PRECANCEROUS DISEASES OF MAXILLOFACIAL AREA

Text book

Poltava – 2017

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
ВИЩИЙ ДЕРЖАВНИЙ НАВЧАЛЬНИЙ ЗАКЛАД УКРАЇНИ
«УКРАЇНСЬКА МЕДИЧНА СТОМАТОЛОГІЧНА АКАДЕМІЯ»

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Precancerous diseases of maxillofacial area

ПЕРЕДРАКОВІ ЗАХВОРЮВАННЯ ЩЕЛЕПНО-ЛИЦЕВОЇ ДІЛЯНКИ

Навчальний посібник

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The publication on the achievements of modern medicine covered issues of etiology, pathogenesis, clinical manifestations, diagnosis and treatment of precancerous diseases of maxillofacial area. The classification of precancerous lesions, which are used both by as dentists and oncologists.

One of the sections is dedicated to the organization of cancer services in Ukraine, organization of cancer care to people in Ukraine. The problems of periodic screening, prophylactic medical examination service, oncological alertness are covered. The manual can be useful for students of dental and medical faculties, interns, medical residents, dentists, family doctors, oncologists and other doctors.

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Рекондовано вченою радою Вищого державного навчального закладуУкраїни «Українська медична стоматологічна академія» як навчальний посібник для англомовних студентів вищих навчальних закладів МОЗ України (Протокол №3 від 22.11.2017 р.)

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У даному виданні висвітлені досягнення сучасної медицини, питання етіології, патогенезу, клінічних проявів, діагностики та лікування передракових захворювань щелепно-лицевої ділянки. Класифікація предраковых уражень, які використовуються як стоматологами, так і онкологами.

Один із розділів присвячений організації онкологічної допомоги в Україні. Обговорюються проблеми періодичного скринінгу, служби профілактичної медичної експертизи, онкологічної перестороги.

Посібник призначений для студентів стоматологічних та медичних факультетів, лікарів-інтернів, клінічних ординаторів, стоматологів, сімейних лікарів, онкологів та лікарів інших спеціальностей.

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INTRODUCTION

The problem of cancer, especially malignant tumors is one of the most pressing of modern medicine. According to WHO, each year nearly 4.3 million people dies from cancer in the world. Cancer is among the three leading causes of death in all age groups after 50 years - both in developed countries and those are in developing.

Malignant tumors of the head and neck (excluding skin, eyes and brain) constitute about 5% of cancers of other locations.Among head and neck malignant tumors cancer of the oral cavity and oropharynx is on second place after the cancer of the larynx, and their ratio is 2 - 10% of all human cancers.

Oral cancer is a major health problem in tobacco users all over the world. It is one of the ten most common cancers in the world. Oral cancer is almost always preceded by some type of precancerous lesion. The precancerous lesions can be detected upto 15years, prior to their change to an invasive carcinoma. It usually affects between the ages of 15 and 40 years. It may be triggered by factors like frequency and duration of tobacco consumption, alcohol, poor oral hygiene etc.

However, this number of patients find significant because the disease leads to extremely severe dysfunction breathing, swallowing, speech and appearance. In these patients serious condition are due, primarily to advanced and often incurable forms of disease, while advanced forms of cancer other locations lead to death from certain metastasis.

Oral cancer ranks as the sixth most common malignancy worldwide, 90% of which consists of squamous cell carcinoma. Morbidity and mortality have not decreased over the past 50 years. Oral cancer early detection, mainly

that of squamous cell carcinoma, is crucial to improve the patient's survival rate. The clinical diagnosis of oral precancerous lesions, leukoplakias and erythroplakias, is one of exclusion. The lesions to be excluded are those belonging to other conditions, such as lichen planus (acknowledging that it has a malignant potential itself), lupus erythematosus, leukoedema, white sponge nevus, and other lesions for which an etiology can be established, such as frictional keratosis, cheek/lip/tongue biting, contact lesions, and smoker's palate. In many cases, a biopsy is mandatory so that such lesions can be discarded. Currently, histological criteria (dysplasia presence and degree) represent the gold standard in precancerous lesion risk evaluation.

SECTION I

CANCER CARE ORGANIZATION TO POPULTION IN UKRAINE

Fighting malignant tumors is a major public health problem in Ukraine. The urgency of this matter is being identified by the constant growth of malignant tumors among the population, early diagnosis difficulties, high cost and difficulty of treatment, high disability and mortality rate of patients.

Each year about 200,000 new cases of malignant tumors are recorded in Ukraine. Medical and social significance feature of malignancies caused the implementation of the state system of cancer care.

Specialized cancer care is the system of measures for cancer diagnostics, treatment and rehabilitation of cancer patients, tracking the population with malignancies cases.

The basis of cancer care providing to patients is the principle of dispensary service, which is the active dynamic monitoring of the health of patients and provide them with necessary medical and diagnostic care.

Ukraine has a unique system of oncological service that has national, regional and peripheral level. The position of chief oncologist who heads the organizational and methodical measures undertaken within the country is provided in the Ministry of Health of Ukraine.

Methodical supervision for oncological care of Ukraine is porvided by Ukrainian Research Institute of Oncology and Radiology.

Regional Oncology Centers (ROC) - specialized health care institutions to provide cancer care to the people are operating in the regional centers. The main objectives of ROC are as follows:

- qualified specialized polyclinic and hospital, consulting and medical assistance to the population in full volume providing according to the standard schemes;
- monitoring the quality of implementation of treatment in medical institutions permitted to treat cancer patients;
- organizational guidance and monitoring of timely diagnosis of malignant neoplasms in all health care settings common network in their regions, as well as studying the causes of late diagnosis;
- organizational and methodic supervision and monitoring of timely diagnosis of malignant neoplasms in all common network health care centers in their regions, as well as studying the causes of late diagnosis;
- increase cancer knowledge through specialization and training of oncological healthcare personnel;
- Implementation in practice of modern methods of diagnosis and treatment of cancer, an analysis of the effectiveness of treatment in all health care centers;
- implementation and provision of full tracking of cancer patients in the region, systematic analysis of morbidity and mortality in the region, analysis of advanced forms of the disease, determine the causes of late diagnosis and the development of measures to their elimination;
- providing clinical supervision for cancer patients;
- preventive examinations of the population to identify primary cancer patients;

– expended health education work providing among all strata of the population explaining the benefits of cancer treatment in the early stages.

Typically, the Regional Oncology Center include organizational and methodological department, outpatient department, outpatient, specialized clinical departments: surgery, radiology, gynecology, department of head and neck tumors, chemotherapy and others. In addition, the clinics provided the X-ray department and radionukleidnoyi diagnostics, endoscopic, ultrasound diagnostics, clinical and cytological laboratory and others. The ROC houses Oncology Departments. Such ROC are called Clinical.

The Department together with basic ROC implementing large-scale development plans oncology science and practice, train students and improve knowledge on medical oncology, provide adequate professional level basic institutions adopting the practice of cancer science achievement and conduct research.

Two research institutes with oncological and radiation oncology specialization, 45 oncology clinics (including 24 regional, 1 republican level), one Cancer Center in the Kyiv city, 699 cancer offices (branches) operated in Ukraine in 1996.

Ministry of Health of Ukraine believes that the treatment of cancer patients (with few exceptions) should be done only in cancer institutions, as the complexity of treatment and the need for complex methods applying (surgery, radiation, chemotherapy) makes this requirement. It was established that the life expectancy of cancer patients treated in ROC in 2.0-2.5 times higher the case when treated at the general hospital network.

Malignant tumors is one of the major biomedical and social and economic problems not only in Ukraine but in the world. The incidence and

cancer mortality steadily growing, increasing their risk due to the unstable economic situation in the country, unfavorable ecological situation and a significant aging population.

Since 1953 in our country compulsory registration of cancer incidence and in 1956 population mortality from malignant tumors were introduced. The study of malignant tumors distribution among the population features, evaluating the effectiveness of anticancer complex measures based on reliable data and reliable use of cancer statistics teaching materials, ensuring the collection, processing, storage and efficient use of materials morbidity and mortality from cancer.

MALIGNANT TUMORS EPIDEMIOLOGY

Oncologic and epidemiologic situation in Ukraine and in some of their regions based on long-term monitoring data is characterized by continuous growth of cancer population morbidity. Thus, in 1980 the number of newly registered patients was 238.3 per 100,000 population in 1996 this value reached 309.4, and in 2010 the incidence of malignant neoplasms in Ukraine amounted to 341.2 per 100,000 population. Each year cancer ill more than 160,000 people. This means that every day in Ukraine arrises 442 new cases of cancer or 18 cases per every hour. This figures indicating on the intensity and magnitude of the process. The risk of getting cancer throu the life has each third or fourth man and every fifth-sixth woman.

It should be noted that cancer is the cause of more than 15% of all deaths in Ukraine, second only to deaths from cardiovascular disease; 35% of deaths from malignant tumors - those of working age. 239 people per day or 10 – hourly die from cancer every day. Over the past 5 years mortality rate decreased from 187,4x100000 to 184,5x100000 population, or for 1.6%.

Malignant tumors are the cause of 21-26% of all disability population.

Rising incidence typical of cancer and mucosa of the mouth, colon and rectum, skin, breast, cervical and uterine, ovarian, prostate, bladder, thyroid, lymphatic and hematopoietic tissue. The largest increase (20 - 50%) morbidity found in malignant tumors of the prostate, kidney, thyroid, colon and rectum, uterine body.

In the structure of the male population morbidity top 5 places are malignant tumors of the lung, stomach, skin, prostate, rectum (52.2% of all malignant tumors).

In the female population the first five places in the structure of morbidity occupy breast cancer, uterine body, colon, uterine cervix (53.5% of all malignant tumors).

The effectiveness of treatment of malignant tumors in the present conditions depends mainly on them early and timely diagnosis. Fatality of cancer is to the greatest extent due to its late discovery. However, the condition of the diagnosis of malignant tumors remains unsatisfying. Only 22-25% of patients with cancer of the oral mucosa enter to specialized cancer facilities in I-II disease stage. The worse situation is with the identification of malignant tumors of the maxillary sinus. According to M.V.Mukhyn, B.D.Kabakov, V.S.Protsyk data that not lost relevance until recent time, timely diagnosis of these tumors was only in 9.1% of patients.

Within recent years the development of a computerized information processing system of cancer patients (ASOI "Oncology"), which allows time and better use of computers based on data as cancer statistics in the field of medical services, and in terms of research.

Thus, oncology service is based on dispensary principle and has strictly defined functions and tasks aimed at prevention, diagnosis, treatment and rehabilitation of cancer patients as well as clinical supervision for them after treatment.

It should be specially emphasized that taking into account the tense oncological situation in Ukraine, to the fight of cancer system should be included not only the cancer institutions, but all the medical institutions including the dental once as well.

SECTION II

POPULATION PREVENTIVE EXAMINATIONS

The main factor that determines the success of treatment and favorable predicting with tumors of the maxillofacial area is early diagnosis.

Maxillofacial area has a good availability for examination as by a doctor and by the patient. However, tumor symptoms could be so mild that the transition of chronic inflammatory or destructive process into malignant growth often goes unnoticed either by specialist or patient.

The large number of neglected cases or absence of cancer suspicion is the evidence of the difficulty of diagnosis of cancers initial stages.

Several authors point out that the lack of different specialties doctors (physicians, surgeons, neurologists, optometrists, physicians district hospitals) awareness as for the early symptoms of dental oncologic diseases in 35.3% is the cause malignant tumors of maxillofacial localization neglect, 40.7% - amount dentists and otolaryngologists errors, 17.5% of patients who later seek treatment due to lack of understanding of the possibility of malignant lesions, often engaged in self-treatment cases.

The most common errors were obzereved in early stages of disease: I stage - 43.53%, 52.76% - in stage II. A biopsy and tumors histology were done in all patients: clinical diagnosis was not confirmed in 13.53% of patients.

Great importance in the public health system has preventive examinations. Comprehensive medical preventive examinations aimed to

detect precancerous diseases and malignant tumors. The entire population of Ukraine at the age of 20 is subjected to oncologic preventive examinations.

The following survey methods should always be used during preventive examinations performing:

1. Skin and visible mucous membranes examination;
2. Lymph nodes all groups palpation;
3. Cytological examination to detect precancerous and malignant tumors (if necessary);
4. Biopsy with histopathological material exanination (if necessary);
5. Radial methods of examination (X-ray, ultrasound diagnostics, etc.);
6. Total blood count.

CANCER PATIENTS EXAMINATION METHODS AND MALIGNANT TUMORS DIAGNOSIS PRINCIPLES

During preventive examinations performing to detect precancerous diseases and early forms of cancer it is necessary first to conduct the most commonly affected with malignant tumors organs examination: the skin of face and neck, lips, tongue and oral cavity mucosa.

When starting the skin examination, pay attention to the cracks that are not heal for a long time, ulcers, age spots, the long existing eczematous rashes, actively growing warts, nodules, skin indurations - especially professional keratoses. Such patients should be detailed examined in dermatological hospitals, if necessary - with conducting morphological or cytological verification (lupus erythematosus, psoriasis, ichthyosis).

Dentists during oral cavity preventive examinations performing for the purpose of rehabilitation and treatment should pay attention to ulceration of the mucous membrane for a long time healing, cracked lips red border, white thick, rough patches of the oral mucosa and lips. If unsuccessful treatment of these damage elements during 7-10 days doctor must send patients to consult a medical oncologist.

Lips, tongue, oral mucosa examination should start with questioning the patient about the presence of his unpleasant, painful sensations, particularly while talking and eating. During the physical examination, special attention should be paid to those areas where the most commonly malignancies are occurred: red border of the lower lip, the side surface of the tongue, the root of the tongue, mucous membrane of the floor of the mouth and cheeks.

During a physical examination on the lower lip attention is paid to dry red border, its matte surface, epithelium induration, cracks, peeling, presence

of cells and rough whitish spots and ulcers, especially with elevated as a roller edges.

During mouth and tongue examination should also pay attention to continuously existing erosions, ulcers, fissures, whitish spots, plaques, nodules and indurations availability. It is important to determine the size of infiltrates around ulcers, soreness and tightness (or indolence) of the mass, its displacement relative to surrounding tissue, benign lesion bleeding tissue. Oral cavity examination should be performed at a sufficient illumination using frontal reflector, binocular magnifier and other tools. It is advisable to wider introduce at stomatoscopy methods using oral cavity mucosa vital coloring.

Very valuable diagnostic feature is the mobility of the teeth, which is not associated with inflammatory diseases of periodontal and periodontal. When having a suspicion for upper jaw tumors the attention is drawn to the face asymmetry presence or absence, the presence or absence of deformation of the alveolar process and palate, the lower edge of the orbit, changing size and shape of the slit eye, exophthalmos. Nasal breathing quality is being checked, headaches complaints, nosebleeds, nasal secretions nature are being found out.

Palpable determine the configuration, texture, size of the salivary glands, determine the status of their excretory ducts, the nature of the secret.

A must is to determine the status of regional lymph nodes pidpidboridnoyi, submandibular areas along kyvalnyh muscles, and lateral carotid triangle of the neck and supraclavicular areas. A must is to determine the status of regional lymph nodes sub-mental, submandibular areas along Sternocleidomastoid muscle, and lateral carotid triangle of the neck and supraclavicular areas. It should be remembered that the cross-metastasis (bilateral and contralateral) is often obsereved.

During thyroid gland palpation draw attention to its increase in size, gland texture, indurations, nodes presence. In the presence of pathological changes ultrasound (US) is necessary, if possible – gland scaning. All nodes formation and indurations of thyroid subject to cytology, and puncture to obtain material should be done under ultrasound conrtol.

In the presence of pathological processes in the maxillofacial area dentist should take smears of ulcers or make a tumor puncture or enlarged lymph nodes for cytology, perform a biopsy.

BIOPSY - lifetime remove a piece of tissue for diagnostic histopathological study. This is the most accurate method for diagnosis of tumors, particularly in their early stages, biopsy reliability - 80 - 98%. A biopsy allows diagnosis and other processes - benign tumors, inflammation, hyperplasia formation. A biopsy is necessary to clarify already established diagnosis and differential diagnosis performing. Repeated biopsy allows to trace the morphological dynamics of pathological process under the influence pharmaceuticals and evaluate the effectiveness of treatment.

There are the following forms of biopsy:

diagnostic;

emergency;

accidental.

Biopsy performing methods:

– *incision biopsy* – excision of one or more pieces of tumors (when tumors are large size). Tissue excision is made with scalpel, electric knife, electric snare, conchotome. Excessive anesthetic infiltration of the tumor

should be avoided during the biopsy, better to apply general anesthesia. Incision biopsy performing requires certain rules:

– a) a biopsy should be performed at the border of healthy tissue, grasping unchanged tissue sa well;

– b) material with necrotic areas, tumors decay areas should not to be taken for the examination;

– c) in the event of small surface formations better to remove them completely (biopsy in toto);

– d) during electric biopsy extracted piece of tissue should be at least 1 cm.

After suspected malignant tumor piece of tissue removing, excision area is subjected to electrocoagulation process or treated with 96 % alcohol. The dimensions of the removed piece determined depending on the nature and location of the pathological focus, it should be sufficient for histopathological study.

During lymph node biopsy should try to remove it or more adjacent nodes to each other completely, without breaking the capsule. Gentle care to tissue, minimum traumtization of it is the necessary condition of properly performed biopsy. Extracted piece of tissue for histological examination immersed in fixing solution (10% neutral formaldehyde solution).

Prior to immersion in formaldehyde it is advisable to do from the piece surface smears for cytology.

– *excision biopsy* – surgical removal of all pathological focus. Most often used for skin tumors, enlarged lymph nodes, small lip and oral mucosa tumors. Often excision biopsy is a therapeutic measure.

– *trepanobiopsy* – receiving column tissue using a needle specially constructed for this purpose (M.P.Fedyushyna, L.Machulskoho and others). Trepanobiopsy can be used in lesions of bone, in lymph nodes dense metastases, in hematology for sternal punctures and other examinations.

– *forceps biopsy* – obtaining a piece of tissue using various designs forceps (conchotomes). It is used within endoscopy in particular. You can use examination in the mouth cavity as well.

Incidental biopsy – the examination, if material is obtained incidentally for the patient, for instance, while bronchial tumor piece expectoration.

Urgent (express biopsy) considered those biopsy aimed to obtaining histopathological conclusion within a few minutes after obtaining the material. Express biopsy is often performed during surgery to clarify the diagnosis and determine further treatment strategy in the short term.

Biopsy is also performed while clinically diagnosed with the aim of:

– histological confirmation of the diagnosis because the clinical data may prove false and lead to unnecessary and sometimes disabling surgery;

– tumor accurate morphological characteristics obtaining, its histological variant formation, the degree of differentiation;

– tumor determining prevalence both in the affected organ and beyond, which enables the rational choice of treatment to be selected;

– individual malignant tumor sensitivity identification to chemotherapy drugs for treatment and selection of the most effective cytotoxic drugs (such studies conducted in vitro or in tissue culture using biopsy material);

– particular treatment type success assessement;

– tumor recurrence detection or exclusion;

– tumor presence documentary evidence, which patient has before was treatment, that has except other things the legal significance, if necessary to confirm the treatment validity, justified only for malignant tumors;

– tumors statistics reliability;

– future malignancies treatment outcomes prognosis prediction and reliable scientific data obtaining.

Being one of the most accurate methods for tumors diagnosis, biopsy is still sometimes gives incorrect results due to non-compliance material obtaining or morphological sample inaccurate interpretation. In such cases, a biopsy should be repeated.

Bleeding, surrounding tissue damage, wound festering, tumor cells dissemination may be biopsy complications.

CYTOLOGICAL EXAMINATION (pathological focus cells screening) is performed with the following methods:

- pathological focus smear is obtained by using gauze swab, spatula or other tool;
- pathological focus reflection is obtained by using a sterile glass or sterile clerical gum;
- retype from obtained smear or reflection;
- aspiration method - sample is obtained by puncture (5.0 or 10.0 ml of empty sterile syringes and needle);
- exfoliative method - sample is obtained during cavity puncture to take fluid or during caviry lavage (rinse water).

For cytology punctates the material sample is taken with dry sterile syringe having tight piston friction and dry needle. After pricking the needle into the pathological focus several suction movements are performed, then the needle content is pushed by the piston onto 2-3 dry fatless slide plates and sliding another plate piece turned into a thin smear. If the material sample is obtained in the form of fluid (serous, hemohrahichnoyi and other), then immediately after taking it from the patient you should add to it a liquid solution of sodium citrate in the rate of 1 ml to 10 ml of liquid; washings, transudates, exudates, must be send to the examination in the full volume.

When taken from erosive or ulcerative surface of skin, lips mucous membrane, mouth, tongue sample material is obtained as a result of stroke, smears, scrape. Before malignancy suspicious surface examination carefully remove dry crusts or pus, necrotic plaque, mucus for having better access to the pathological focus.

In all cases the material sample is taken for cytology by doctor who examined or performed surgical operation to the patient. In the referral to cytology to smears (tubes, bottles) you must write the name and number of patient histories or outpatient cards, department, institution, office, where patient is examined or operated. Be sure to specify from which area the material is taken (body anatomical area), which way (print, punctate, washings, etc.), what macroscopic appearance it has.

Clinical diagnosis and performed treatment should be specified. Material samples for cytological examination should be delivered immediately after receiving it from the patient.

Conducted the patient examination department is taken responsibility for material samples delivery. Atypical cells presence in the material samples is not a reliable basis for malignant tumors diagnosis, thus may be several cytological examinations. Proper cytology provides the reliability of diagnosis in 78-90% of cases.

Excepet these methods the following methods are used for the diagnosis: stomatoscopy, radiation methods, radioisotope methods, inductive methods, wave (ultrasound) and other methods as necessary.

Thus, there is a wide range of different methods for the diagnosis of precancerous diseases and malignant tumors. However, the percentage of abandoned cases among newly diagnosed cancer patients is very high, what also caused high mortality rate within the first year after diagnosis.

The main reasons for this situation are medical errors, patients late appeals for help, refusal from examination, hidden disease course, about which 60 years ago wrote A.V.Melnikov. During this passed time period the situation had improved. The main reason for this is to be considered a lack of oncologic alarm.

The term *"Oncological alarm"* was introduced by A.Sh.Stavytskyy in 1948 and included three main components:

- suspicion of cancer;
- careful case history;
- compulsory examination methods usage.

Later B.E.Peterson had proposed to consider the cancer alarm the following:

1. Malignant tumors symptoms knowledge at early stages;
2. Precancer knowledge and their traetment;

3. Oncology care knowledge, medical institutions network and with urgent sending clarified or suspicious pathological process patients as intended;

4. Each patient who applied to the doctor of any specialty careful examination to detect possible cancer;

5. The habit to think about atypical or malignant tumor complicated course in severe cases diagnosis possibility.

According to Yu.F.Hryhorchuk and H.P.Ruzin term *"cancer alarm"* includes the following provisions:

- precancers clinical manifestations knowledge for their early detection;
- precancers main initiating and predisposing development agents knowledge to eliminate them;
- determined visually oral cavity and skin malignant tumors early clinical manifestations knowledge;
- providing cancer care structure and system knowledge for patient timely direction for examination and treatment;
- minimum required dental clinic examination knowledge when suspected precancerous disease;
- deontology principles knowledge in dealing with cancer patients;
- dental oncologic patients rehabilitation in dental clinic main provisions knowledge, depending on clinical group.

The main rule for doctors during the patients examination should be a full patient survey. This tactic can be explained by the following points:

- local lesion may be a reflection (distant metastases) of tumors that initially localized in a completely different place;

- multiple primary tumors (bazaliomy, melanoma) simultaneous occurrence is possible;
- satellite evident pathology can be detected during a full examination of the patient that may affect the amount of additional examination, establishing the exact diagnosis and treatment nature.

After the physical examination, the doctor should decide what additional diagnostic methods should be applied in this case and should perform a full scope of examination.

All patients in whom during periodic screenings processes that were suspected of belonging to precancerous diseases or malignant tumors were revealed, are subject to mandatory further thorough examination in outpatient health care facilities. In the event of necessity, the examination should be performed in a hospital or special general medical establishment.

Enhance examination of persons with suspected malignancy should be completed in preventive and treatment institutions within 7 days. Examination results data are entered in the patient's medical card and records keeping in preventive examinations form to control the patient arrival for enhance examination.

Organized (decreed) population in cities preventive examinations are performed:

1. within industrial enterprises – by means of medical units (MU) resources;

2. within enterprises and organizations that do not have their own MU, by means of preventive and treatment facilities to which they are attached.

3. unorganized population (pensioners, housewives and others) preventing examinations performing relies on regional clinics.

Employed and unemployed population in rural areas preventive examinationsare made in Rural District Hospital (RDH) or rural medical stations, and enhanced examinations are performed by Central District Hospital (CDH).

In some areas where the population due to the specifics of production location or remoteness of settlements removed from schools of general hospital network, preventive examinations are carried out by expeditionary or brigade methods are used.

For all detected during preventive examinations patients with malignant neoplasms discovered the disease doctor must complete notification of newly diagnosed cancer (form number 90/u, approved by order of the Ministry of Health of Ukraine № 1030 dtd. October 4, 1980) and in three days forward it to Cancer institution in the patient place of residence. Patients precancerous and tumor diseases are registered in clinical records by relevant specialists, for each patient a control card is filled in, form №30 (clinical patients registration form). For each patient with newly diagnosed malignant tumor in stage IV of the disease, while the visual localization of tumors - in stage III (all localization in maxillofacial area) the "Protocol in case of detection in a patient the neglected form of malignant tumors" (form number 027-2/u) is composed.

All taken under medical supervision patients should be allocated to following clinical groups:

1. *group Ia* – suspicious for malignancy diseases patients;
2. *group Ib* – precancerous diseases patients;

3. *group II* – special complex treatment subjected malignant tumors patients;

4. *group IIa* – radical treatment subjected malignant tumors patients;

5. *group III* – practically healthy individuals after malignant tumors radical treatment;

6. *group IV* – palliative or symptomatic treated malignant tumors common forms patients.

Ia clinical group includes patients with unclear clinical picture, having the presence of suspected malignancies disease. When the final diagnosisis confirmed Ia group patients is striked off the clinical records or transferred to other clinical groups. Ia clinical group patients enhanced examination should be organized no later than 7 days after taking on the clinical records. Patient may stay in Ia clinical group no longer than 10 days.

Ib clinical group includes patients with precancerous diseases.

II clinical group includes patients with malignant tumors, which are due to the use of modern treatment regimens can be completely cured from malignant tumors, and patients with achieved prolonged remission.

IIa subgroup is dedicated as part of *II clinical group* - patients subjected to radical treatment. By radical treatment is understood the tumor treatment modern methods usage aimed to complete patient cure from tumor.

III clinical group - a group of healthy individuals include patients who received radical treatment (surgery, radiation, combined or complex treatment), with no recurrence and metastasis. These individuals are the object of observation and rehabilitation. Controlling examinations are performed within first year after radical treatment on a quarterly basis; within the second year of controlling examinations are performed twice a year; within the third

and subsequent years – controlling examinations should be carried out once a year. Individuals of this clinical group, in the case of recurrences are transferred to II (IIa) group for specialized treatment (surgery, radiation, etc.). or in IV group if special treatment is not required due to the prevalence process.

IV clinical group – progressive form of malignant tumors - include patients special treatment for where is not possible. These patients are mainly receiving symptomatic and palliative treatment. This heavy contingent of patients requires special attention from the medical staff. For these patients is required prompt analgesic therapy and elimination of vital dangerous complications.

Malignant tumors treatment can be successful only when it is performed at early stages of the disease and even better if you begin treatment at precancerous changes. Head and neck precancerous patients can seek treatment to dentists, ENT specialists, surgeons, dermatologists and others. Therefore, these specialists should be familiar with head and neck precancerous diseases clinical signs, malignancy signs and cancer early signs in their respective areas.

One of the most important measures in solving anticancer control compliance problem is systematic population comprehensive preventive examinations performing, as well as general outpatient care organization, during which any patient's examination performed by a doctor would be both preventive examinations aimed to detect the most common cancer locations and precancerous diseases.

All precancerous diseases patients should be under respective specialties doctors medical observation. High incidence malignancy precancerous patients are subjected to systematic monitoring and treatment in

oncologists (clinical group 1B). Within precancerous diseases surgical treatment removed tissue histological examination is compulsory. After performed precancerous diseases radical treatment the patients should be under active medical observation in a 6 - 12 months. Patients received therapeutic treatment medication, should be under active medical observation in a 3-6-9-12 months, within the second year – in a 6-12 months, if recurrence or continuation of the disease is not detected, the patient is transferred to entire population annual clinical examination system where they are included to the malignancies increased disease risk group. If during the process of obzervation the patient required surgical treatment, it is carried out in a required specialist.

After performed treatment the patient should be under active medical observation in a 6 and 12 months if not detected recurrence or continuation of the disease, the patient is transferred to entire population annual clinical examination system where they are included to the malignancies increased disease risk group. Refused treatment patients should be under active medical observation every 2-3 months.

According to acting Ministry of Health of the USSR Order of the №192 dtd. 07.04.1986 patients with malignancies and precanser disease high-risk groups formation is carried out by specialists involved in population annual clinical examination performing.

Oncologist provides methodological assistance during these groups formation, controls registration, examination timeliness and completeness, an clinical supervision and recreational activities effectiveness annual analysis performs together with other specialists.

During population annual clinical examination performing or when the patient is sicking for medical care, family doctor, dentist and other specialties

doctors taking into consideration the list of risk factors include examined patient into increased risk group. The related record is made in patient's outpatient card.

Persons included in the precancer diseases high risk patients group clinical supervision is carried out in residence territorial medical facility at the or in the clinic at the place of work. Dispensary observation control card (form №030-U) is created for each detected patient.

Above mentioned patient population annual clinical supervision the necessary amount of examinations are carried out required for the component to oncological clinical examination.

Within the next dispensary patients examination departmental guidelines listed diagnostic procedures are applied. In addition, precancer tumors patients are enrolled in annual clinical examination in the amount provided for the entire population.

Patients treated from precancer tumor deseases should be enrolled into specialist control examination in a 6-12 months, afterwards they can be transferred to entire population annual clinical examination system where they are included to the malignancies increased disease risk group.

Main risk factors list:

1. *Age.* Male and female, 45 and older – all localizations.

2. *Bad health habits*:

- alcohol ingestion – all localizations;
- smoking – all localizations;
- excessively hot and spicy foods - oral mucosa, tongue;
- local drugs (weed chewing, and etc.) – oral mucosa, tongue.

3. *Prolonged industrial hazards (10 years and more)*:

- Outdoors working in the field of agriculture, construction, marine transport - lip skin;

- Lips red border frequent burns during the metallurgical, chemical and glass blowing business - lip, skin, oral mucosa, tongue;

- Automobile transport workers; workers employed in oil production and processing, employed in nickel and chrome plating processes, in the wood industry - malignant tumors of the nose, sinuses, lips, oral mucosa, tongue;

- X-ray and radiation, chemical carcinogens performance in industrial environment (oil, nitropaint) influence on skin - skin malignant tumors, lips.

4. *Internal causes*:

- family (blood) relatives malignant neoplasms presence – all localizations;

- melanoma presence in relatives – all localizations.

MAXILLOFACIAL PRECANCEROUS CONDITIONS
PRECANCER CONCEPT

Precancers - pathological conditions, preceding within the long period the tumors appearance, but not always turn to them and is a stage of carcinogenesis. The term “precancer” (praecancer) was proposed in 1986 at the International Congress of Dermatologists in London by M.V.Dyubreyl. He raised the question of keratosis, a condition preceding the occurrence of malignant skin tumors. Since the term "precancers" is widely used in clinical medicine, but it should be noted that long before, cases of cancer at the site of various pathological conditions were known. Nevertheless, there is still no consensus on the importance preceding pathological processes in the development of malignant tumors. Some experts believe that the term "precancer" should encourage and not to consider it obligatory phase in the development of tumors. Other authors believe that every cancer has its own precancer, but not each precancer always turns into cancer.

It is experimentally and clinically proved that certain pathological processes precede tumors development.

A.V. Melnikov, a leading Ukrainian onkomorfologist, gives the following a definition of precancer: precancerous is local (hereditary, born or acquaired) benign skin epithelial disease, mucous membrane or parenchymal organ, which, located in the typical places, subjected to constant irritation (nonspecific) and being neglected, with stratification endogenous causes quantity, becomes malignant tumor.

A.V.Melnykov conventionally identified four stages precancer to cancer transformation:

a) hyperplasia and tissue restructuring;

b) lesion hyperplasia;

c) benign tumor formation;

d) benign tumor to malignant transformation with specific infiltrative and destructive growth.

L.M.Shabad identifies 4 stages in cancer development:

1. Morphologically and functionally modified uneven diffuse hyperplasia.

2. Lesion growths on diffuse hyperplasia background from multycentral anlages; immaturity signs, atypia.

3. Focal proliferates, merge to form a unit separated from the surrounding tissue (benign tumor).

4. Malignization.

Some authors identify three histological precancerous stages: stage A - corresponds to the I stage of cancer according to Shabad and characterized only diffuse or multiple hyperplasia of epithelium; Stage B - meets the II and III stages according to Shabad, characterized by focal proliferation, with initial signs of atypia (basophilia, cytoplasmic and nuclear polymorphism); Stage C represents a sharp atypia and actually have the original cancer.

Most authors consider directly precancerous stages 2 and 3, ie, focal proliferates and benign tumors. They propose to distinguish precancers from background diseases.

In practice listed anove stages moves from one to another without clear boundaries; malignant tumor formation may arise without 3-rd stage.

Thus, precancer is a dynamic state that can transferred into cancer due to constant changes in the cells properties toward malignancy. Precancer to cancer transformation occurds not only by quantitative changes (time, weight) as a result of biological changes in cells, specific for malignant cells qualities accumulation in them.

Precancers missing one or more characterisitics differs them from cancer. precancers lesion cells feature is great sensitivity to factors that cause cell reproduction.

Precancers lesions dynamics varies:

- cancer progression and development;
- benign tumor formation;
- regression.

The reasons for these changes are unknown at this time, but they are directly dependent on immuno-biological condition of the body, duration and intensity of oncogenic factors.

Venkei and Shugar, comparing their clinical classification with histological stages, concluded that most of the changes that belong to the group of optional precancer in a broad sense, histologically belongs to A precancer stage; most of the changes that belong to the optional precancer in a narrower sense, histologically "pushed" to B precancer stage, and finally changes belonging to obligate precancer, histologically correspond to group C.

Especially revealing precancer value is determined in lips and mouth red border mucous membranes localization process. This is connected with patients monitoring availability and obviously the fact that most cancers arise from this location due to to the external carcinogenic factors.

According to various statistics, oral and lips cancer precancerous changes precede from 92% of cases (L.A.Epshteyn) to 26% (V.A.Hremilov). Yet, most of the leading scientists (M.M Petrov, I.T. Shevchenko and others) believe that most maxillofacial localization cancers arising from precancerous lesions progression.

PRECANCER PROVOKING FACTORS

Along with lip cancer features spatial distribution as one proof of solar radiation important role in the etiology of cancer localization several authors presented data that villagers whose work is associated with prolonged stay in the open areas, having lip cancer more often than the urban population.

Several authors noted that the vast majority of patients with lip cancer had prior various precancer diseases and pathological conditions (erythro- and leukoplakia, limited hyperkeratosis, papilloma, diffuse dyskeratoz and etc.). So far there is no consensus concerning which from a large number of lips diseases should really be recognized precancerous diseases.

Climate factors, particularly insolation, sudden changes in temperature, significant wind speed, often lead to dry lips and cracking and disceratosis on basis of which lips cancer may develop.

In various parts of the world, including Ukraine, the risk factors for cancer and oral cavity mucosa and pharynx vary. Most authors connect these tumors development with smoking and strong alcoholic beverages consumption.

Published data analysis shows regional factors presence that influence maxillofacial area malignant tumors development and that must be considered during screening process planning and within clinical observations proces.

These include the systematic use of alcohol combined with intensive tobacco smoking that increase oral cavity and pharynx cancer risk in 14.5 times because within combined usage alcohol and smoking

carcinogenic effects synergy is observed, but these factors may contribute to oral cavity cancer development independently.

Some authors assume that at deterring from alcohol and smoking tobacco usage the mouth and throat cancer incidence in male decreased to 76%, with contributions from smoking cessation, perhaps, would represent 33%, as a result of the exclusion of alcohol - 43%.

The incidence of oral cavity and pharynx tissues squamous cell carcinoma in patients, who abuse alcohol and smoking, progressively increases with the drinking of alcohol and the number of cigarettes smoked.

Tobacco role serious study in oral cavity cancer developing confirmed the clinical assumption that it acts as a carcinogen.

Most studies indicated that alcohol is a risk factor for oral cavity, pharynx, larynx, esophagus, liver and lungs carcinoma in people abused him.

It is established that alcohol can act as an etiological factor in reducing cellular immunity: head and neck cancer unusual for alcoholics with normal immune defense.

The assumption was made that alcohol promotes tobacco carcinogens adsorbtion. Perhaps malnutrition in people consuming large quantities of alcohol, makes epithelial cells that keratinize more susceptible to malignant transformation.

Malignant neoplasms high incidence of population in some countries is associated with regular, often begins with childhood, salted fish consumption. The authors believe that the causative factor may be present in dried and salted fish dimetylnitrozamin that is a strong organotropic carcinogen for laboratory animals.

Oral mucosa most famous carcinogenesis example resulting in people nutrition imbalance is iron deficiency or Plummer-Vinson syndrome.

Typical symptoms - cracks or sores in the corners of the mouth, yellowish skin tone, smooth red tongue and dysphagia. Confirmed the link between mucous membrane atrophy on esophageal tract top and mouth, pharynx and esophagus carcinoma development susceptibility. Improving nutrition, through understanding the problem, resulting in lower incidence as Plummer-Vinson syndrome and head and neck cancers among women of Northern Sweden.

Clinical studies have confirmed that under certain conditions, depending on the dose and duration of exposure, x-ray radiation can cause cancer.

It is recognized nowerdays that one of the groups at high risk of cancer developing were people that being a child receiving therapeutic doses of X-rays or radium applications on the head, neck or upper chest on various benign processes (enlarged thymus, enlarged tonsils or adenoids, mastoiditis, sinusitis, keloids, dermatomycosis heads, acne, etc.). In this part of population statistically noted a significant increase in thyroid cancer incidence and (to a lesser extent) the salivary glands, and other tissues. It develops latent within 3–35 years after initial exposure.

Another type of head and neck iatrogenic tumors caused by radiation - is osteosarcoma. The researchers determined exposure possible role in causing malignant changes in bone among 11 patients with osteogenic sarcoma developed through a 6–22 years following X–ray or gamma therapy.

From bone sarcoma after radiation 17 observations, which first reported from clinic Meyo, in 3 cases the tumor was localized in the region of the head: one – the lower mandible, two – at the upper. In another clinic Meyo study jaws and facial bones of the skull osteogenic sarcomas reported 19 cases of sarcoma of the lower mandible, 14 of upper mandible and 11 - in the area of maxillary sinuses.

There is no evidence that intermittent exposure during dental radiography has a carcinogenic effect, especially now, when applied exclusively high X-ray films and devices with low doses.

Some people because of genetic traits are at risk of cancer. There are three types of genetic factors that contribute to cancer:

1) chromosome, characterized by an imbalance in the genetic structure, particularly the lack or, conversely, an excess of certain genetic material;

2) localized in a particular gene, when the disease is caused by mutations or in one of the units, as in the dominant sign, or in the first team, as with recession sign;

3) polygenic, which can operate at a large number of genes (this includes environmental factors), and no factor or gene does not play a major role.

In the 161 monogenic disorders type examined patients were tumor or pre-cancerous manifestations or complications. Excluding monogenic trait typical for skin, thyroid and parathyroid cancer, three other symptoms remains associated with head and neck malignant tumors.

The first of them - a syndrome basal cell nevus that appears in the basal cell carcinoma, medulloblastomi, jaw cysts and fibroids (ovarian carcinoma).

The second - a Gardner syndrome, manifested intestinal polyps, osteomas, fibroma, atheroma and carcinoma of the colon, oral faterova pancreas, thyroid and adrenal glands. Third disorder - a cherubism, which is characterized by numerous giant cell tumor, can lead to situations that pose a threat to life, such as asphyxia.

Among all the possible microbial factors real value has only viruses in carcinogenesis. If they really cause cancer in humans, it is associated with specific recipient factors, such as time of infection, immune status, also accompanied by other diseases, genetic predisposition and cellular immunity decreasing.

Since then, when in cell cultures of Berkytt African lymphoma identified Epstein-Barr virus (EBV), collected evidence of significant side connection of the disease with Berkytt African lymphoma. In almost all cases are EBV antibody serum, and their average titers in patients compared with patients from the control group significantly increased. Non-tropical Berkytt tumors tisssues do not obviously contain EBV DNA.

In several authors studies is reported a significant incidence of syphilis in men with oral cavity cancer, particularly lips and tongue cancer. But other authors do not mention syphilis in their viruses and other microbes as etiological factors of mouth cavity cancer analysis.

Thus, the link between the disease and oral mucosa cancer is very doubtful, because in each case it can be easily argued that men with syphilis were certainly not young, abuse tobacco and alcohol, often have not good nutrition all these factors may be important in causing cancer.

Chronic injury from destroyed tooth sharp edges, substandard restorations and poorly fitting dentures is the cause of oral mucosa cancer. The authors specify that in 20 million US citizens who use dentures, mouth mucosa and alveolar jaw bone carcinoma amounts about 11%.

Thus, lips, oral mucosa and pharynx malignant tumors dynamics and forecast incidence suggests its growth among population. Increased oral mucosa cancer risk is caused by several factors, such as nutrition, immunological disorders, infections caused by viruses (including herpes type 1-alpha), phungi Candida, presence of chronic injury from exposure of carious teeth or poorly fitting dentures, oral hygiene underexposed and others.

Among precancer should be noted oral mucosa erythroplakia and leukoplakia, destructive leykokeratosis, submucosal membranes fibrosis, trophic ulcers and long-existing papillomas, and various inflammatory processes should be attributed to the background diseases and conditions.

Thus, precancer causes can be environment negative effects (exogenous factors), as well as the whole body condition disorders (endogenous factors).

Exogenous factors

1. Mechanical stimulants: coarse food, different kinds of poor quality prostheses, filings manufacturing defects, abnormal bite, dentitions defects, teeth uneven worn, bad habits (keeping in mouth pencil, pens and so on.).

Some mechanical factors include occupational hazards (N.F.Danylevskyy, 1966): iron ore, lead, silicate dust contributes oral mucosa hyperkeratoses of employees in the corresponding entrprises. Mucous membrane irritation is promoted by aluminum buses due to galvanic currents arrising (Penev, Todorov, 1970).

2. Chemical stimulants can be devidie into two groups: household and occupational. Household chemical irritants include spices, highly concentrated solutions of alcohol, tobacco (smoking, chewing), quicklime (betel). Spicy foods with lots of spices, which is widespread among residents of the south where the high frequency leukokeratosis and oral cancer is observed.

Tobacco has a rough irritant action to the mucous membrane of the mouth. While smoking the body gets about 20% tabaco smoke, which contains a number of products for extremely strong irritant effect: pyrydinovi foundations - the most harmful side of influence, hydrocyanic acid, cyanide sister compounds, fatty acids, phenol and tar sediment. In addition, tobacco smoke, except polycyclic hydrogens contains 3 - 4 bensperen and arsenic. Increased tobacco products usage leads to increasing patients quantity with leukoplakia and oral cancer.

One of the annoying points of smoking is the heat factor. Keratosis often occurs in those who puff at pipe, smoke up cigarette to the end so that the lips are being burned.

Operational stimulants: alkalis, acids in the form of vapors, aerosols and other chemicals depending on the concentration and action duration may lead to acute or chronic chemical injury.

The temperature stimulants: hot food, a cigarette burning lips, hot air during working at some enterprises. With prolonged exposure contributes to precancerous diseases development.

Meteorological factors - is a environment negative agents complex that affect skin tissues of the face and lips. This includes the effect of sunlight, dust, wind, aerosols, salt water at low temperatures and high humidity.

Biological factors: yeasts, pale spirochete, Chopsticks Koch contributing the tongue, mouth mucous membrane keratinization emergence, causing temporary

infringement keratinization in some areas of the oral mucosa and increases tendency to malignancy.

Endogenous factors

Anatomical and physiological features: increased keratinization oral mucosa tendency due to its origin from the ectoderm. The tendency to keratinization increases with age due to cells dehydration. Hormonal changes (especially in women) influence the keratinization process. Some diseases of different etiologies (chronic anemia, diabetes, etc.) disrupt the keratinization processes.

Listed above factors both in isolation and together are constant companions of human life and render permanent effect on oral mucosa keratinization processes:

- stress conditions: acute psychic trauma value in the event of dyskeratosis appearing (eg. lichen planus);
- gastrointestinal tract diseases: within chronic gastritis, enteritis, colitis arising para- or hyperkeratoses states;
- febrile states;
- diffetent ethialogy xerostomias;
- Lupus erythematosus, psoriasis, ichthyosis.

PRECANCER CLASSIFICATION

Recently, a broad implementation in practice acquired precanser - classification proposed by Hungarian authors - Venkei and Shugar, according to which all precancers are devided into obligate (mandatory) and optional. Optional precancers therefore are devided into optional precancers in the broadest sense and optional precancers in a narrow sense.

T. Venkei and Ya. Shugar precancers classification

I. Optional precancers

1) Optional precancer processes in the broadest sense (main diseases).
2) Optional precancer processes in a narrow sense (keratopreccanserosis).

II. Obligate precancerous conditions or intradermal cancers.

Precancerous conditions in the broad sense are characterized by the fact that the probability of their malignancy is below 10% of cases. These include senile skin atrophy; chronic ray, radiation dermatitis; dermatitis caused by the action of tar, arsenic, scars, chronic inflammation, including lupus, benign tumors and others.

To optional precancers in the narrow sense belongs so called keratoprekarcenosis (senile keratosis, keratoakantoma, cutaneous horn, sores). Probability of malignancy at 20-30% of cases.

To obligate skin precancers belong xeroderma pigmentosum, Bowen's disease, eritroplasia Keira, Paget's disease.

Similar principles in the distribution of lip and oral mucosa precancers underlying the classification established by A.L.Mashkilleyson (1970), which is followed both by dentists and oncologists.

There are the following oral mucosa and lips red border precancers forms.

A.L.Mashkilleyson precancers classification

I. Obligate precancers:

1) Bowen's disease and Kejer's erythroplasia;

2) warty or nodular lips red border precancer;

3) abrasive precancerosis cheilitis Manganotti;

4) lips red border limited precancerous hyperkeratosis.

II. Optional precancers with high potential malignancy:

1) erosive and verrucous leukoplakia;

2) papilloma and papillomatosis of palate;

3) cutaneous horn;

4) keratokantoma.

III. Optional precancers with less potential malignancy:

1) flap leukokeratosis;

2) oral mucosa chronic ulceration;

3) lips red border lupus erythematosus and red flap leave hiperkeratotical and erosive forms;

4) chronic lips cracks;

5) postirradiation cheilitis and stomatitis;

6) meteorological and actinic cheilitis.

Obligate precancers - processes which are with the greatest frequency transformed into malignant tumors in a relatively short time. Optional precancers are less likely to turn into cancer at a long exposure.

Thus, all oral mucosa and lips red border precancerous changes are divided into three groups: the obligate precancerous conditions, facultative precancerous conditions with greater potential malignancy, characterized by transformation into cancer in 15-30% of cases, and precancerous conditions with less potential malignancy in which the malignancy occurs not more than 6-10% of patients. In regard to histological first and second groups of diseases belong to the focal proliferates or so-called benign tumors (as per L.A.Shabad terminology), while the diseases classified in the third group, presented as diffuse, pathologic uneven hyperplasia. In the first group included diseases, histological structure of which meets the condition referred to as cancer in situ, so-called "offset" cancer that under international histological precancers classification refers to precancerous disease (Bowen's disease and Kejer’s erythroplasia).

Comparing A.L. Mashkilleyson classification to Venkei and Shugar classification, it is noted that three groups precancerous lesions according to Mashkilleyson almost entirely correspond to three pathomorphological phases A, B and C. For example, a disease included in the first group corresponds histology characteristic of phase A; diseases of the second group - Phase V; diseases of the third group corresponds to stage B-C or C.

OBLIGATE PRECANCERS

Bowen's disease was first described in 1912. The etiology and pathogenesis is unknown.

The clinical picture is diverse; often localized in oral mucosa (palatine arch, tongue root, soft palate) posterior part, seldom in retromolar and anterior arears, on lips red boder. Affected area has irregularly shape. May show spotty-nodular lesions that gradually increase in size may have torulose surface and papillary proliferation. Prolonged existence light atrophy is observed, affected areas sinks down slightly, it may be erosioned, affected areas may merge, forming polycyclic contours plaques, plaque size from 0.1 to 1.0 cm. The surface area is hyperaemic, smooth or velvety with small papillary growths, slight desquamation and itching are possible.

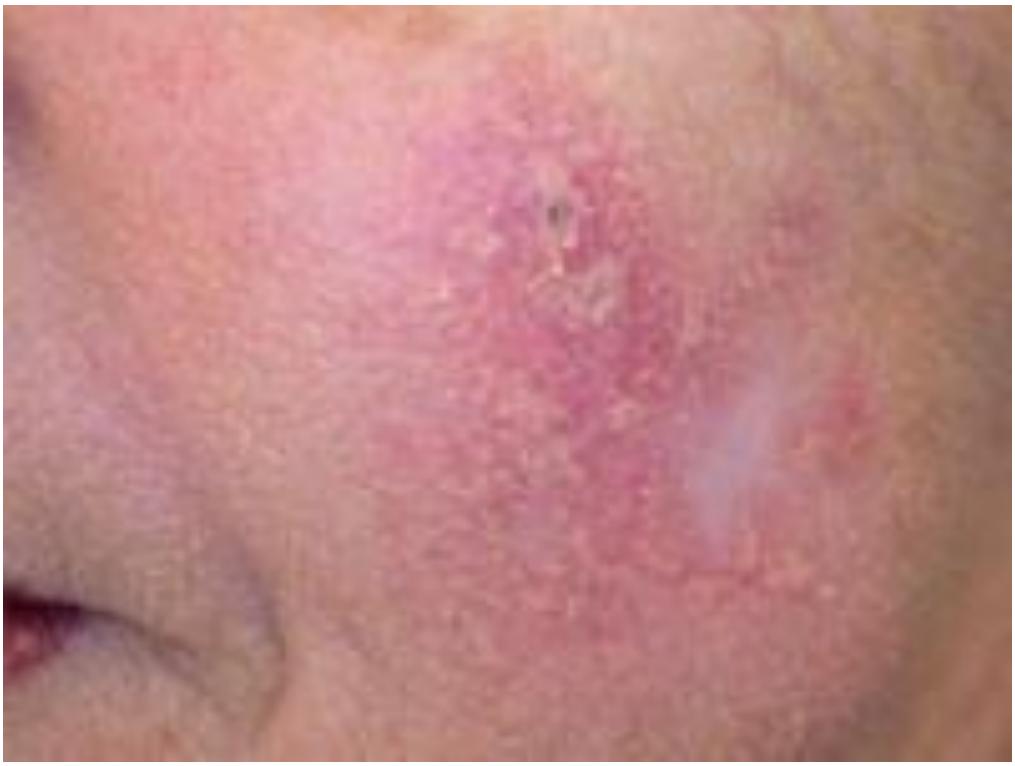

Fig 1. Bowen’s disease

To differentiate is necessary from leukoplakia, lichen ruber planus, syphilis. Diagnosticate is only on histological examination results.

According to clinical manifestations Bowen's disease four forms are:

1) papules and furfuraceous;

2) papules and crusted;

3) atrophic;

4) weeping.

Histologically, there are giant cells in stratum spinosu with cores agglutination as lumps. Individual cells keratisation in malpighian layer, infiltrate composed of lymphocytes and plasma cells in stroma may be observed.

Treatment. Electrosurgical wide lesions removal or cryogenic destruction. If surgical treatment is not possible awailable areas close-focus roentgenotherapy is applied. If invasive growth is detected, combined treatment method is used.

Keyr's erythroplasia was described in 1921. Histological picture corresponds to Bowen's disease (embedded in the concept "carcinoma in situ"), therefore Bowen's disease is being interpreted by some authors as a further stage of Keyr's erythroplasia development. Other researchers do not see the need to separate Bowen's disease and Keyr's erythroplasia.

The disease starts with strictly limited bright red lesions with hardly noticeable thickening at the base appearing on lips, cheeks mucous membranes. Lesions are slightly increased over the mucosa surface. Lesions surface is smooth, hyperemic, some velvety. Gradually on lesion surface ulcers is appeared and disease becomes a cancer, may metastases in lymph nodes. This disease is characterized by slow motion. Treatment is only radical surgical; radiation therapy is less than effective, conservative methods - quite ineffective.

Abrasive precancerous Manhanotti's cheilitis - refers to obligate lips precancers**.** Among numerous cheilitis groups Manhanotti in 1933 highlight one form the feature of which is very frequent transformation in cancer. This form was often described by many oncologists like "destructive disceratosis." Cheilitis Manhanotti clinical manifestation differs with some varriety. The disease affects only the lower lip, manifesting itself in the form of one or more erosions oval or irregular in shape, size 0.5-1.0 cm, often with a smooth, polished surface having intense red color. In some patients erosion surface is partially covered with a thin transparent epithelium. Quite often crust (bloody or serous), which held quite firmly on the surface occur on erosion surface.

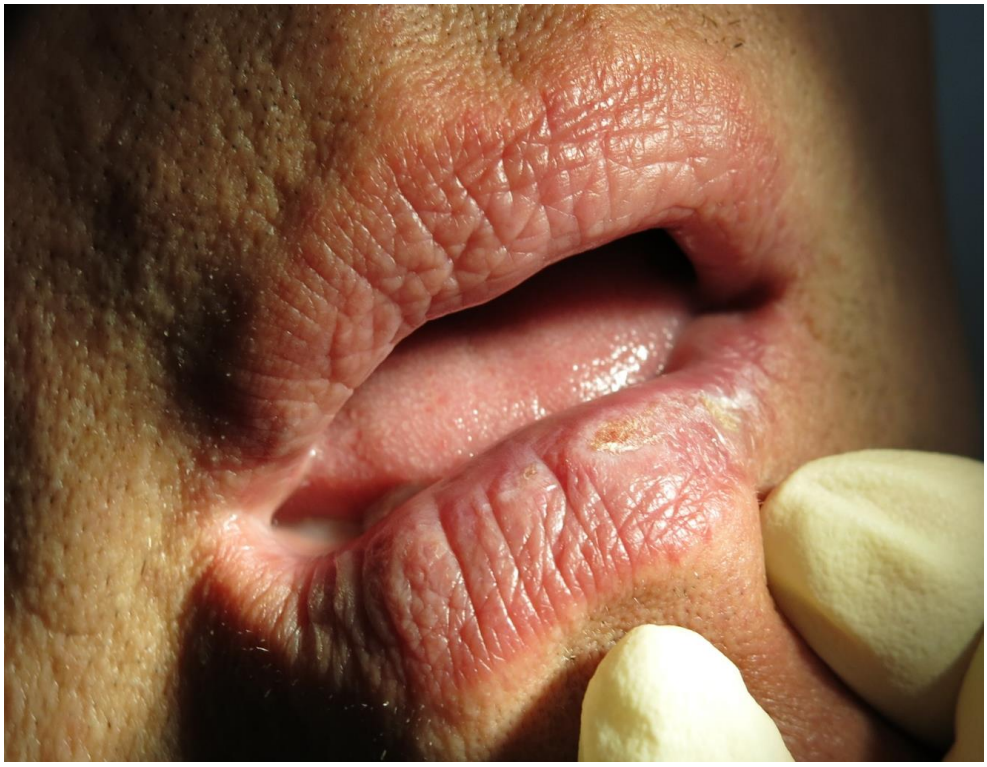

Fig.2. Abrasive precancerous Manhanotti's cheilitis

Crusts removal causing minor bleeding, while erosive surface without crusts minor trauma does not cause bleeding. Erosion epithelization is often observed and then recidive. Erosion is often located on the side of the lip,

sometimes - in the center. In some cases, erosion is placed on a slightly infiltrated and hyperemic basis, and the inflammatory response is observed upto 1.0-1.5 cm beyond erosion boundaries. Malignization is possible in within the period of several months to several years - with the formation of squamous cell carcinoma. Signs of malignancy: loss trends to epithelialization, proliferation on the background of erosion formations similar to granulation, increased as a roller edges of erosion, bleeding from erosion, compaction at the base of erosion, the emergence of a significant keratinization directly around erosion. Finally, possible malignant transformation process question can be resolved by morphological examination. It should be noted that sometimes, even in the absence of these malignancy clinical signs, histological examination can reveal a picture of spinocellulare (squamous cell) cancer.

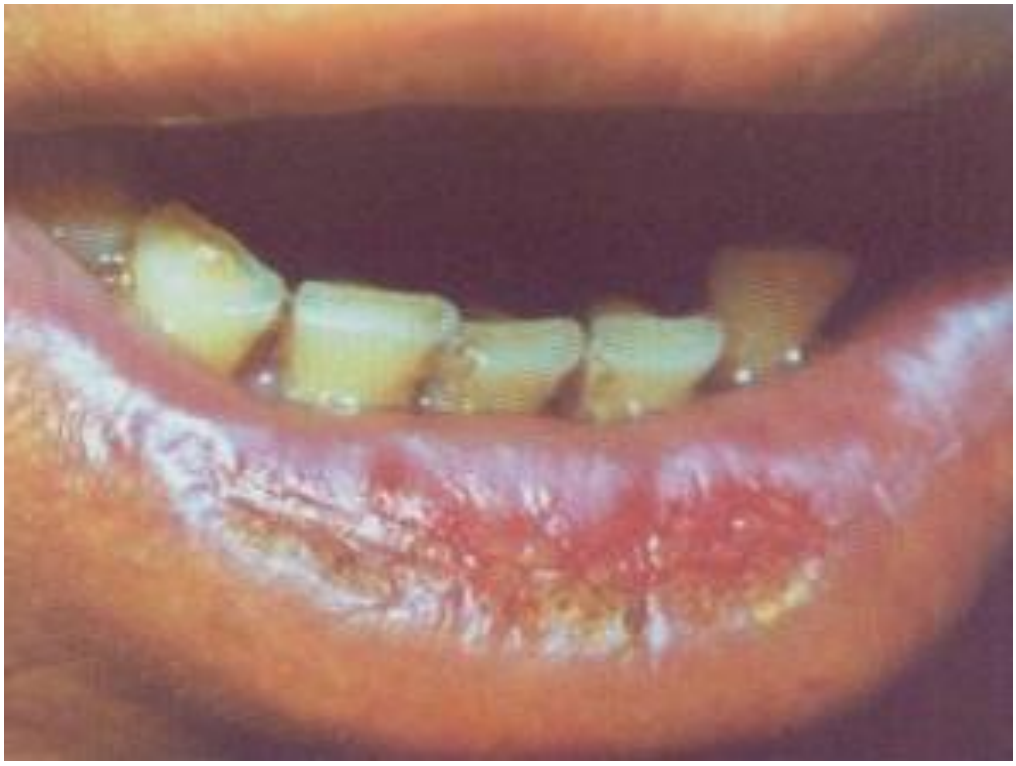

Fig. 3. Abrasive precancerous Manhanotti's cheilitis

Cheilitis Manhanotti differential diagnosis should be made with pemphigus, herpes, thrush, lichen planus, lupus erythematosus, erosive leukoplakia, eczema of the lips, ulcerative form lips cancer.

Abrasive precancerous cheilitis Manhanotti treatment involves the use of drugs that stimulate epithelization erosion - retinol, thiamine chloride, riboflavin, niacin. Treatment should begin after irritating factors removal, oral cavity sanation, gastrointestinal tract pathology treatment. If the process is not amenable to conservative treatment, or when there are signs of malignancy, it should be applied surgery - removal of the lesion within healthy tissue layer with mandatory histological examination by layers. Clinical monitoring of such patients is carried out both dentists and oncologists (this applies to all patients with obligate precancers).

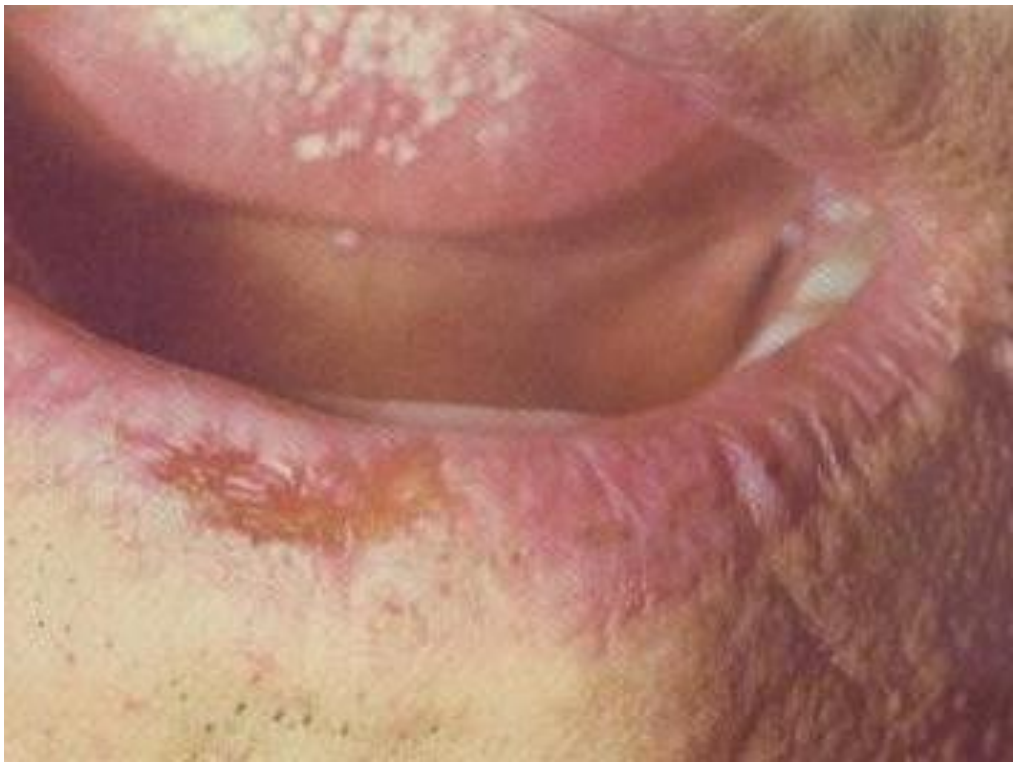

Fig.4 Abrasive precancerous Manhanotti’s cheilitis

Cheilitis Manhanotti differential diagnosis should be made with pemphigus, herpes, thrush, lichen planus, lupus erythematosus, erosive leukoplakia, eczema of the lips, ulcerative form lips cancer.

Abrasive precancerous cheilitis Manhanotti treatment involves the use of drugs that stimulate epithelization erosion - retinol, thiamine chloride, riboflavin, niacin. Treatment should begin after irritating factors removal, oral cavity sanation, gastrointestinal tract pathology treatment. If the process is not amenable to conservative treatment, or when there are signs of malignancy, it should be applied surgery - removal of the lesion within healthy tissue layer with mandatory histological examination by layers. Clinical monitoring of such patients is carried out both dentists and oncologists (this applies to all patients with obligate precancers).

Nodular or warty (verrucous carcinoma) lips red border precancer. The disease was described by A.L. Mashkilleyson in 1970. In comparison with Manhanotti cheilitis is more common in younger people. Typically, the lesion is localized a side from the center of lips, mostly in lower lip, within the red border without spreading to the skin or in the Klein zone.

Clinically the lesion is similar to papilloma or wart, has clear limits. Element size from 4 mm to 1.0 cm, semispheric form above the level of the surrounding red border of 3-5 mm, has a dense texture. The color changes from red border normal color to stagnant red. In most patients usually nodule surface is covered with a small number of scales that cling to the surface without stripping while rubbing. In such cases, the surface becomes grayish-red. Nodule palpation is usually painless. Most often this element is situated on not changed red boder, sometimes – having slight inflammation background.

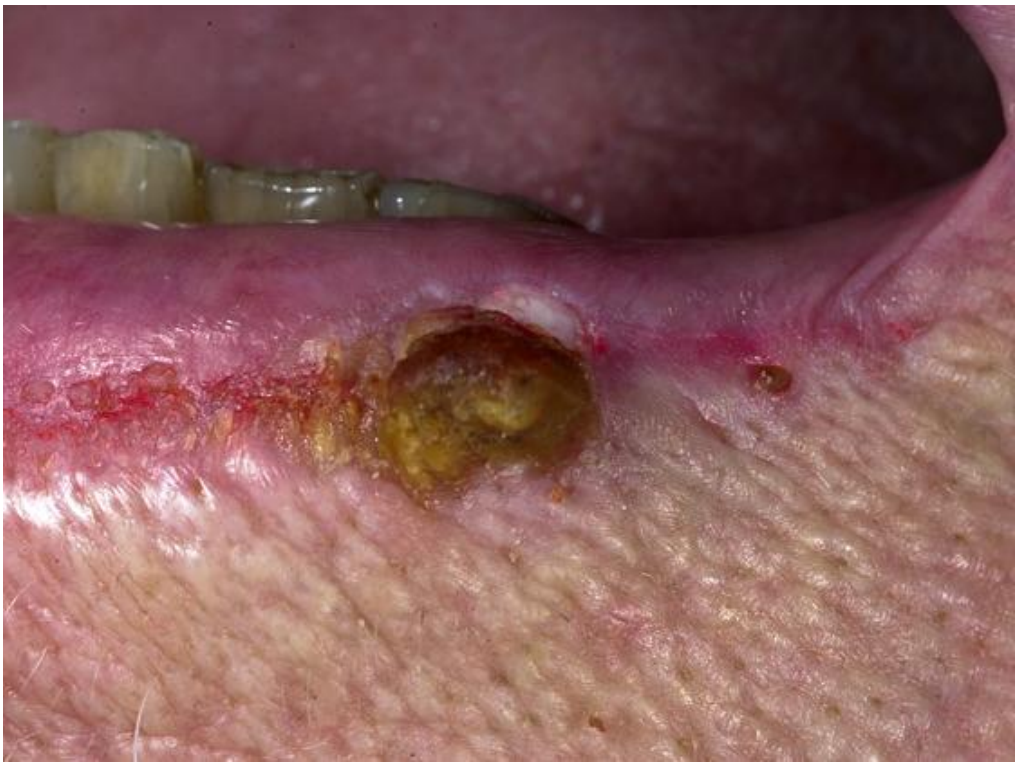

Fig 5. Verrucous carcinoma

Verrucous carcinoma course is pretty fast. Malignization process may happen after 1-2 months after the onset of disease, although in some patients this process continues for 1-3 years.

Verrucous carcinoma differential diagnosis should be done with ordinary warts, papilloma, keratoacanthoma, pyogenic granuloma.

To verrucous carcinoma malignancy signs must be referred growth acceleration, surface nodule enhance keratinization processes. Great importance should be given to the induration forming at element base and pain arrising. But we should point out the relativity of these signs, which may sometimes be absent during malignancy.

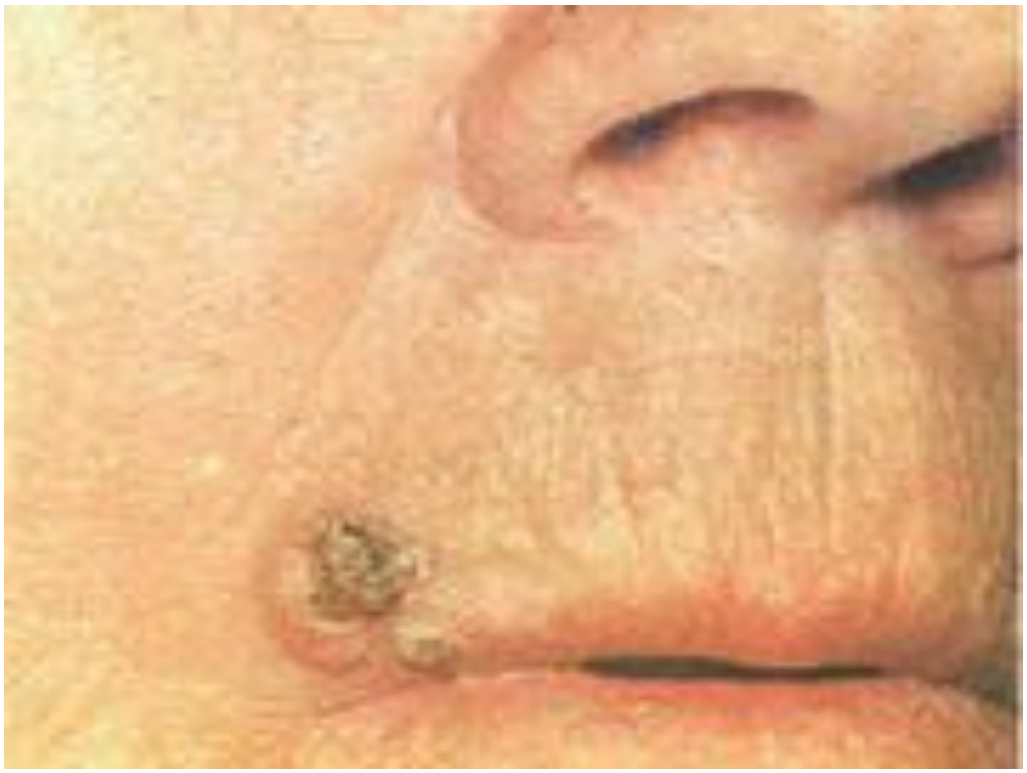

Fig. 6. Warty lips red border precancer

Lips red border verrucous carcinoma treatment consists of complete surgical removal of lesion area with the following optional morphological examination. Lesion excision is best to be performed by electric knife within the healthy tissue limits. Electrocoagulation and cryodestruction in its purest form should never be done, because they deprive the possibility of morphological verification process performing.

Clinical monitoring is carried out both dentist and oncologist, because there is a high probability of malignancy, if lesion removal within healthy tissue is not timely performed.

Preventive measures. Protection from the effects of adverse weather factors and above all the insolation. Avoid lips red border trauma. Lips chronic inflammation timely treatment, systematic oral cavity sanation. Smoking forbidden.

Lips red border limited precancerous hyperkeratosis. Described by A.L.Mashkilleyson in 1965. Prior to that clinicians treated the disease as leukoplakia. But from leukoplakia limited precancerous hyperkeratosis differs not only clinically, but in fact by its progress process because it has much more potential malignancy compared with leukoplakia and belongs to obligate precancers. Unlike other precancers young and middle age people mostly affected in this group. The process also localized mainly on the lower lip, but more often - about halfway between the center of the lips and mouth angle.

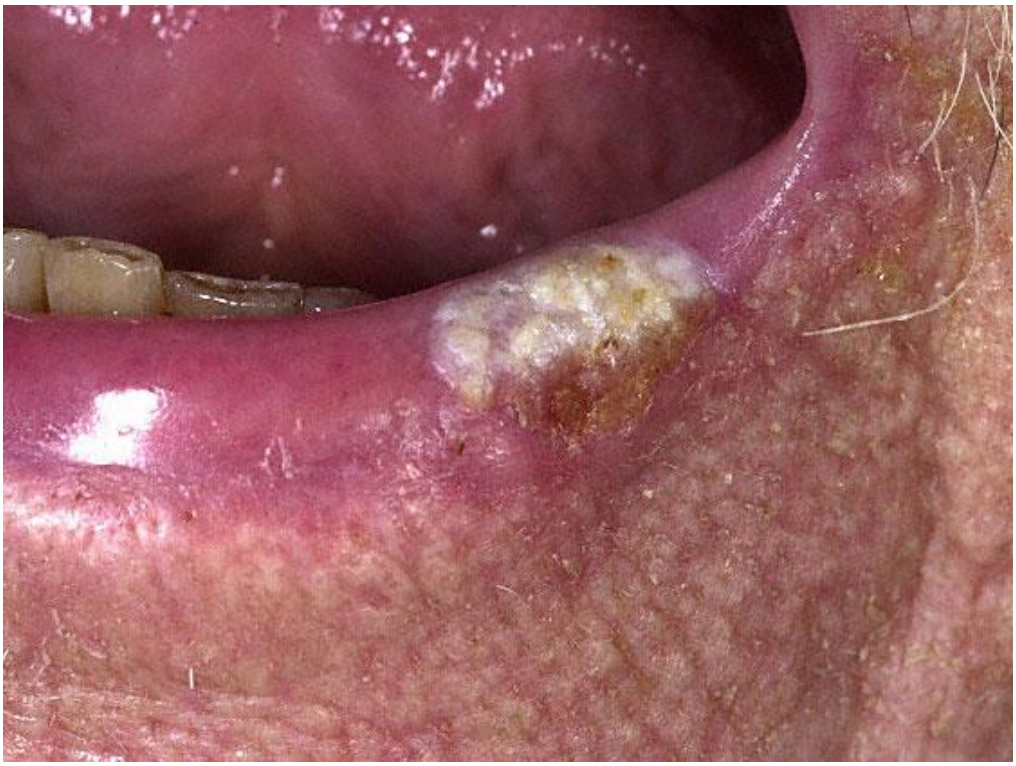

Fig. 7. Red border lower lip precancerous hyperkeratosis

Clinically limited precancerous hyperkeratosis is manifested in the form of limited areas, which often polygonal shape, with size of 0.2 to 1.5 cm. Most patients lesion surface does not rise above the surrounding red border, but often the opposite seems slightly reduced, light, surrounded by a thin

whitish roller. The surface area covered by such agglutination tightly-spaced scales grayish and brown color. During palpation the lesion is painless, soft.

Limited precancerous hyperkeratosis course is slower compared with precancer nodular form. Affected areas can exist without malignancy for several years, but sometimes malignancy may occur during the first year of the disease and even during the first months. Limited precancerous hyperkeratosis large quantity malignancy cases are the basis for putting this form to a group of obligate precancers.

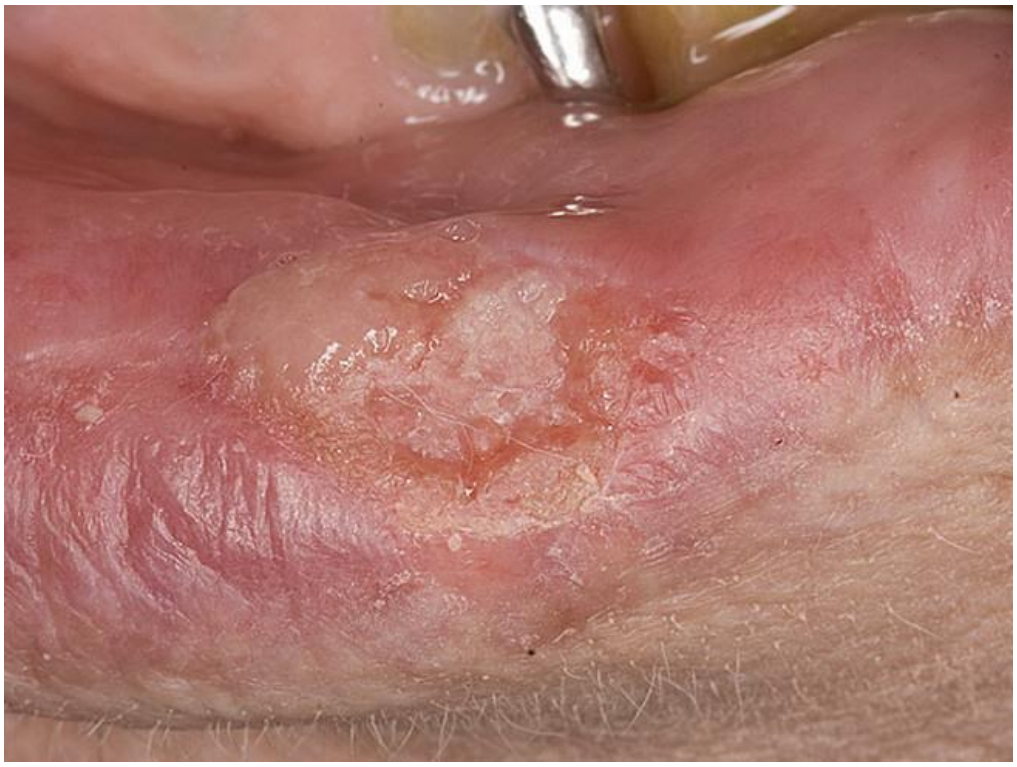

Fig. 8. Red border lower lip precancerous hyperkeratosis

Limited precancerous hyperkeratosis differential diagnosis should be made with leukoplakia, exfoliative cheilitis, lichen and red flaps lupus erythematosus. During lips red border precancerous limited hyperkeratosis patient examination the most difficult is the question whether the malignancy process has already occured. With clinical signs that are at least partially help to address this issue, Mashkilleyson specified three ones: strengthening

keratinization process, formation of erosion on the surface and formation of the seals at the base of lesion. Therefore, the only reliable means of diagnosis is biopsy, which is recommended as soon as possible.

Limited precancerous hyperkeratosis treatment is surgical removal of the lesion within healthy tissues limits. Better to perform elektroexcesion. Removed tissue samples must be histologically examined. The outcome of subsequent therapy depends on the results of the above histological examination.

OPTIONAL PRE-CANCEROUS DISEASES WITH GREAT POTENTIAL MALIGNANCY

Leukokeratosis verrucous. Localization: cheeks, mouth floor, tongue, lip mucous membrane. Expressed keratinization process. It has two forms. Warty form - indurated, bumpy, sometimes grayish-white milky formation of the warty growths on the surface. Plaque form -smooth sharply restricted irregularly shaped plaques, towering above the surrounding mucosa milky white cloured, with a rough surface.

Treatment. Lesion surgical removal.

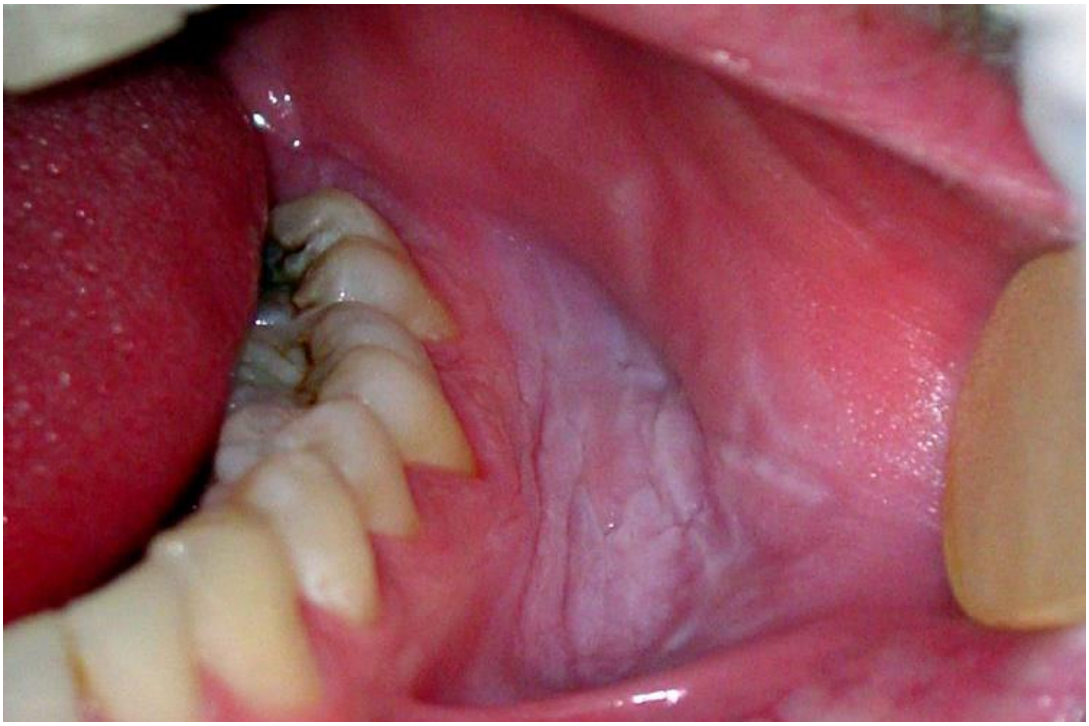

Fig. 9. Leukokeratosis verrucous

Preventive measures. Refusal from smoking, oral mucosa sharp teeth edges chronic trauma elimination, with malocclusion poorly made dentures, eliminating irritating foods, alcohol. Prosthetic using homogeneous metal to prevent galvanization.

Erosive leukokeratosis. Arrises as flap or verrucous leukokeratosis consequency. On the background of flap or verrucous leukokeratosis lesions cracks or erosion occur, accompanied by pain, heartburn, etc., especially when taking foods. Cracks are periodically increased or epithelialized.

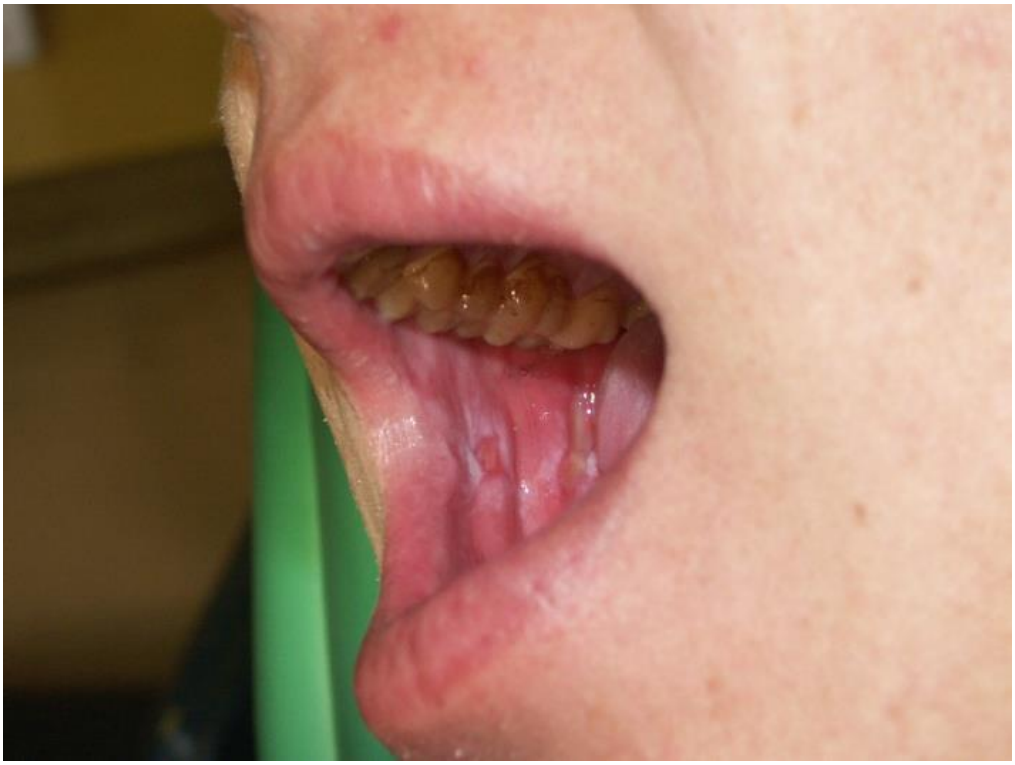

Fig. 10. Erosive leukokeratosis

Treatment. Therapeutic medication that accelerate epithelization (gel "Solcoseryl"), with the failure - remove surgically.

Preventive measures. Avoid insolation, lubricate lips with cream, fat, occasionally take vitamin A concentrate 10 drops 3 times per day within two months, refusal from smoking.

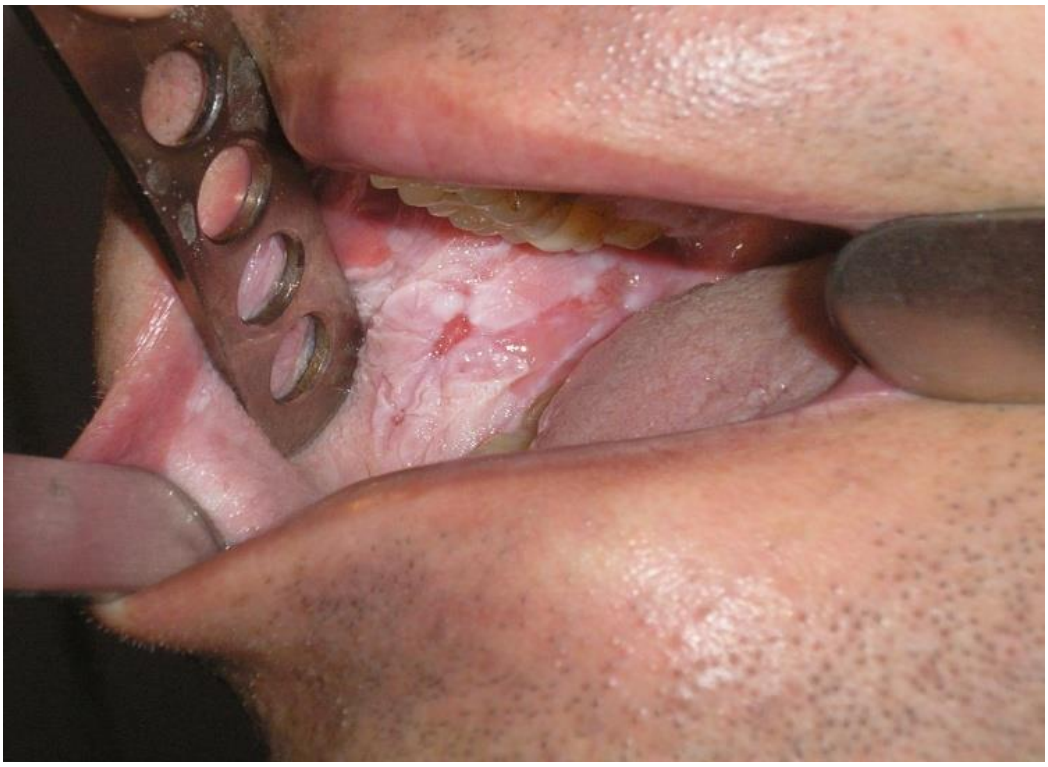

Fig. 11. Erosive and verrucous leukokeratosis

Papilloma. The tumor on the shank or on a wide basis, may resemble a wart or cauliflower, sometimes on the surface can be villi. It is distinguished grayish-white keratinizing and nonkeratinizing papillomas - the color does not differ from the color of the tissue on which it is located. Localized on the skin, lips, oral mucosa and tongue.

*Treatment. S*urgical removal.

Preventive measures. Avoid traumatization.

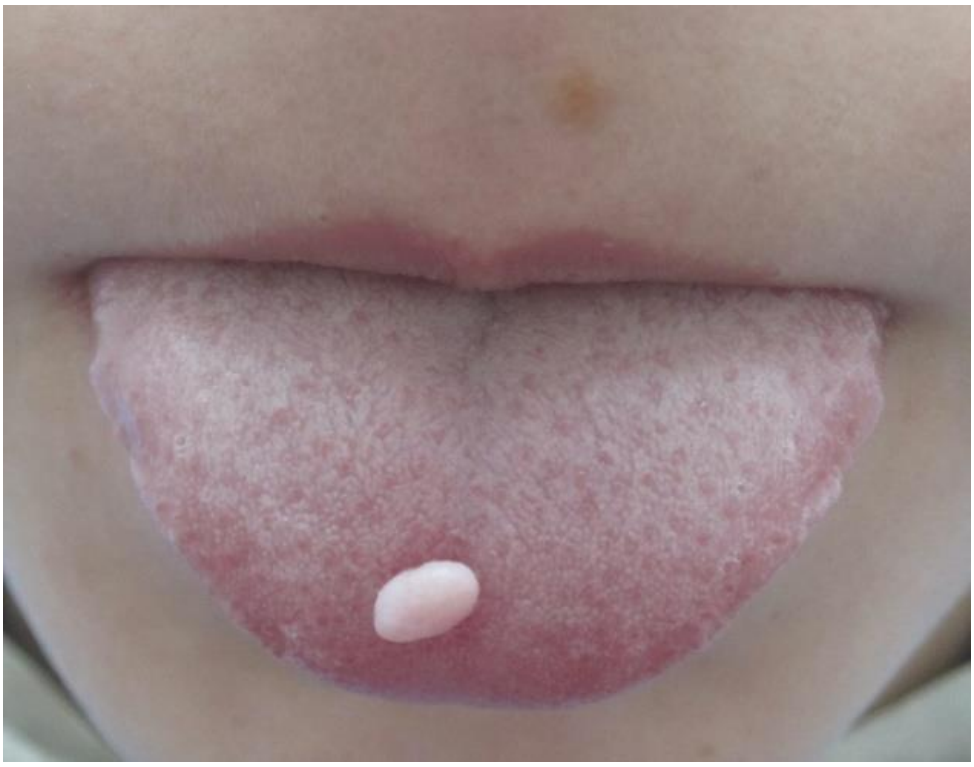

Fig. 12. Tongue papilloma

Papillomatosis. Multiple papillomas proliferation on a separate part of the skin, lips or oral mucosa and tongue. Appeared dense knots, well shaped, congestive red, towering above the surrounding surface, hemispherical shape, size 0.2 - 0.4 cm.

Fig. 13. Side surface toungue papillomas

Sometimes nodules coalesce. Their surface due to keratinization may take grayish-white colour. Favorite localization - hard and soft palate mucous membrane.

Treatment. Surgically removal.

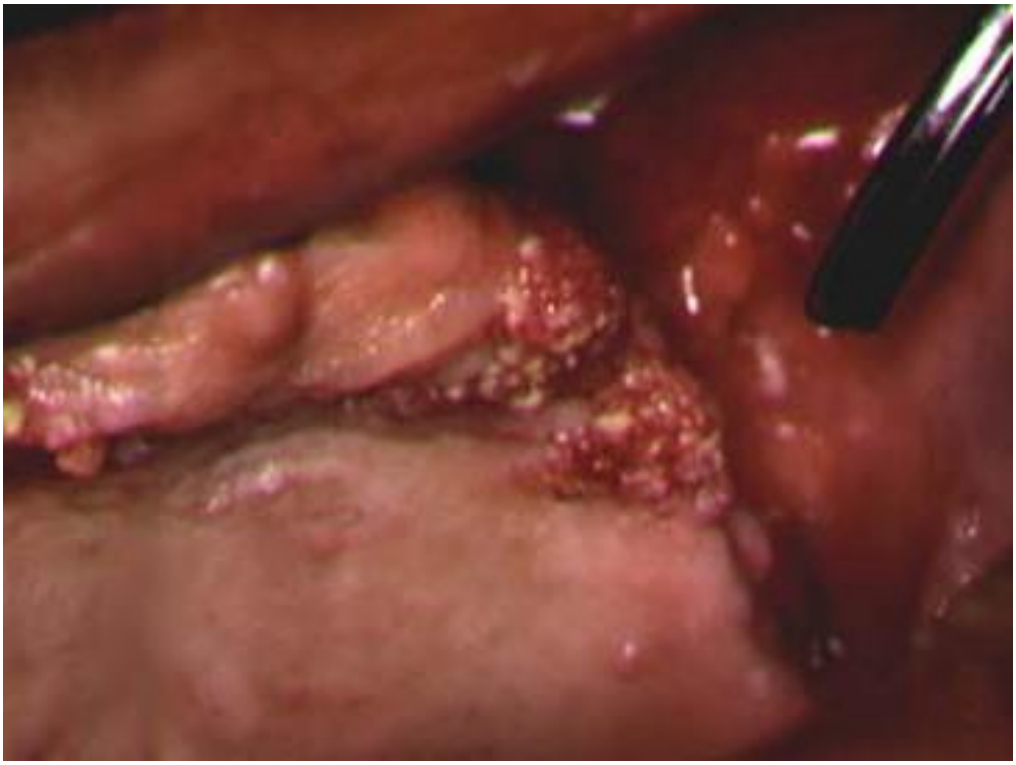

Fig. 14. Oral cavity papillomatosis

Preventive measures. Oral cavity sanation with rational prosthetics. Sparing diet. Smoking and alcohol consumption prohibition.

Keratoakantoma. Thick bundle round shape grayish-red, size 1 - 1,5sm in diameter, with sealed edges and distinctive bell-shaped hollow in the center, filled with horny masses freely removed.

Teratment. Surgically removal.

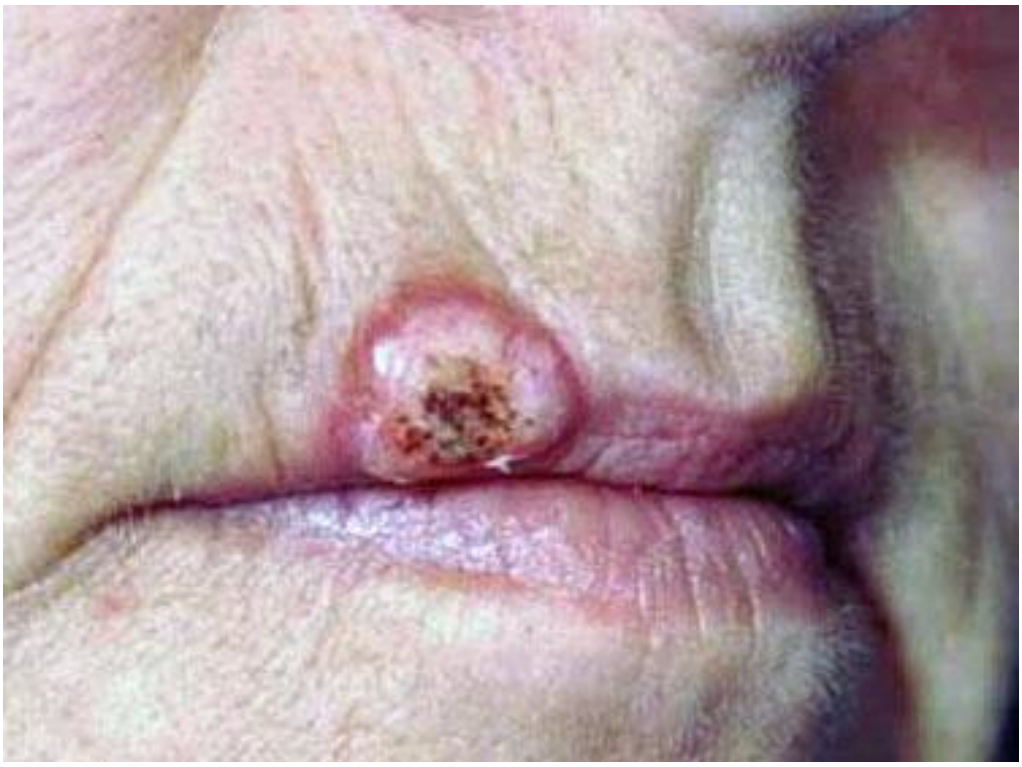

Fig.15. Upper lip keratoakantoma

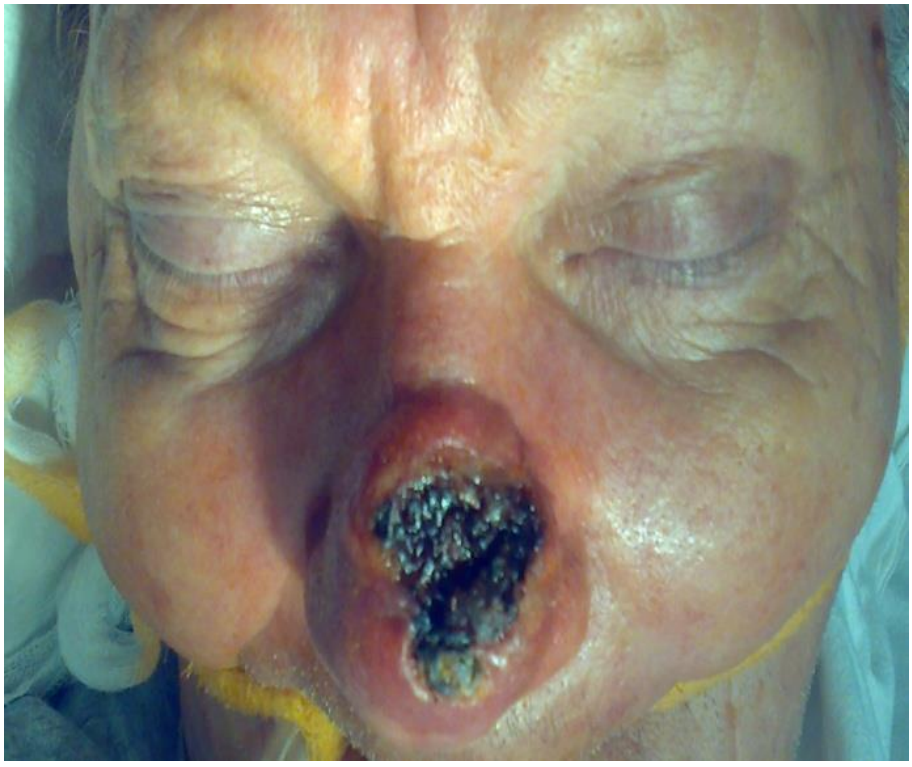

Fig. 16. Nasal tip keratoakantoma

Cutaneous horn looks clearly limited lesions with 0.3 - 0.5 cm diameter at the base, from which conical shape formation departs with height 0.5 cm -1 grayish color, tightly adhered to the base.

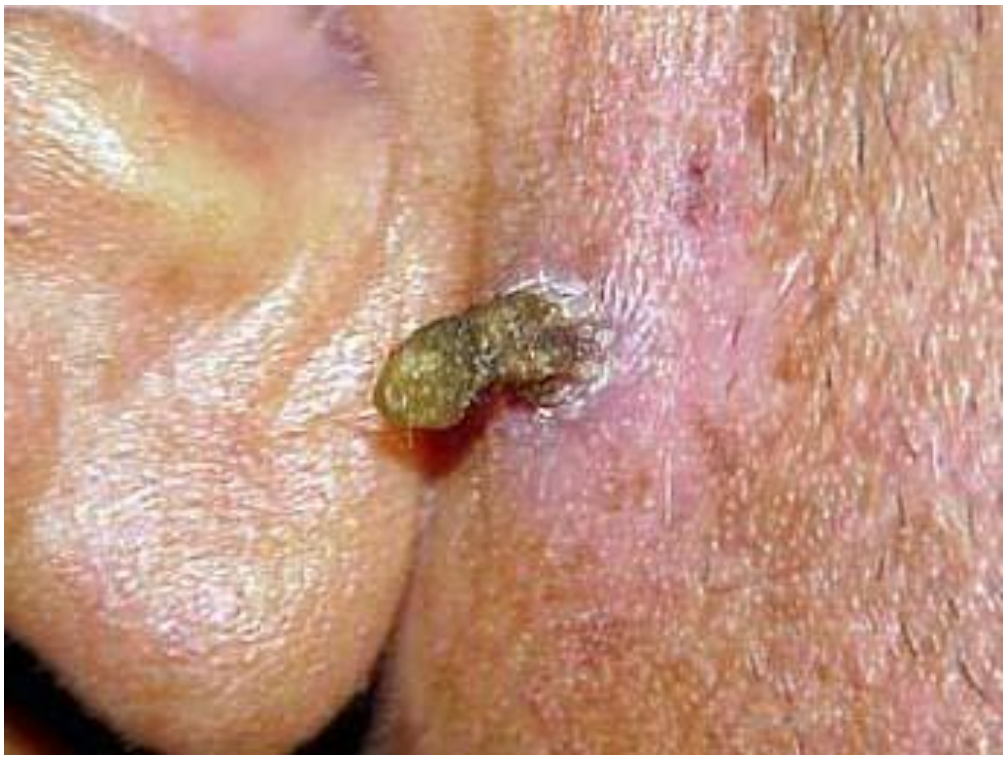

Fig. 17. Cutaneous horn

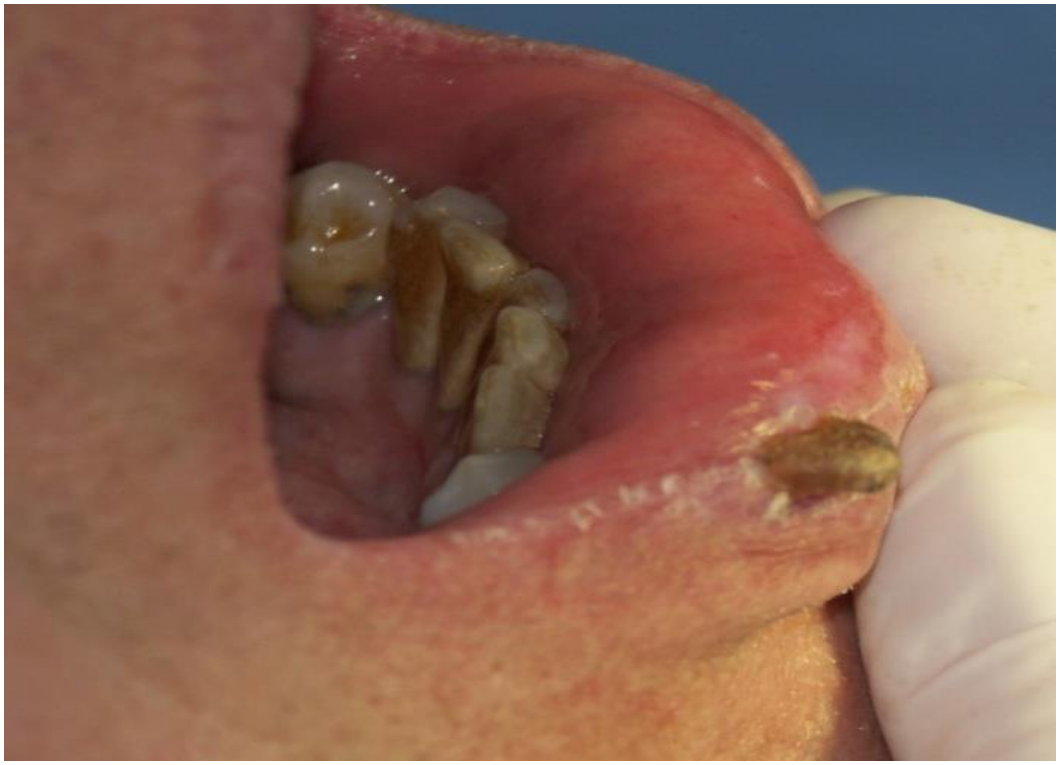

Fig. 18. Lower lip cutaneous horn

More often one lesion is developing, but may be more. Location: leather or red border of the lips. It affects the elderly people.

Treatment. Surgical removal.

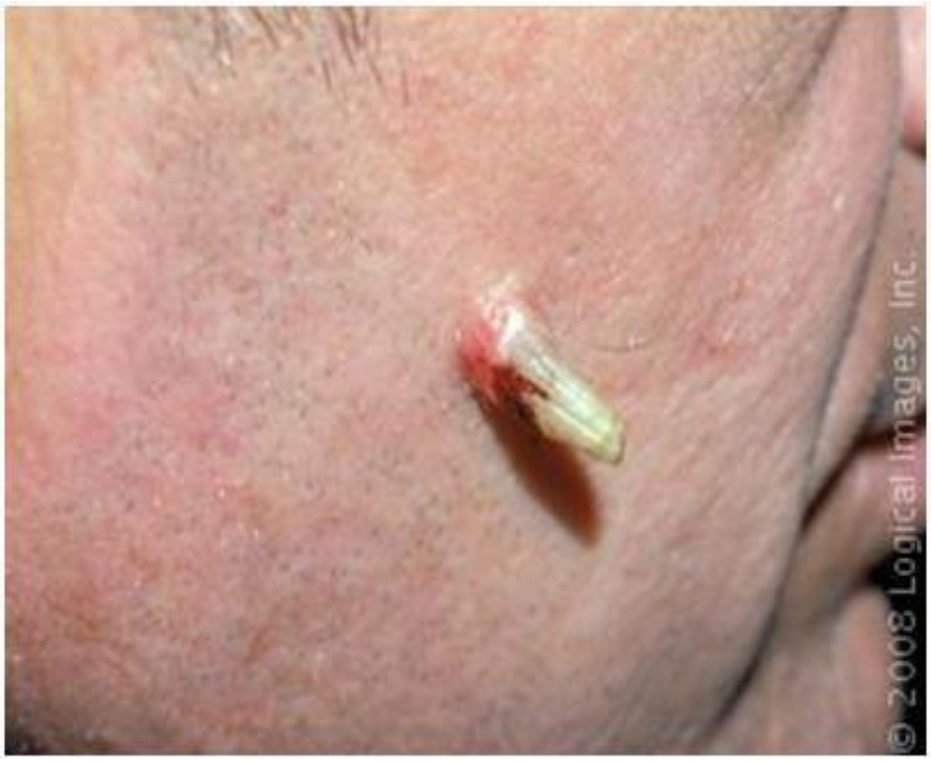

Fig. 19. Cheek cutaneous horn

Preventive measures. Lips and skin red border inflammatory processes timely treatment.

OPTIONAL PRE-CANCEROUS DISEASES WITH LESS POTENTIAL MALIGNANCY

Leukoplakia plana is observed as limited nidus of keratinization, different shapes and sizes, not increased above the surface of the mucous membrane; the surface can be folded, grayish-white color, matte; sometimes, around the nidus, may be inflammation. The most common localization: mucous membrane of the cheek, retro-molar areas, at least – oral floor, tongue, mucous membrane of the lips.

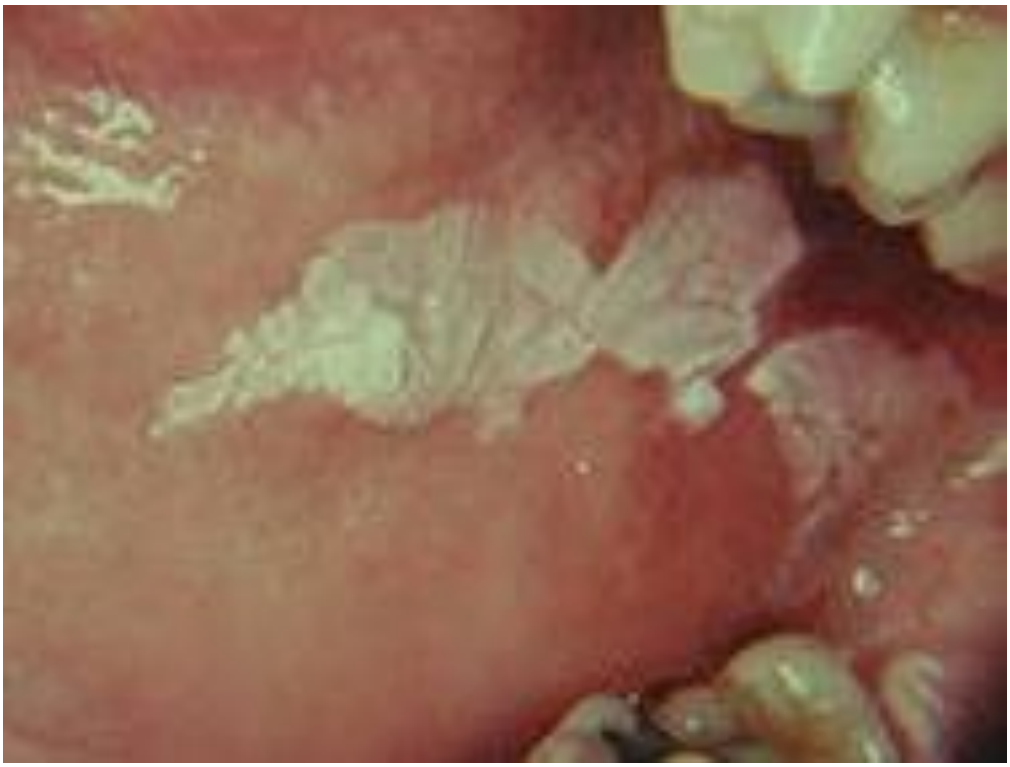

Fig. 20. Leukoplakia plana of buccal area

*Treatment is c*onservative, medication (sea buckthorn or wild rose oil, "Aekol", "Aevit").

Preventive measures are refusal from smoking, elimination of chronic trauma of the oral mucosa by sharp edges of teeth, by poorly made dentures at

malocclusion, elimination of irritating foods, alcohol; prosthetic by homogeneous metal to prevent galvanization.

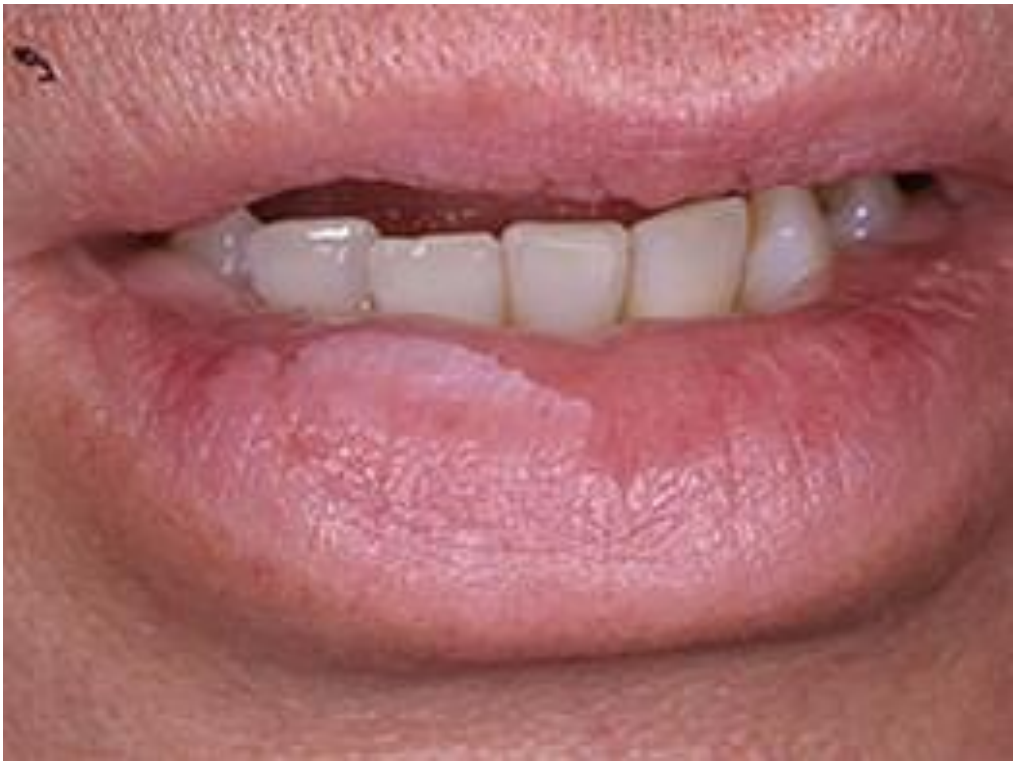

Fig. 21. Leukoplakia plana of lower lip

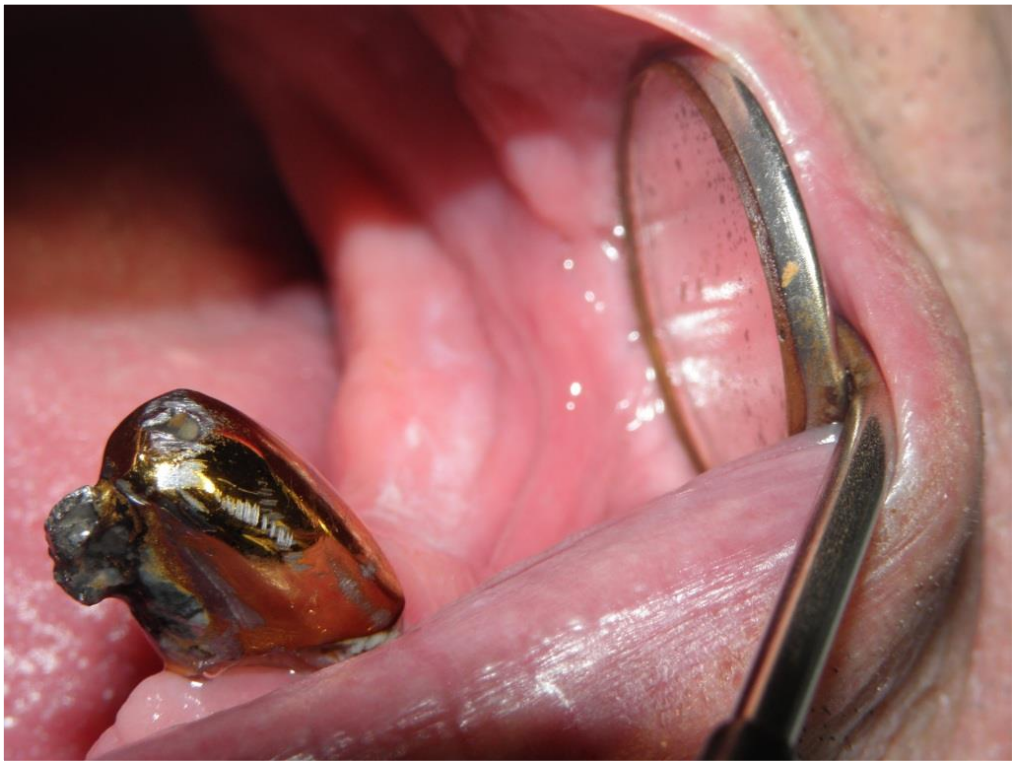

Fig. 22. Leukoplakia plana of mucouse membrane of alveolar process.

Erosive-ulcerative and hyperkeratotic forms of lupus erythematosus and lichen ruber planus. The manifestations of lupus erythematosus are happened more often on exposed skin, red border of lips and oral mucous membranes.

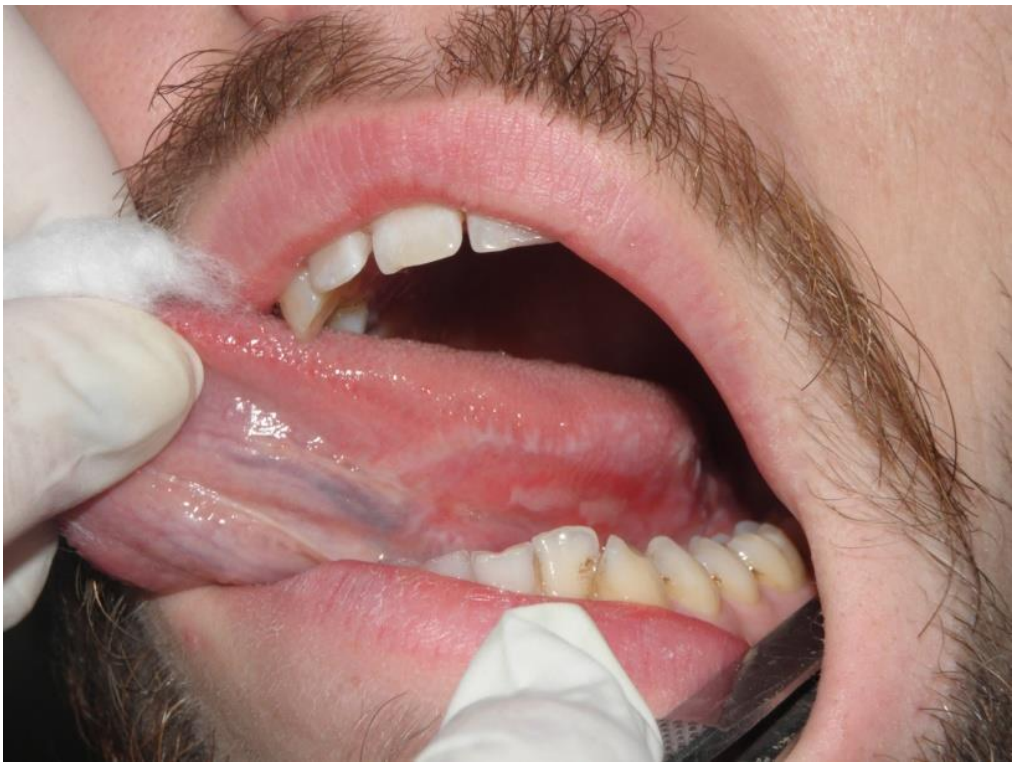

Fig. 23. Erosive-ulcerative forms of lichen ruber planus

There are erosions with clear borders that bleed easily, are not subject to epithelialization, and with an infiltration of the base against hyperaemia at erosive-ulcerative form of lupus erythematosus. Hyperkeratosis is small.

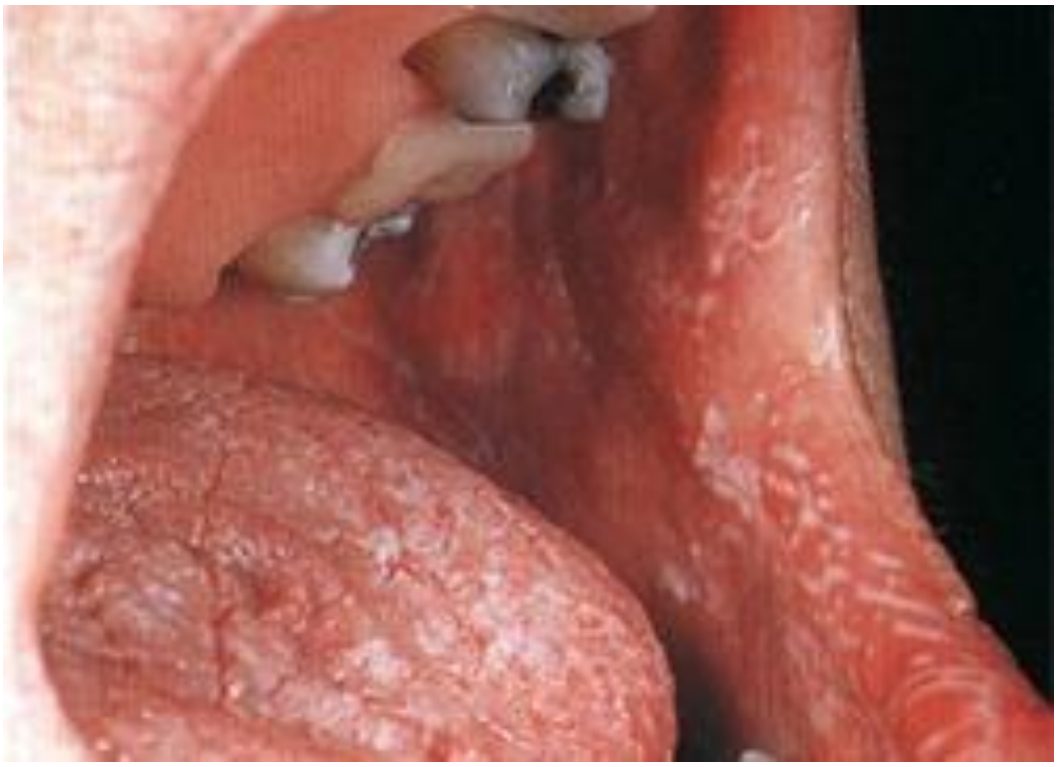

Fig. 24. The lichen ruber planus (generalizating form)

Treatment is synthetic antimalarial drugs with small doses of corticosteroids (prednisone, dexamethasone) and B vitamins, especially, nicotinic acid. Locally – application of ointments with corticosteroids.

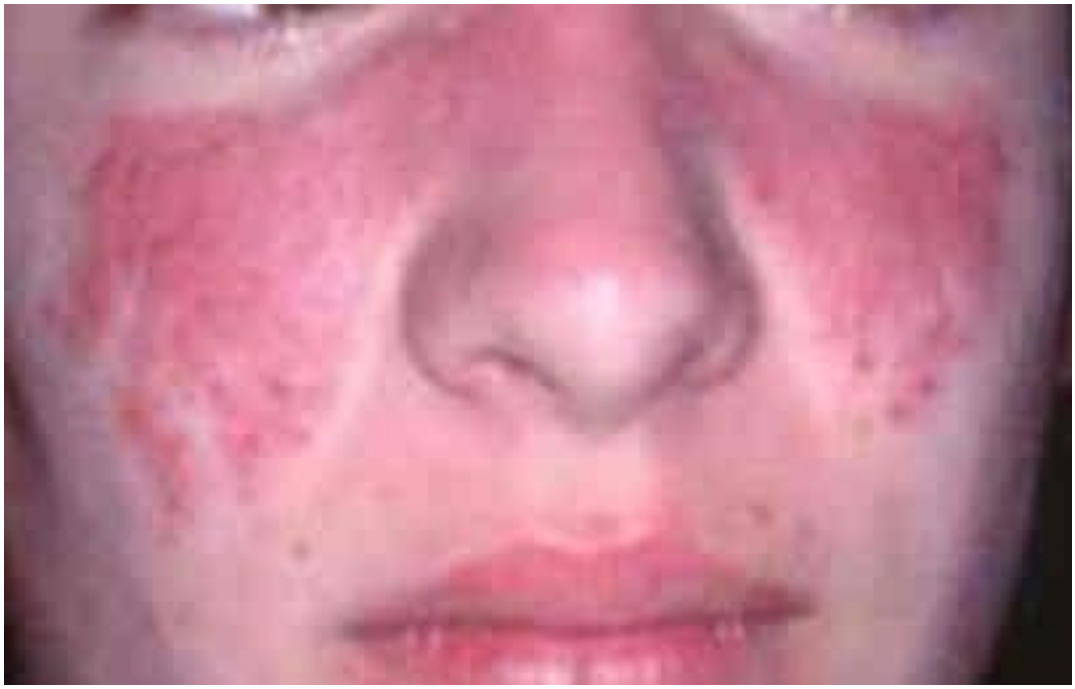

Fig. 25. Systemic lupus erythematosus

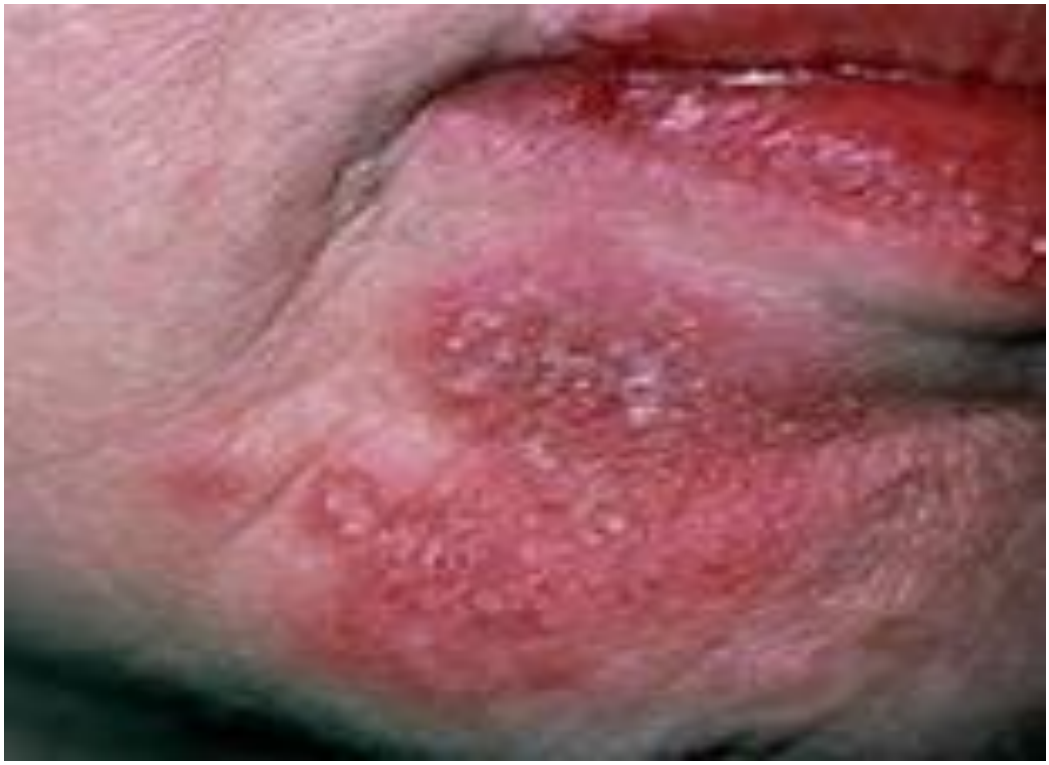

Fig. 26. Systemic lupus erythematosus

Preventive measures are avoidance of excessive insolation. It is necessary to use ointments that contain sunscreen agents, fenilsalitsylat 10%, 5% quinine to protect from UV rays. These ointments should be applied in the autumn and spring and summer regardless of the presence or absence of lesions of hyperaemia.

The pathological nidus at lichen ruber planus are observed on the buccal mucosa in the region of the last molar on teeth joing line; on tongue; lip and palate are affected rare.

The erosive form of lichen ruber planus is charactirizated by erosions and ulcers that are covered by fibrinous coating and bleeds after its removal. There are typical papular cellular-like eruptions around erosions and ulcers hyperemic and swollen base. The hyperkeratotic form of lichen ruber planus

is characterisated by stagnant hyperkeratosis that increase the level of red border of the lips as leukoplakia-like plaques.

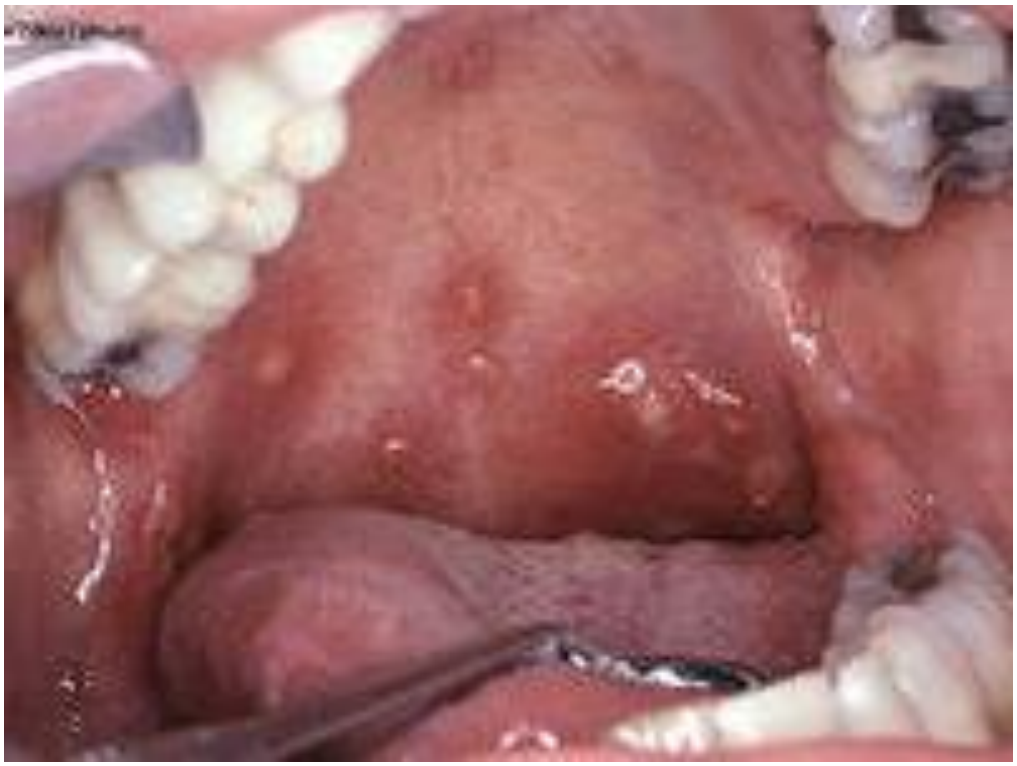

Fig. 27. Systemic lupus erythematosus

Treatment is acceptance of prednisolone and delagil inside. If there are contraindications to the appointment of corticosteroid drugs inside, it can be used hydrocortisone injections in the mucous membrane under nidus, ointments "Holisal", "Solcoseryl" and “Prednizolon”. In case of failure of treatment it is necessary to do surgical removal of the nidus.

Preventive measures are timely treatment of lichen ruber planus, avoidance of injury, excessive insolation, refusal from smoking, rational prosthesis.

Cheilitis after irradiation. The clinical symptoms are: hyperaemia of lips dryness, cracks, erosion, atrophy. On the surface may be warty or hyperkeratosis growths of the epithelium.

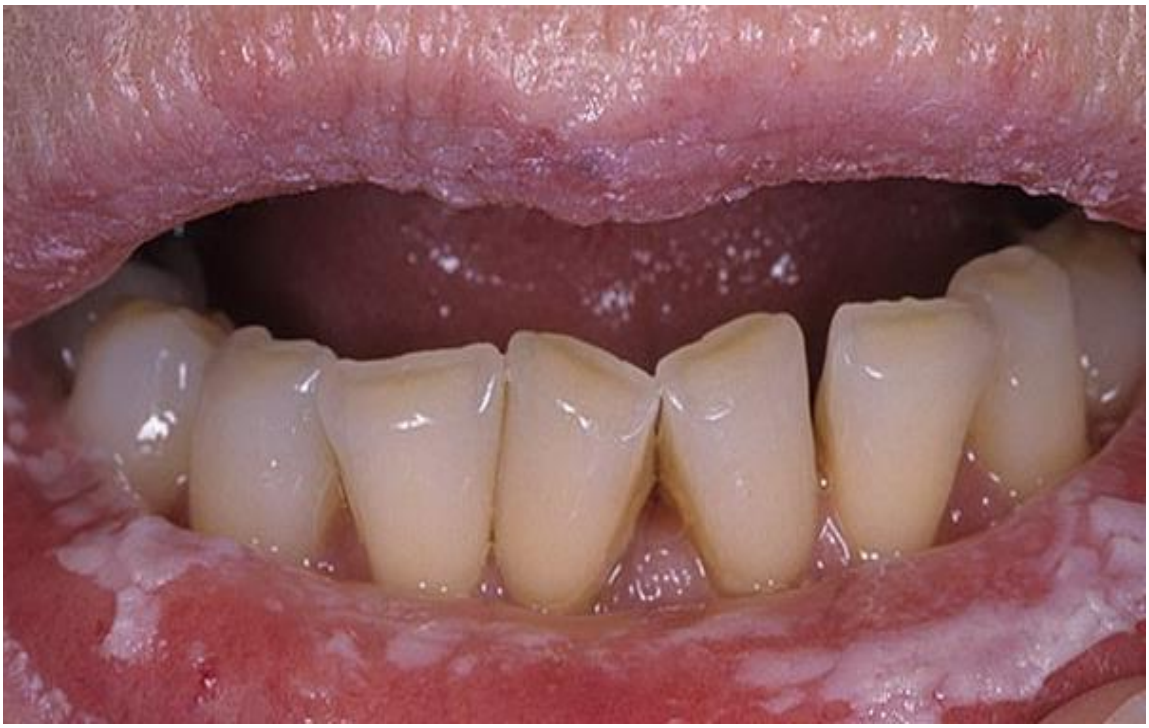

Fig. 28. The cheilitis after irradiation

Treatment is using of ointments with corticosteroid drugs methyluracil, sometimes quinoline series drugs are prescribed inside.

Preventive measures are avoidance of excessive UV-insolation.

Stomatitis after irradiation. The humid mucositis sometimes with erosive-ulcerative character is happened on the oral mucosa and the tongue. Epithelial cover in the area of irradiation may be exposed by keratinization.

Treatment is applications of rose hips or buckthorn oil, and other fatty substances. Rinse by antiseptic solutions, including metacil or chlorophyllipt solution.

Preventive measures are avoidance of excessive UV-insolation.

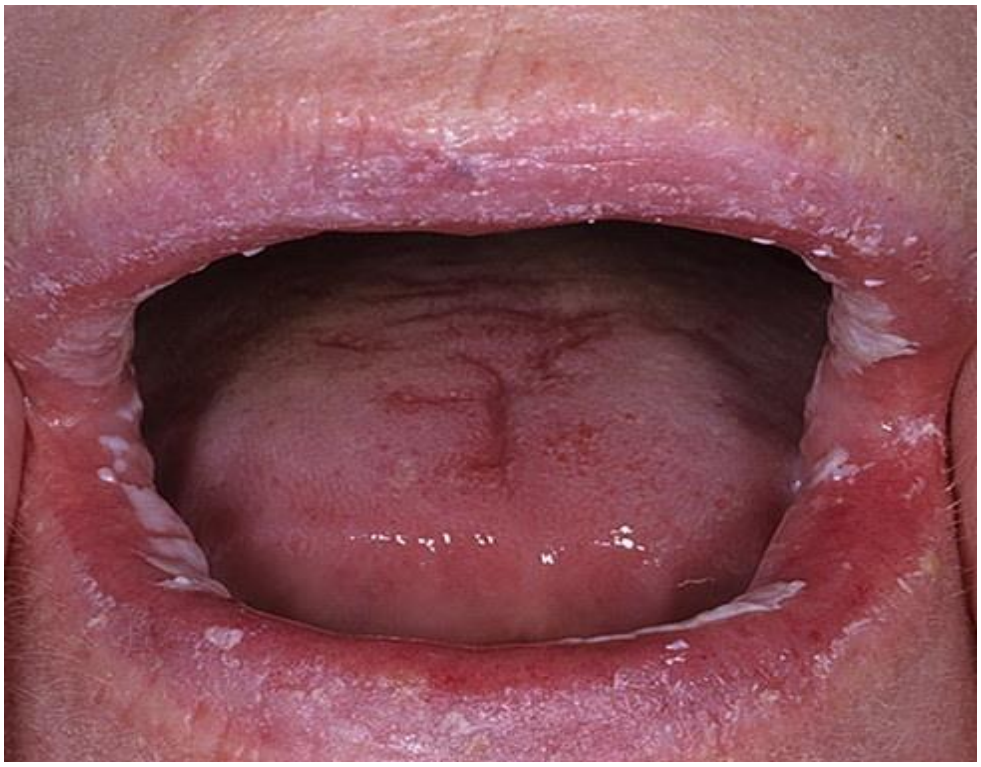

Fig. 29. The stomatis after irradiation

Actinic and weather cheilitis is damaged of red border of the lips, which occurs during prolonged exposure to sunlight. Clinically distinguish two forms: exudative, which is characterized by edema and hyperemia, the emergence of papulas on this background, erosions, crusts, scales, cracks; and dry form. This form is characterizated by bright red border that is covered with grayish-white scales that after removal happend again. Then the red border becomes dry, rough, easily vulnerable; patients complane on feeling of burning, pruritus, pain. This disease is characterized by relapses in the spring and summer.

Treatment istherapeutic with use of drugs: protective creams, rosehip and sea buckthorn oil, “Solcoseryl”.

Preventive measures are protection of the lips from excessive action of sunlight, use sunscreen ointments.

PRECANCEROUS DISEASES OF FACE SKIN

Obligate precancerous skin diseases

Xeroderma pigmentosum. The mode of inheritance is autosomal-recessive. In the event of illness there is important role of blood kinship parents and innate sensitivity to sunlight. The skin of patients is extremely sensitive to sunlight and its changes lead to malignancy.

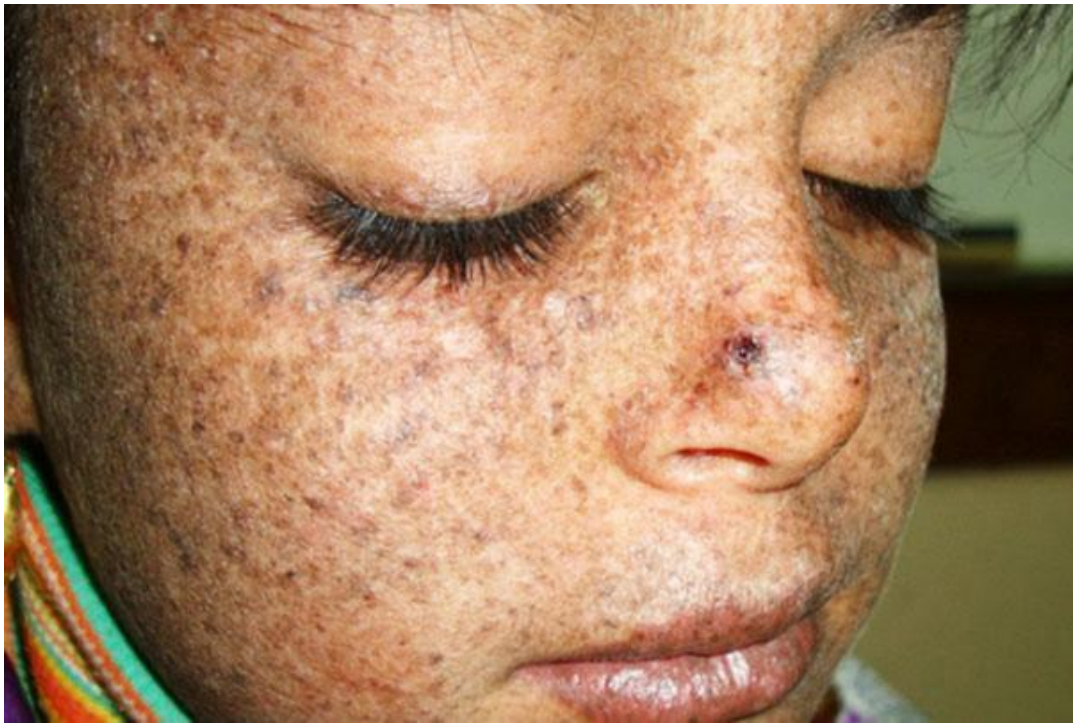

Fig. 30. Xeroderma pigmentosum

Clinical picture. 2-3-year-olds children get redness, peeling, dryness of open areas of skin (face, neck, hands) in the spring and summer. There are swollen erythematouse areas without clearly separations after exposure to the sun. It is formed the pigmentation as lentigo and freckles after the resolution of erythema. In superficial pigmentation appear white atrophy, telangiectasias, keratoses. Number of pigmentation increases, the skin becomes colorful, and areas of atrophy can cause atresia of mouth, ectropion. In addition, skin lesions are accompanied by conjunctivitis and photophobia.

Atrophic changes lead to thinning of the ears and nose, loss of eyelashes. The warty growths develop from keratosis that eventually transformed into epithelioma, and sometimes, sarcoma and melanoma. Neoplasms can metastasize to internal organs. In addition, bone dystrophy, microcephaly, retarded physical and mental development are noted at these patients. Most patients die before the age of 15.

Treatment. Bracing therapy.

Preventive measures. Maximum restraint from solar and ultraviolet insolation.

Bowen's disease. It is the precancerous dermatosis that is inherently intraepidermal cancer. Sometimes it is localized on the face. It is characterizated by uneven growthing of on the periphery of the lesion, its diversity because of the erosive areas, superficial atrophy, hyperkeratosis and foci of increased peripheral rollers.

Fig. 31. Bowen's disease

The central area is ingrained, rough, slightly warty, covered with scales and crusts, under which there is uneven papilomatouse surface with erosions. Ulcer can rarely decay. Announced border gets more intense color. If the dense tumor within pockets is formed, with disposision to ulceration, Bowen's disease becomes into squamous cell carcinoma.

Treatment. Wide excision, diathermocoagulation, cryosurgery, laser and X-ray therapy. Simultaneously etretynat is administered at a dose of 1 mg/kg of body weight.

Preventive measures. Avoid trauma.

Barrett-Yadasson's epithelioma. It affects the elderly people.It is intradermal tumor. Usually it gets one nidus, plaque is round or oval, pink or broun color, smooth or warty, shiny or covered with scales that exfoliate. If there are ulcers thay usually cancerate. It should be differentiated from psoriasis, nevus, papilloma.

Treatment. Surgical removal.

OPTIONAL PRECANCEROUS SKIN DISEASES

Keratoma (senile atrophy). The skin becomes dry, thin, wrinkled. It appears yellowish-brown spots that rise, covered with a thick crust that is difficult to remove. At prolonged traumatization the senile keratoma can get the malignization.

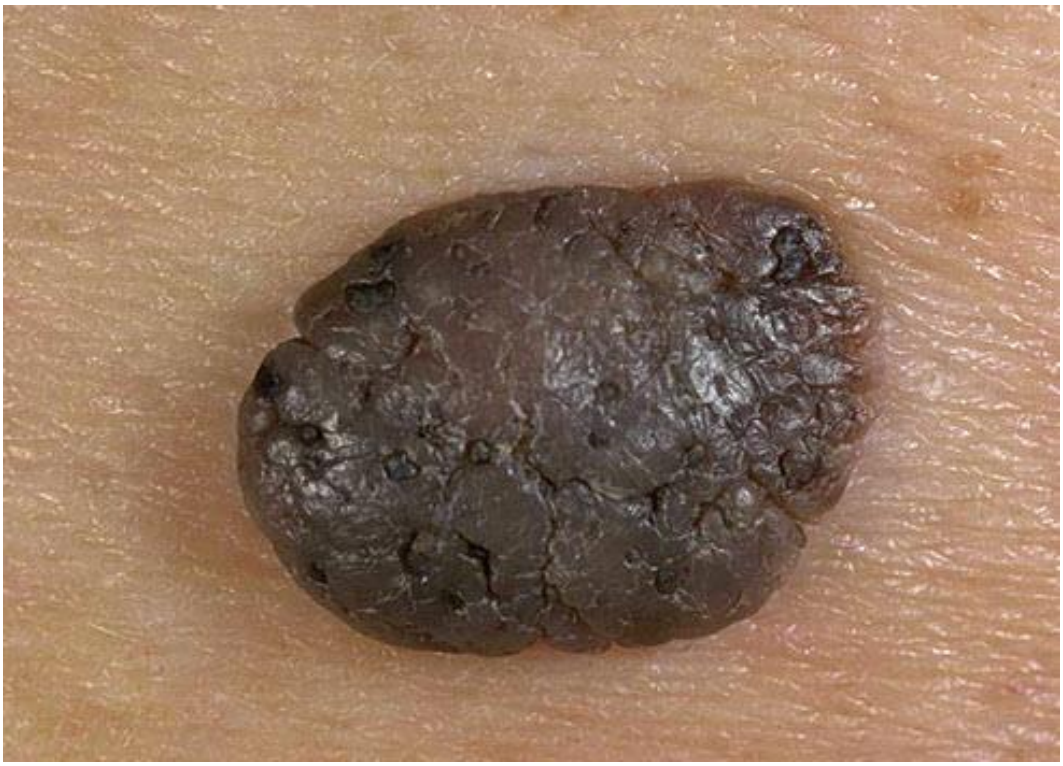

Fig. 32. Seborehating teratoma

Treatment. Surgical treatment, electroinsision, laser removal, short-focal radiotherapy

Actinic keratosis – is a type of seborrheic (senile) keratosis on dystrophic skin of face (sailors and people who working for a long time on the open air).

Treatment. Electrocoagulation or cryosurgery of keratosis niduls. Vitamine A.

Preventive measures. To ezclude the adverse weather action.

Late radiation ulcers. This is the skin ulcer that heals hardly, with areas of atrophy and telangiectasias around the site of radiation action (can be many years after it).

Treatment is unirritating local anti-inflammatory and epithelizating treatment, vitaminotherapy. Surgical removal in case of indacation.

Preventive measures. Eliminate re-radiation effects and UV insolation.

Tryhoepithelioma. It is a benign tumor of the skin appendages. This is usually hereditary congenital disease. This tumor arises on the face, sometimes on the scalp in the form of multiple, dense, tumor-like nodules, the size of 0.3-0.5 cm, round shape, color is from light pink to yellowish, with venouse lake on the surface. Tryhoepithelioma exists for a long time, grows slowly and can be transformed into basalioma.

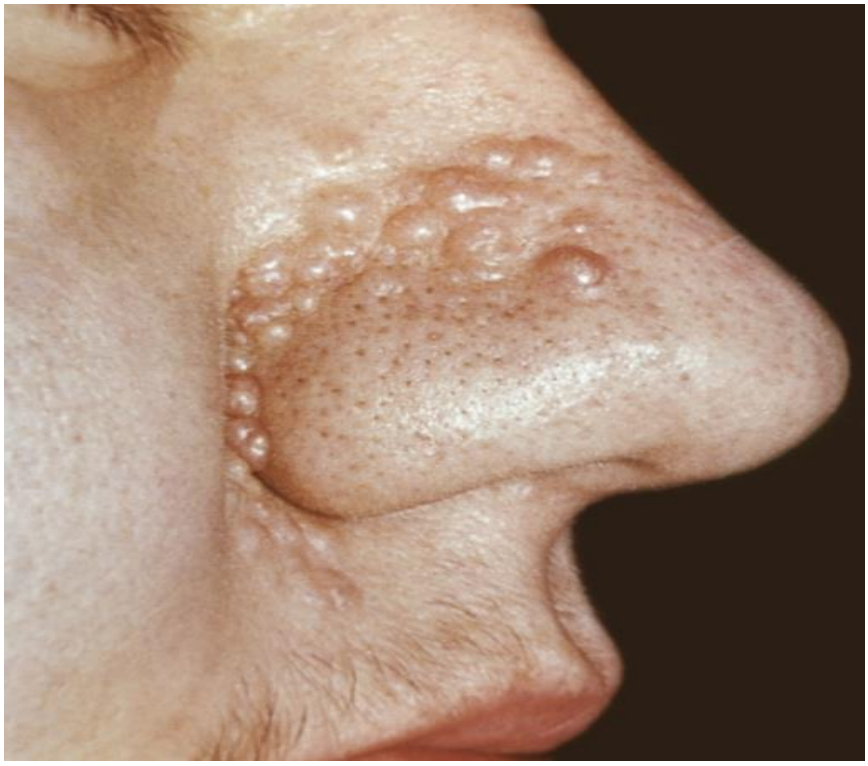

Fig. 33. Tryhoepithelioma

Treatment is surgical: wide excision of rash elements, electrocoagulation, cryosurgery, laser removal, dermabrasion.

Preventive measures. Avoid traumatic injuries.

Skin horn. It is a benign epithelial tumor, which mainly located on the face, scalp. Usually it developes on plase of senile keratoma at the elderly people, but it may occur in areas of scars, papilloma, focal tuberculous lupus, after chronic X-ray lesions of skin. Tumor is cone formation from horny masses of yellowish-brown or dark colors, length is several centimeters. The base of tumors is dense, the surface is covered by longitudinal and transverse grooves. Inflammation signs are abcent. Often this tumos can transform into skin cancer in old age.

Treatment. The best result is obtained by the use of liquid nitrogen with curettage; application of 70% glycolic acid for 3-5 minutes should prevent the curettage. It is possible to use diathermocoagulation, laser therapy.

Preventive measures. Timely treatment of keratomas, papillomas and others diseases that precede the appearance of skin horn.

Papilloma. It is the most bening tumor of skin. It developed from the surface epithelium.

Papillomas are diagnosed as solitary (single) and multiple (papillomatosis). Approximately 20% of patients papilloma can become malignant. Papillomas localized in different areas of the face.

Their clinical symptoms varied: a thin or thick stalk, round or oval, smooth or wrinkled surface with papillary excrescences of keratinizing or non-keratinizing epithelium of various size (0.5-2.0 cm). The presence of multiple papillomas is determined as papillomatosis of skin. Papillomas with keratinizing changes often becom/e malignant.

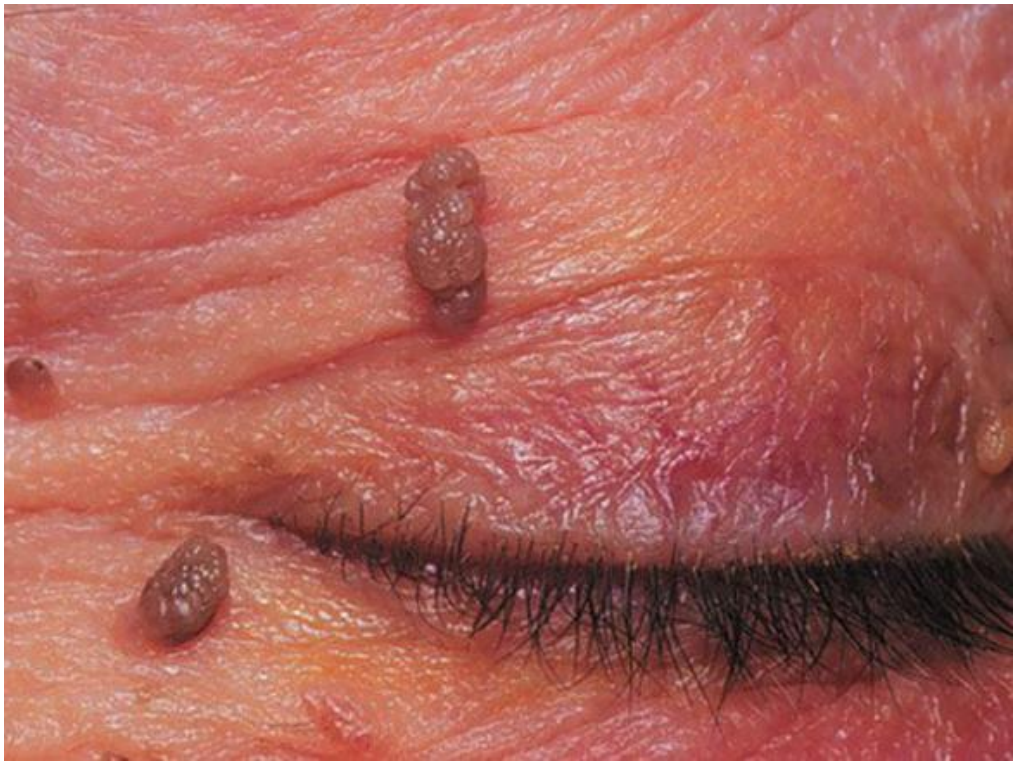

Fig. 34. Papilomas of upper eyelid

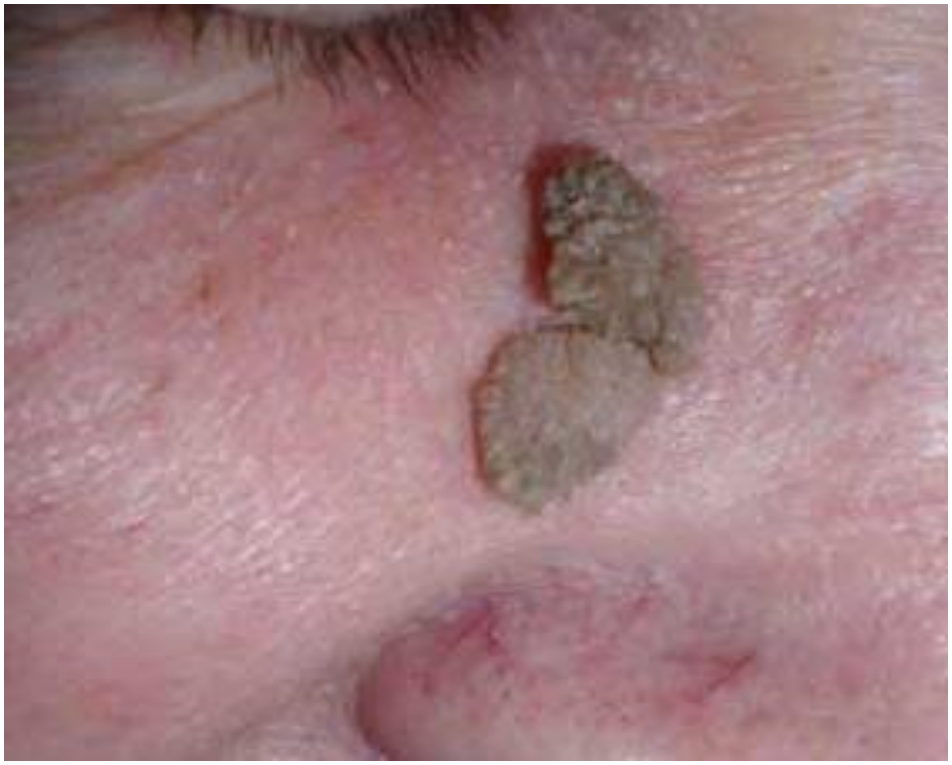

Fig. 35. Papilomas of upper eyelid

Naevus. It is pigment formation on the skin of neuroectodermal origin, which includes nevus cells with melanin.

The most complete classification of pigmented nevus is the classification by M.Z. Segal, which is shown in the thesis ob A.S.Abdullin (1967), in which tumors are divided as follows.

1. The appearance:
a) plana;
b) plana-lumpy;
c) papilomatose;
d) knotted;
d) on the leg;
h) warty.
2. The size:
a) speckled;
b) medium;
a) large;
d) gigant.
3. The color:
a) gray-brown;
b) brown;
c) black;
g) dark blue.
4. The presence of hair:
a) with hair-covering;
b) without hair-covering.
5. For the clinical course:
a) those buried;
b) complicated.

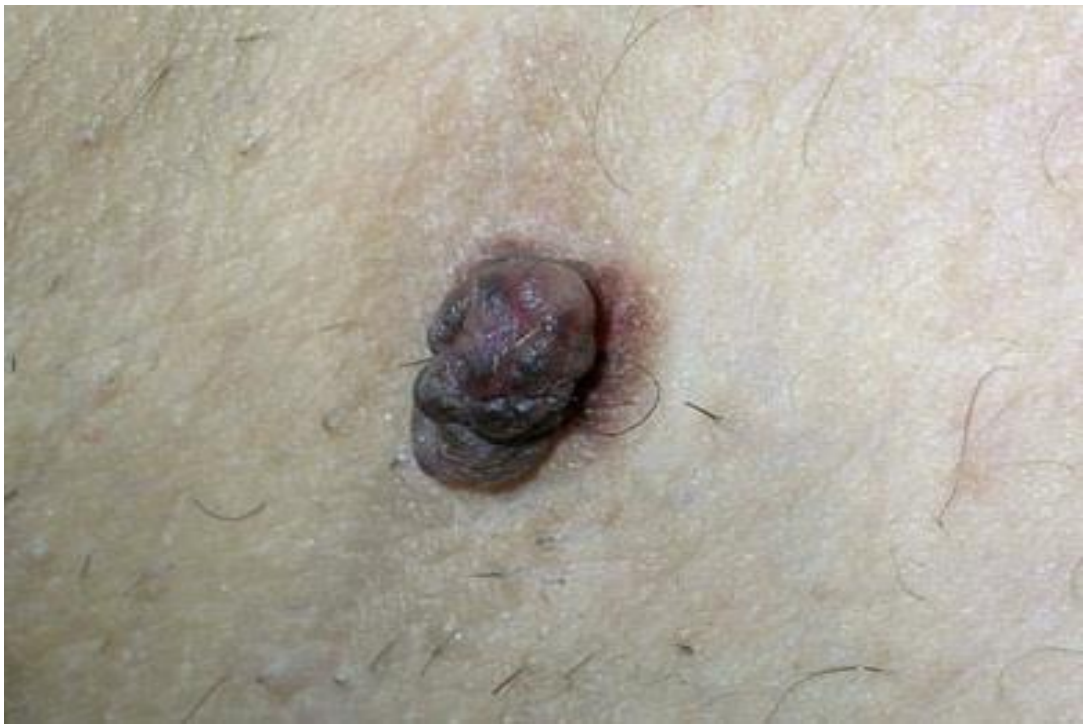

Fig. 36. Naevus

A A.I. Paches (1983) has noted that the size and color of nevus is extremely diverse, they are not factors which determine the nature of the process and are unlikely to be the basis for classification.

In practical work A.I.Paches (1983) has proposed the following clinical and anatomical form nevus:

1. The plana nevus – it increases slightly above the skin surface, it is smooth, black or brown, sometimes with hair.

2. Tubercular nevus – it is also with clear boundaries, but the surface is bumpy. often color is brown, with hair.

3. Papilomatose nevus – its forms are multiple, there are papillary eminences, the color is varied, eminences often have no pigment, texture is soft, hair is usually abcent.

4. Nodular nevus - node is smooth, dense, color is brown or blue, sometimes the nodule has a foot that looks like a mushroom, hair is abcent.

5. Warty nevus – the neoplasme with grooves of varying depth, often black color, hair is present.

Warty or plana nevuses are frequently observed on the face skin. Papilomatose nevus is observed on the red border of lips, sometimes at external margin of orbit. According to the literature, boundary nevus often becomes malignant, at least - blue.

Congenital pigmented nevi usually grow slowly in children, before puberty period growth may stop. In patients with congenital nevi rarely happened their malignancy. Nevi that were extrauterine period in child development, tend to malignant transformation.

Treatment. Remove Nevi that are located at the sites of constant irritation, trauma or for cosmetic indications should be removed.

Preventive measures. Avoid traumatic and irritating factors, excessive action of solar insolation.

Limited precancerous melanosis of Dubrey. The disease mostly elderly and senile age. The main localization is face. Usually – the one focus with uneven pigmentation disorders, flaking, sometimes - erosion.

Treatment. Complete removal of neoplasme within healthy tissues.

Preventive measures. Avoid trauma and sunlight.

SECTION III

APPLICABILITY OF PHOTOTHERAPY BY DEVICE «UFL-122» IN COMBINATION WITH GEL "SOLCOSERYL" FOR THE TREATMENT OF PRECANCEROUS LESIONS OF THE ORAL MUCOSA AND LIPS (EROSION, FISSURES, ULCERS THAT PROLONGED HEALING).

The spectra of light radiation of multifunctional machine «UFL-122» (firm Lux-dent, Kyiv) is studied in this work. The ability to use light sources «UFL-122» for phototherapy with Solcoseryl (gel) of precancerous lesions of the oral mucosa and lips (erosion, fissures, ulcers, prolonged healing) is prooved. The absorption capacity of the gel Solcoseryl and its optical density are studied.*

With the advent of lasers which give a strong, coherent monochromatic, polarized light, began the development and implementation of a variety of optical methods in medical practice. The good therapeutic effect can be obtained by quasi-monochromatic light [9].

Phototherapy is based on photo-biological processes. One of its variants is photodynamic therapy (PDT) [8]. Antimicrobial PDT is effectively used for the treatment of infectious inflammation of periodontal tissues [1, 5] and root canals, periodontal pockets, the periimplantitis, deep caries [7].

This seems to be an easy, safe and noninvasive system capable of helping the dentist to better visualize lesions, as well as its edges. Another point to consider is that the lesion seems to be bigger under chemiluminescence light. One disadvantage is that this system is expensive and a stick is used for each patient. Furthermore, chemiluminescence light

seems to be nonspecific as it does not identify the lesion etiology — whether inflammatory, neoplastic benign, or neoplastic malign — and this could lead to unnecessary biopsies

For achievement of desired therapeutic effect during using of phototherapy methods it should be pick up the light of a certain wavelength and ensure its access to tissues that require therapeutic intervention. It is important to know the effective of wavelength at which maximum system absorbs light energy and as a result generates free radicals, which in turn affects the chemical reactions and biological processes.

So the light absorption has the important role in a phototherapy. The positive effect will be better with more absorption of light energy, but on the other hand less light will penetrate to the tissues located deeper, which will reduce the therapeutic effect.

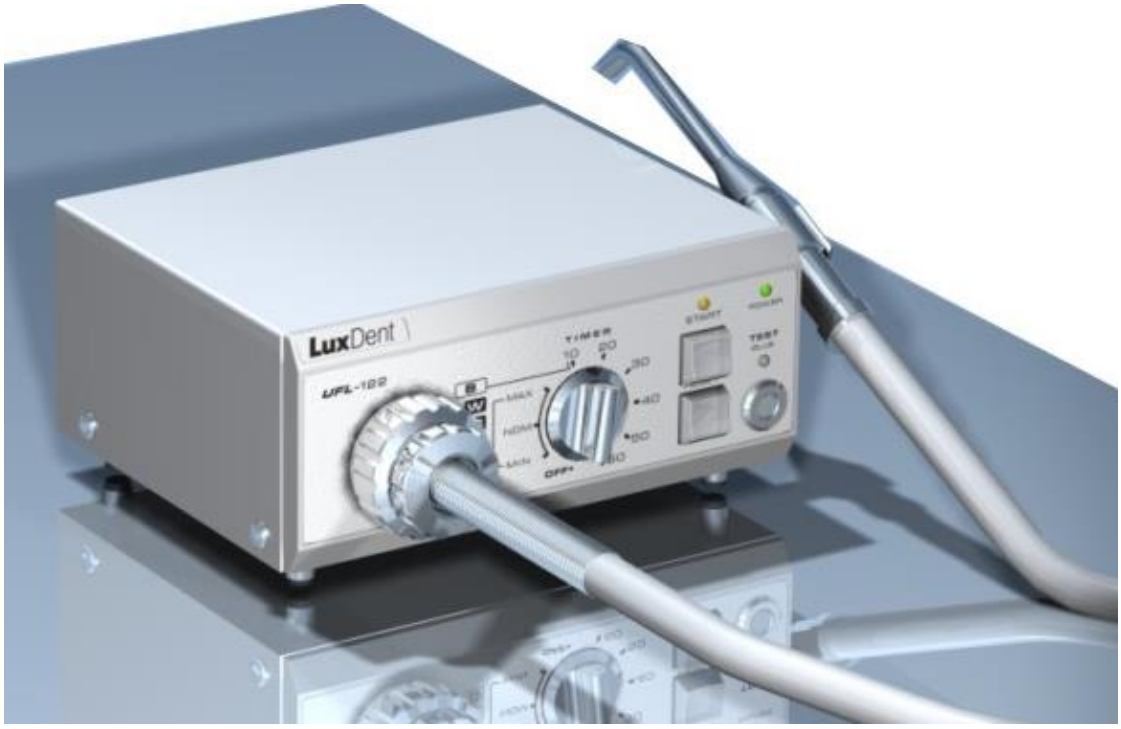

Fig. 37. Quasilaser «UFL-122»

In absorption colorimetric it is exercised transmittance measurement τ ($\tau = \frac{I}{I_0}$,where I - the intensity of the light that has passed through the object, I_0 - the intensity of the incident parallel beam) and the optical density of the medium D ($D = \lg \frac{1}{\tau}$) a narrow range of wavelengths of light.

The basis is colorimetric analysis by Bouguer - Lambert - Beer, whereby the intensity of the beam at the output layer of the substance is given by:

$$I = I_0 e^{-k_\lambda h},$$

where h - the thickness of the material; k_λ - Absorption coefficient, which depends on the wavelength of the incident light, the chemical nature and state of matter, but depends on its intensity.

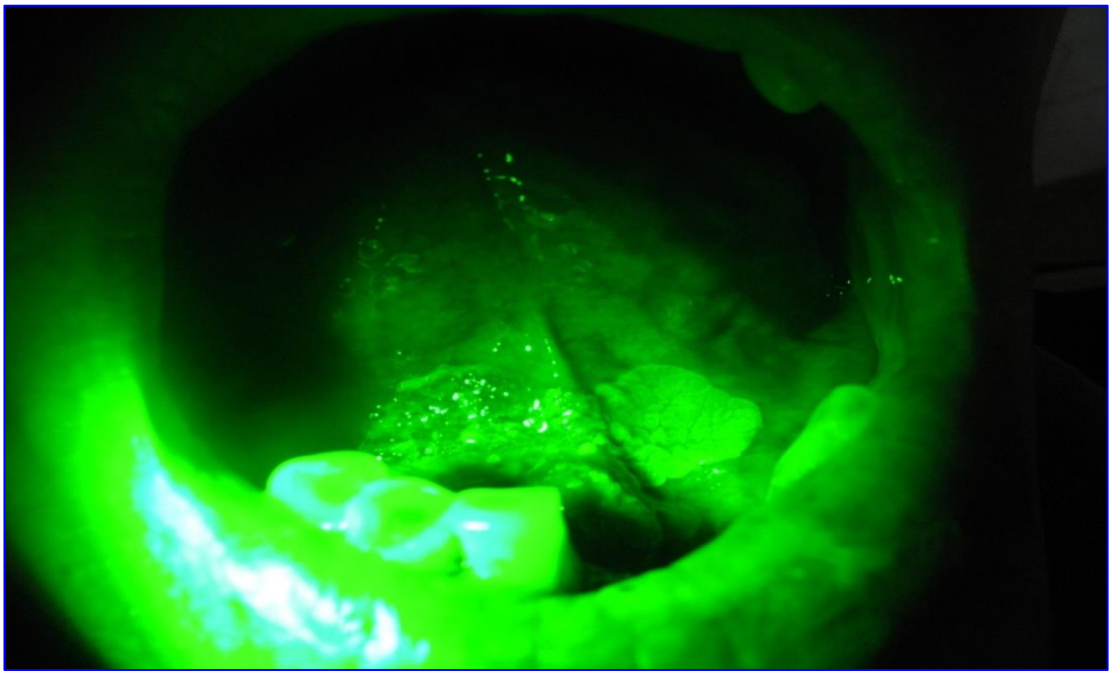

Fig. 38. Leukoplakia plana of oral floor. Diagnostic by quasilaser «UFL-122», green color.

In dental clinics the device «UFL-122» is used, the source light flux which has a quartz-halogen lamp Philips (13164) power 200W. System of

interference filters makes it possible to provide the necessary range of areas and absorb most other components, including ultraviolet and infrared. It provides optical radiation in five different spectral bands of the visible area of the spectrum. Analysis of the radiation spectrum shows that the maximum for UF filter corresponds to $\lambda = 487нм$ for G - G – $\lambda = 567nm$, for R - $\lambda = 602nm$.

The intensity or flux of density at the output of the fiber may lie within 50 - 300 mW/cm2 - for red and 100–1300 mW/cm2 - to orange light.

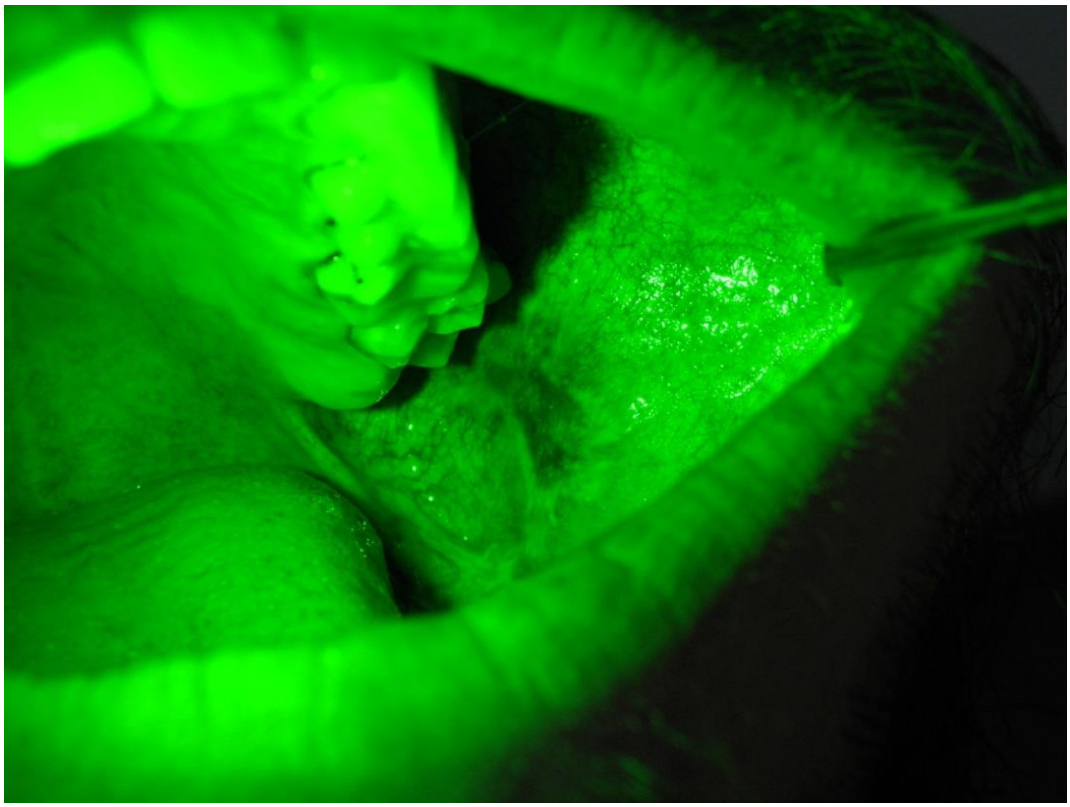

Fig. 39. Erosive-ulcerative forms of lichen ruber planus. Diagnostic by quasilaser «UFL-122», green color.

The aim of our study was to study the absorption of light by damaged mucosa in the treatment of precancerous lesions of the oral mucosa and lips (erosion, fissures, ulcers, prolonged healing) and without using SOLCOSERYL (gel). Rate change in the intensity of red and orange light with its depth of penetration into the tissue of the damaged mucosa. To prove

the possibility of using «UFL-122» as a light source for phototherapy implementation.

Materials and methods.

To determine the transmittance coefficient of mucosal tissue special designs were produced by standard technology. They were the slices of tissue taken at 1 mm, 2.5 mm, 4,5 mm levels, thickness from 4 till 40 micrometers placed on glass slides.

Two types of tissue were studied that was the squamous-cell with keratinization (malignant) and overgrowth of dense connective tissue soft plasmocells infiltrates and hemorrhages without tumor (benign). The experiment was carried out based on the photoelectric colorimeter FEK-2, which makes it possible to conduct a study on the narrow spectral ranges with peaks that correspond to wavelengths of 400, 440, 490, 540, 590, 670, 750 nm. A beam of light, limiting diaphragm and placed in his way without a substantive piece of glass cut tissue.

Changing the sensitivity of the gauge set up the arrow on the scale. In light path placed the sample and fixed display gauge - transmittance τ tissue. Similarly it was conducted experiment with “SOLCOSERYL” by placing it in a standard cell device.

The results of research and discussion.

Dependence of transmittance coefficient from wavelength for benign tissue sections at the same thickness, taken at three levels are presented in Fig. 1 and for malignant tissues - in Fig. 1b. Maximum absorption for all investigated tissues responsible wavelength ranges to 500-700 nm with a

maximum at 550 nm. No significant differences in the nature of absorption of benign and malignant tissue were found. Fig. 1 shows the dependence of a transmittance coefficient of wavelength for “SOLCOSERYL” layer thickness is 2mm. Absorption of light is low and clearly not dependent on the wavelength.

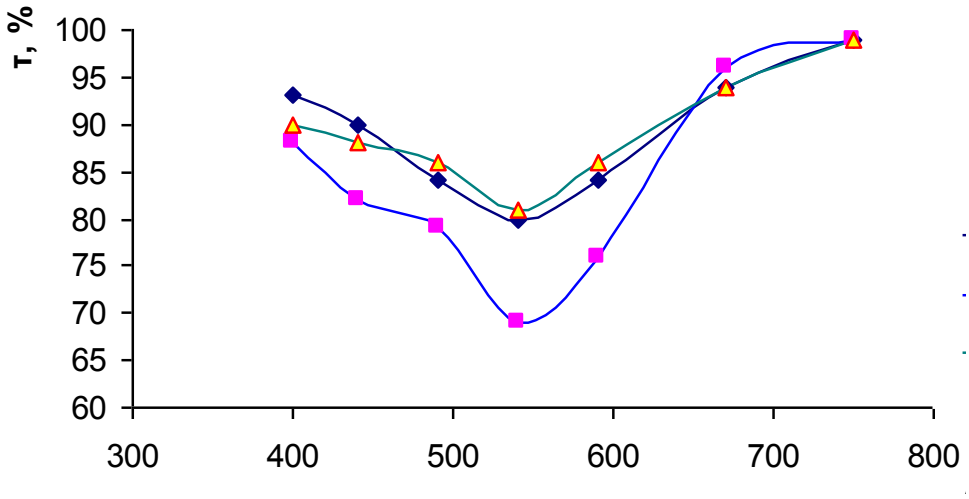

Fig. 40. A diagrame of dependence of transmittance versus wavelength for tissue with benign formaions.

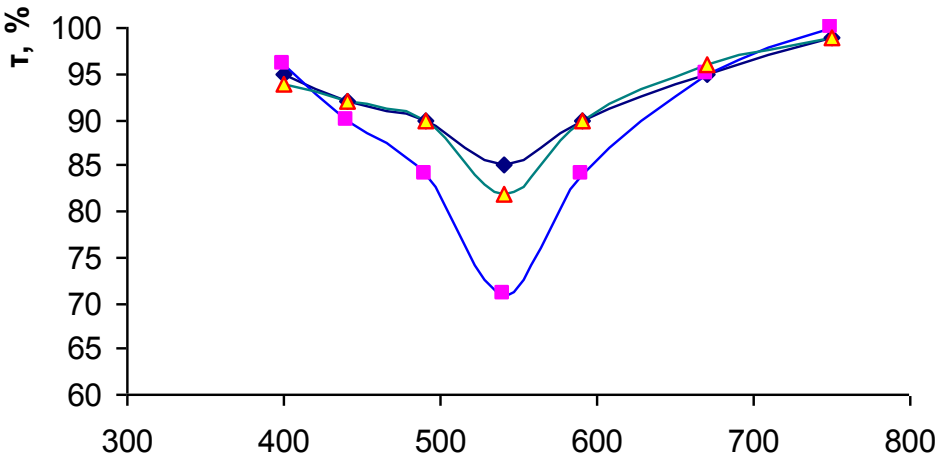

Fig. 41. A diagrame of dependence of transmittance versus wavelength for tissue with malignant formaions.

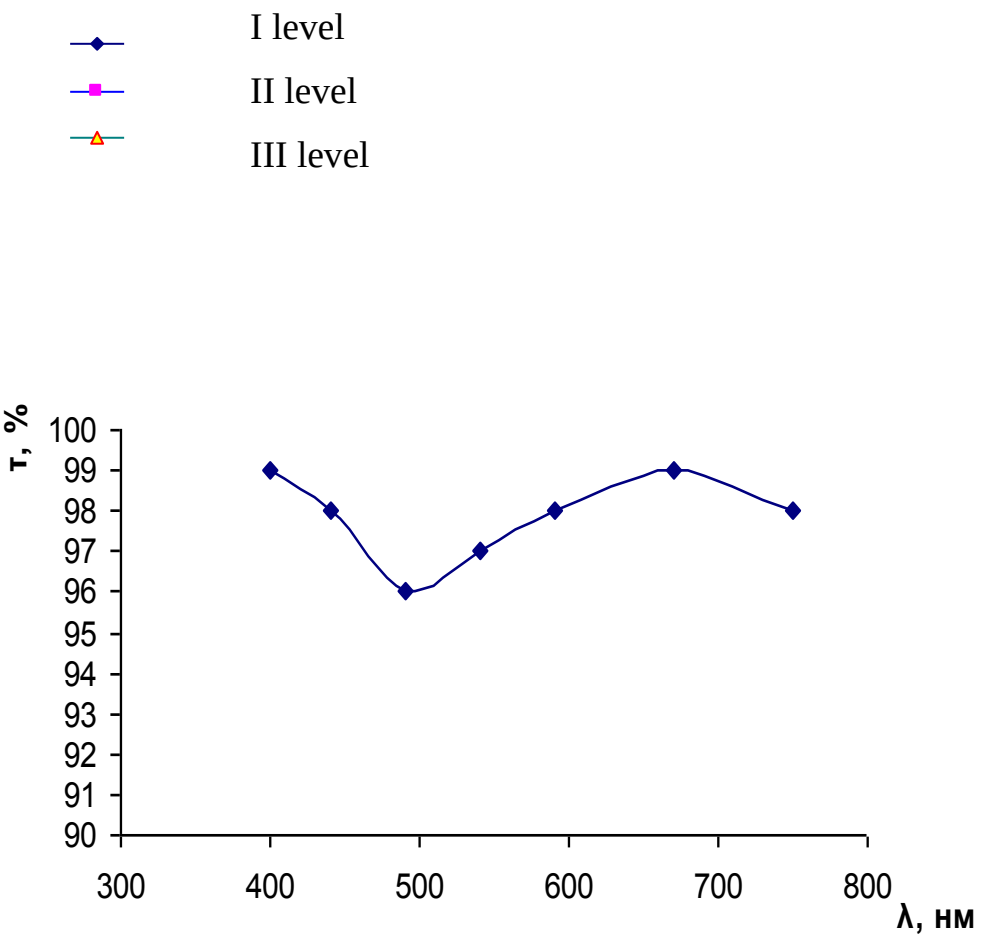

Fig. 42. A diagrame of dependence of transmittance versus wavelength for Solcoseril.

Comparing the absorption specters it can be concluded that the greater effect is achieved when irradiated with light in the wavelength range 550 - 650nm, which has color from yellow-green to red.

During study of dependence of light absorption on the thickness of malignant and benign tissue, taken at different levels using the same filters colorimeter, there was no significant difference in the nature of absorption. Fig. 2 presents graphs showing the dependence of the optical density of the substance D material thickness in micrometers for wavelengths belonging to four spectral intervals. The figure shows that with decreasing wavelength of

the optical density of the medium grows faster with increasing depth of penetration of light.

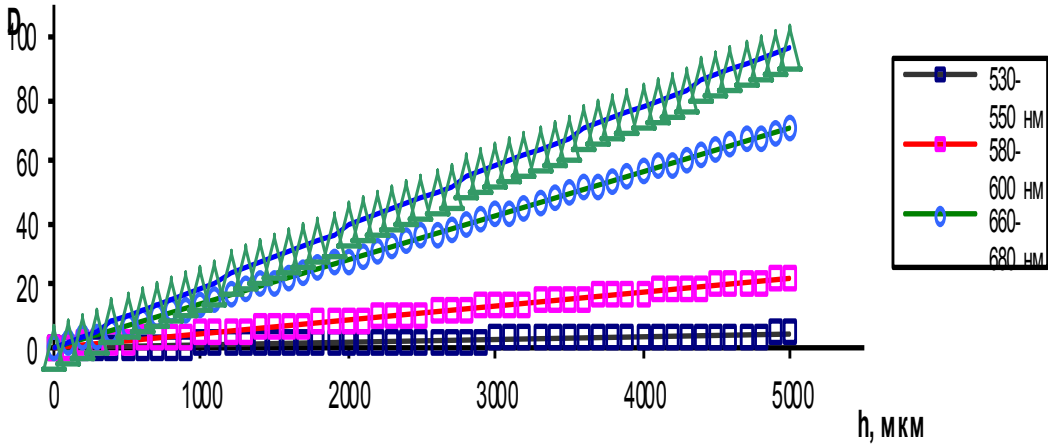

Fig. 43. A diagrame of dependence of absorbance mucosal tissues of thickness for wavelengths in four intervals

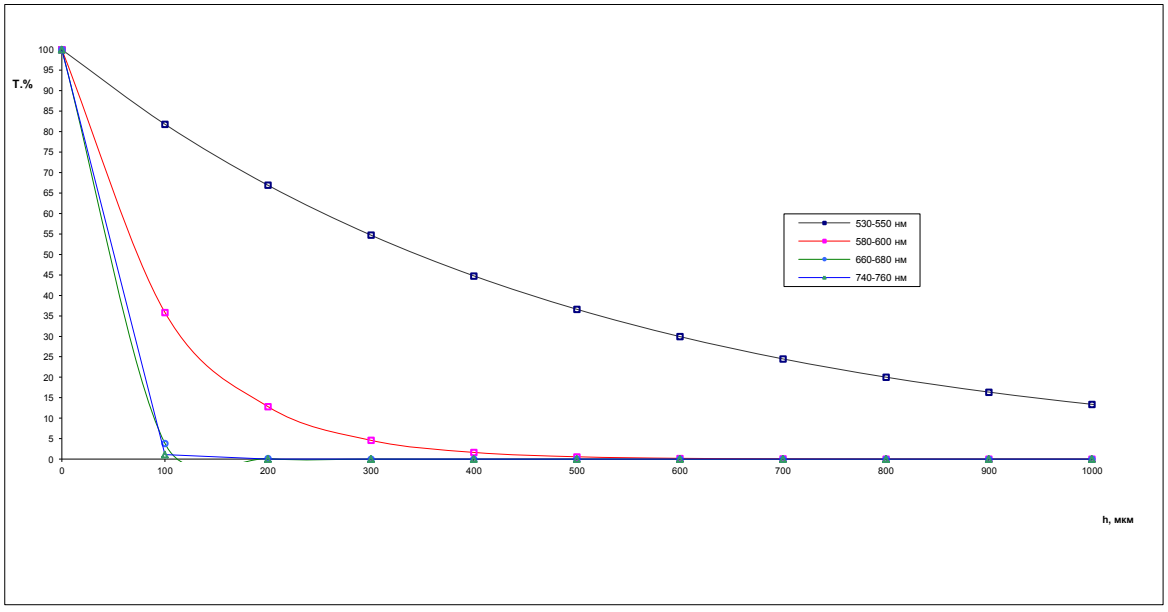

Fig. 44. A diagrame of dependence of absorbance mucosal tissues of thickness for wavelengths in four intervals

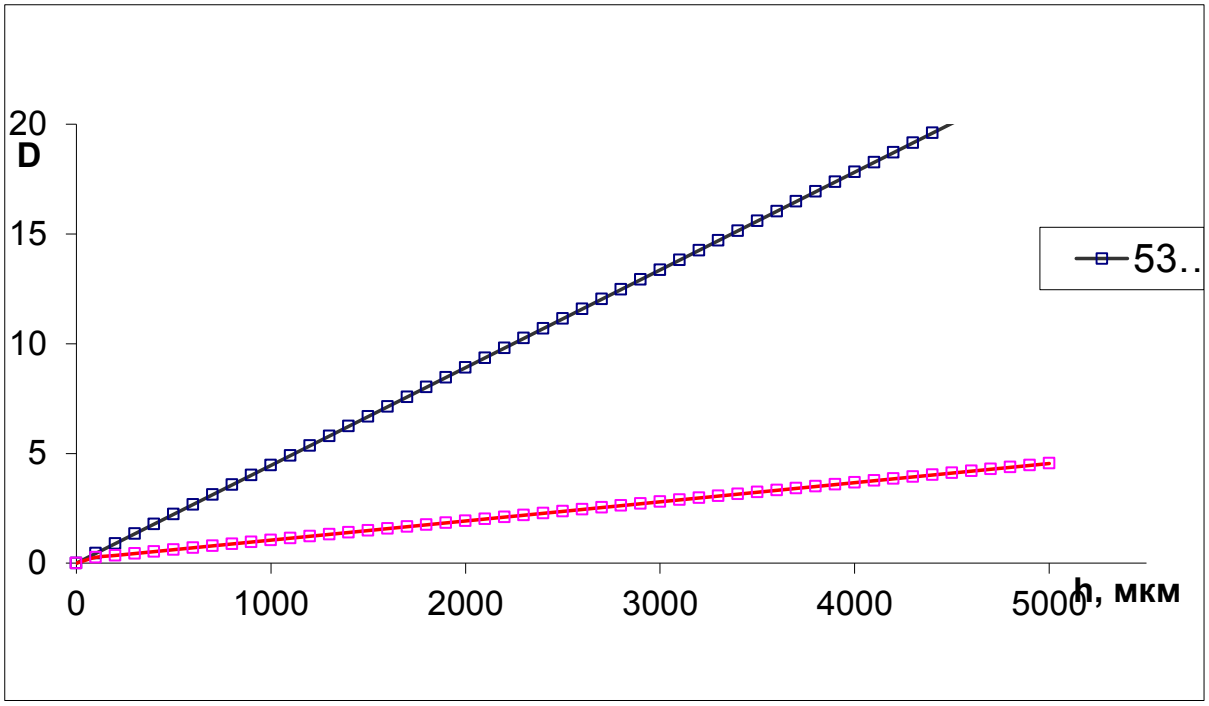

Fig. 45. A diagrame of dependence of absorbance mucosal tissues of thickness for wavelengths 660-68- nm with and without Solcoseril in four intervals

Dependencies of transmittance coefficient of mucosal tissues with the thickness of absorbing layer for different wavelengths are presented at Fig. 3. The intensity of light red is reduced by about 10 times during passage through tissues layer thickness of 1 mm, and the intensity of green light is reduced 10 times at a distance 100 mkm.

So permeable ability of light depends on the wavelength of light and it is the largest for light red. This makes it possible to use as a light source the quasi-monochromatic red light by device «UFL-122", which accounts for maximum radiation wavelength $\lambda = 602nm$.

According to averaged experimental data, plots of optical density on the thickness for benign and malignant tissues using and without Solcoseryl for the spectral range of 660 - 680nm are presented in Figure4. The graph

shows that the introduction of Solcoseryl is slightly reduced the absorption of upper layers of tissue that provides its penetration to the deeper layers.

Conclusions

So, significant differences in the nature of light absorption for benign and malignant tissue, taken at various levels, were not found. More light absorption is occurred in the wavelength range 550 – 650 nm, which has color from yellow-green till red. The optical density of matter for both kinds of tissues is linearly increased with the increasing of layer thickness. The optical density is faster increased at decrease of thickness of tissue with the decrease of wavelength. Introduction of Solcoseryl slightly reduces the light absorption of upper layers of tissue. Red light is more permeable. So, red and orange lights that are produced by «UFL-122» can be used for the implementation of phototherapy."

PROSPECTS OF OPTIMIZING OF THE DIAGNOSIS AND TREATMENT OF PRECANCEROUS DISEASES OF THE MUCOUS MEMBRANE OF THE ORAL CAVITY. TREATMENT. PREVENTION.

The role of active stomatological examination of patients increases for early detection of precancerous diseases and prevent their malignancy that is based on the characteristics of clinical manifestations of late treatment of patients. The importance of modern diagnosis and treatment of precancer of the oral mucosa and lips red border are extremely increased. However, practical implementation of this topic is inadequate.

Data of analysis of number of medical institutions revealed poor results of providing specialized aid to the numerous patients. It became apparent that one reason for rising incidence of malignant transformation of precancer is the ratio of doctors to some of its common shapes (leukoplakia plana, ulcers with prolonged healing) as to background diseases that are not dangerous. The same number of causes is long-term therapeutic (conservative) treatment that is not provided the criterion of radical transition. The lack of opportunities for stomatoscopy and other methods of additional diagnostics cause prevention of reasonable choice of treatment and establishment of indications for biopsy.

According to several studies it is known that many general practitioners and dentists do not diagnose precancerous conditions of the oral cavity [2, 6, 18, 58, 67] due to improper treatment or due to lack of knowledge of this disease. For example therapists from the UK [28] believe that dentists are responsible primarily for identifying oral cancer.

Research of J.D. Krisman indicates that the US therapeutics stomatologist could not immediately establish the diagnosis of oral floor

cancer, because they confuse it with traumatic or infectious inflammatory lesions.

Therapists stomatologist have a unique opportunity to identify malignant tumors of the oral cavity on early stages. But studies show that general practitioners do not hold oral examination to identify this pathology. J.M. Elwood has noted that 94% of patients at a late stage oral cancer were inspected by therapist for one year already having the disease. G.R. Lynch and M.N. Prout have found that only 3% of stomatologist documented that they had a full screening assessment of oral cancer for their patients with high risk of cancer development.

It was noted that dentists get mistakes and not diagnosed in time the early manifestations of precancer formations and oral cancer.

According to J.F. Shnetler stomatologists are less familiar with the diagnosis and early detected of precancerous lesions than general practitioners. B.T. Mahir has indicated that only 14% of all doctors-stomatologits carried out intraoral examination in full.

In previous reports J. Scotland, M.A. Pohrel have stated that dentists passed twice asymptomatic cancer cases of oral cavity than reveal. F. Coffin has noted that dentists could not identify oral cancer in 69% of cases presented to them. At the same time as another study that focused on both general practitioners and for doctors - dentists found that 15% of patients had cases of incorrect diagnosis or a delayed diagnosis of oral cancer.

Recent studies have reported that clinicians often do not know about the habits of their patients associated with high risk of malignant tumors of the oral cavity. According to research data of B.T. Mahir, 64% of dentists are not aware of the habit of smoking patients, and 40% did not know about addiction to alcohol. T.A. Dolan has observed that only 35% of US dentists

asked all or almost all of their patients about smoking habit. Even less than 15% of dentists ask patients about their habit of chewing tobacco.

Adult population of Ukraine and other countries are not sufficiently informed about the symptoms and signs of precancer and oral cancer.

From the data of world literature it is knows that cytologists, who are studying the oral mucosa, describe a new diagnostic method to obtain tissue samples for histological analysis. The doctor uses a stiff brush to the oral mucosa under significant pressure to make the bleeding point to ensure proper sampling of the deeper layers of the epithelium. Further, cell samples can be analyzed by variety of unique diagnostic techniques such as cytomorphometry, DNA cytometry, immunocytochemical analysis.

The newest computer system Oral CDx, (Brush test) allows to do the brush-biopsy analysis using a computer program for morphological and cytological analysis of tissue samples. Computerized analysis cell divides, based on the number of abnormal cells, which are then available to cytologist for further distribution and classification.

Oral CDx test sensitivity varies from 71% till 100%, specificity is 27% - 94%. It has 100% coincidence with results of usual avulsed biopsy, but has the advantage, it is painless; it can be used by all doctors-stomatologits, not just oral surgeons. It can be used in patients with numerous lesions of the oral cavity, as smooth and beneficial to patients who are afraid of normal biopsy.

A biopsy is the main and most accurate method of diagnosis and sometimes of treatment of tumors. Sometimes a biopsy gives wrong results (due to non-compliance taking of material or misinterpretation of morphological drug). In such cases, it should be carried out repeated studies.

Cheilostomatoscopy is used for differential diagnosis of precancerous lesions and malignant tumors of oral cavity.

AI Yatskiv proposed the color test with 1% aqueous blue toluidine solution. It is recommended using this test for suspicious areas to determine the oral mucosa, and for differential diagnosis of benign and malignant tumors. Vital toluidine blue coloration has high sensitivity but low specificity, due to accumulation of stain in areas of dysplasia and inflammation. This test, according to its information content is similar to immediate biopsy.

At advanced stomatoscopy it is possible to carry out differential diagnosis of precancerous lesions with the initial stages of cancer.

At the same time, T.S. Dvornikova (2000) has noted that extended stomatoscopy results in the diagnosis of precancerous diseases of the oral mucosa are not incontestable. Sensitivity of buccal biopsies was 96%, specificity - 97%, but for verification of diagnosis it is necessary to do avulsed biopsy. Therefore, the effective non-invasive detection of malignancy of cancer remains a serious problem.

Fig. 46. Vizilite Plus

Chemiluminescent light, based on systems Vizilite Plus, MicroluxDL, is used for visualization of pathological processes of oral mucosa, which is not visible in normal light bulb. 1% acetic acid is used for rinsing the mouth to remove desquamated epithelial cells before the state value of to oral health assessment using light. When illuminated normal epithelium absorbs light (becomes light blue), while abnormal tissue reflect light (appears white color), they can be seen TB blue marking system containing fenotiazin.

Vizilite Plus, Microlux DL, these competing technologies are very similar, they are the best methods to determine areas with high DNA content; have a high degree of sensitivity. Disadvantages are low specificity, can detect the light conditions of the mucosa, which is not abnormal. These technologies are better than visual inspection, but they do not determine the true boundaries of the lesion.

There is a screening system Identafy 3000 ultra for oral mucosa precancerous lesions visualization improving, which can not be revealed during casual examination. But, unlike other fluorescent technologies and supravital color, Identafi is a multispectral system with three different lengths and colors waves, that making it easier to diagnose morphological changes in lesions, thereby reducing the likelihood of false-positive results.

Vizilite Plus system uses toluidine blue, for further assistance in evaluating oral mucosa lesions. It can detect abnormal areas located under mucous membrane and are invisible under normal examination using day light from incandescent lamps. According to three studies evaluation system, its sensitivity was 100%, the number of positive results was 18-80% falsenegative 0-100%..

Autoflyuorescent research methods, describe the impact of a specific wavelength of the light beam on epithelial tissue, it is expressed excitement cellular fluorophores and radiation energy as fluorescence. Within normal

tissue morphology disruption in dysplastic lesions fluorescence is collected and dispersed, resulting in tissues discoloration.. According to this principle Velscope works, a device for mucosa precancerous changes early diagnosis. Normal, healthy oral mucosa with this lighting rendered pale - green, while the pathological areas - dark because it does not flyuorescenting..

It is known from the data of world literature that Velscope is used as oral mucosa pathological areas edges auxiliary definition while surgical manipulation; as a screening technique for determining the precancerous lesions and their early manifestation in the oral cavity.

According to some authors, the accuracy in determining tissue auto fluorescence is 98-100%, 100-78% specificity.

Typically, the primary method of diagnosis is a visual examination of tissue using lamps with white light, but existing design: Velscope, Identafi, Vizilite Plus, Microlux and Oral CDx. Scientists around the world continue to experiment with modern optical technologies: fluorescence spectroscopy, autoflyuorecence imaging, confocal microscopy, optical coherence tomography. Unfortunately, all the above-mentioned current screening technologies are too expensive for widespread application in Ukraine, making the new system unavailable today for dental doctors in public institutions, and the more in rural clinics.

Light curing unit series UFL-122 was invented by local scientific and production company Lux Dent. Unit developers have used four light spectrum (blue, green, red, orange) (G - to diagnose oral mucosa lesions and etc., O - for oral mucosa diseases, deep lesions treating), the unit can be used for caries and its complications, oral mucosa and periodontal tissues diseases diagnosis and treatment.

Transillimination method is formed the basis of unit usage. Learning (training), secondary and hidden approximal caries, mouth mucous membrane lesions, dental hard tissues lesions diagnosis is possible by means of this unit usage. Unit Lux Dent UFL-122 series are used in clinical practice since September 1998 and up to date at the Department of Postgraduate Education Physicians Dentists HSEEU UMSA.

The Periodontal and oral mucosa disease dynamics study during complex treatment using laser demonstrate improved general condition after 2-3 treatments (exacerbation of ulcerative gingivitis). Good results are obtained using R- and O mode with purulent sinusitis, temporomandibular mandibular arthritis, lymphadenitis, abscesses and face phlegmon. Unfortunately, there is no data in literature on the use of these modes in the practice of oral cavity mucous membrane precancerous screening assessment.

The latest development from american scientists team is painless non-invasive mouth cavity oncodiagnosis technology creation, as an alternative to traditional sampling tissue for histological examination. This nano - biochip, like a toothbrush, reqired for diagnoses a few minutes, just touching the affected areas of tissue on the tongue, cheeks, throat or mucous of patients.

Immunohistochemical methods have to establish the localization of antigens in specific components of tissues, cell types and cell structures using specific antibodies. Currently, mutations in the gene P53 or loss of this gene in the chromosome 17p most common genetic abnormality that observed in human malignant tumors of epithelial origins (from 40% to 60%). And the biggest percentage amounts oral mucosa cancer (60-80%).

Mutation in the gene expression of P53 and protein p53 is considered an initial event in the development of carcinomas in the mouth and aerodigestive way and is a measure of pathological phenotype progression that has already genetic changes in cells. Protein KI-67 expression level

determining can objectively evaluate the epithelial tumor genesis proliferative activity.

Treatment methods depend on the type of precancer, stage of disease, they can be therapeutic and surgical, so good results were obtained while use Solkovahina and Lizomukoyida as adjuvant therapy of oral mucosa leukoplakia (splash and verukosis form). Heliy-neon laser scheme of physical treatments of leukoplakia reasonable use is possible.

Surgical treatment methods (lesion excision within healthy tissue areas, cryosurgery, microwave hyperthermia, laser surgery) - used while curing Keyer erythroplasia, cutaneous horn, Bowen's disease, papilloma, warty precancer restricted hyperkeratosis, verukosis form of leukoplakia, keratoakantoma, in case of unsuccessful treatment erosive forms of cheilitis and leukoplakia Manhanotti etc. They are performed within a short time after diagnosis, but with oral cavity pretreatment. To do this, it is necessary to remove the metal construction, replace seals made of metal, sometimes with polymers, avoid wearing dentures. Furthermore, it should strictly prohibit smoking, chewing tobacco and tabaco mixture, exclude selftreatment.

For faster healing after surgery is recommended to rinse with the herb or their mixtures, oil solution (malavit, stomatofit, stomatofit A), application of vitamins A, E, applying ointments, Solcoseryl, under its influence diminishes spasm of arteries and arterioles, there is the growth of new collateral vessels, improves trophic tissues, increased utilization of oxygen content of normal breast and pyruvic acid, increased proliferation and migration of fibroblasts, increases collagen synthesis.

F.M. Mamedova and co-authors studied Meturakol film (based on Methyluracilum collagen) efficiency for the treatment of patients with flat red lichen.

R.V. Ushakov and co-authors used a film Dyplen Dent containing comprising dexamethasone, lincomycin, chlorhexidine.

D.S. Abakarova substantiated soluble films with SOLCOSERYL efficiency at various traumatic and inflammatory lesions of the oral mucosa.

Within the short term of oral cavity sanation in order to protect the lesion with epithelial defect (erosion, ulceration, cracks) symptomatic treatment is performed using painkillers, antiseptic and epitelising medicines. Primary form of leukoplakia is treated conservatively. It is recommended to apply vinilin mixture, 10% metyluratsyl emulsions and oil solution of vitamin A in the form of application to 20 minutes for affected areas. In the presence of erosions and if they formed recently (10-14 days old), ointments prescribed hormones (prednisone, synalar, flutsynar, hydrocortisone, etc.), aekolu oil solution application, lubricating ointments patron, calendula, etc.), sea buckthorn oil, "Ayekol" "Aevit" and others.

For erosive and ulcerative hyperkeratosis leave red flap form treatment synthetic anti-malarial drugs with small doses of corticosteroids (prednisolone, dexamethasone, dermoveyt, advantan) and vitamin B is used. Ointments with corticosteroids and others are used fir local applications. In evident severe inflammation, for local therapy except antiseptic and keratolytic agents, anti-inflammatory, analgesic, antibacterial and epithelizing action medications should be prescribed. These properties have: 1% alcohol citral solution, 0.1% sodium salt mefenamin solution, artificial lysozyme, Givalex, stomatydyn et al., Decoctions, tinctures and herbal gel and combinations thereof; quercetin granules, stomatofit, piralveks and others. These medications are used for rinsing baths and oral applications (3-4 times a day) as well as sebidyn tablets with vitamin C, trahisan, lisobakt etc.

Shumsky A.V. recommends to include to precancerous diseases complex therapy and perform as to indication the following:

- *immunomodulatory therapy with glutaksym, thymogen, immunofan, derynat, galavit;*
- *antioxidant therapy (vitamins A, E, C, selenium medications, meksydol);*
- *metabolism correcting (vitamins, adaptogens, herbal medications).*

Oral cavity malignant tumors prevention primary task in Ukraine has significant limitations and refusal of alcohol, and promote good nutrition, occupational cancer prevention, carcinogenic pollution fighting, prevention of exposure to excessive ultraviolet radiation and hereditary caused malignant tumors prevention . Because cancer effects of the Chernobyl accident special attention requires malignancies due to ionizing radiation primary prevention measures.

Oral mucosa chronic trauma eliminating with teeth sharp edges, poorly made dentures, lubricate lips with cream regularly, take vitamin A concentrate of 10 drops., 3 times a day within 2 months.

When literature analysis summarising first should be noted oral cancer diagnosis and treatment complexity problem. Taking into account all known developments and successes in this area, yet a significant number of problem aspects remains valid today, and it requires further study and clarification.

Malignant tumors incidence significant increase is marked within recent years, but still most of the patients "appears" in the late stage of the disease. This requires complex and expensive treatment and long-term outcomes remain unsatisfactory. At the same time, doctors of all specialties in their practice regularly meet with patients various localizations latent stages cancer carrier.

But in most cases, the tumor is detected in the metastatic stage. To detect early malignancies physician should have modern ideas about cancer development process features.

Immunohistochemical detection of separate proteins p53 and Ki-67, as the latest and modern methods of oral cavity mucous membranes precancerous diseases early diagnosis and malignant neoplasms histological diagnosis allows us to identify early signs of malignancy in the early stages of the disease, and the percentage of the likely degeneration of precancerous lesions in malignancy. Malignant tumors process development patterns knowledge will facilitate early detection of tumors and more effective treatment.

It is important to perform oral cavity mucous membrane precancerous diseases and cancer screening by the dentist during regular outpatient examination. Fot this purpose we believe that appropriate is the use of localy manufactured unit UFL-122 Lux-dent company, for diagnosing oral mucosa and lips diseases, periodontal (G -Mode) and for treatment of these conditions, along with traditional treatment methods.

Relevant upto today is the use of congratulatory painting suspicious sites oral cavity and lips red border mucous membrane with 1% toluyidyn blue solution, marking clear boundaries pathological lesion for subsequent extensive biopsy, etc.

This method of malignancy early detection is available to all dentists and informative diagnosis metho, easy to use, almost having no contraindications, except for hypersensitivity to product components.

In processed literature there is no data on the use of localy manufactured unit UFL-122 Lux-dent company in different spectra of light

for oral mucosa and lips precancerous diseases diagnosis and early detection - modes ("O" and «R») - as part of its comprehensive treatment.

That is why we consider appropriate to examine and investigate more thoroughly its diagnostic and therapeutic effect.

ORAL CAVITY PRECANCEROUS STATES AND CANCER HISTOLOGICAL DIAGNOSTIC OBJECTIFICATION BY BIOMARKERS P-53 AND KI-67 ON BIOPSY MATERIAL

Oral cancer constitutes about 3% of all cancers and is a major worldwide health problem. Despite significant progress in methods of treatment, 5-year survival rate has not improved over the last few decades and is still about 50-60%. More than 80% of oral cavity cancers are squamous cell carcinoma, which develops from the epithelium through the progression from hyperplasia to dysplasia and carcinoma *in citu* and further on to invasive cancer. A significant proportion of squamous cell carcinoma develops from premalignant damages.

Despite oral cavity availability for clinical examination, a large percentage of tumors are diagnosed at no precancerous states, but at the last stages of the disease. Oral mucosa cancer early detection is critical for treatment, because survival terms are significantly improved if oral mucosa pathology is qualified diagnosed and detected at an early stage. It should be specified that oral mucosa premalignant conditions and early cancer occurring mostly asymptomatic. Oral mucosa precancerous states significant percentage can be detected not only by oncologists and dentists, ENT doctors during oral cavity examination in patients treated with their disease profile.

Currently, mutations in the gene p53 or loss of this gene in the chromosome 17r most common genetic abnormality that observed in human malignant tumors of epithelial origin (from 40% to 60%). And the biggest percentage amounts oral mucosa cancer (60-80%). Suppressor gene product p53 main function in tumor growth in the cell is in the regulation of normal cell proliferation, and genes involved in DNA repair when it is

damaged transcription activation, and apoptosis regulation. Mutations in the p53 gene and overexpression of p53 protein are being considered a primary event in the development of carcinomas in the mouth and aerodigestive way and are a measure of pathological phenotype progression that has already genetic changes in cells. The protein Ki-67 protein belongs to the cell cycle regulators.

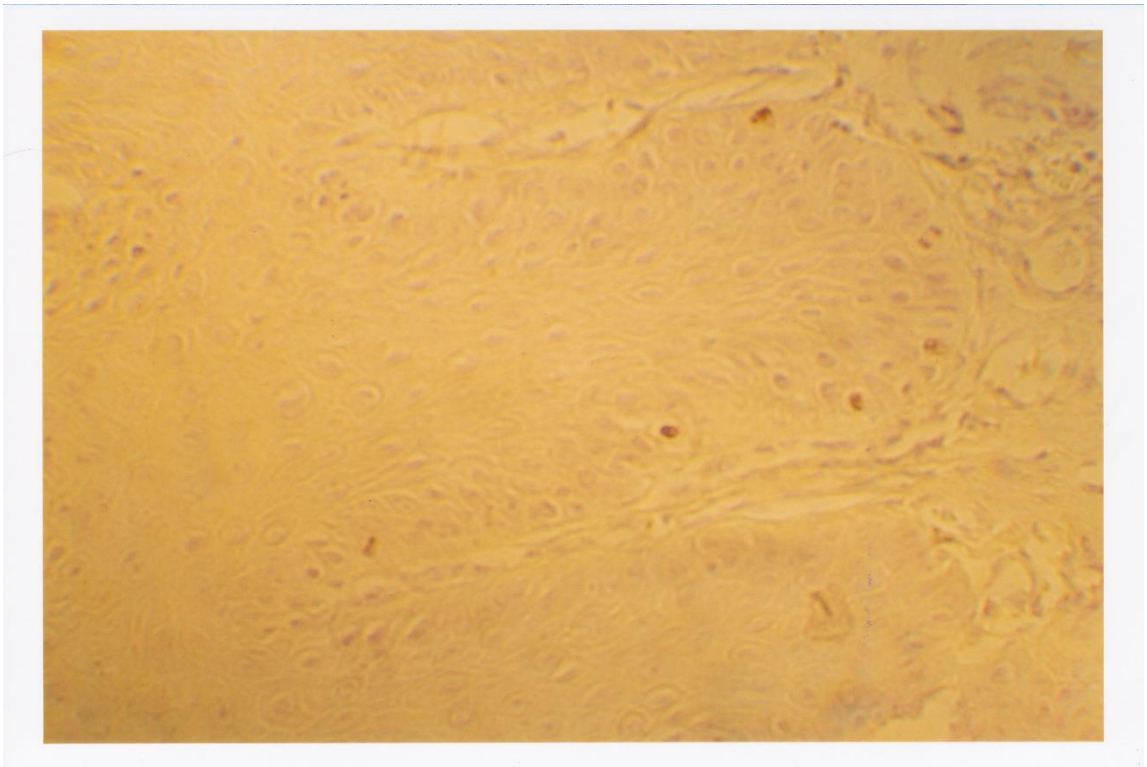

Fig. 47. Papilloma area photomicrograph. Diagnosis: papillomatosis (left maxillary sinus blastoma). Single CI-67 in the epithelium. Immunohistochemical reaction with KI-67. Hematoxylin-eosin colored. Histological sample No. 49895/08. Enl.×1000.

Tumor cell growth rate is a key characteristic that determines the tumor aggressiveness. Determining Ki-67 protein level expression can objectively evaluate epithelial origin tumors proliferative activity. In order to prevent oral mucosa precancerous conditions degeneration, multiple address screening methods for risk groups (smoking combined with alcohol abuse, professional prolonged contact with mutagens and

carcinogens) are required to detect precancerous conditions and objectification diagnostic methods using modern definition technologies biomarkers that precede cancer development.

Cells with expression p53 and Ki-67 performed analysis revealed individual characteristics as in the expression levels of biomarkers studied, and their distribution in the examined observations. Thus, among histologically defined papillomatosis (squamous papilloma) in the mucous marked difference in the expression of p53 and Ki-67. One observation has the slight signs of dysplasia (low), where cells with p53 were not found, only solitary cells with Ki-67 in hyperplastic papillomatous epithelium separate fields were noticed.

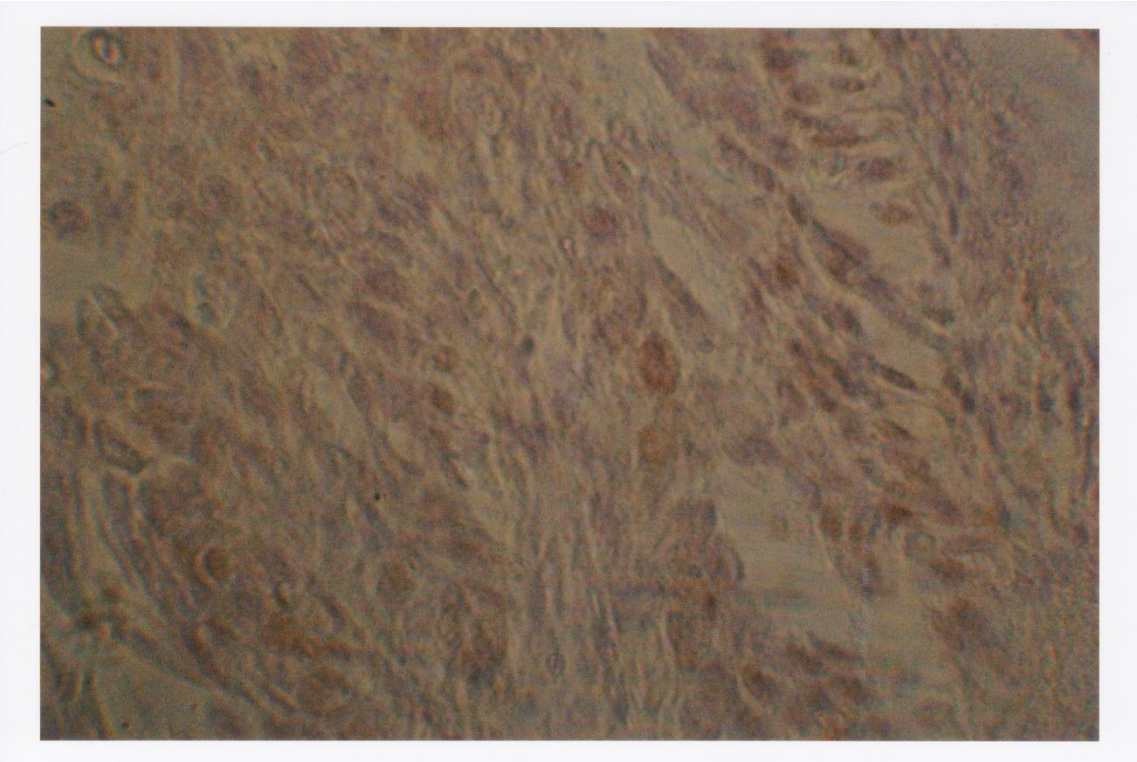

Fig. 48. Papilloma area photomicrograph. Diagnosis: papillomatosis with malignancies (left maxillary sinus tumor). Average dysplasia. P53 cells in epithelium basalis, parabasalis layers. Immunohistochemical reaction wioth p53. Hematoxylin-eosin colored. Histological sample No. 49891 - 2/08.

The second observation shows stratified squamous epithelium papillomatous proliferation cells with dysplasia signs and p53 expression in cells in the zone of proliferating cells, in suprabazalis layer cells directly parabasalis layer of epithelial cells. In some papillomatous outgrowths areas single cells with p53 in basal and parabasalis cell layer and in the surface layers and suprabazalis cells expressing Ki-67 in field cages with signs of dysplasia were found. Cells with p53 and Ki-67 labeling index (LI) was 29.6% with range in individual fields from 19% to 42% and 17.2% with range of 10% -24%, respectively.

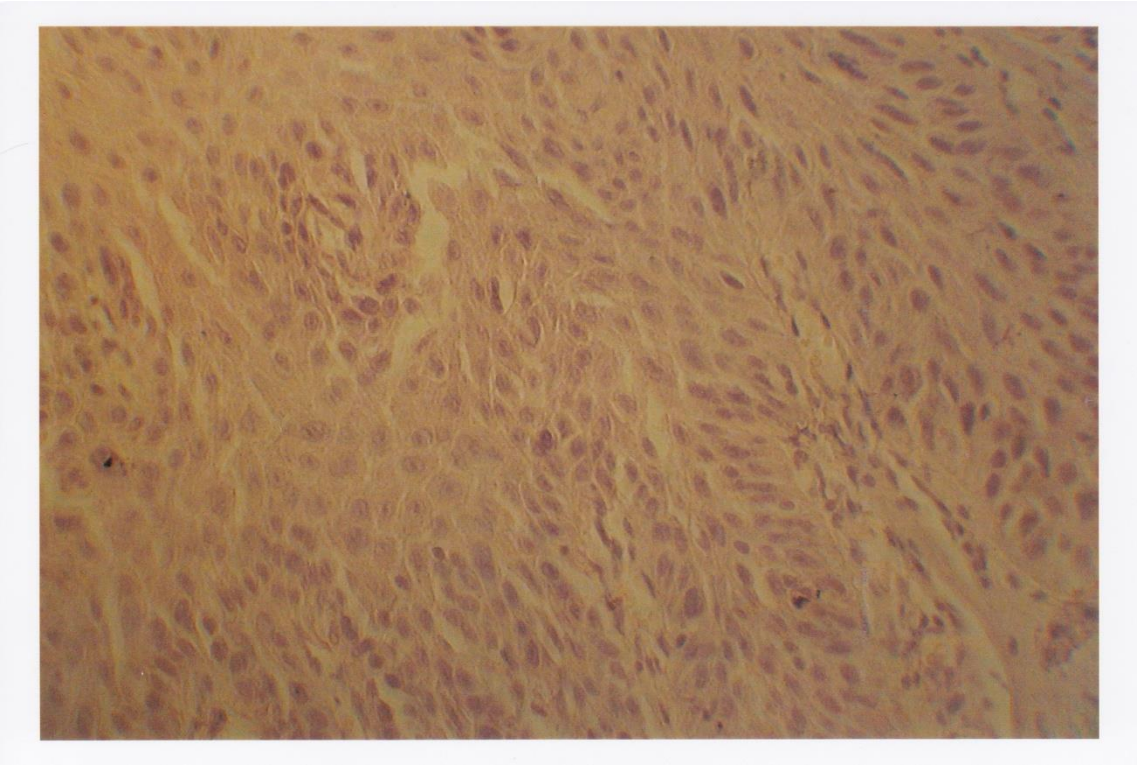

Fig. 49. Mucosal area photomicrograph. Diagnosis: Mouth bottom mucous membrane cancer. Histological sample No. 37437/08. Single KI-67. Dysplasia (low). Immunohistochemical reaction with KI-67. Hematoxylin-eosin colored. Enl.×1000.

It should be noted that dysplasia in this observation morphological was the low level, subjectively at the secondary level, but the definition of essential cells with p53 in cells, and particularly suprabazalis surface layers

and proliferating cells of Ki-67 gave reason to decide in favor of malignancy.

This observation demonstrates how determined biomarkers examination and its topography allow histologist to get rid from subjective evaluations while diagnosis and objectify individual diagnostics.

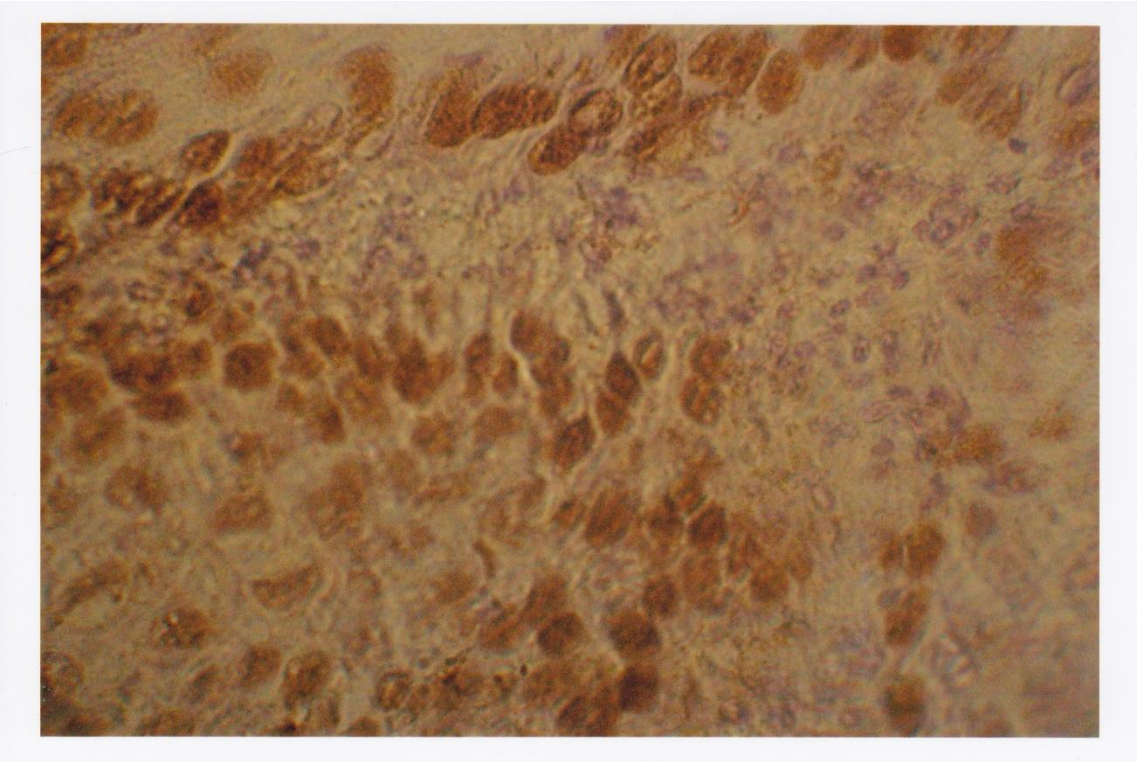

Fig. 50. Lower lip red border area photomicrograph. Clinical diagnosis: Lower lip red border hyperkeratosis. Histopathological diagnosis: leukoplakia (high dysplasia). Histological sample No. 24134. Immunohistochemical reaction with p53. Hematoxylin-eosin colored. Enl. × 1000.

Among surveyed leykoplakias in one observation cells were detected with neither p53 nor with Ki-67, indicating a relatively quiet epithelium conditions in biopsy material of this leukoplakia. The second observation was diagnosed with leukoplakia signs of dysplasia and cell proliferation basal cells and a significant level cells with p53 (LI 24.6%, range 12% - 33%) and Ki-67 (14.5% LI, range 6% -21%, respectively), which may

indicate a breach gene p53 tumor suppressor and its protein p53, leading to disturbances in the normal regulation of cell proliferation, DNA repair and apoptosis. This is evidenced by the marked proliferation of epithelium basal layer cells and a certain level of proliferating cells in this leukoplakia.

The literature has accumulated historical data about such leykoplakias malignancy and cancer development from them after a certain period of time and such leukoplakias require monitoring after performed treatment.

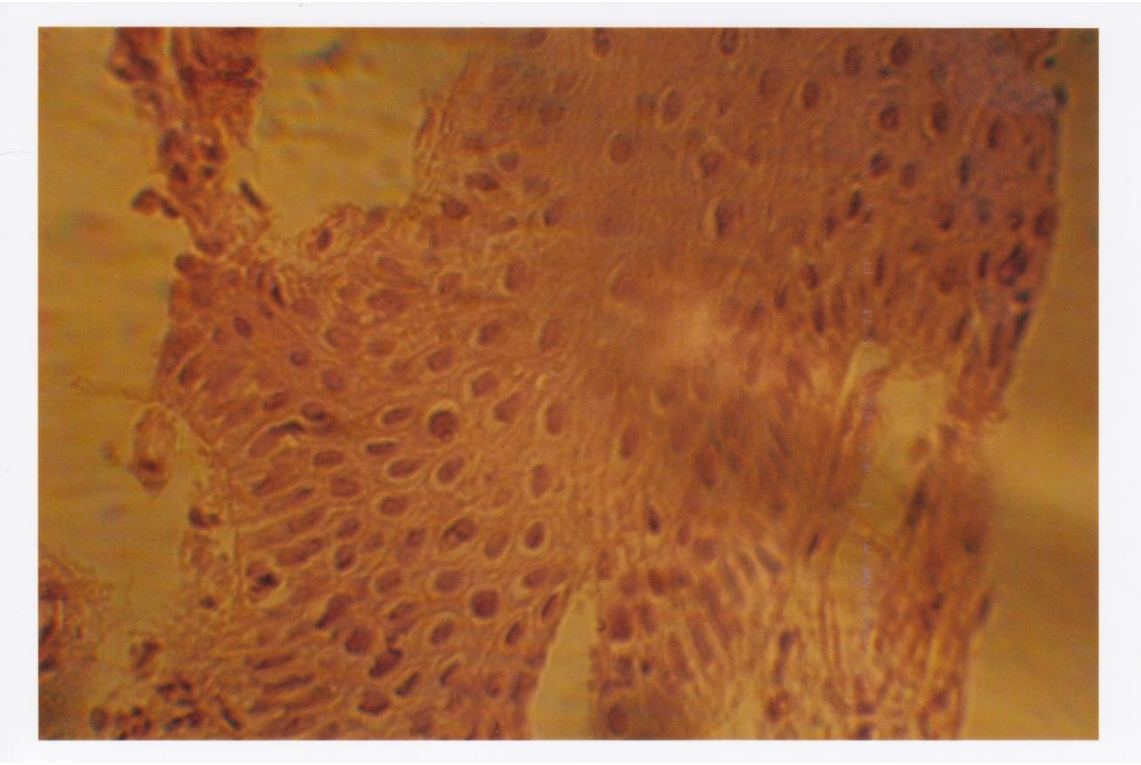

Fig. 51. Lower lip red border areas photomicrograph. Clinical diagnosis: Lower lip red border suspected cancer. Histopathological diagnosis: Epithelium high dysplasia. Intraepithelial carcinoma. Histological sample No. 5697/04. An intense expression of p53. Immunohistochemical reaction with p53. Hematoxylin-eosin colored. Enl. × 1000.

Among diagnosed mucosa epithelium dysplasias in one observation with small cell dysplasia squamous epithelium (dysplasia low to medium) cells with p53 and Ki-67 was not found.

The second observation squamous multylayred epithelial with dysplasia margins (low) isolated cells with p53 with very weak immunoexpression were revealed (LI 1% range 1-2%) and single cells expressing Ki-67 (LI 0.4% range 0 -2%).

For the third observation, within which cytomorphologically multilayred squamous epithelium with signs of dysplasia (average) was found, in a large segment of histological sections within immunohistochemical study cells with high p53 and Ki-67 (p53, LI 44.9%, range 35-55%, Ki-67, LI 27.5%, range 20-34%, respectively) were identified. Specific for this observation were placed, without merging with each other, isolated groups of cells that look like clones of individual cells with intense expression of p53 in suprabasalis epithelial layers.

According to the literature, founded p53 suprabasalis immuno expression is clearly associated with the degree of such dysplasia and malignancy risk of dysplasia manifestation.

Table 1.

Histopathological diagnosis and cells level with p53 and Ki-67 examined biopsies distribution.

Pos. No	Biopsy No.	Clinical diagnosis	Histopathological diagnosis	p53 (LI %) Range	Ki67 (LI %) Range
1	2	3	4	5	6
1	49895/ 08	Left maxillary sinus blastoma	Papillomatosis	0,0	0,2 0-2
2	49891-2/08	Left maxillary sinus tumor (B1)	Papillomatosis with malignancies (average dysplasia)	29,6 19-42	17,2 10-24
3	13743/ 04	Tongue lateral surface leukoplakia	Leukoplakia	0,0	0,0
4	24134	Lower lip red border hyperkeratosis	Leukoplakia (high dysplasia)	24,6 12-33	14,6 6-21
5	29118-20	Lower lip red border separated hyperkeratosis	Epithelium dysplasia (low)	0,0	0,0
6	4814/0 4	Palate mucosa cancer	Epithelium dysplasia (high)	44,9 35-55	27,5 20-24
7.	37437/ 08	Mouth floor mucosa cancer	Epithelium dysplasia (low)	1,0 1-2 (weak expression in single cells)	0,4 0-2
8.	5697/0 4	Possible lip cancer	Epithelium dysplasia (high), intraepithelial carcer	8,0 2-6	8,4 5-12

9.	48891-2/08	Possible mouth floor mucosa cancer	Epithelium dysplasia (high), intraepithelial carcer	34,9 10-60	1,5 1-2
10.	20539/04	Possible lip cancer	Epithelium dysplasia (high), intraepithelial carcer	69,2 62-77	9,6 7-12
11.	44888/08	Mouth floor mucosa area with postradiation cicatricial tissue	Squamous cell cancer remains with tumor cells penetration into granulocytic tissue	3,1 1-6	1,7 1-7
12	35951/05	Soft palate mucosa cancer	Squamous cell cancer	1,0 0-3	1,0 1-2
13	49839/08	Possible lip cancer	Squamous cell cancer	3,75 0-15	8,1 3-26
14	4812/04	Hard palate mucosa cancer	Squamous cell cancer	15,5 6-32	0,4 0-2
15	30059/04	Mouth floor mucosa cancer	Squamous cell cancer	27,6 13-59	7,8 5-14
16	30058/04	Mouth floor mucosa cancer	Squamous cell cancer	39,3 28-47	16,3 0-48
17	49893/08	Left maxillary sinus tumor piece	Squamous cell cancer	34,5 16-45	16,4 4-26
18	4603/04	Possible lip cancer	Squamous cell cancer	30,4 21-45	4,2 0-9
19	49894/08	Left maxillary sinus tumor piece	Squamous cell cancer	18,1 2-38	10,8 6-23
20	4602/03	Possible lip cancer (B1)	Squamous cell cancer	23,4 10-43	22,3 10-43
21	29120/04	Lower lip red border local hyperkeratosis	Squamous cell cancer	15,3 9-22	13,2 7-22
22	19406/04	Possible lip cancer	Keratinizing squamous cell carcer	0,0	0,0

Intraepithelial carcer (3-rd observation) was also diagnosed with cells p53 and Ki-67 involvement to histological level characteristics in these observations.

For two observations typical were high performance dysplasia and examined studied biomarkers values (p53, LI 69.2%, range 62% -77% and LI 29.6%, range 19-42%, Ki-67, LI 9.6% range 7-12% and 17.2% LI, range 10-24%, respectively for these two observations in stratified squamous epithelium areas with signs of cells dysplasia with high p53 and Ki-67 prevailed in the superficial suprabasalis epithelium layers. In one observation high dysplasia is marked by cytomorphological signs in stratified squamous epithelium, but with not significant levels of cells with p53 and Ki-67 (p53, LI 8.0%, range 2.6%, Ki-67, LI 8.4%, range 5-12%, respectively).

But determined expression of these proteins in surface suprabasalis epithelium layers of cell nuclei and significant proliferating cells indicator as well at surface suprabasalis layers level where naturally proliferating cells are almost absent (in some areas their level reached 12%) allowed in the examined biopsy material to diagnose not a dysplasia but intraepithelial carcer.

This observation clearly demonstrates how by means of p53 and Ki-67 biomarkers immunohistochemical examination on biopsy material histopathological changes in mouth mucosa can be objectively diagnosed.

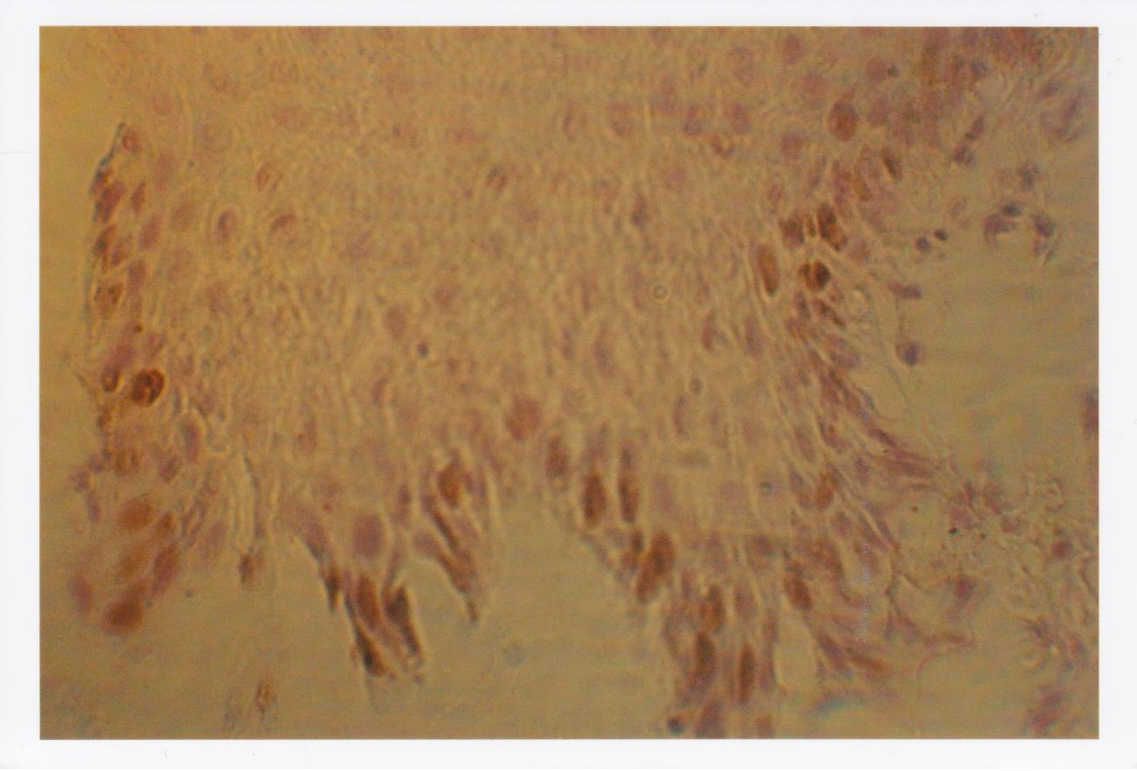

Fig. 52. Mouth floor mucosal areas photomicrograph. Clinical diagnosis: Mouth floor mucosal possible cancer. Histopathological diagnosis: High dysplasia. Intraepithelial carcer. Histological sample No. 48891-2 / 08. p53 intense expression. Immunohistochemical reaction with p53. Hematoxylin-eosin colored. Enl. × 1000.

According to the study, using histological analysis potential cancer threat in the mucosal precancerous conditions can be determined, but its further biological behavior is not possible to predict. However, investigated p53 and Ki-67 biomarkes expression determination allows to get objective approach to precancerous condition individual dysplasia level assessment and subsequent treatment strategy.

Among biopsies (12 observation), where oral mucosa squamous cell carcer was cytomorphologicaly diagnosed individual characteristics were found also as in studied biomarkers expression levels, and their distribution in the investigated tumors, allowing to make their malignancy and

proliferative potential individual assessment. Thus, in one observation where keratinizing cancer was diagnosed, cells with p53 and Ki-67 were not revealed. Squamous cell cancer observations exist when mutated gene protein p53 immunohistochemicaly can not be detected in tumor cells, but this does not exclude mutations in the p53 gene.

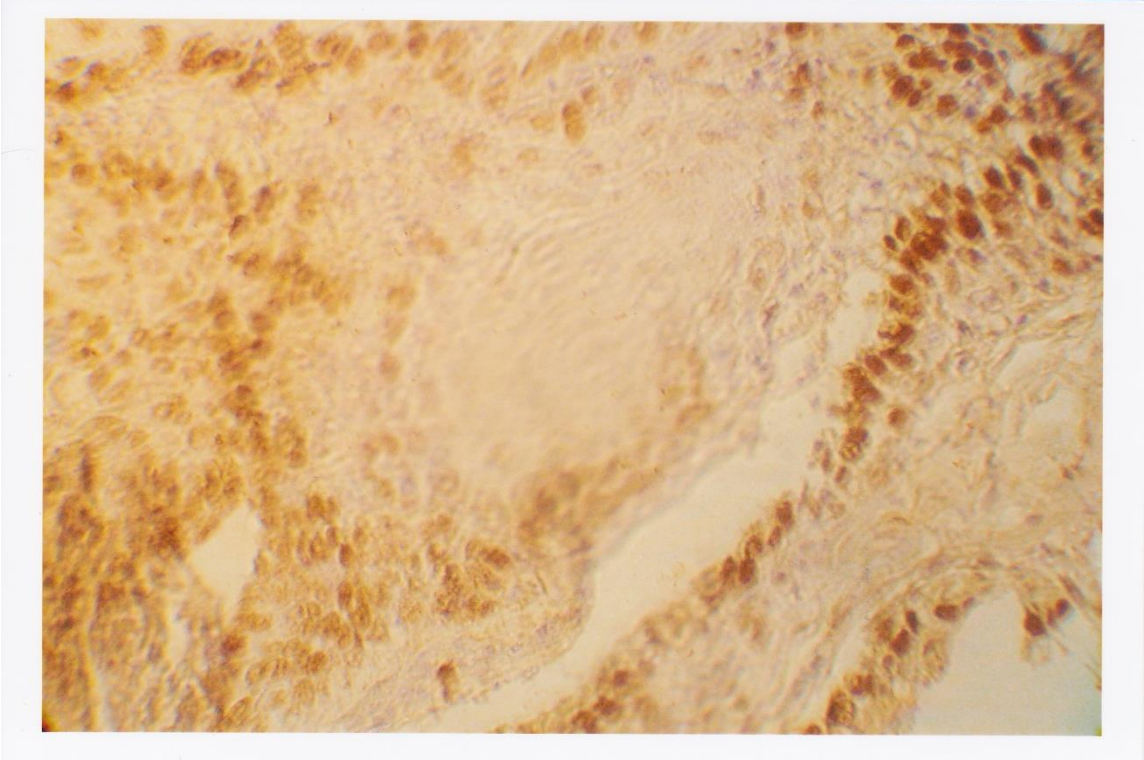

Fig. 53. Hard palate mucosa areas photomicrograph. Clinical diagnosis: Hard palate mucous membrane cancer. Histopathological diagnosis: High epithelial dysplasia. Histological sample No. 4814-2 / 04. p53 intense expression. Immunohistochemical reaction with p53 and Ki-67. Hematoxylin-eosin colored. Enl. × 1000.

Two observations identified cancer cells with low levels of biomarkers examined, which in one case was due to the fact that the histological sections for immunohistochemistry did not get tumor

essential part cut (p53, LI 1% range 0-3% Ki-67, LI 1% range 1.2%, respectively) and the second observation p53- LI 3.75%, but range in the level of p53 in tumor cells examined fields from 0 to 15% and with significant level of cell with Ki- 67 (LI, 1% range 3-26%).

In one observation diagnosed with squamous cell oral mucosa cancer after radiation (biopsy tissue scar after radiation) among granulation tissue field epithelial cells with signs of radiation pathomorphosis and fields of cells with signs of dysplasia (high) were detected and immunohistochemistry identified cells with p53 (LI 3 1% range 1 - 6%) and Ki-67 (MI 1.7%, range 1% -7%).

Tumor cells with p53 saving, which has significant malignancies and proliferating cells including demonstrates tumor recurrence in the scar area possibility formation after radiation exposure. This observation demonstrates an opportunity within immunohistochemical examination of cells with p53 and Ki-67 more accurately assess mucosa condition after received treatment. In other squamous cell carcer observations (9 observation) LI cells with p53 fluctuated in the range of 15.3% to 39.3%, and LI cells with Ki-67 was in the range of 0.4% to 22.3%, respectively.

Molecular biomarkers p53 and Ki-67 high expression level in oral cavity squamous cell carcer indicates these tumors high malignant potential. The level of tumor cells with p53 is determining individual biomarker of oral cavity malignant squamous cell carcer assessment.

Fig. 54. Hard palate mucosa areas photomicrograph. Clinical diagnosis: Hard palate mucous membrane cancer. Histopathological diagnosis: High epithelial dysplasia. Histological sample No. 4812/04. Ki-67 intense expression. Immunohistochemical reaction with Ki-67. Hematoxylin-eosin coloured. Enl. × 1000.

Thus, cells level with p53 and Ki-67 on biopsy material oral mucosa precancerous conditions and cancer performed analysis shows that the use of immunohistochemical technologies protein gene suppressor tumor growth p53 and protein proliferating cells Key 67 determining while histological diagnosis allows us to give more objective assessment of individual processes that occur in oral mucosa precancerous conditions, evaluate malignancy risk, proliferative potential and predict tumor malignancy.

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