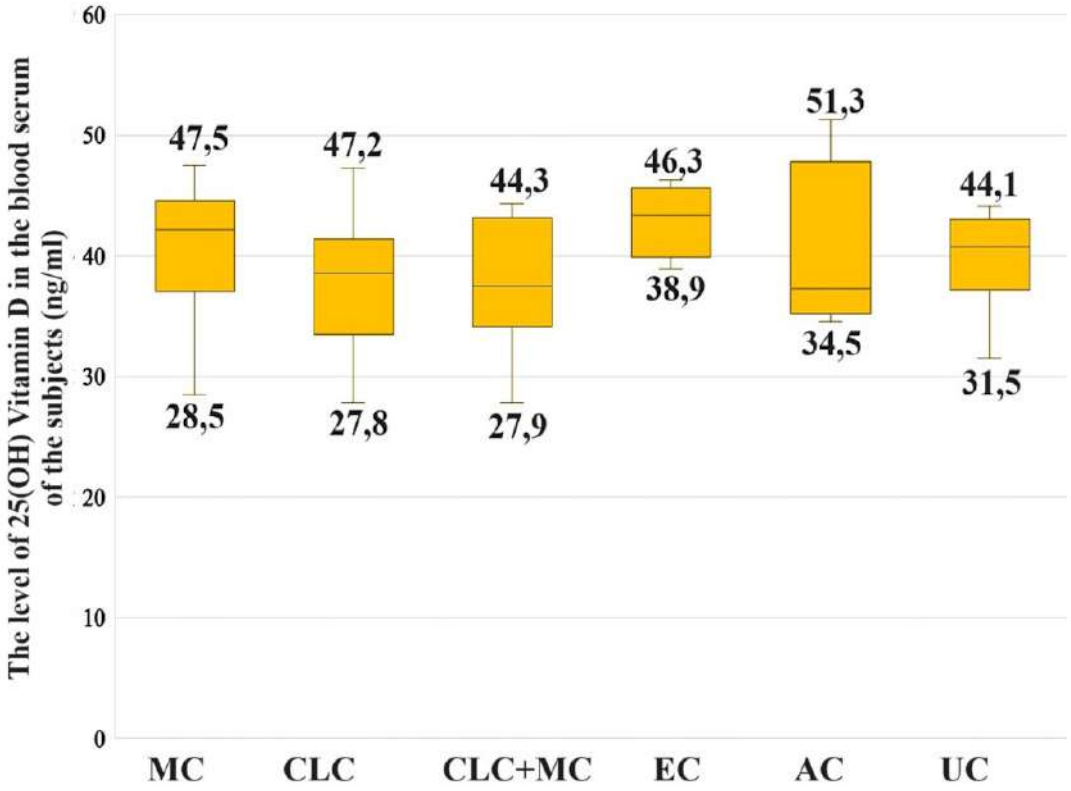

Figure 15. Vitamin D levels in patients of the main group (by nosology) after 12 months

A statistical study of the vitamin D content in the blood serum of the subjects of the main group found that the average vitamin level in the subjects increased by 115.04% after 6 months and amounted to 40.6±6.78 ng/ml compared with the measurement at the initial visit before the start of treatment (18.88±3.88 ng/ml).

Repeated analysis of laboratory parameters after 12 months (39.47±5.08 ng/ml) revealed a decrease in the average values of vitamin levels in patients by 2.78% compared with previous indicators after 6 months (Figure 16). In our opinion, this is due to the cumulative property of vitamin D in the body and its ability to constantly spend it on metabolic processes in the body, in addition, according to the patients themselves, the subjects 6 months after the start of the recommendations for prevention irregularly took vitamin D in maintenance doses of 500-1000 IU.

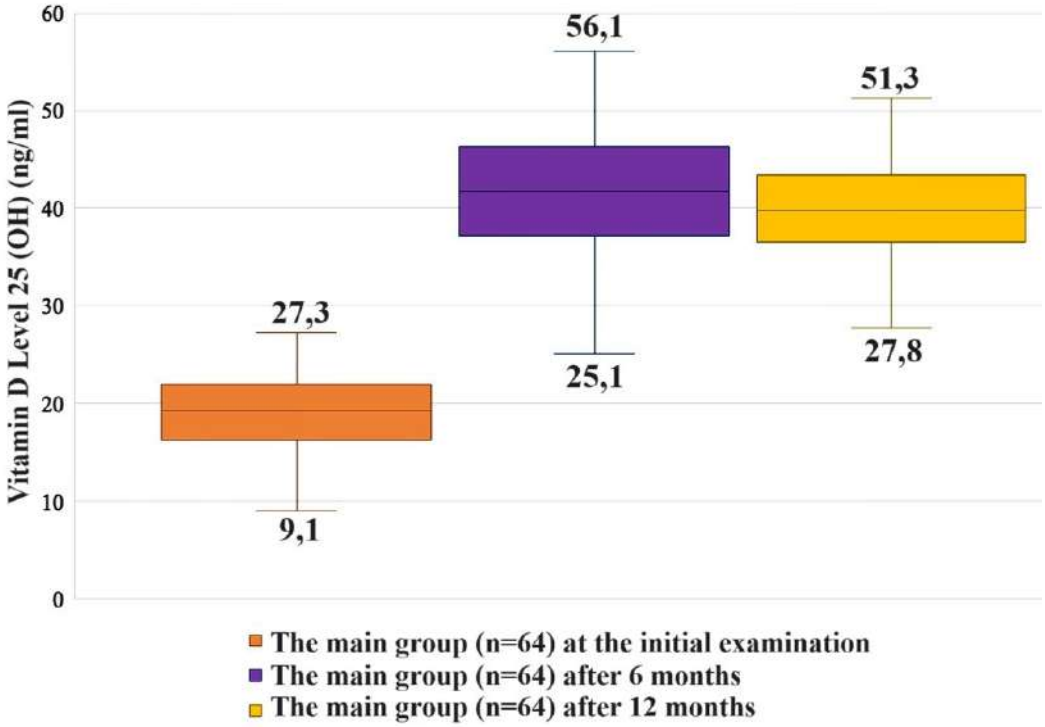

Figure 16. General diagnostic picture of vitamin D serum levels in the main group of subjects

The prevalence of vitamin D deficiency and insufficiency in the regions of the Far North is especially high, while vitamin D is an indispensable steroid prehormone, it is involved in the process of metabolism, cell metabolism, accelerating the healing process, including in inflammatory diseases of the lip skin. Vitamin D plays an important role in regulating local immune responses and reducing excessive production of T-cell responses by modulating keratinocyte proliferation, differentiation and apoptosis. Since the absence of vitamin D deficiency and

deficiency provides favorable conditions for the regeneration of the skin, mucous membrane and red border of the lips, we consider it necessary to include vitamin D drugs in the comprehensive treatment plan for various forms of cheilitis in the Far North.

When evaluating the results of vitamin E analysis in patients of the main and control groups, the results were as follows: 93.16% of the subjects (n=109) had vitamin E levels at the initial examination within the reference values: for the control group (n=53) 8.24±2.01 mcg/ml, for the main group (n=64) 8.65±1.29 micrograms/ml.

The results of a laboratory study on the determination of α-tocopherol in blood serum in patients of the main and control groups by nosology are presented in Table 14.

Table 14 – The level of Vitamin E in the blood serum during the initial examination

Group	M±SD (mcg/ml)*	min↔max (mcg/ml)*
Control (n=53)	8,24±2,01	4,8 – 12,4
CLC (n=16)	8,02±2,25	4,8 – 11,8
MC (n=18)	8,05±2,21	5,3 – 12,4
CLC+MC (n=7)	8,54±1,3	6,3 – 9,7
AC (n=3)	7,43±1,53	5,4 – 9,1
EC (n=3)	8,36±1,79	6,9 – 10,9
UC (n=6)	9,14±1,29	7,9 – 11,1
Main (n=64)	8,65±1,29	5,1 – 12,2
CLC (n=18)	8,2±1,86	5,1 – 12,2
MC (n=21)	9,12±1,72	5,3 – 12,1
CLC+MC (n=9)	8,47±1,78	5,8 – 11,1
AC (n=4)	9,05±1,34	6,8 – 10,2
EC (n=4)	8,85±1,35	8,1 – 10,8
UC (n=8)	8,3±1,94	4,8 – 11,1

*$p < 0,05$ – reliability in comparison between the main and control groups

Of the total number of subjects, 6.84% (n=8) showed a decrease in serum vitamin E levels: in the control group, 9.26% (n=5) with meteorological cheilitis (n=2), with chronic lip crack (n=2), with atopic cheilitis (n=1), in in the main group, 4.68% (n=3) had angular cheilitis (n=1), meteorological cheilitis (n=1), and chronic lip crack (n=1) (Figure 17). However, the recorded level of vitamin E deficiency was close to the reference values from 5.5 to 18 micrograms/ml and was equal to 5.09±0.22 micrograms/ml (Figure 18).

A-tocopherol, detected in the blood serum of patients, is one of the most common forms of vitamin E, which is actively involved in cellular repair and is an antioxidant. Vitamin E prevents cell damage during lipid peroxidation, neutralizes free radicals, which are a companion of "polar stress" and adverse environmental factors of the Arctic zone of the Far North.

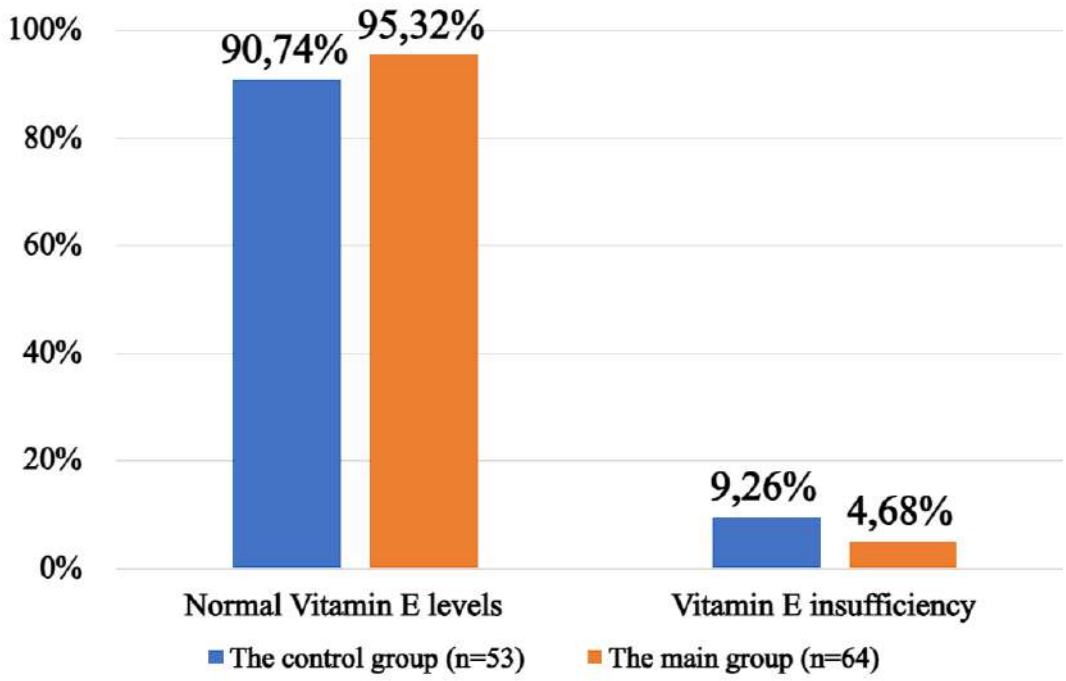

Figure 17. Distribution of subjects (n=117) by serum α-tocopherol level at the beginning of the study

Vitamin E has regenerative and membrane-protective properties, and when applied topically, it can have an anti-inflammatory effect. The optimal level of this fat-soluble vitamin in the body of patients supports the antioxidant balance and

barrier-repair function of cells and tissues, including the skin of the lips. The inclusion of this vitamin in the program of complex treatment of various forms of cheilitis in the Far North is necessary due to its properties, the absence of vitamin E deficiency creates conditions for ensuring long-term remission of cheilitis.

The overall picture of vitamin E level results reflects a low percentage of vitamin deficiency in the subjects (Figure 18). Due to the fact that tocopherols are found in many foods, unlike vitamin D, food intake into the human body occurs daily in small amounts. Based on the results of a laboratory study of vitamin E, patients in the main group were prescribed the drug Aevit according to the scheme: in case of insufficiency, 1 capsule 1 time per day for 30 days, with reference values up to 10 mcg /ml, 1 capsule 1 time per day for 14 days for the period of treatment. In patients with a result of more than 10 mcg /ml of vitamin E in serum, the drug Aevit was not prescribed.

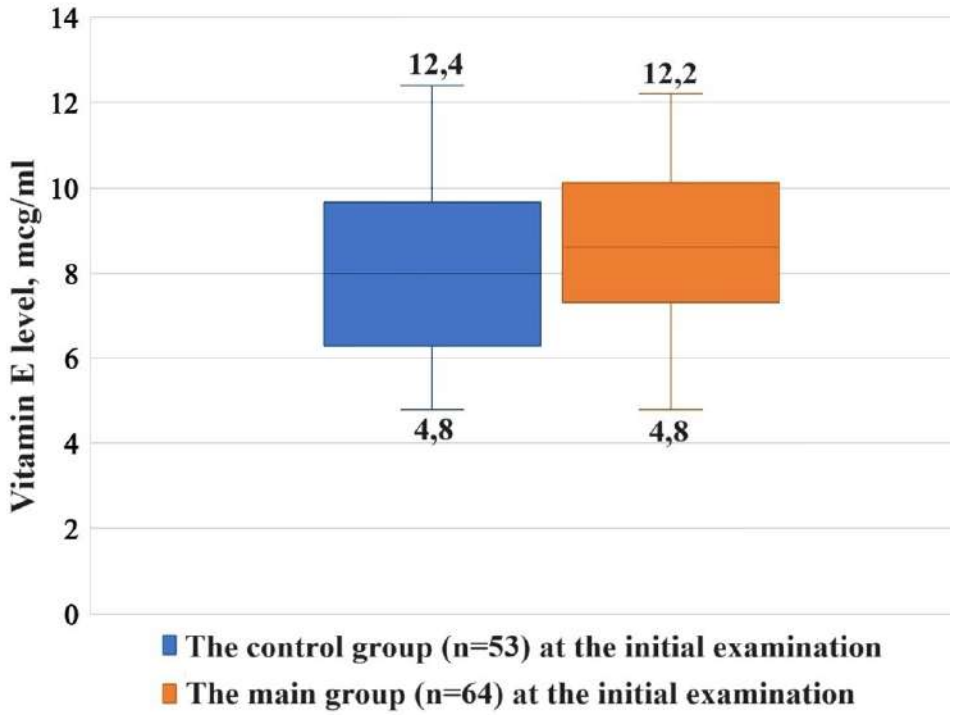

Figure 18. The serum levels of vitamin E in patients of the main (n=64) and control (n=53) groups

Despite the fact that all patients were somatically healthy at the time of the study, analysis of the level of malondialdehyde found that 21.37% of the subjects

(n=25) had an increased indicator of oxidative stress marker. It was found that in patients of the control group, the serum MDA level was 1.09±0.43 nmol/ml, in patients of the main group 1.06±0.39 nmol/ml. There was no statistical significance for comparing the difference in laboratory diagnosis of MDA both between the examined groups and within the nosology groups (Figure 19).

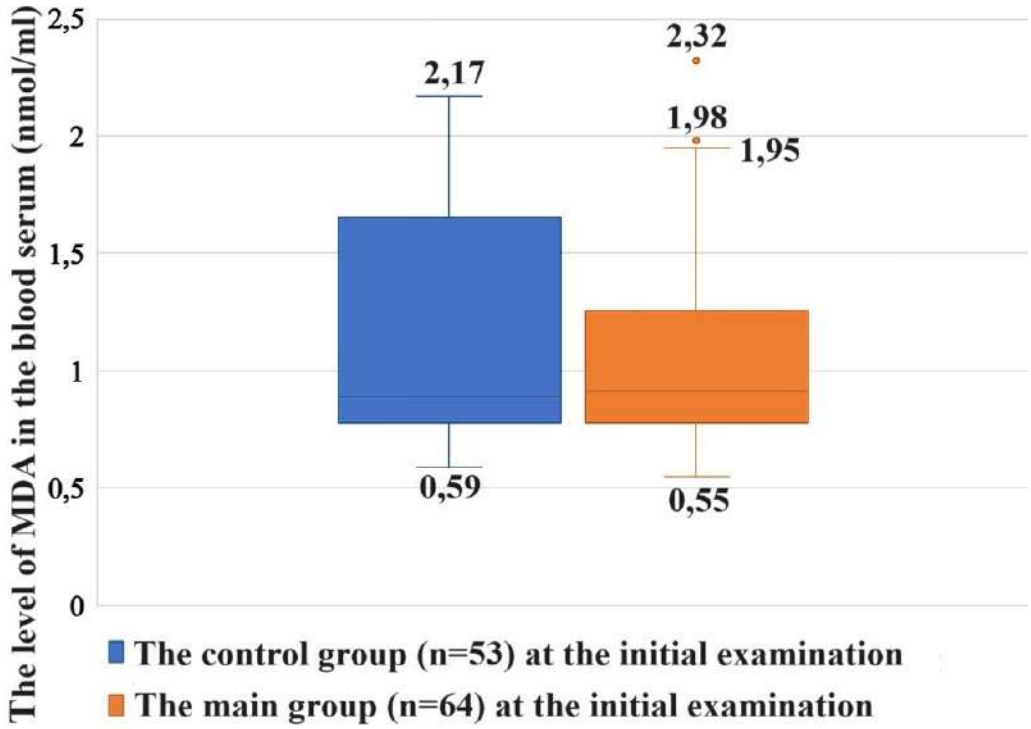

Figure 19. The serum level of malondialdehyde in patients of the main (n=64) and control (n=53) groups

Oxidative stress is a concomitant factor of a wide range of nosologies, through the mechanisms of the damaging effect of reactive oxygen species on cells, for example, direct oxidation by reactive oxygen species (hydroxyl radical, peroxynitrite). Another important mechanism of cell damage mediated by oxidative stress is impaired transmission of redox signals. Despite the lack of statistical significance between the groups and within the nosology groups, we noted that among patients who had an increased marker of oxidative stress, vitamin E deficiency was observed when analyzing the study of vitamin E levels (n=8), the remaining 17 subjects with elevated levels of malondialdehyde had an index no higher than 6.9

mcg/ml. It was also found that the level of MDA in the blood serum was higher in the subjects who had been living in the extreme conditions of the Far North for a longer time.

Thus, we can conclude that the level of malondialdehyde in the blood serum depends on the indicators of the body's antioxidant defense system and increases with a decrease in antioxidant levels (for example, vitamin E in our study). Since the leading pathophysiological mechanism of "polar stress", which triggers a cascade of damaging effects on the cellular and tissue structures of organs, is free radical oxidation, in case of violation of the processes of formation of a stable system of antioxidant protection of the body associated with their increased consumption in the Far North, it is advisable to prescribe drugs with an antioxidant effect. In our study, patients in the main group received Mexidol.

3.2. Results of microbiological and bacteriological studies

There are numerous associations of microorganisms on human skin. The microbiome of the skin strongly depends on the localization of areas of the skin and plays a significant role, including in maintaining the health of the skin of the lips. The main function of the epithelial cover is barrier, which is to protect the body from potential invasion of microorganisms. The epithelial integuments of the red border of the lips anatomically have many linear microlayers, which become the habitat of a wide range of microorganisms. The skin part and the red border of the lips are in permanent contact with the external environment, thus, like the rest of the human skin, they make up a biotope that is colonized by many microorganisms.

Unlike the cutaneous part, where there are sebaceous glands that support the lipid and water-salt balance of the skin, which reduce pH, reduce colonization and growth of microorganisms, the red border of the lips is devoid of many protective mechanisms. When the balance of microorganisms is disturbed or adaptive and

protective mechanisms decrease, the growth of microflora occurs, respectively, the damaging effect of bacterial toxins on cells of all epithelial layers increases.

In 100% of cases, chronic lip cracks, according to the results of a bacteriological study, are accompanied by a massive increase in bacterial colonization. Most of the microflora is represented by gram-positive cocci. Among the examined patients with CLC and CLC+MC, the following microorganisms were isolated in smears from the depth of lip cracks (Figure 20): Staphylococcus aureus in 38% of cases (n=19), Staphylococcus saprophyticus 24% (n=12), Staphylococcus epidermidis 84% (n=42), Streptococcus viridans spp 38% (n=19), Candida spp. 30% (n=15), Staphylococcus pseudintermedius 14% (n=7), Pseudomonas aeruginosa 28% (n=14), Enterococcus spp. 16% (n=8) figure. At the same time, differentiation was carried out from the total number of smears where fungi of the genus Candida (n=15) were established: Candida albicans was isolated in 53.33% of cases (n=8), Candida parapsilosis 20% (n=3), Candida glabrata 26.67% (n=3) (Table 15.16).

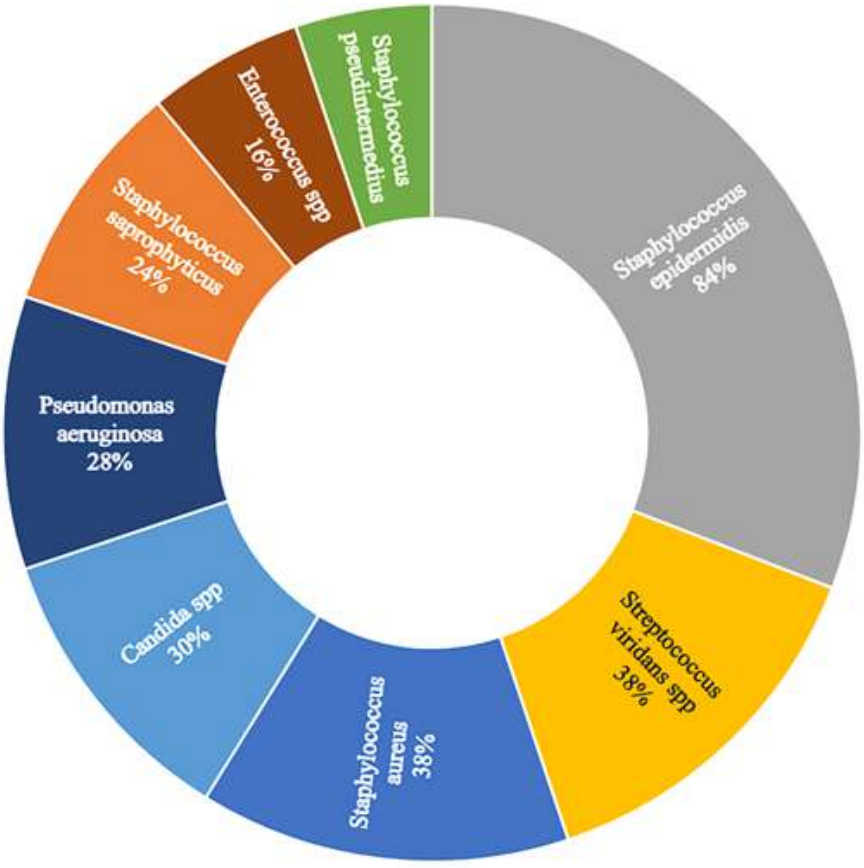

Figure 20. Incidence of microorganisms in smears in patients with chronic lip crack and chronic lip crack complicated by meteorological cheilitis (n=50)

The study established a high degree of microbial contamination of cracks in the red border of the lips in the order of counting colony-forming units (from 10^2 to 10^8 CFU in 1 ml of nutrient medium).

The microflora is represented by conditionally pathogenic microorganisms, which normally persist on the skin or in the human oral cavity, but with damage to the skin, changes in host resistance, conditionally pathogenic microorganisms begin to act as an attached secondary infection with activation of the corresponding pathogenicity factors in the tissues of microorganisms. Communities of microorganisms create a biofilm that prevents the healing of chronic lip cracks, polymicrobial communities of bacteria and fungi formed around the cracks and in their depth are surrounded by an extracellular matrix, common wound-associated bacteria such as Staphylococcus, Streptococcus and Pseudomonas aeruginosa produce exotoxins that cause cell damage and disruption of normal cellular metabolism, which leads to aggravation the infectious process. In this study, we recorded two-three-four-component associations of microbial biofilm with different degrees of growth.

Table 15 – Characteristics of microbial biofilm in patients with chronic lip crack complicated by meteorological cheilitis (n=16), with determination of the degree of microbial contamination (CFU/ml)

An established microorganism	Frequency of occurrence (%),number of reported cases	Concentration in samples (CFU/ml)
Candida albicans	31,25% (n=5)	10^2-10^3
Candida parapsilosis	12,5% (n=2)	10^3
Candida glabrata	25% (n=4)	10^2-10^3
Staphylococcus aureus	25% (n=4)	10^4-10^5
Staphylococcus epidermidis	100% (n=16)	10^4-10^6
Streptococcus viridans spp.	50% (n=8)	10^5-10^7
Pseudomonas aeruginosa	31,25% (n=5)	10^2-10^3

Staphylococcus saprophyticus	25% (n=4)	10^3-10^5
Enterococcus spp.	18,75% (n=3)	10^2-10^4

*p < 0,05

Microbial films with statistically significant concentrations of Pseudomonas aeruginosa (CFU/ml >103) and/or Staphylococcus aureus in association were found in 38.23% (n=13) of patients with chronic lip cracks, namely with severe and moderate severity and frequent relapses. Some strains of Candida spp. and Enterococcus spp. had poor growth and were statistically insignificant (Table 16).

Table 16 – Characteristics of microbial biofilm in patients with chronic lip crack (n=34), with determination of the degree of microbial contamination (CFU/ml)

An established microorganism	Frequency of occurrence (%)*, number of reported cases	Concentration in samples (CFU/ml)
Candida albicans	8,82% (n=3)	10^2-10^3
Candida parapsilosis	2,94% (n=1)	10^2
Staphylococcus aureus	44,12% (n=15)	10^3-10^6
Staphylococcus epidermidis	76,47% (n=26)	10^4-10^8
Streptococcus viridans spp.	32,35% (n=11)	10^4-10^6
Pseudomonas aeruginosa	26,47% (n=9)	10^2-10^3
Staphylococcus saprophyticus	23,53% (n=8)	10^3-10^5
Enterococcus spp.	14,71% (n=5)	10^2-10^3
Staphylococcus pseudintermedius	20,58% (n=7)	10^2-10^4

*p < 0,05

A small growth of Candida spp. (Figure 21) was found in chronic cracked lips with a lateral location. Nevertheless, there are statistically significant indicators in the determination of fungi of the genus Candida, therefore it is advisable to prescribe a complex ointment containing an antimycotic component.

Staphylococcus aureus (Figure 22) and Pseudomonas aeruginosa were isolated in associations with moderate and severe degrees (Figure 24) in 70% of the subjects (n=24).

Staphylococcus saprophyticus, which is the causative agent of urinary tract infections, was found in statistically significant amounts on chromogenic agar Uriselect (Figure 25) in 25% (n=4) in patients with chronic lip crack complicated by meteorological cheilitis and in 23.53% (n=8) in patients with chronic lip crack.

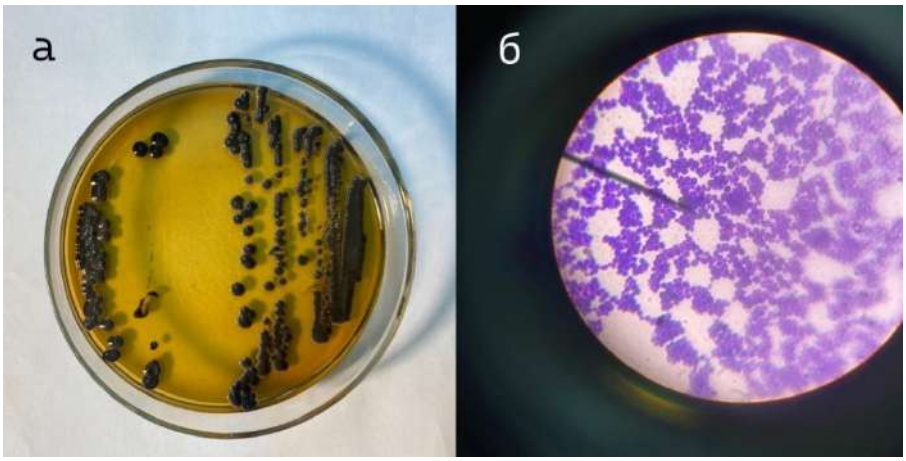

Figure 21. Bacteriological and microscopic studies of Candida spp (a - growth of fungi of the genus Candida when sowing a smear from the depth of a lip crack on Saburo medium; b – yeast-like cells (Candida spp.), Gram-stained, uv. 100x)

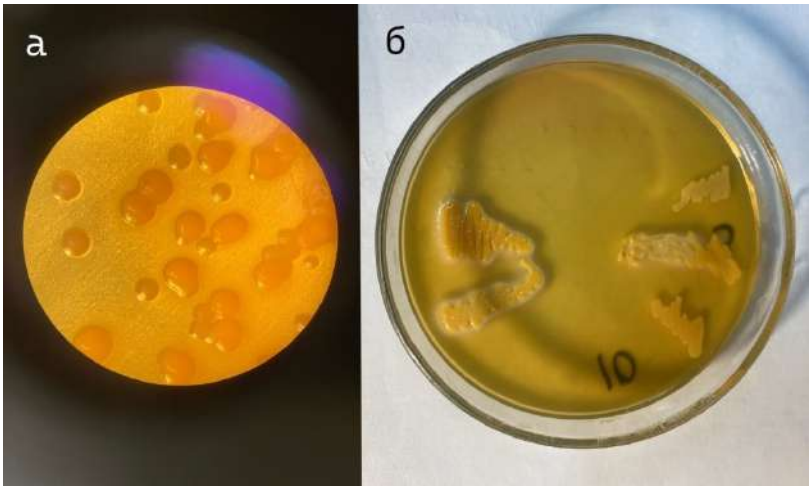

Figure 22. Bacteriological examination of S. aureus (a – growth of S. aureus on yolk-salt agar, uv. 4x; b – separation of S. aureus culture on medium No.10, with determination of positive litsinase activity)

The most frequently seeded microorganism in the subjects was Staphylococcus epidermidis, which was isolated (Figure 23) in 100% of cases (n=16) in patients with

chronic lip crack and a complication in the form of meteorological cheilitis and in 76.47% (n=26) in patients diagnosed with chronic lip crack.

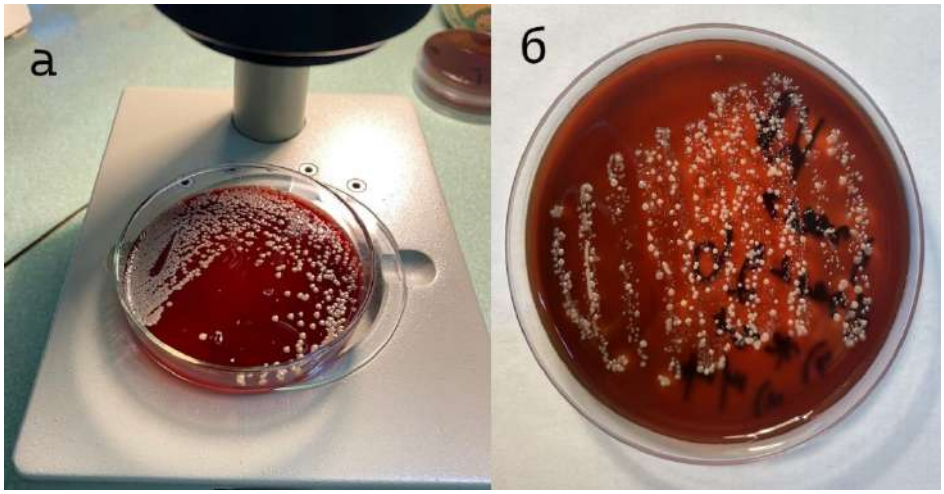

Figure 23. Bacteriological examination (a,b – crops for Staphylococcus epidermidis blood agar)

Figure 24. Patient S., 24 years old, diagnosed with severe chronic lip crack, in whom microorganisms were detected: Candida albicans 103 CFU/ml, Staphylococcus aureus 105 CFU/ml, Staphylococcus epidermidis 108 CFU/ml

Thus, when analyzing the microbial flora from the depth of chronic lip cracks, we observe a symbiosis of the microflora of the oral cavity and the skin. Microorganisms aggravate the course of chronic lip cracks, prevent the healing of linear defects. The factor of microbial colonization on the lip surface in cheilitis causes the inclusion of local drugs containing antibacterial and antifungal components in the treatment plan. The spectrum of bacterial flora on the surface of

the red border of the lips of the subjects is diverse (Figure 26), associations of opportunistic pathogens with various virulence factors are determined in the smears of patients, in one patient, Staphylococcus aureus and bacteria of the Enterobacteriaceae family can be isolated simultaneously from the depth of the crack in the microbial association (Figure 27).

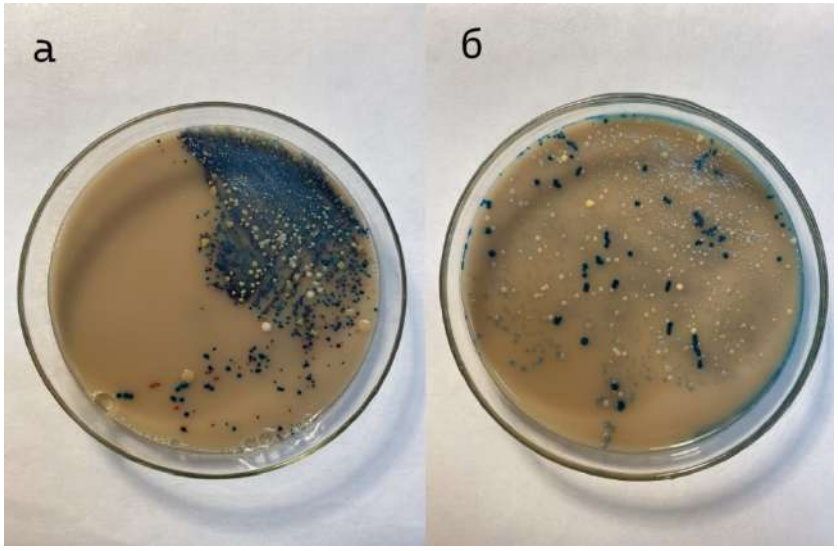

Figure 25. Crops for chromogenic Uriselect agar (a,b)

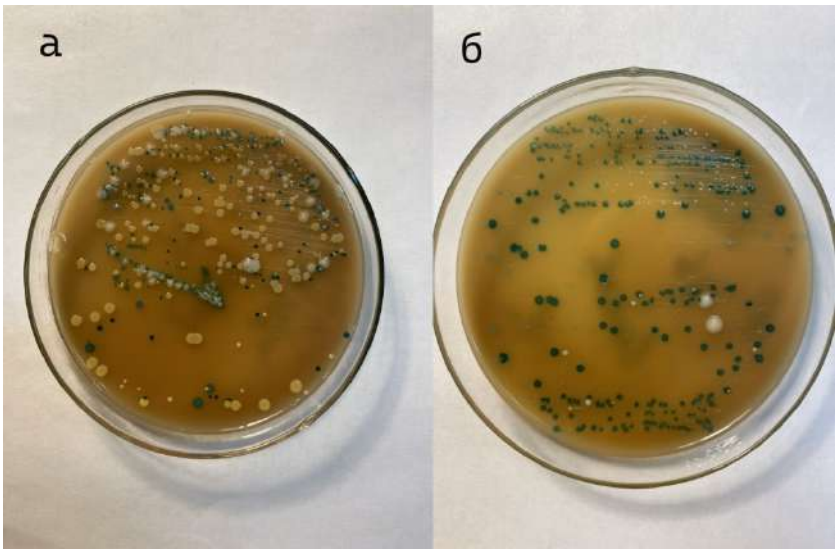

Figure 26. Crops for Levin's environment (a,b)

Therefore, under aggravating living conditions in the Far North, the appointment of complex ointments with broad-spectrum antibacterial components as one of the pathogenetic links in complex treatment is justified.

Unfavorable climatic and geographical factors of the regions of the Far North lead to chronic damage to the stratum corneum of the lip epithelium, which is

colonized by microorganisms. After starting a cascade of peroxidation reactions, lip tissues become even more vulnerable to invasion by microorganisms. Microorganisms create stable biofilms and interfere with the healing process. Due to the constant exposure of bacterial endotoxins to damaged tissues, the process takes on a chronic form.

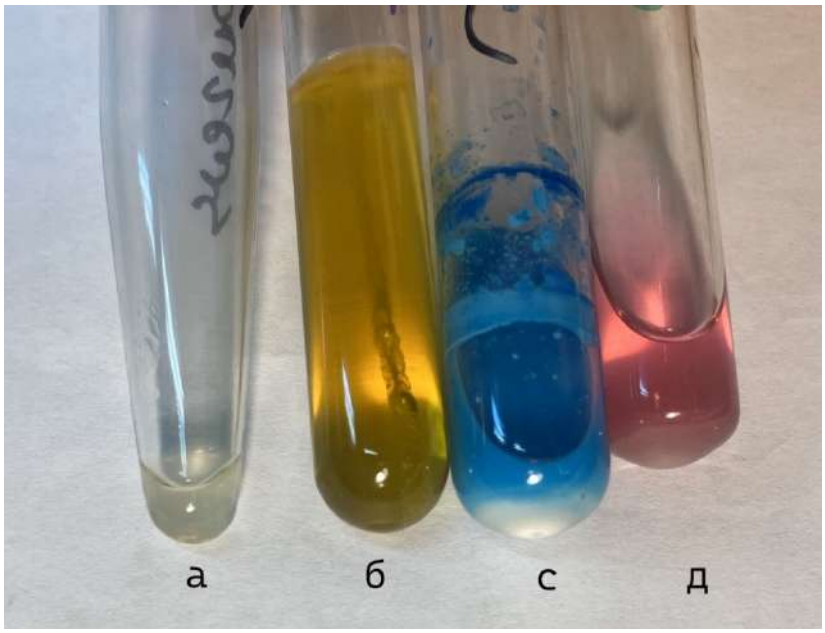

Figure 27: Bacteriological analysis of the flora of a patient with chronic lip crack (biochemical properties of Staphylococcus aureus: a – coagulase–positive reaction (rabbit plasma), b - mannitol fermentation; biochemical properties of the Enterobacteriaceae family: c – reduction of methylene blue in milk, d – fermentation of sorbitol)

Pimafucort and Triderm ointments used in complex therapy contain broad-spectrum antibacterial components natamycin and gentamicin, respectively, to which microorganisms isolated during bacteriological examination are sensitive. The above ointments also contain antifungal components (natamycin, clotrimazole), which are active against yeast-like fungi of the genus Candida, also isolated in our study.

3.3. The results of the patient survey

According to the results of the patented questionnaire of interest in the treatment of chronic lip crack, it was found that the maximum, as well as the

minimum scores according to our QIT-CLF questionnaire, were not registered in any study participant, however, the predominant share of the survey results belongs to the conclusion "high interest" (Table 17,18).

When processing the data from the questionnaire of interest, which patients underwent on the 7th day of the study, it was found that out of the total number of subjects (n= 50), no lack of interest in treatment was revealed, we assume that potential subjects with low scores of this test refused to participate in our study already at the stage of sampling patients. 26% of the surveyed (n=13) had a low level of interest, and 74% (n=37) had a high level of interest.

Table 17 – Results of the questionnaire of patients with chronic lip crack in the main and control groups

	No interest	Low interest	High interest
The main group (n=18)	0% (n=0)	22,22%* (n=4)	77,78%* (n=14)
The control group (n=16)	0% (n=0)	31,25%* (n=5)	68,75%* (n=11)
Total (n=34)	0% (n=0)	26,47%* (n=9)	73,53%* (n=25)

*p < 0,05 – reliability in comparison between the main and control groups

Table 18 – Results of the questionnaire of patients with chronic lip fracture complicated by meteorological cheilitis, main and control groups

	No interest	Low interest	High interest
The main group (n=9)	0% (n=0)	33,33%* (n=3)	66,66%* (n=6)
The control group (n=7)	0% (n=0)	14,28%* (n=1)	85,71%* (n=6)
Total (n=16)	0% (n=0)	25%* (n=4)	75%* (n=12)

*p < 0,05 – reliability in comparison between the main and control groups

The average result of the questionnaire of interest in treatment was 38.66±5.96. For subjects diagnosed with chronic lip crack, the average was 38.53±6.18, with a diagnosis of chronic lip crack complicated by meteorological cheilitis – 38.93±5.55.

If we analyze the indicators of the control and main groups, the result of the control group of patients is slightly higher and equal to 38.83±6.16, and the main 38.52±5.79.

Analyzing the data from the questionnaire of interest in the treatment of chronic lip crack, we concluded that 26% of the subjects did not follow the treatment regimen with general and local drugs in accordance with the prescriptions. Non-compliance with the treatment regimen may become a factor affecting the outcome of treatment, if the patient of our study does not adhere to his treatment plan, then he may not achieve the expected results in the treatment of chronic recurrent lip crack.

Non-compliance with the prescriptions of complex treatment may be due to personal discipline, violation of the frequency of taking local and general drugs, unpleasant taste of local drugs, unpleasant sensation when applying ointment, oils, frequency of meals during the day, bad habits that the patient does not want to get rid of: smoking, biting and licking lips, etc.

The questionnaire of patients' interest in the treatment of chronic lip fissure (QIT-CLF) is of great importance, unlike other diagnosed forms of cheilitis in our study due to the increased risk of malignancy.

3.4. The results of a statistical study of the incidence of various forms of cheilitis in the Far North

When analyzing the statistical processing of dental office data for 2021, 2022, 2023 in the polyclinic of branch No. 3 of FSGI "1469 NCH" of the Ministry of Defense of the Russian Federation, it was found that various forms of cheilitis were diagnosed in 22.62% of cases (3701 people) out of 16362 primary visits over three years.

The structure of morbidity is dominated by the meteorological form of cheilitis, due to unfavorable climatic conditions over a long period of time throughout the year. Meteorological cheilitis accounts for 1,815 cases (49.04%) of all forms of inflammatory lip diseases over three years out of the total number of inflammatory lip diseases. Chronic recurrent lip crack was recorded in 942 cases, which is 25.45% in the structure of morbidity over three years. Angular cheilitis was determined to be the third most common, the incidence rate was 21.02% and 778 cases, respectively (Figure 29). The remaining forms of cheilitis accounted for 4.49% of the total number or 166 cases (Figure). In the period from 2021 to 2023, 50 cases (1.35%) of atopic cheilitis, 92 cases (2.48%) of exfoliative cheilitis, 10 cases (0.27%) of glandular cheilitis, 11 cases (0.29%) of other forms of cheilitis were recorded (Figure 28). By other forms of cheilitis in our statistical study, we mean: infectious and hypovitaminous forms of cheilitis (candidiasis, herpetic cheilitis, symptomatic cheilitis in diseases of the gastrointestinal tract and impaired absorption of vitamin B6, established at an appointment with a general practitioner).

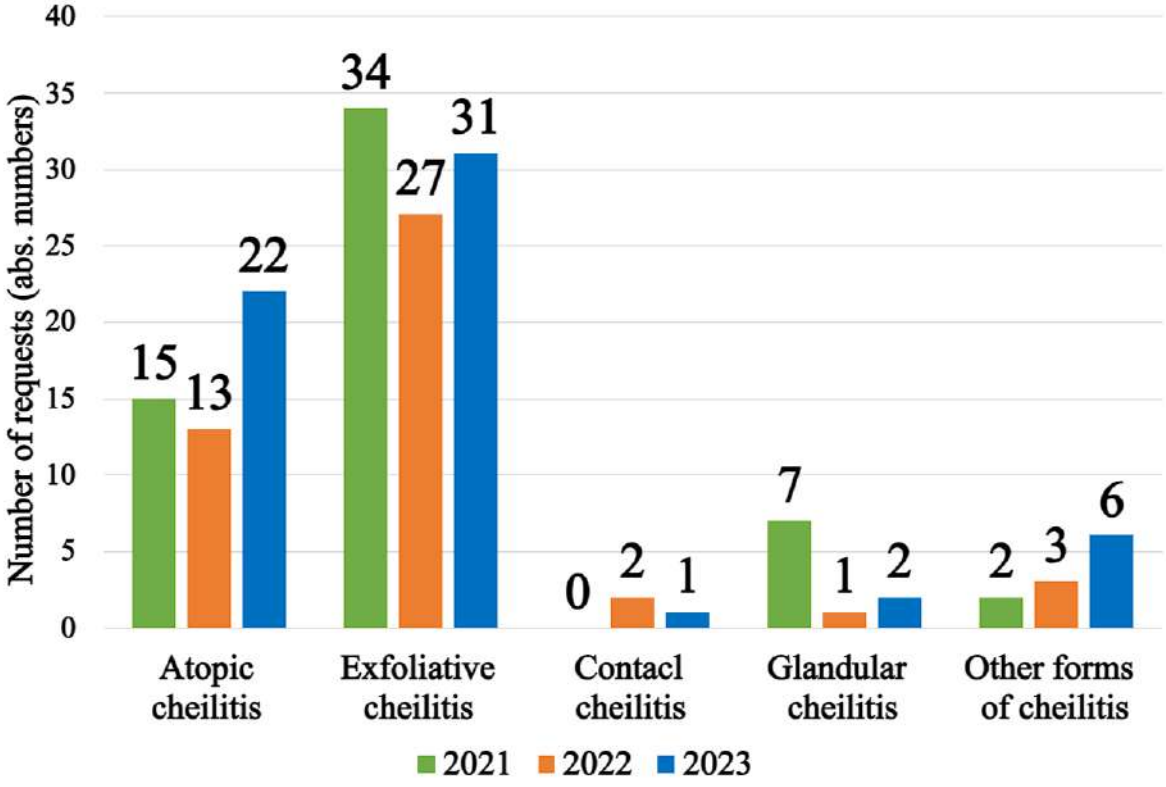

Figure 28. The number of cases of diagnosis of various forms of cheilitis in 2021-2023.

The least common pathology was contact cheilitis, the incidence rate is 0.08% and 3 cases, respectively. As a rule, it was important not only the rarity of allergen exposure in this area, but also the fact that when the first signs of an allergic reaction appear, the patient mainly turns to a dermatologist, therefore this category of patients is often not the object of research by dentists [19,48].

In 2021, out of 5,636 cases of primary visits, 23.19% (1,307 cases) were various forms of inflammatory lip diseases. Of the total number of primary visits, meteorological cheilitis accounts for 654 cases (11.6%), chronic recurrent lip cracks – 338 (5.99%), angular cheilitis – 257 (4.56%), atopic cheilitis – 15 (0.27%), exfoliative cheilitis – 34 (0.6%), glandular cheilitis – 7 (0.12%), other forms of cheilitis – 2 (0.03%).

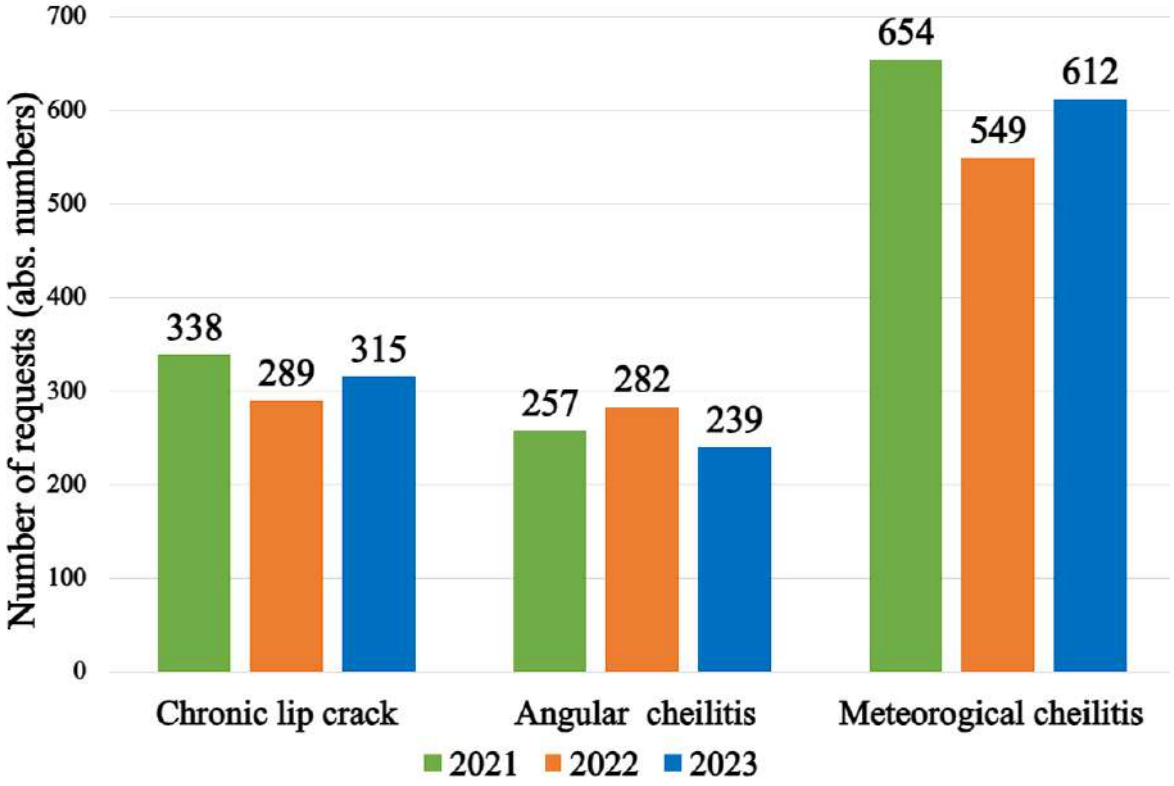

Figure 29. The number of cases of diagnosis of various forms of cheilitis in 2021-2023.

In 2022, out of 5,134 cases of primary visits, 22.71% (1,166 cases) were various forms of inflammatory lip diseases. Of the total number of primary visits, meteorological cheilitis accounts for 549 cases (10.69%), chronic recurrent lip cracks – 289 (5.63%), angular cheilitis – 282 (5.49%), atopic cheilitis – 13 (0.25%),

exfoliative cheilitis – 27 (0.53%), glandular cheilitis – 1 (0.02%), other forms of cheilitis – 3 (0.06%).

In 2023, out of 5,592 cases of primary visits, 21.96% (1,228 cases) were various forms of inflammatory lip diseases. Of the total number of primary visits, meteorological cheilitis accounts for 612 cases (10.94%), chronic recurrent lip cracks – 315 (5.63%), angular cheilitis – 239 (4.27%), atopic cheilitis – 22 (0.39%), exfoliative cheilitis – 31 (0.55%), glandular cheilitis – 2 (0.04%), other forms of cheilitis – 6 (0.12%).

Thus, according to our statistical studies, the incidence of cheilitis does not tend to decrease.

3.5. Evaluation of the results of treatment and prevention of various forms of cheilitis in the Far North

According to the results of the study, the average epithelialization time of morphological elements of inflammatory lip diseases in patients of the control and main groups was determined (Table 19).

Epithelialization is an important component of the healing of damaged tissues, in this study the term is used as a determining criterion for the success of the treatment of inflammatory lip diseases in the subjects, in its absence, pathologically altered lip tissues cannot be considered a healing process. Since the violation of the epithelial barrier creates conditions for the invasion of microorganisms in all forms of inflammatory lip diseases and causes the inability of keratinocytes to maintain the barrier, the absence of the epithelialization process in clinical manifestations of cheilitis may contribute to the recurrence of some forms of cheilitis.

In our study, lip epithelialization was assessed continuously for 20 days after the start of treatment. The1 results were evaluated visually using basic examination methods. In our study, epithelialization in various forms of cheilitis is defined as the process of regeneration of the lip epithelium, the elimination of morphological

elements. For epithelization, we took the process of creating a new barrier between the skin of the lips and the environment through the migration of epithelial cells. Upon examination, patients showed the absence of disturbed skin, ulceration, bleeding, edema and hyperemia, while pigmentation is allowed.

The average time of lip epithelization in patients of the control group was: 13.7±0.5 days for chronic lip crack, 6.6±0.4 days for meteorological cheilitis, 14.2±0.2 days for chronic lip crack complicated by meteorological cheilitis, 15.3±0.8 days for exfoliative cheilitis, 7.1±0.4 days for atopic cheilitis, 13.4±0.6 days for angular halite. The average time of lip epithelization in patients of the main group is less than the time of epithelization in chronic lip crack by 44.52±5.73% and amounted to 7.6±0.3 days, in meteorological cheilitis by 25.76±2.85% - 4.9±0.2 days, in chronic lip crack complicated by meteorological cheilitis by 45.07±3.38% - 7.8±0.4 days, in exfoliative cheilitis by 46.41±7.49% - 8.2±0.5 days, with atopic cheilitis by 25.35±2.04% - 5.3±0.2 days, with angular cheilitis by 36.57±4.21% - 8.5±0.3 days ($p<0.05$).

Table 19 – Average epithelialization time of morphological elements in various forms of cheilitis in patients of the main and control groups

Diagnosis	Average epithelialization time, day (M±SD)*	
	The main group (n=64)	The control group (n=53)
CLC	7,6±0,3	13,7±0,5
MC	4,9±0,2	6,6±0,4
CLC+MC	7,8±0,4	14,2±0,2
AC	5,3±0,2	7,1±0,4
EC	8,2±0,5	15,3±0,8
UC	8,5±0,3	13,4±0,6

* $p < 0,05$

Thus, the average duration of epithelialization of inflammatory lip diseases in the control group is 11.7±0.4 days, compared with the main group, where the average duration of epithelialization is 7.05± 0.1 days, this indicator is 39.74± 6.43% less. In

the main group with meteorological cheilitis, patients noted the absence of a feeling of tightness, pain, redness on the lips on average already on the 4th day, peeling, hyperemia and edema were not observed during examination.

With chronic recurrent lip fissure, the average epithelialization period was 7.6 days, when examined on the 7th day, the linear defect had only pigmentation, tissue integrity violations were not noted, a similar pattern was observed with angular cheilitis on average on the 8th day after the start of complex treatment. With exfoliative cheilitis, the absence of crusts and hyperemia during examination was not observed on the 8th day, in parallel, drugs for psychoemotional correction were prescribed to patients. Patients with atopic cheilitis had no peeling of the red border and the skin of the lips on the 5th day.

The average remission time of inflammatory lip diseases in patients of the main group was: 10.2±0.4 months for chronic lip crack, 11.2±0.3 months for meteorological cheilitis, 10.3±0.5 months for chronic lip crack complicated by meteorological cheilitis, 6.8±0.3 months for exfoliative cheilitis, 8.5±0.4 months for atopic cheilitis, 8.2±0.7 months with angular cheilitis. The average remission time of inflammatory lip diseases in patients of the control group is less ($p<0.05$) than the epithelialization time in chronic lip crack by 54.91±6.38% and amounted to 4.6±0.3 months, in meteorological cheilitis by 75.01±4.87% - 2.8±0.3 months, in chronic lip crack complicated by meteorological cheilitis by 54.37±6.52% - 4.7 ± 0.4 months, with exfoliative cheilitis by 36.76 ± 3.29% - 4.3 ± 0.2 months, with atopic cheilitis by 51.76±8.82% - 4.1 ± 0.5 months, with angular cheilitis by 29.27 ±5.23% - 5.8± 0.4 months (Table 20).

Table 20 – Average remission periods of various forms of cheilitis in patients of the main and control groups

Diagnosis	Average remission time, months (M±SD)*	
	The main group (n=64)	The control group (n=53)
CLC	10,2±0,4	4,6±0,3
MC	11,2±0,3	2,8±0,3

CLC+MC	10,3±0,5	4,7±0,4
AC	8,5±0,4	4,1±0,5
EC	6,8±0,3	4,3±0,2
UC	8,2±0,7	5,8±0,4

* $p < 0,05$

In the control group of patients, a decrease in remission time was observed by 56.63±8.37% compared with the main group, which averaged 3.8±0.2 months and 8.8±0.3 months, respectively ($p<0.05$).

Separately, for patients with chronic lip crack and patients with complications in the form of meteorological cheilitis (n=50) of both groups, the relationship between the results of the questionnaire of interest in treatment and the results of epithelialization and remission periods was established. Thus, in the main group, the worst epithelialization rates of chronic lip crack (n=4) averaged 10.8±0.3 days, and in chronic lip crack complicated by meteorological cheilitis (n=3) – 12.4± 0.5 days.

At the same time, the remission period significantly decreased in patients with low indicators of the questionnaire of interest in the treatment of the main group: in patients with chronic lip crack (n=3), the average remission period was 6.5±0.8 months, in patients with chronic lip crack complicated by meteorological cheilitis (n=2), the average remission period was 5.1±0.6 months. In the control group, in patients with low interest rates and diagnosed with chronic lip crack (n=5), the average epithelialization time was 15.6 ± 0.5 days, while in 40% (n=2) of the total number of patients in the control group with low interest rates, treatment goals were not achieved. These patients were referred for surgical excision of a chronic recurrent lip crack, since conservative therapy methods with a low level of patient participation in treatment did not bring a therapeutic effect.

In one patient of the control group with a chronic lip fissure complicated by meteorological cheilitis, low interest was revealed, treatment also did not bring positive results, the patient was referred for surgical excision of a linear defect.The average remission period in patients with chronic lip crack and low scores of the questionnaire of interest in treatment was 2.5±0.3 months.

Thus, the appointment of complex therapy of various forms of cheilitis, subject to constant exposure to adverse factors of the Far North, is the key to successful treatment and achieving stable remission. In addition to carefully collecting anamnesis, the dentist must take into account the peculiarities of the influence of adverse environmental factors, taking into account which to choose treatment tactics.

The results of our study have determined that treatment based only on the topical application of complex ointments is ineffective. The best treatment results were achieved by prescribing combined ointments based on glucocorticoids and antibacterial/antifungal components in combination with physiotherapy procedures, vitamin and antioxidant therapy. The inclusion of vitamins A, E, and D in the treatment plan in order to stimulate the regenerative ability of the lip skin, maintain the protective function of the epithelium from exposure to cold and wind as part of the treatment of inflammatory lip diseases in the Arctic zone of the Far North is the key to successful treatment and long-term remission (Figure 30).

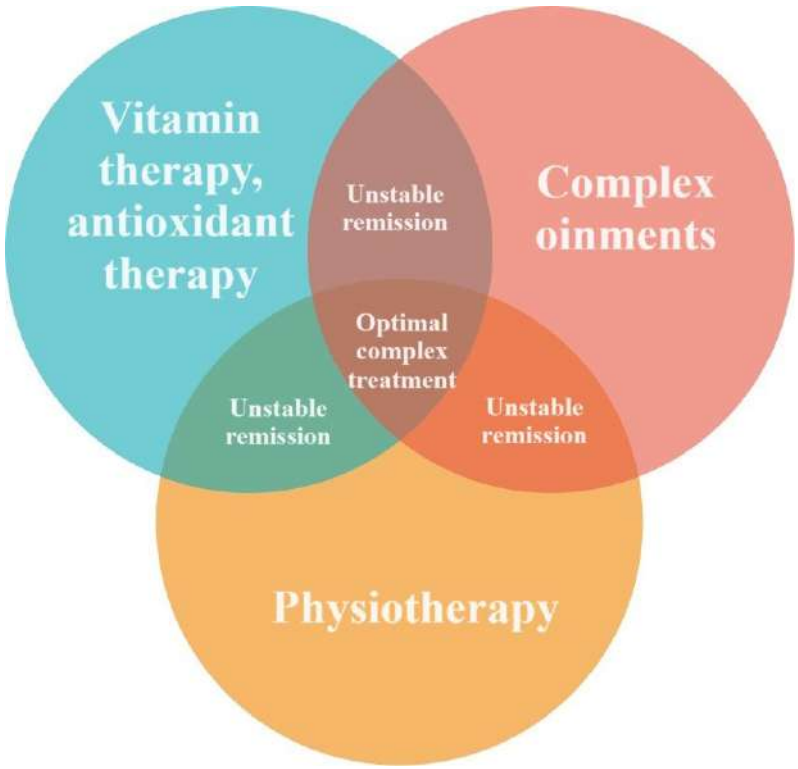

Figure 30. The optimal content of complex treatment of cheilitis in the conditions of the Far North

3.6. Review of clinical cases of the study

Clinical case No. 1. A 36-year-old woman with a diagnosis of exacerbation of chronic periodontitis of the tooth 3.6 applied for an appointment. During a dental examination and a survey, a concomitant diagnosis was established: meteorological cheilitis. From the patient's medical history: inflammation of the lips is noted with the onset of the cold season, with exacerbations and remissions. In the summer or when leaving the Far North region, lip inflammation does not manifest itself. The use of hygienic lipsticks reduces peeling, but the pain and swelling of the lips do not decrease (Figure 31).

Figure 31. Patient M., 36 years old. Diagnosis: meteorological cheilitis. Before the start of treatment

In addition to the treatment of the main diagnosis: exacerbation of chronic periodontitis of the tooth 3.6. the patient agreed to participate in our study, and blood was taken. The patient was prescribed a comprehensive treatment for meteorological cheilitis, including vitamin therapy, antioxidant therapy, local treatment according to the scheme: from day 1 to 5 Pimafucort ointment 2 times a day, from day 6 to 14 Methyluracil ointment 10% 3 times a day, as well as physiotherapy with the Svetozar

device for 5 sessions. At the initial intake, the results of laboratory tests: vitamin D 15.7 ng /ml, vitamin E 8.6 mcg /ml, MDA 0.97 nmol /ml.

Upon repeated examination 4 days after the start of treatment, edema, hyperemia and peeling are completely absent, the patient does not experience discomfort (Figure 32). For 14 days after the start of treatment, the lip tissues had a pale pink color, the skin was clean, without signs of inflammatory phenomena. After completing the course of treatment, the patient was offered a preventive remedy based on Elabium oils according to the instructions for use developed by us on an ongoing basis.

6 and 12 months after the start of treatment and in compliance with the established preventive measures, the patient had no cases of recurrence of meteorological cheilitis. Hygienic lip balm did not cause unpleasant sensations. After 6 months, the level of vitamin D in the blood serum rose to 38.5 ng/ml, after 12 months, the result of vitamin D was 42.1 ng/ml.

Figure 32. Patient M., 36 years old. Diagnosis: meteorological cheilitis. 4 days after the start of treatment

Clinical case No. 2. The patient, a man, 30 years old, went to see a dentist for a preventive examination as part of a medical examination. Upon examination of the lip skin, the diagnosis was established: chronic recurrent lip crack (Figure 33).

Localization: laterally on the right side of the lower lip, mild severity. The patient was offered a comprehensive treatment of meteorological cheilitis, including vitamin therapy, antioxidant therapy, local treatment according to the scheme: from day 1 to 7 Pimafucort ointment 2 times a day, from day 8 to 14 Methyluracil ointment 10% 3 times a day, at night the use of adhesive films with solcoseryl, Diplen Denta C, as well as physiotherapy treatment with the Svetozar device 7 sessions.

Figure 33. Patient A., 30 years old. Diagnosis: chronic lip crack.
Before the start of treatment

At the initial intake, the results were: vitamin D 22.2 ng/ml, vitamin E 9.4 mcg/ml, MDA 1.18 nmol/ml. The result of the microbiological study was the detection of Staphylococcus saprophyticus 104 CFU/ml and Streptococcus viridans spp. 105 CFU/ml in the smear.

7 days after the start of treatment, there were no signs of bleeding cracks during examination, active epithelialization of the linear defect of the lower lip on the right was visualized, but pigmentation at the site of skin disorders persists (Figure 34).

After 10 days, not only complete epithelialization was observed at the site of a chronic lip crack, but also the absence of pigmentation on the skin of the lip, a secondary morphological element of infection caused by the Herpes simplex virus

was visualized on the lower lip (Figure 35). The patient continued treatment for this disease.

Figure 34. Patient A., 30 years old. Diagnosis: chronic lip crack.
7 days after the start of treatment

Figure 35. Patient A., 30 years old. Diagnosis: chronic lip crack.
10 days after the initial visit

After the course of treatment, the patient was given recommendations regarding the prevention of cheilitis (the use of the balm "Elabium", vitamin therapy). After 6 and 12 months, there was no recurrence of chronic lip crack, and at the appointments the patient did not complain about the recurrence of a linear lip defect both at the treatment site and in other lip locations. After 6 months, the level of

vitamin D in the blood serum rose to 42.4 ng/ml, after 12 months, the result of vitamin D was 37.3 ng/ml.

Clinical case No. 3. Patient, 23 years old, diagnosis: chronic recurrent lip crack, moderate severity, localization of the middle (Figure 36).The patient has been living in the Far North for 5 years, he observes the presence of a lip crack in different months of the year, during the time when he travels to more southern latitudes, the manifestations of the linear defect decrease to complete epithelialization. Upon examination, a median linear defect of 6 mm in size is noted, the crack is bleeding, there is hyperemia and slight swelling around. The patient is concerned about the appearance of the lips, pain when smiling and eating.

Figure 36. Patient D., 23 years old. Diagnosis: chronic lip crack.
Before the start of treatment

At the initial intake, the results were: vitamin D 11.4 ng/ml, vitamin E 5.5 mcg/ml, MDA 1.72 nmol/ml. The results of the microbiological study were the detection of Staphylococcus aureus 103 CFU/ml and Staphylococcus epidermidis 106 CFU/ml in the smear.

The patient's treatment regimen: in the first 7 days, the use of Triderm ointment 2 times a day, the next 7 days, Methyluracil ointment 10% 3 times a day, at night, the use of adhesive films with solcoseryl, Diplen Denta C, physiotherapy with Svetozar

apparatus 10 sessions. Complex drug therapy: vitamins, antioxidants according to the scheme. Facial rest, control of biting and licking lips.

Figure 37. Patient D., 23 years old. Diagnosis: chronic lip crack. 9 days after the start of treatment

7 days after the start of treatment, edema and hyperemia were not detected, the crack did not bleed, the size of the crack decreased to 3 mm and was in the stage of active epithelialization. After 9 days, against the background of regenerative local therapy, the linear defect was completely epithelized (Figure 37).

After treatment, the patient followed a set of preventive measures throughout the study. At the control sessions, after six months and a year, the clinical picture remained at the level of persistent remission. The patient indicated during the survey that there was no recurrence of linear lip defects (Figure 38).

Figure 38. Patient D., 23 years old. Diagnosis: chronic lip fracture.

6 months after the initial visit

After 6 months, the level of vitamin D in the blood serum rose to 34.7 ng/ml, after 12 months, the result of vitamin D was 32.3 ng/ml.

Clinical case No. 4. Patient D., 36 years old. I applied for an appointment for chronic recurrent aphthous stomatitis. He did not complain about the aesthetic condition of the lips.

After collecting the medical history, it was found that the patient has a habit of uncontrollably biting his lower lip. When examining the skin of the red border of the lips: in the Klein zone, turning into the red border of the lips, yellow-brown crusts are visualized, the lips are dry, prone to peeling, at the point of transition to the mucous part of the lips, slight hyperemia, puffiness and a dental imprint are also noted.

Figure 39. Patient B., 38 years old. Diagnosis: exfoliative cheilitis.

Before the start of treatment

From the anamnesis: the patient noted the long-term condition of his lips with the presence of dryness and scales, a state of emotional tension, which is the cause of obsessive lip biting. In addition to treating the underlying disease, the patient agreed to participate in the study according to the diagnosis: exfoliative cheilitis, dry form (Figure 39). In addition to vitamin and antioxidant therapy, the patient was prescribed local treatment according to the scheme: Hydrocortisone 1% ointment for 5 days 3 times a day, Methyluracil ointment 10% from day 6 to 14. Physiotherapy treatment of

7 procedures. To correct the psychoemotional status, the patient was referred to doctors of the appropriate profile, the patient was also recommended to consult a general practitioner and an endocrinologist for examination.

After signing the informed consent, blood sampling was carried out with the determination of vitamin D 21.6 ng/ml, vitamin E 7.2 mcg/ml, MDA nmol/ml.

After 7 days, upon examination, the surface of the lips had no scales and crusts, no signs of inflammation were noted, however, the patient's habit of biting his lips persisted, the patient continued the course of treatment, and in parallel underwent concomitant pathological condition therapy from doctors of other specialties. 10 days after the start of treatment for exfoliative cheilitis, the patient has no manifestations of this disease, the red border of the lips is pale pink, moderately moistened, without pathological elements.

The complex of preventive measures included the use of vitamin therapy, Elabium lip balm, control of lip biting habits, including working with a specialist to correct anxiety levels.

6 months after the start of treatment, the patient, who followed all the recommendations, no longer sought medical help for exfoliative cheilitis, 12 months after the initial visit, no recurrence of this disease was established. After 6 months, the level of vitamin D in the blood serum rose to 45.7 ng/ml, after 12 months, the result of vitamin D was 42.9 ng/ml.

Clinical case No. 5. A 19-year-old girl applied for an appointment in order to conduct professional oral hygiene. The diagnosis of atopic dermatitis is present in the anamnesis, however, the patient complained of a crack in the corner of the lip on the right side, in the form of pain, its bleeding. On examination, dryness and peeling of the skin and the red border of the lips are visualized, a 3 mm lip crack and areas of hyperkeratosis around it are noted in the area of the lip commissure on the right side (Figure 40a).

Figure 40. Patient A., 19 years old. Diagnosis: atopic cheilitis (a – before the start of treatment, b – 12 days after the start of treatment)

It follows from the anamnesis that peeling of the patient's lips is year-round, but lesions of the corners of the mouth have periods of remission and exacerbation several times a year, in winter the cracks persist, and in summer, when leaving for more southern latitudes, they disappear before returning to the subarctic climatic zone. Since the lichenization of the corners of the lips in atopic cheilitis is leading in the development of angular cheilitis in a patient, after receiving consent to participate in the study, the patient was prescribed laughter treatment: Pimafucort cream 3 times a day with an emphasis on a crack in the corner of the mouth on the right for 7 days, the next 7 days the use of Methyluracil ointment 3 times There are 7 physiotherapy treatments per day. The results of laboratory tests at the initial visit: vitamin D 19.7 ng/ml, vitamin E 6.8 mcg/ml, MDA nmol/ml.

The results of the application of Pimafucort cream on the 6th day of the examination showed the absence of peeling and lichenization of the red border of the lips and the skin of the lips, when examining the crack in the corner of the mouth, the process of epithelialization of the lesion was noted, the absence of bleeding, the skin in the area of the cheilitis diagnosed on the first visit had a physiological color in the area of the skin and the red border of the lips with preservation lichenization sites in the area of lip commissures. On the 12th day after the start of treatment, the skin and the red border of the lips were without peeling, physiological color, the skin of the lip

contours on the right and left were clean, without pathological elements, physiological color (Figure 40b).

6 months after the initial treatment and subject to compliance with preventive measures, a positive trend in the development of remission of atopic cheilitis was established. During 12 months of dynamic follow-up, the patient did not notice any manifestations of atopy in the lip area and/or angular cheilitis. Against the background of regular preventive measures, the symptoms of skin manifestations of atopic dermatitis in the lip area were reduced, the epidermal barrier was restored, and there were no recurrences of angular or atopic cheilitis during the entire study period. After 6 months, the level of vitamin D in the blood serum rose to 56.1 ng/ml, after 12 months, the result of vitamin D was 51.3 ng/ml.

Clinical example No. 6. A 28-year-old man came to the reception complaining of a non-healing crack on his lower lip for several years.

The patient complained of pain when smiling and eating, prolonged non-healing linear ulcer, bleeding, and also asked to be referred to a maxillofacial surgeon for excision of a cracked lip. From the anamnesis: the crack of the lower lip appeared several years ago, it practically does not heal.

Figure 41. Patient K., 28 years old. Diagnosis: chronic fracture of the lower lip.
4 days after the start of treatment

Objectively: a linear defect on the lower lip on the right measuring 5 mm, the location is lateral, around hyperemia, edema, hyperkeratosis phenomena. A diagnosis was made: chronic recurrent lip crack (Figure 41).

Figure 42. Patient K., 28 years old. Diagnosis: chronic crack of the lower lip.
9 days after the start of treatment

The patient was offered conservative treatment, after signing informed consent to participate in the study, the patient was prescribed local therapy: Triderm ointment 3 times a day for 7 days, Methyluracil ointment 3 times a day for the next 7 days, at night Diplen Denta S. Physiotherapy treatment with Svetozar apparatus, a course of 10 procedures. Vitamin therapy and antioxidant therapy according to the scheme. Mimic peace.

At the initial intake, the results of laboratory tests: vitamin D 17.5 ng /ml, vitamin E 5.1 mcg /ml, MDA nmol/ml. Microbiological examination revealed the presence of lip crack microorganisms: Candida albicans 102 CFU/ml, Streptococcus viridans spp. 104 CFU/ml, Enterococcus spp. 102 CFU/ml.

7 days after the start of treatment, the linear defect of the lower lip on the right significantly decreased, there were no signs of inflammation around the crack, hyperkeratosis and pigmentation bordering the crack persisted. After 9 days, the crack was completely epithelized, pigmentation phenomena persist on the skin of the lips (Figure 42). Areas of traumatization are marked on the red border of the lower lip on the left (according to the patient, lip biting). Within 12 months after the start of

treatment, the patient, who was recommended a scheme for the prevention of inflammatory lip diseases, did not complain about a recurrence of the crack. The serum vitamin D level was 45.6 ng/ml after 6 months, and 40.1 ng/ml after 12 months. We recommended that the patient actively use the Elabium lip balm at all seasons of the year in the Far North.

Clinical case No. 7. Patient, male, 31 years old. Applied for an appointment as part of a medical examination in order to undergo an annual preventive examination.on. The oral cavity is sanitized, however, upon examination of the skin of the lips, the presence of a 6 mm medio-lateral crack of the lower lip on the left was noted, the lips are dry, cracked and hyperemic. Diagnosis: chronic lip crack complicated by meteorological cheilitis (Figure 43).

The patient agreed to participate in the study and signed an informed consent to participate in the study. The patient was prescribed local therapy: Triderm ointment 3 times a day for 7 days, Methyluracil ointment 3 times a day for the next 7 days, at night Diplen Denta S. Physiotherapy treatment with Svetozar apparatus, a course of 8 procedures. Vitamin therapy and antioxidant therapy according to the scheme. Mimic peace.

When analyzing the microbiome, the cracks of the lip are determined: Staphylococcus aureus 103 CFU/ml, Staphylococcus epidermidis 107 CFU/ml.

Figure 43. Patient J., 31. Diagnosis: chronic lip crack. Before the start of treatment

At the initial intake, the results of laboratory tests: vitamin D 16.7 ng/ml, vitamin E 7.4 mcg/ml, MDA nmol/ml.

7 days after the start of treatment, the crack of the lower lip decreased to 3 mm, the crack did not bleed, was in the stage of active epithelialization, there was no peeling and hyperemia of the lips (Figure 44). After 10 days, the crack was completely epithelized, the lips were pale pink in color, moderately moistened without signs of inflammation. After undergoing treatment for inflammatory lip disease, the patient was prescribed a course of prevention: during 12 months of dynamic follow–up, the patient did not complain of a recurrence of the crack, while the level of vitamin D in the blood serum was 41.9 ng/ml after 6 months, 37.5 ng/ml after 12 months. After the end of the study, we recommended that the patient actively use the Elabium lip balm at any time.

Figure 44. Patient J., 31. Diagnosis: chronic lip crack. 7 days after the start of treatment

3.7. Diagnostic protocol for the management of patients with inflammatory lip diseases in the Far North

The course of inflammatory lip diseases in the Arctic zone of the Far North is complicated by climatic and geographical features and the adverse influence of environmental factors. The diagnostic approach to patients with manifestations of various forms of cheilitis should first of all take into account the etiological diversity

and the similarity of the clinical picture with other forms of cheilitis [18,20,48]. Some forms can be diagnosed by characteristic clinical signs, but most inflammatory lip diseases manifest a non-specific picture. In the absence of clinical recommendations (treatment protocols) for the diagnosis of cheilitis, it is necessary to develop a structured algorithm for the diagnosis of various forms of cheilitis (Figure 45). At a medical appointment, the doctor must inspect not only the lips, but also the oral cavity, establish primary and secondary morphological elements, determine the presence of seals, assess the localization, the degree of tissue damage. Carefully collect anamnesis (including family history), study the patient's medical history, determine the presence of concomitant diseases, if necessary, send for consultation to a doctor of another profile.

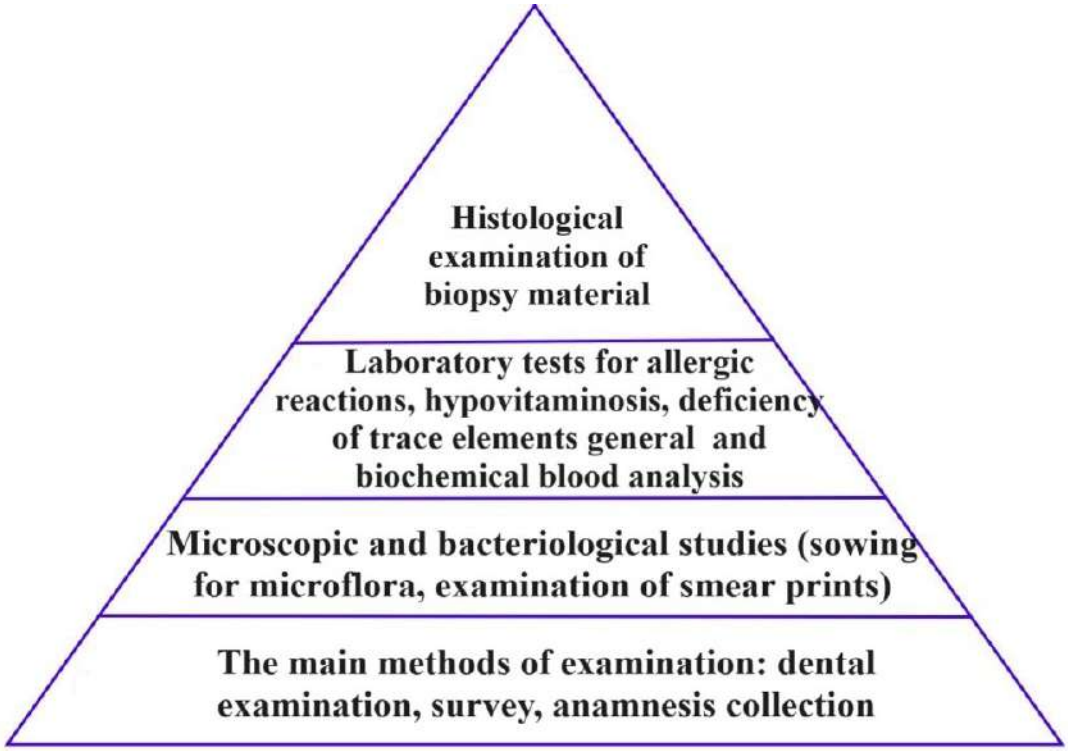

Figure 45. The scheme of diagnostic measures for patients

It is important to establish the duration of residence in the Far North and other regions with harsh climatic conditions of the Arctic, the nature of work (including outdoor activities), bad habits, recent contact with substances potentially causing an allergic reaction, immune status, concomitant diseases, heredity, taking medications

or biologically active substances.active additives. Anamnesis collection is important in establishing a definitive diagnosis.

In some forms of cheilitis (angular cheilitis, chronic lip crack), as well as in the case of frequent relapses and unstable remissions, it is necessary to take a smear to determine the conditionally pathogenic microflora, infection caused by yeast-like fungi. The study of the microbiota of lip lesions is the identification of microorganisms in a sample of smears from the surface of the lips or the depth of cracks, as well as the determination of sensitivity to antibiotics will determine the choice of topical antibacterial drugs in case of ineffectiveness of the initial choice of the drug. Due to the fact that microorganisms of a chronic wound (chronic recurrent lip crack) form a stable and stable colonization by microorganisms with multiple antibacterial resistance, they are able to disrupt the healing of chronic inflammatory diseases of the lips.

If it is impossible to establish a diagnosis and prescribe treatment based on the basic examination methods, it is necessary to prescribe additional diagnostics: laboratory tests of blood serum for biochemical shifts, hypovitaminosis, deficiency of trace elements. The results of additional research methods can also make a correct diagnosis. For patients with suspected contact cheilitis, along with the determination of general and specific immunoglobulins in the blood serum, if it is impossible to reliably identify an allergen based on anamnesis, it is necessary to conduct allergological application testing or scarification tests, which is the main method of diagnosing this disease with the determination of a sensitizing substance. Diagnosis of contact cheilitis is necessary in conjunction with an allergist.

Patients with precancerous lip diseases or suspected malignancy need histological and cytological examination of the biopsy, especially this research method is important in the absence of positive dynamics in treatment in order to make a differential diagnosis and prescribe effective treatment. In addition, establishing the presence of a history of concomitant systemic or dermatological disease is also a method of the diagnostic stage. An effective diagnostic approach can also be achieved if doctors have an understanding of the classification of

inflammatory lip diseases, etiopathogenetic factors, including those caused by the subarctic climate, and the peculiarities of the occurrence and course of the disease when living in unfavorable conditions of the Far North [47]. This is especially important in cases where abnormalities or potentially malignant diseases need to be detected at an early stage.

Despite the fact that cheilitis as a term identifying inflammatory diseases of the lips has been isolated and studied for a long time, there are no clinical recommendations or other clear protocols for diagnosis, treatment and prevention for this diagnosis. Thus, in the course of the study, we conducted clinical methods of examining patients, processed data on laboratory parameters of patients, established the content of vitamin D in blood serum and determined the antioxidant status, analyzed bacterial and fungal colonization of chronic lip crack. An additional method of examining patients with chronic lip crack was their interest questionnaire. After the received diagnostic data, a comprehensive treatment plan for the appropriate form of cheilitis was drawn up individually for patients.

Statistical data on the incidence of inflammatory lip diseases have been processed, and the most common forms of cheilitis in the Arctic of the Far North have been identified. The results of prescribing individual complex treatment to patients of the main group and the results of the treatment to patients of the control group are analyzed. The results of the developed tactics of preventive measures for inflammatory lip diseases in the Arctic zone of the Far North are determined.

Based on the data obtained, a basic algorithm for the diagnosis and determination of specific forms of inflammatory lip diseases was formulated.

CONCLUSION

The regions of the Far North are a unfavorable region to live in due to their geographical location, harsh climatic conditions, on which metabolic shifts in the body depend. Despite the adverse environmental factors, the Far North is a strategically important territory of the country, where the Northern Sea Route passes, oil producing enterprises and large deposits of natural resources are located. An economic term, the Arctic zone of the Russian Federation is a diverse region with many complex ecological and socio—economic systems. The population of the region is in conditions of atmospheric pressure fluctuations, oxygen deficiency, high humidity, strong winds, extremely low temperatures, magnetic field instability, prolonged frosty winter, desynchronosis, under the influence of these factors, a "polar metabolic type" is formed, shifts occur in all organs and systems.

The purpose of our study was to identify the features of the course of various forms of cheilitis, optimize the treatment and prevention of various forms of this disease in the Far North. To achieve this goal, we performed the following tasks: we analyzed the structure of the incidence of various forms of cheilitis in residents of the Far North regions, assessed the influence of adverse factors of the polar region on the antioxidant and vitamin status of patients with various forms of cheilitis in order to optimize diagnosis based on laboratory studies, conducted a survey of patients interested in the treatment of chronic lip crack, an algorithm of complex treatment has been formulated and methods of prevention of the most common forms of cheilitis in the conditions of the Far North have been improved.

After conducting the main examination methods, it was found that relapses of various forms of cheilitis in patients are characteristic of the period of residence in the Far North, when traveling to more southern latitudes, regardless of the time of year, the symptoms of diseases decrease up to a state of remission. Also, patients purposefully do not seek medical help for inflammatory diseases of the lips. Of the total number of participants in our study (n=117), only 5.13% (n=6) complained of uncomfortable sensations and unsatisfactory lip aesthetics associated with a long course of chronic lip cracks. The remaining 94.87% (n=111) initially sought an

appointment with a dentist for other dental diseases or as an annual follow-up. This trend persists beyond the scope of our study: patients with inflammatory diseases of the lips, precancerous red border of the lips do not seek medical help, often self-medicate with ineffective means, thereby increasing the risks of malignancy of the chronic inflammatory process of the lip epithelium. According to statistics, targeted visits to a dentist about inflammatory lip phenomena were registered in contact cheilitis in 100% of cases in 2022 (n=2) and in 2023 (n=1), with chronic lip crack 1.48% (n=14) in 2021-2023.

One of the objectives of our study was to assess the impact of adverse factors of the subarctic climate of the Far North on the antioxidant and vitamin status of patients with various forms of cheilitis in order to improve diagnosis. The assessment of the vitamin status of patients revealed the most acute problem of residents of the Far North – vitamin D deficiency. In 100% of cases, the subjects had laboratory values of vitamin D below the reference values before the start of treatment. Data on vitamin E deficiency show that 6.84% (n=8) of the subjects have vitamin deficiency, but the recorded level was close to the reference values.

An equally important laboratory indicator in assessing the influence of climatic and geographical factors on the health of patients was the level of malondialdehyde, a marker of oxidative stress. Oxidative stress occurs as a result of an imbalance of the antioxidant defense system and the action of reactive oxygen species, the combination of these phenomena leads to cell damage. The process is mediated by free radicals, which are formed during the formation of "polar stress" in the conditions of the Far North. Since the processes of oxidative stress have a damaging effect on the epithelium, including the lips, it is becoming increasingly obvious that oxidative stress is involved in the pathophysiological mechanism of the development of cheilitis in the Far North. An increased level of the oxidative stress marker (MDA) was detected in 21.37% (n=25) of the subjects. At the same time, it was also noted that 100% (n=8) of patients with vitamin E levels below the reference values have an increased MDA index. In our study, the definition of vitamin E had an applied significance, which was associated with its function of increasing the effectiveness of

the body's antioxidant defense system and preventing damage by free radicals, which certainly play an important role in the pathophysiology of "polar stress".

A statistical study of the vitamin D content in the blood serum of the subjects of the main group found that the average vitamin level in the subjects when measured after 6 months increased by 115.04% compared with the measurement at the initial visit before the start of treatment. Repeated analysis of laboratory parameters after 12 months revealed a decrease in the average values of vitamin levels in patients by 2.78% compared with previous indicators after 6 months.

Since the processes of oxidative stress create a microenvironment in tissues that significantly reduces the resistance of cells to external influences and promotes the formation of microbial biofilm, our study analyzed the microbial flora of patients with the most difficult to treat lip disease and at the same time being a precancer with the risk of malignancy, chronic recurrent lip crack. Of the total number of cases of chronic lip crack in 66% of patients (n=33), namely, with moderate and severe disease course, pathogens of many purulent-inflammatory diseases Staphylococcus aureus and Pseudomonas aeruginosa were isolated in associations. When analyzing the microbial flora, which was mainly represented by commensal microorganisms, a massive growth of Staphylococcus epidermidis was recorded in 84% of the subjects (n=42), Streptococcus viridans spp in 38% of the subjects (n=19), Staphylococcus pseudintermedius in 14% of the subjects (n=7). Colonization and invasion of microorganisms in the depth of the lip crack slowed down the healing and regeneration of chronic linear defects.

A survey using the questionnaire of interest in the treatment of subjects with chronic lip crack gives an idea of the interest of patients in the treatment of pathology, so it was found that 26% (n=13) of patients with chronic lip crack, as well as a complication in the form of meteorological cheilitis, had a low level of interest. The remaining 74% of patients (n=37) showed a high level of interest in treatment. The absence of patients in whom patient interest has not been established is explained by their refusal to participate in the study at the sampling stage.

The treatment of patients in the control group (n=53) was limited to local therapy with glucocorticoid drugs with antimycotic and antibacterial components for 5-7 days, depending on the clinical picture, as well as the appointment of a local keratoplastic drug in the form of sea buckthorn oil. Patients of the main group (n=64) also received local treatment with complex glucocorticoid ointments, the regeneration stimulant Methyluracil, with chronic lip cracks, the use of Solcoseryl in the form of films was additionally prescribed. A mandatory component of the local treatment of patients in the main group was physiotherapy with the Svetozar device.

In combination with local treatment, patients were prescribed general vitamin therapy with colecalciferol, AEvit and the antioxidant drug Mexidol course. As is known, the production of vitamin D in the skin depends on the effects of ultraviolet radiation from sunlight, which is practically absent in the autumn-winter season, it is necessary to include vitamin D preparations in the comprehensive treatment plan for inflammatory diseases of the lips in order to ensure an adequate level of vitamin D in the blood serum to maintain metabolic processes in tissues, as well as the use of a complex vitamin AEvit. Vitamin E is also found in many products of daily consumption, tocopherol deficiency in our patients seems to be associated with an unbalanced diet, however, to exclude pathology of the gastrointestinal tract, these patients were nevertheless referred for consultation to a gastroenterologist. Given the antioxidant status with an increased content of the lipid peroxidation product, it is necessary to prescribe a course of antioxidant drugs.

Routing to doctors of other specialties was organized for patients with exfoliative and atopic cheilitis of both groups. Patients with exfoliative cheilitis were primarily referred for consultation to a neurologist, patients with atopic cheilitis received a referral to a dermatologist for the treatment of the underlying disease (atopic dermatitis) and relief of other skin manifestations of atopy. Patients with angular cheilitis, depending on the cause and course of the disease, were prescribed appointments by other specialists: a general practitioner, an orthodontist and an orthopedic dentist.

After the treatment, conclusions were drawn about the results of complex treatment in the groups of subjects. The average time of lip epithelization in patients of the control group was: 13.7±0.5 days for chronic lip crack, 6.6±0.4 days for meteorological cheilitis, 14.2±0.2 days for chronic lip crack complicated by meteorological cheilitis, 15.3±0.8 days for exfoliative cheilitis, 7.1±0.4 days for atopic cheilitis, 13.4±0.6 days for angular halite. The average time of lip epithelization in patients of the main group is less than the time of epithelization in chronic lip crack by 44.52±5.73% and amounted to 7.6±0.3 days, in meteorological cheilitis by 25.76±2.85% - 4.9±0.2 days, in chronic lip crack complicated by meteorological cheilitis by 45.07±3.38% - 7.8±0.4 days, in exfoliative cheilitis by 46.41±7.49% - 8.2±0.5 days, with atopic cheilitis by 25.35±2.04% - 5.3±0.2 days, with angular cheilitis by 36.57±4.21% - 8.5±0.3 days ($p<0.05$).

Thus, the algorithm of complex treatment of the most common forms of cheilitis in the Far North should be reduced to the etiopathogenetic aspects of the development and course of these pathologies, which is based on the local application of ointments with a glucocorticoid component. In conditions of constant exposure to adverse environmental factors on the human body, short periods of remission, it is necessary to include topical glucocorticoid anti-inflammatory drugs in the form of ointments for a period of 5-7 days. In the presence of persistent invasion of microorganisms in the area of the affected lip tissues, it is necessary to use glucocorticoid ointments with an antibacterial and antifungal component. No less important in the complex treatment of cheilitis is physiotherapy with red-spectrum laser light using the Svetozar device. The appointment of physiotherapy treatment with a course of 7 to 10 procedures will provide anti-inflammatory and metabolic effects and accelerate the healing of damaged lip tissues.

According to the results of the survey, it was also found that patients with low interest in our study (n=13) had a longer treatment period and a shorter remission period for chronic recurrent lip fissure. Thus, the questionnaire allows us to determine the tactics of local treatment of patients with chronic lip fissure and low

interest: the appointment of complex ointments with a strong glucocorticoid component in combination with physiotherapy.

The tactics of preventive measures in patients of the main group (n=64) included taking preventive doses of vitamin D and using preventive lip balm "Elabium" with a high oil content on a daily basis. The patients of the control group (n= 54) were not given special methods of prevention, the recommendations were reduced to recommendations on compliance with work and rest, proper nutrition, especially in autumn and winter, and oral sanitation. Separately, work has been carried out to teach proper and regular oral hygiene.

An analysis of statistical data on the timing of remission found that in the control group of patients, a decrease in remission time was observed by 56.63±8.37% compared with the main group, which averaged 3.8±0.2 months and 8.8±0.3 months, respectively ($p<0.05$). Also, when analyzing the medical documentation of patients, it was found that the shorter the treatment time of patients and the faster the epithelization of the disturbed lip tissues occurs, the longer the remission period.

Since the population of residents of regions beyond the Arctic Circle should be considered a high-risk group for vitamin D deficiency. The use of vitamin D to maintain normal levels of vitamin in blood serum is an essential element of preventive measures for inflammatory lip diseases, which helps to improve lip skin regeneration, supports the barrier function of the epithelium, reduces the number of recurrences of inflammatory lip diseases. On an ongoing basis, it is necessary to use protective lip balms with a high content of natural oils, proper nutrition, maintaining a healthy lifestyle, observing work and rest, sanitation of the oral cavity, vitamin therapy is necessary with vitamin D, which is most deficient in northern latitudes.

Thus, research aimed at optimizing the diagnosis, treatment and prevention of cheilitis in the Far North refers to the development of medical care for the population of the polar region, as one of the directions of socio–economic improvement of the Arctic zone of the Russian Federation. The optimization of diagnostics is based on the assessment of the vitamin and antioxidant status of the patient, analysis of microflora and interest in treatment for chronic lip crack, the basis of treatment is

complex therapy aimed at reducing the effects of adverse factors of the Far North on the patient's body, local physiotherapy, the use of complex glucocorticoid ointments and local stimulators of tissue regeneration. Preventive measures should be limited to maintaining an optimal level of vitamin D, the use of lip protectors based on oils, the treatment of major concomitant diseases, oral sanitation and maintaining a healthy lifestyle.

FINDINGS

1. It was found that various forms of cheilitis are diagnosed in 22.62% of people living in the Arctic zone of the Far North. The structure of the incidence of cheilitis is dominated by meteorological cheilitis 11.09%, chronic recurrent lip crack 5.76% and angular cheilitis 4.75%. The remaining forms of cheilitis are less common and account for 1.01%.

2. An increased level of the oxidative stress product, malondialdehyde, was detected in the blood serum of somatically healthy people in 21.37% of cases, indicating active processes of free radical oxidation, pronounced deficiency was diagnosed in 1.72%, deficiency in 47.86% and vitamin D deficiency was determined in 50.42% of the subjects, vitamin E deficiency was diagnosed in 6.84% of the surveyed, however, the recorded level was close to the reference values.

3. The developed algorithm for the complex treatment of cheilitis in the Arctic zone of the Far North, including the administration of colecalciferol, vitamins A and E, antioxidants, the use of complex glucocorticoid ointments, local regeneration stimulants, exposure to laser light of the Svetozar apparatus of the red spectrum at a wavelength of 665 ± 15 nm, has shown its effectiveness in the treatment of 92.19% of cases.

4. Preventive measures consisting of regular use of balms with a high content of oils without fragrances and preservatives, taking preventive doses of colecalciferol, treatment of concomitant diseases together with internists can increase the remission period by 2.3 times.

PRACTICAL RECOMMENDATIONS

1. Given the fact that most patients do not seek medical help for lip diseases, practicing dentists are recommended to identify this pathology on an outpatient basis.

2. Treatment of inflammatory lip diseases in the Arctic zone of the Far North requires an individual and comprehensive approach. In patients with chronic lip crack, when prescribing a course of treatment, it is necessary to determine the mild, moderate and severe degrees of severity of the course of this disease, as well as the results of the questionnaire of interest in treatment.3. Before prescribing antioxidant drugs, vitamin D, E, it is recommended to conduct laboratory tests to assess vitamin and antioxidant statuses.

4. In case of low interest in the treatment and / or severe course of chronic lip crack, patients are recommended to prescribe complex ointments with a highly active glucocorticoid component. In terms of treatment, it is necessary to route patients for consultation with doctors of other specialties, depending on the form of cheilitis: a general practitioner, endocrinologist, gastroenterologist, neurologist, dermatologist, etc.

6. After the end of treatment and the achievement of goals, it is necessary for patients to independently carry out regular preventive measures to maintain the lipid barrier of the red border of the lips from the effects of adverse meteorological factors in the Arctic zone of the Far North, the appointment of vitamin therapy with colecalciferol preparations.

LIST OF ABBREVIATIONS AND SYMBOLS

ATP – Adenosine triphosphate

ROS – reactive oxygen species

AC – atopic cheilitis

HIV – human immunodeficiency virus

NCH – Naval Clinical Hospital

ng/ml – nanograms per milliliter

nm – nanometer

MDA – malondialdehyde

ICD – International classification of diseases

mcg/ml – micrograms per milliliter

MD RF – Ministry of Defense of the Russian Federation

MC – meteorological cheilitis

QIT-CLF– Questionnaire of patients' interest in the treatment of chronic lip crack

PUFA – polyunsaturated fatty acids

LPO – lipid peroxidation

PCR – polymerase chain reaction

TBA – thiobarbituric acid

FBIS - Federal Budgetary Institution of Science

FSGI – Federal State Government institution

CLC – chronic lip crack

CLC+MC – chronic lip fissure, complicated by meteorological cheilitis

CRI – Central Research Institute

UC – angular cheilitis

EC – exfoliative cheilitis

COVID – 19 – coronavirus infection in 2019

CRS – Confocal Raman spectroscopy

DRESS – drug rash with eosinophilia and systemic symptoms

EGFR – epidermal growth factor receptor

IgE – immunoglobulin E

IL – interleukin

ICMJE – International Committee of Medical Journal Editors

KGFR – keratinocyte growth factor receptor

PDGF – Platelet-derived growth factor

Th1/Th2 – T–lymphocytes

TLR2 – toll–like receptor 2

VDR – vitamin D receptor

VDRE – vitamin D response element

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