

**ASTRAKHAN STATE MEDICAL UNIVERSITY**

**SIBERIAN STATE MEDICAL UNIVERSITY**

**L.G. Tarasova, O.V. Filinyuk**

**OROFACIAL TUBERCULOSIS:  
clinic, diagnosis,  
differential diagnosis**

Translation from Russian N.F. Koksharova

**TUTORIAL**

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Current data on tuberculosis of orofacial localization are presented. Issues of etiology, classification, pathogenesis, risk factors, clinical features, diagnosis, differential diagnosis are disclosed. An algorithm is presented for examining patients with suspected orofacial tuberculosis and features of the treatment of the disease

In view of the rare localization of the disease, the training material is illustrated by the clinical data of patients with verified orofacial tuberculosis, which are publicly available and published on the Internet in specialized journals.

Tests are presented in various modifications, the answers to situational tasks are oriented to practice, which completes the high-quality and complete development of the academic discipline.

The manual has been developed for the work program of the module “Infectious Diseases, Phthysiology” in the phthysiology unit for the direction of preparation 05.31.03 - Dentistry for students of higher medical educational institutions and is recommended for use for independent preparation for classes and in-depth study of the material.

**Reviewers:**

**Anna V. Mordyk**, head of the phthysiology, phthysiosurgery and infectious diseases Division DMedSc, MD, Professor, Omsk State Medical University.

**Lyudmila V. Poddubnaya**, head of the phthysiopulmonology Division DMedSc, MD Novosibirsk State Medical University.

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# INTRODUCTION

## BASIC INFORMATION ABOUT TUBERCULOSIS

Tuberculosis is a chronic infectious granulomatous disease caused by microorganisms that form the Mycobacterium tuberculosis complex group (7 species). In most cases, the disease in humans is caused by Mycobacterium tuberculosis.

Mycobacterium tuberculosis (MBT) is a large, slightly curved or straight bacterium in the form of a stick of 1-10 microns, 0.2-0.6 microns in diameter. Bacteria are motionless, do not form spores and capsules, and do not secrete exotoxins.

### **The main species properties of MBT:**

- obligate aerobes;
- slow reproduction (the division cycle is 18-24 hours, which leads to slow growth on nutrient media and during cultivation);
- high resistance to external factors due to the unique cell wall containing a large number of mycolic acids linked to fatty acids, complex waxes, sulfatides, glycolipids and arabinogalactan;
- MBT can withstand heating up to 80-90° C and low temperatures - up to -260° C, are resistant to drying, are well preserved in a humid environment, and are resistant to most chemical and physical factors (except for ultraviolet radiation and direct sunlight);
- pronounced polymorphism under the influence of adverse environmental factors with the ability to L-transformation and the formation at the genetic level of drug-resistant strains that pose a serious public health problem around the world – the spread of multidrug-resistant tuberculosis (MDR) MBT (resistant to at least two essential drugs isoniazid and rifampicin);
- pathogenicity and virulence.

Tuberculosis is an anthroponosis infection.

**TB infection source:** sick person (bacterial excretion), sick animal.

**Ways of MBT excretion:** with sputum (most often), with urine, feces, pus (in case of tuberculosis of bones, peripheral lymph nodes).

**Ways of infection:**

- 1) aerogenic (90%): air-dust (most often) and airborne;

- 2) alimentary (meat, milk, cheese, eggs) – 1-2%;
- 3) contact (through damaged skin and mucous membranes) – 2-5%;
- 4) transplacental (rare).

The main source of infection for others is a patient with tuberculosis, who releases MBT by airborne transmission. As a rule, these are patients with pulmonary tuberculosis. The most dangerous are patients with abundant, constant bacterial excretion, which is detected by microscopy. These patients can excrete a billion or more causative tuberculosis agents with sputum per day.

Tuberculosis infection can be due to the direct contact with a TB patient that transmits MBT when coughing, sneezing, by droplets of saliva when talking, kissing, etc. A contacting person inhales the created cloud of aerosol containing MBT. However, infection is possible without the direct contact with the patient; it can happen due to the contact with infected items, underwear, dust particles containing dried sputum, other material containing mycobacterium (air-dust infection). The danger of airborne dust infection increases if the patient does not follow the rules of personal hygiene, with insufficient disinfection or its absence, with poor-quality cleaning of the room.

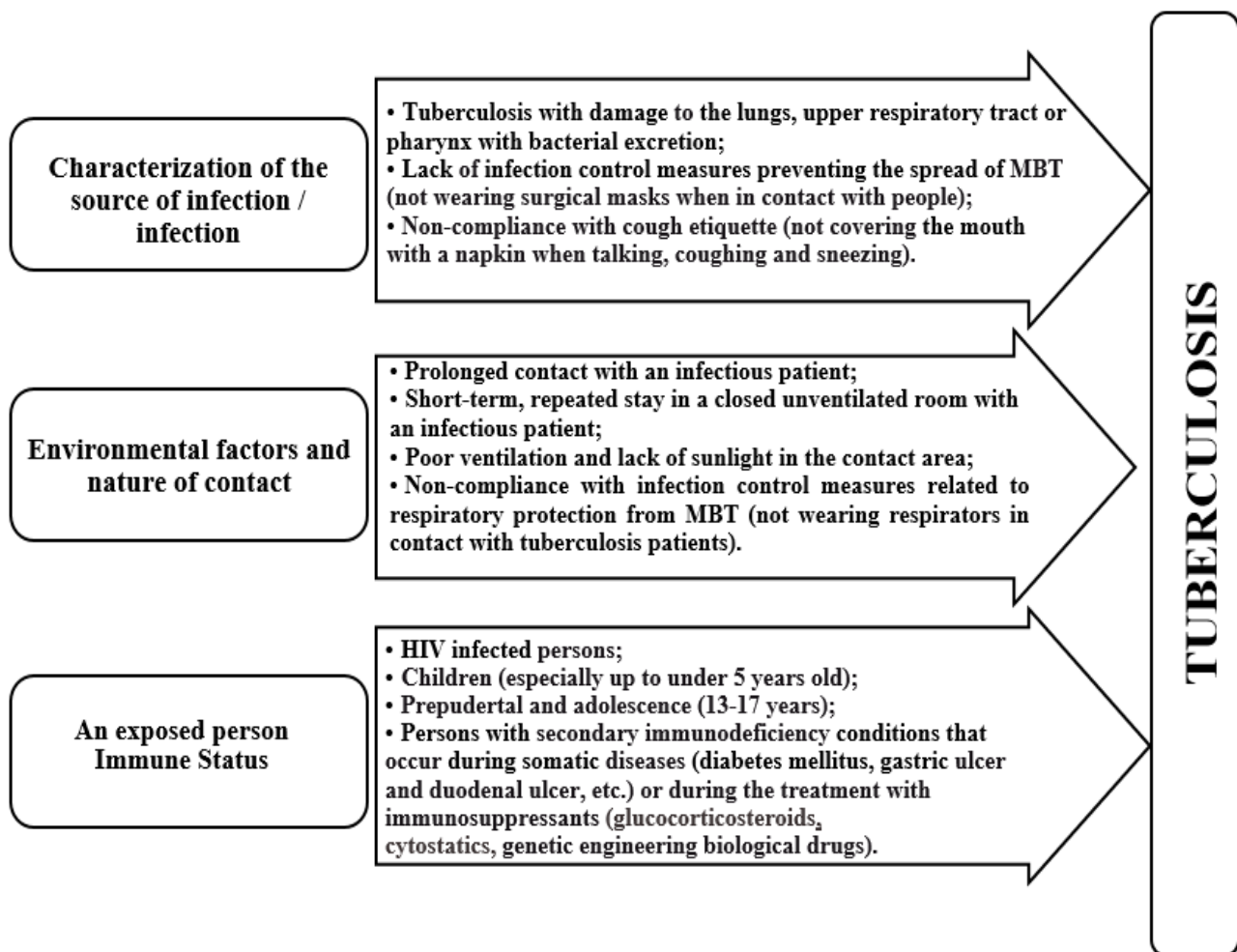
Patients with extrapulmonary forms of tuberculosis, secreting MBT (tuberculosis of the kidneys and urinary tract, fistulous tuberculosis of bones and joints, peripheral lymph nodes and other organs) are also considered dangerous to others because of the risk of infection of the latter. Annually, a person with bacterial secretion can infect 10-15 people.

**The risk of MBT infection depends on:**

- massive bacterial excretion of the patient;
- time of contact with the patient;
- proximity of contact and size of the room in which contact with the patient occurs;
- the presence of risk factors in the exposed person (Fig. 1).

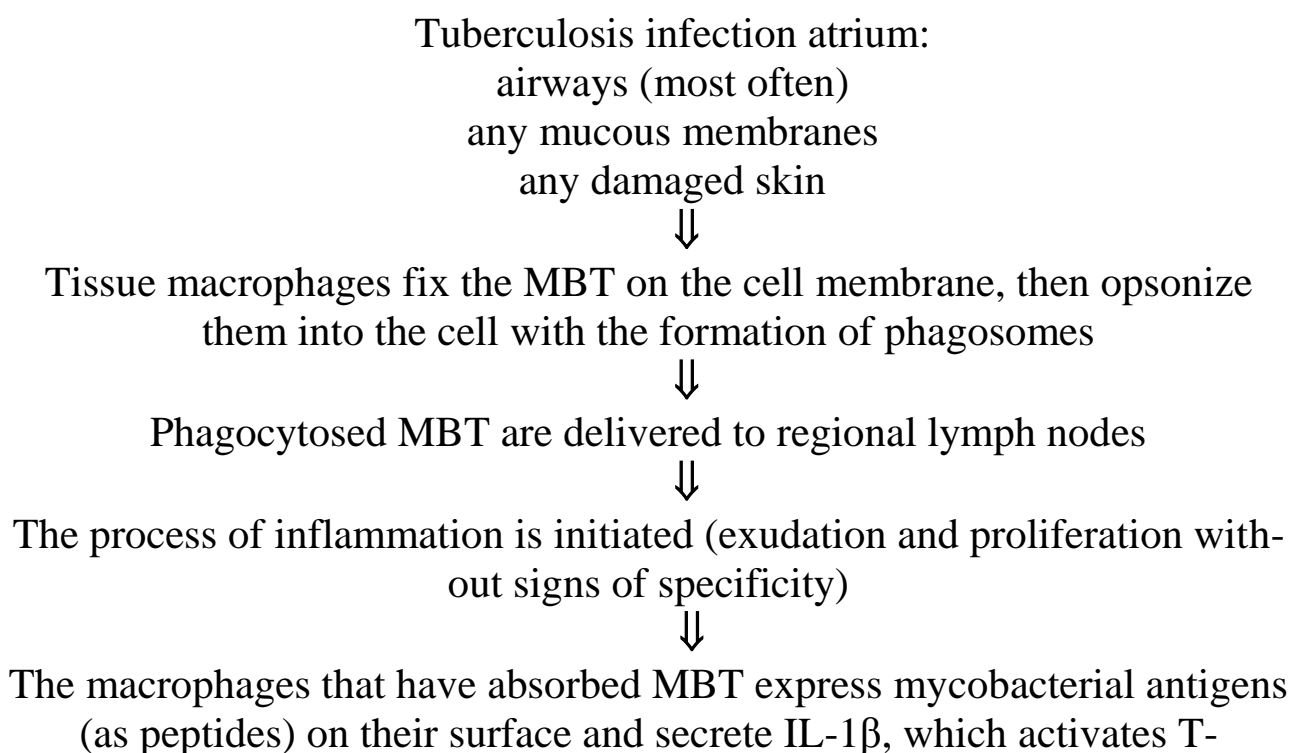
In Russia, people become infected with tuberculosis in childhood. In most cases, infection does not lead to the disease due to humans' high congenital resistance to tuberculosis.

In the development of tuberculosis as a disease, two periods are distinguished: primary and secondary. Primary tuberculosis occurs as a result of primary infection.



**Figure 1. High risk factors for tuberculosis**

**A brief scheme of the MBT interaction with a human body**



lymphocytes (CD4 +), into the intercellular space



Activated (sensitized) CD4 +, CD8 + produce effector cytokines IFN- $\gamma$  and TNF- $\alpha$ , IL-2, which attract cells from the capillaries to the site of inflammation that can restrict and eliminate MBT: macrophages, lymphocytes, histiocytes, granulocytes



A tuberculous granuloma is formed, in the center of which there is caseous necrosis, including the remains of dead macrophages, MBT and organ tissue elements surrounded by epithelioid cells, Pirogov-Langhans multinuclear cells and lymphocytes

In the pathogenesis of tuberculosis, two phenomena are distinguished - infection and disease. Infection is the penetration of MBT into the human body in the absence of appropriate clinical symptoms and local manifestations. The disease is characterized by the appearance of morphological, clinical, radiological, and microbiological signs of tuberculosis infection. Therefore, depending on the adequacy of the immune response, the development of the tuberculous process occurs in two versions:

1. favorable course - MBT reproduction stops, their number decreases sharply, granulomas are calcified and scarred (MBT L-forms are preserved in the granuloma). The condition is interpreted as latent tuberculosis infection (LTI). In humans, due to the formation of anti-tuberculosis immunity, positive skin reactions to tuberculin, a recombinant tuberculosis allergen (diaskintest), IGRA tests in the absence of clinical and radiological signs of active tuberculosis are observed.

2. Under the influence of adverse factors that reduce the resistance of the human body, with an insufficiently active immune response, tissue specific inflammatory processes progress with the formation of the disease and, possibly, the generalization of the process.

It is believed that about 5% of the number of infected people develop primary tuberculosis. The risk of developing primary tuberculosis remains until completion of the reverse development of morphological tuberculosis changes with the formation of petrification. From the moment of infection to the reverse development of changes, at least 3 years pass.

Secondary forms of the disease are formed as a result of endogenous reactivation of tuberculosis against the background of weakened immunity, are characterized by the formation of local forms, however, they can al-

so develop as a result of repeated penetration of MBT into the body from the external environment - exogenous superinfection.

Although pulmonary tuberculosis is the most common form of the disease, specific inflammation can occur in other organs and tissues, including the oral cavity and the area of the head and/ or neck.

**Orofacial tuberculosis** is a rare localization of extrapulmonary tuberculosis and can affect the tongue, palate, oral mucosa, red border of the lips, gums, bones of the facial skeleton, and lymph nodes. The incidence of orofacial tuberculosis makes up from 0.5 to 1.5% of all tuberculosis cases.

Tuberculosis of the maxillofacial region can develop as an independent form or as a secondary one, or on the background of pulmonary tuberculosis. From the outbreak in the lung tissue, MBT can enter the oral mucosa in a contact way (with sputum during coughing) or through the hematogenous route. At the same time, the fact is well known that not all people infected with mycobacteria develop tuberculosis; their risk during life is 10%. People with weakened immune systems have an increased risk of developing the disease. Predisposing causes may be HIV infection, prolonged immunosuppressive therapy, diabetes mellitus, pregnancy, alcoholism and drug addiction, and malignant neoplasms. Local risk factors for the development of maxillofacial tuberculosis are the presence in patients of various chronic pathologies in the oral cavity from common deep caries, pulpitis, up to complete tooth decay, as well as the state after tooth extraction and other dental operations and chronic injuries.

The oral mucosa has a natural resistance to infections due to the presence of lysozyme and a number of enzymes (amylase, maltase, etc.) in the salivary fluid. The penetration of an infectious agent into the mucosa and the development of maxillofacial tuberculosis is possible due to the lack of local protection mechanisms against infections, which are tissue antibodies, saliva, saprophytic flora, which lives on the mucosa and, in fact, the multilayer oral mucosa (OM). However, various damage to the natural barrier of oral mucosa by foreign agents (as a result of trauma, inflammation, tooth extraction, etc.) may be an open gate for the penetration of mycobacteria into the mucous membrane. A mucosal defect leading to a violation of its barrier function can also occur due to poor hygiene of the maxillofacial region and (or) smoking.

Orofacial tuberculosis does not have specific symptoms and is characterized by various clinical manifestations, both general (intoxication syndrome) and local, which creates a serious problem for the timely diagnosis

of this localization of a specific process. So, for example, it is extremely difficult to recognize the first symptoms of tuberculous damage to the tissues of the lips and the perioral region (cheilitis), due to the fact that the inflammatory process is presented as a painless local or diffuse edema, the occurrence of which may have other reasons (infection, trauma, allergic reaction, neoplasm).

The main condition for the correct diagnosis of tuberculosis is a comprehensive examination of the patient, the analysis of laboratory and instrumental methods of research. The disease is verified with the help of microbiological and histological studies defined in the standards for the diagnosis of tuberculosis and allowing us to establish the true nature of the disease.

Thus, the dentist must know the main symptoms of this pathology, the principles of its diagnosis and therapy. Due to the fact that in recent years the number of HIV-infected patients has significantly increased, the knowledge of the features of the course of this lesion is of diagnostic value in the provision of dental care to these patients.



## CHAPTER 1

### CLASSIFICATION OF OROFACIAL TUBERCULOSIS

According to the current clinical classification, tuberculosis of the oral cavity and maxillofacial area refers to the extrapulmonary localization of specific inflammation and is defined with codes **A15 – A19** in the 10<sup>th</sup> revision of International Statistical Classification of Diseases and Related Health Problems (ICD)

**Tuberculosis of other organs (A15.8** — bacteriologically and histologically confirmed; **A16.8** — without mentioning bacteriological or histological confirmation): tuberculosis of the oral mucosa: tuberculosis of the tongue, tuberculosis of the gums, tuberculosis of the mucous membranes of the lips and buccal mucosa, tuberculosis of the hard and soft palate, tuberculous lupus erythematosus, miliary ulcer tuberculosis; tonsil tuberculosis, pharyngeal tuberculosis.

#### **Tuberculosis of other organs and systems**

1. Tuberculosis of bones and joints of the facial skull (**A18.0**).
2. Tuberculosis of the peripheral lymph nodes (**A18.2**).
3. Tuberculosis of the skin and subcutaneous tissue (**A18.4**).
4. Tuberculosis of other organs: tuberculosis of the salivary glands (**A18.8**).

Patients who have mycobacterium tuberculosis – from fistulas, in smears from the mucous membrane of the oral cavity and skin of the face - detected by any method of etiological diagnosis, are considered bacteria excretors (MBT +).

Primary lesions of the oral mucosa are extremely rare, they are commonly observed in children and adolescents (less commonly, in adults who were not infected with MBT in their childhood). A specific primary infiltrative-ulcerative lesion of the oral mucosa is accompanied by an increase in regional (submandibular, submental and cervical) lymph nodes.

Secondary lesions are often associated with a specific inflammatory process in the lungs, observed in patients of any age group, more often in middle-aged and elderly patients. According to the systematic reviews of articles on this subject published in English for the period from 1950 to

2016, tuberculosis of the maxillofacial region mainly affects middle-aged men (65%) (about 40 years old), having a tuberculosis history in 25% of cases. The share of children and adolescents aged 1 to 17 years is about 20% [1, 2].

Tuberculosis can have any localization in the oral cavity. More often, it occurs on the mucous membrane of the buccal mucosa, in the vestibule of the oral cavity, on the gums, palate and tongue. The retromolar region is less commonly affected by a specific process.

Morphologically, tuberculous inflammation in the mucous membrane of the oral cavity manifests itself in the form of various elements, such as edema with hyperemia (infiltration), erosion, fissures, ulcers, whitish-yellow tubercles, periapical granulomas.

Inflammatory elements can be singular and multiple. Erosions and ulcers can be shallow or some millimeters deep, oval or oblong, with underlined scirrhous edges, with necrotization in the central part and with edema and hyperemia in the periphery.

In addition to changes in oral mucosa, tuberculous inflammation affects the craniofacial bones, salivary glands and peripheral lymph nodes with the formation of extra-oral fistulas.

## CHAPTER 2

### DIAGNOSIS OF TUBERCULOSIS

Diagnosis is the process of recognizing a disease and assessing the individual biological and social characteristics of a subject, including targeted medical examination, interpretation of the results and their generalization in the form of a diagnosis.

The main principle of the diagnosis of tuberculosis is the identification of direct signs that make it possible to establish the etiology of the disease (MBT), and indirect manifestations that reveal the effects of the etiological agent on the patient's body.

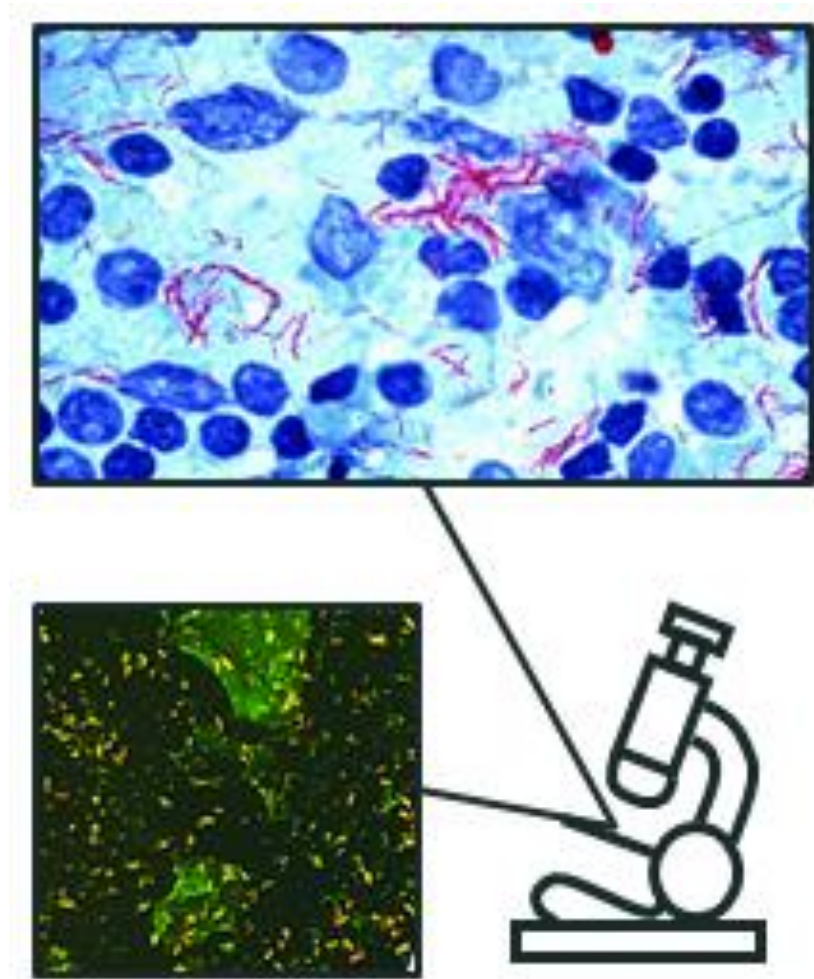
In case of tuberculosis, direct methods include microbiological diagnostic technologies (microscopy and culture) and molecular genetics methods (MGM), which determine the presence of deoxyribonucleic acid (DNA) of the pathogen in the diagnostic material (sputum, urine, feces, discharge from fistulas, and also smears and prints from scrapings of pathologically changed tissues and exudates, including oral mucosa). The etiological diagnosis of tuberculosis is the basis of diagnostic measures for tuberculosis of the respiratory system. The priority is to confirm / exclude the presence of MBT in the diagnostic material by methods with the maximum available sensitivity and specificity. In order to minimize the likelihood of discrepancies in the results obtained by different methods, a comprehensive study should be carried out from one sample of diagnostic material.

#### **Microscopic diagnosis of tuberculosis:**

- Ziehl-Nielsen microscopy;
- luminescent microscopy;
- LED microscopy.

**With simple / light bacterioscopy**, the diagnostic material is stained by the Ziehl-Nielsen method. MBT do not accept conventional aniline dyes, as a result of which acid-resistant mycobacteria are stained in raspberry red, and other microorganisms and cell-based sputum cells are blue. Microscopic examination does not allow differentiating MBT from non-tuberculous mycobacteria (NTM); therefore, the result of the study deter-

mines the presence or absence of acid-fast bacteria (AFB) (Fig. 2). AFB under the microscope look like oblong rods, pink-colored on a blue background.



**Figure 2. Microscopic results of diagnostic material for the detection of acid-resistant mycobacteria: Ziehl-Nielsen staining (top) and fluorescent dyes (bottom)**

***Method Advantages:***

- allows you to quickly (within 1 hour) and with minimal financial costs to identify the most epidemiologically significant patients with tuberculosis and evaluate the intensity of bacterial excretion;

***Disadvantages of the method:***

- the diagnostic sensitivity of the microscopy method is usually not more than 50%, as it allows you to identify the pathogen if 1 ml of sputum contains at least 5,000-10,000 MBT.
- with a small amount of MBT in sputum, the method is ineffective.
- lack of differentiation of MBT from NTM.

**Fluorescence microscopy** – optical research of microobjects stained with special dyes (fluorochromes) emitting a glow when exposed to ultraviolet rays. The essence of the method is the ability of MBT, stained with special fluorescent dyes (auramine, rhodamine), to glow when irradiated with ultraviolet rays. A luminescent microscope is used at low magnifications. As a result of staining against a dark background, golden-yellow MBT are determined.

***Method Advantages:***

- the ability to conduct research with small magnifications of the microscope, which allows viewing more fields of vision in a short time;
- the probability of detecting MBT is increased by 10-15% compared with conventional bacterioscopy.

***Disadvantages of the method:***

- lack of differentiation of MBT from NTM.

**Bacteriological culture methods** are based on the cultivation of MBT contained in the diagnostic material on dense (Fig. 3) and liquid artificial media.

For MBT, a long cultivation time (up to two or more months) and specific requirements for the composition of the nutrient medium are characteristic. The most common for detection of MBT are dense environments based on chicken eggs — the Levenshtein - Jensen and Finn-2 environments (Fig. 3).



**Figure 3. MBT colonies grown on Levenshtein - Jensen medium**

### *Advantages of Dense Cultivation:*

- the sensitivity of the culture method is 80 - 85%, the detection is 10 - 100 MBT in 1 ml of diagnostic material.
- specificity 98%;
- species identification allows you to immediately differentiate MBT from NTM and non-specific microflora;
- determination of the mass of bacterial excretion by counting the number of colonies grown in test tubes;
- determination of drug sensitivity (DS) of MBT to 4 first-line anti-TB drugs: to isoniazid, rifampicin, ethambutol, streptomycin; to 7 anti-TB drugs of the 2<sup>nd</sup> line: to kanamycin, ofloxacin, ethionamide, protionamide, capreomycin, cycloserine, PAS.

### *Disadvantages of the method:*

- a long period of obtaining results (from 1 to 3 months).

**Liquid media** (especially Middlebrook 7H9 medium) can reduce the time of MBT cultivation. They are mainly used in automated systems such as BACTEC MGIT.

The methodology is based on the invention of the MGIT-Mycobacteria Growth Indicator Tube, in the bottom of which a fluorescent oxygen sensor is integrated.

The contents of the MGIT are a nutrient broth, due to which a more efficient excretion of mycobacteria and their accelerated growth is achieved. The tube contains 7 ml of Middlebrook 7H9 sterile nutrient broth, which is supplemented with an enrichment supplement to stimulate MBT growth before use. The bottom of the tube contains an oxygen-dependent fluorochrome dye. During bacterial growth, O<sub>2</sub> is absorbed and is replaced by CO<sub>2</sub>. As O<sub>2</sub> is consumed, the inhibition of fluorochrome is terminated. The fluorescence becomes visible under UV irradiation and is automatically detected by the device photosensors. Glow intensity is recorded in growth units (GU). On average, the appearance of MBT growth is up to 11 days. The device evaluates the sample as negative in the absence of growth for six weeks (42 days). The growth data is entered into the computer, where it can be saved. Computer analysis of growth curves can provide the information on the presence of various mycobacteria pools, including non-tuberculosis, and also helps to evaluate the growth properties of mycobacteria.

### ***Advantages of the Method:***

- high sensitivity and specificity;
- productivity (up to 8000 tests per year);
- automatic monitoring of MBT growth and detection of drug sensitivity;
- automatic quality control;
- determination of MBT drug sensitivity for 5 first-line anti-TB drugs: isoniazid, rifampicin, ethambutol, streptomycin, pyrazinamide; to 10 anti-TB drugs of the 2<sup>nd</sup> line: amikacin, capreomycin, ofloxacin, levofloxacin, protionamide, moxifloxacin, ethionamide, protionamide, linezolid, kanamycin, PAS.

### ***Disadvantages of the method:***

- it is necessary to use expensive nutrient media for cultivating;
- the complexity of processing pathological material;
- a third level laboratory is needed.

**Molecular genetics methods** are based on the polymerase chain reaction (PCR). PCR is a molecular biology method that allows in vitro to achieve a significant increase (amplification) of low concentrations of certain (specific) DNA fragments in an almost unlimited amount.

#### ***Types of PCR:***

- Real-Time PCR;
- PCR with further hybridization on biological microarrays;
- PCR with further hybridization on strip membranes (Line Probe Assay);
- PCR in cartridge (GeneXpert).

### **Stages of PCR:**

**Stage 1.** Isolation of DNA from Mycobacterium cultures.

**Stage 2.** PCR amplification of mycobacterium gene fragments.

**Stage 3.** Hybridization of PCR products with DNA probes immobilized on a test strip. Such DNA probes are DNA sections strictly specific for each type of mycobacteria.

**Stage 4.** Visualization of the results of hybridization; in this case mycobacteria belonging to a certain species is determined.

The conclusion about the presence of MBT in the diagnostic material is based on the detection of MBT DNA, and the conclusion on drug re-



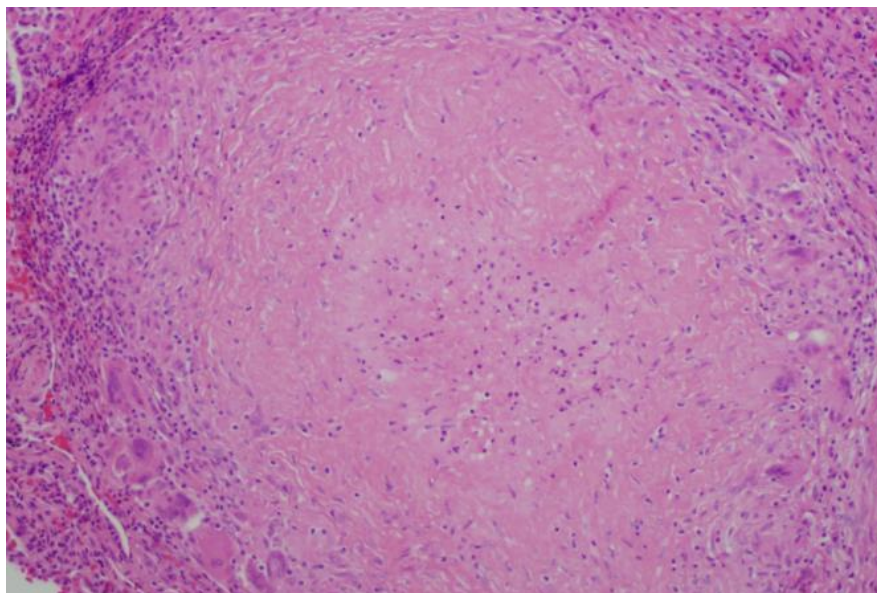
sistance is based on the detection of mutations in the target sections of the MBT genes associated with drug resistance.

***Advantages of MGM:***

- high sensitivity, less than 10 microbial bodies per 1 ml of material are needed;
- quick results;
- high specificity;
- obtaining a positive PCR result does not require additional identification of MBT from NTM;
- automated sample preparation (for GeneXpert system);
- contamination at any stage of the device operation is excluded (for the GeneXpert system).

A sufficient basis for the etiological confirmation of the diagnosis may be the detection of MBT in at least one sample. A single detection of MBT DNA without confirmation by microscopic or cultural methods requires careful interpretation of the positive result and coordination with clinical and anamnestic data.

Reliable signs of tuberculous inflammation include **morphological (histological) studies** of the affected organ with the identification of a typical tuberculous granuloma (Fig. 4).



**Figure 4. Tuberculosis granuloma**

Its center is formed by amorphous tissue detritus - caseosis (result of alteration); along the periphery there is a granulation shaft of epithelioid cells, among them large multinucleate Pirogov-Langhans cells (the result



of type IV hypersensitivity, proliferation; nonspecific for tuberculous inflammation, they are found in other granulomatoses); in the lower layer of the tubercle are lymphoid and plasmatic cells, fibroblasts.

Tuberculosis does not have specific signs, its clinical manifestations are diverse, the disease can affect various organs and tissues, sometimes localizing in several organs simultaneously. The main condition for the correct diagnosis of tuberculosis in the absence of a direct etiological factor of the disease is a comprehensive examination of the patient with the analysis of clinical, anamnestic, radiological, laboratory and instrumental methods of research.

*Indirect criteria for establishing a diagnosis of tuberculosis are based on the following data:*

- medical history: the duration of intoxication symptoms and other complaints, episodes of hemoptysis, lack of effect from non-specific treatment, contact with a patient with tuberculosis;
- immunodiagnostic tests (positive skin and / or in vitro);
- laboratory data: moderate inflammatory changes in the general blood analysis, lymphocytosis, anemia;
- X-ray data: an increase in intrathoracic lymph nodes, the presence of focal, infiltrative, cavitory lesion in the lung tissue, the presence of sequestra, cavitory lesion in bone structures with a satisfactory general condition of patients.

**The immunodiagnosis of tuberculosis** is carried out with the aim of detecting the sensitization of the body (infection) to MBT. Depending on the test method, they are divided into two groups: “in vivo” and “in vitro”, and various biological substances (antigens) are used to formulate these tests - tuberculin with 2 tuberculin units (TE) PPD-L (Mantoux test), recombinant tuberculosis allergen (RTA) in standard dilution (diaskintest) antigens ESAT-6, CFP-10, TB7.7 (so-called IGRA tests (Interferon Gamma Release Assays-IGRAs)) - T-SPOT.TB and QuantiFERON-TB, which are based on the detection of secretion of interferon-gamma (IFN- $\gamma$ ) by peripheral blood mononuclear cells as a result of their interaction actions with the corresponding specific proteins of mycobacterium tuberculosis).

Allergy to tuberculin and a recombinant tuberculosis allergen is a phenomenon of increased sensitivity of the slow type to MBT antigens. At the site of intradermal administration of allergens, a specific delayed-type allergic reaction develops in the form of an infiltrate in 24-72 hours. Pathomorphologically, the infiltrate is characterized by edema of all skin

layers with a mononuclear and histiocytic reaction. The peak of the reaction occurs at 48-72 hours, when the non-specific component is minimal and the specific component reaches a maximum. The result of the reaction (hyperemia, papule, infiltrate) characterizes the degree of allergy - a change in the sensitivity or reactivity of the body to tuberculin, but is not a criterion for assessing immunity.

Immunological tests make it possible to detect the fact of infection of a human MBT, to determine the presence of actively propagating virulent strains of the MBT, to decide the question of the effectiveness of vaccination against tuberculosis, the risk of developing the disease, the need for preventive therapy. The tests help in the differential diagnosis of tuberculosis, determine the activity of the tuberculosis process and etc. Currently, in the Russian Federation, the Mantoux test with 2TE is used to select individuals for BCG revaccination and to detect MBT infection in children under 7 years old, from 8 to 14 years old, a diaskintest is performed to screen for active tuberculosis infection. IGRA tests are alternative in vitro tests. Comparative characteristics of immunological tests are presented in table 1.

**Table 1****Comparative characteristics of immunological tests**

<b>The properties</b>	<b>Diaskintest</b>	<b>QuantiFERON-TB</b>	<b>T-Spot.TB</b>
Antigens (specific, absent in BCG and other NTM strains)	ESAT-6, CFP-10	ESAT-6, CFP-10, TB7.7	ESAT-6, CFP-10
Test procedure / number of visits to the doctor	Intradermal test / 2 visits	Determination of free IFN- $\gamma$ in blood serum; 1 visit	Calculation of the number of active lymphocytes producing IFN- $\gamma$ ; 1 visit
Specialized laboratory required	No, in vivo test; clinical interpretation	Yes, in vitro test, fresh blood sampling is needed	Yes, in vitro test, fresh blood sampling is needed to isolate mononuclear cells
Effect of BCG vaccination on test result	Not	Not	Not
Booster effect	Not	Not	Not
Threshold values	Unique (there is a dubious result)	Unique (there is a dubious result)	Unique (there is a dubious result)
Differences between LTBI and active tuberculosis	Not	Not	Not
MBT infection timing (recent or prolonged)	No differences	No differences	No differences
MBT correlation	Yes direct	Yes direct	Yes direct
Immunosuppression accuracy (including HIV)	With CD4 + less than 350-200 cells / $\mu$ l –anergy	High, there may be false negative results with CD4 + less than 200 cells / $\mu$ l	High
Sensitivity *	94-99%	73-82%	86-93%
Specificity **	94-99%	94-100%	86-100%

Note \*: percentage of positive cases of tuberculosis confirmed by culture methods;

\*\* : the percentage of negative cases in people at low risk of contracting tuberculosis.

### **Interpretation of Diaskintest results:**

- negative - no infiltrate or hyperemia;
- doubtful - hyperemia of any size;
- positive - in the presence of an infiltrate (papule) of any size;
- hyperergic - in the presence of an infiltrate of 15 mm or more in size, or vesicles, necrosis, lymphangitis of any size.

A positive test result with RTA and / or in vitro testifies in favor of an actively metabolizing population of MBT (breeding), which requires a more thorough examination to exclude the local form of tuberculosis. In order to diagnose a disease of any localization, it is recommended to use RTA or alternative in vitro tests - IGRA tests. The sensitivity of these tests in patients with extrapulmonary localization of the tuberculosis process is low, 6-20%.

Immunological diagnostic tests in people with HIV infection with a CD4-lymphocyte count of less than 350-200 cells /  $\mu$ l cannot be an informative method for diagnosing tuberculosis, since in almost 90-95% of cases they give a negative result.

A diagnosis of tuberculosis is considered **probable** if there are clinical signs suspicious for tuberculosis and a positive test with a recombinant tuberculosis allergen or other positive tests for determining the release of gamma interferon (IGRA tests).

A diagnosis of tuberculosis is considered **established** if the patient has clinical and radiological signs of the disease, but there is no bacterial excretion and histological confirmation of the diagnosis.

The diagnosis is considered **verified** if the patient, along with the clinical, laboratory and radiological signs of tuberculosis, has the MBT identified by any microbiological and molecular genetic method and / or the results of a histological examination are obtained, indicating the presence of tuberculous granuloma in the affected organ.

If MBT is detected without clinical, radiological, and laboratory signs of the disease, an in-depth examination using instrumental diagnostic methods is required. A single detection of AFB by microscopy or MBT DNA using molecular genetics methods (MGM) in the absence of other signs of the disease requires dynamic monitoring of the patient.

Studies of extrapulmonary diagnostic materials are carried out with the aim of differential diagnosis of tuberculosis of extrapulmonary localization with other diseases in specialized medical institutions. The priority is to confirm / exclude the presence of MBT in the diagnostic material by

the methods with the maximum available sensitivity and specificity. In this regard, the main methods are culture studies of pathological material on liquid and solid nutrient media and MGM. PCR and the automated system BACTEC MGIT are mainly used.

### **Tuberculosis risk factors:**

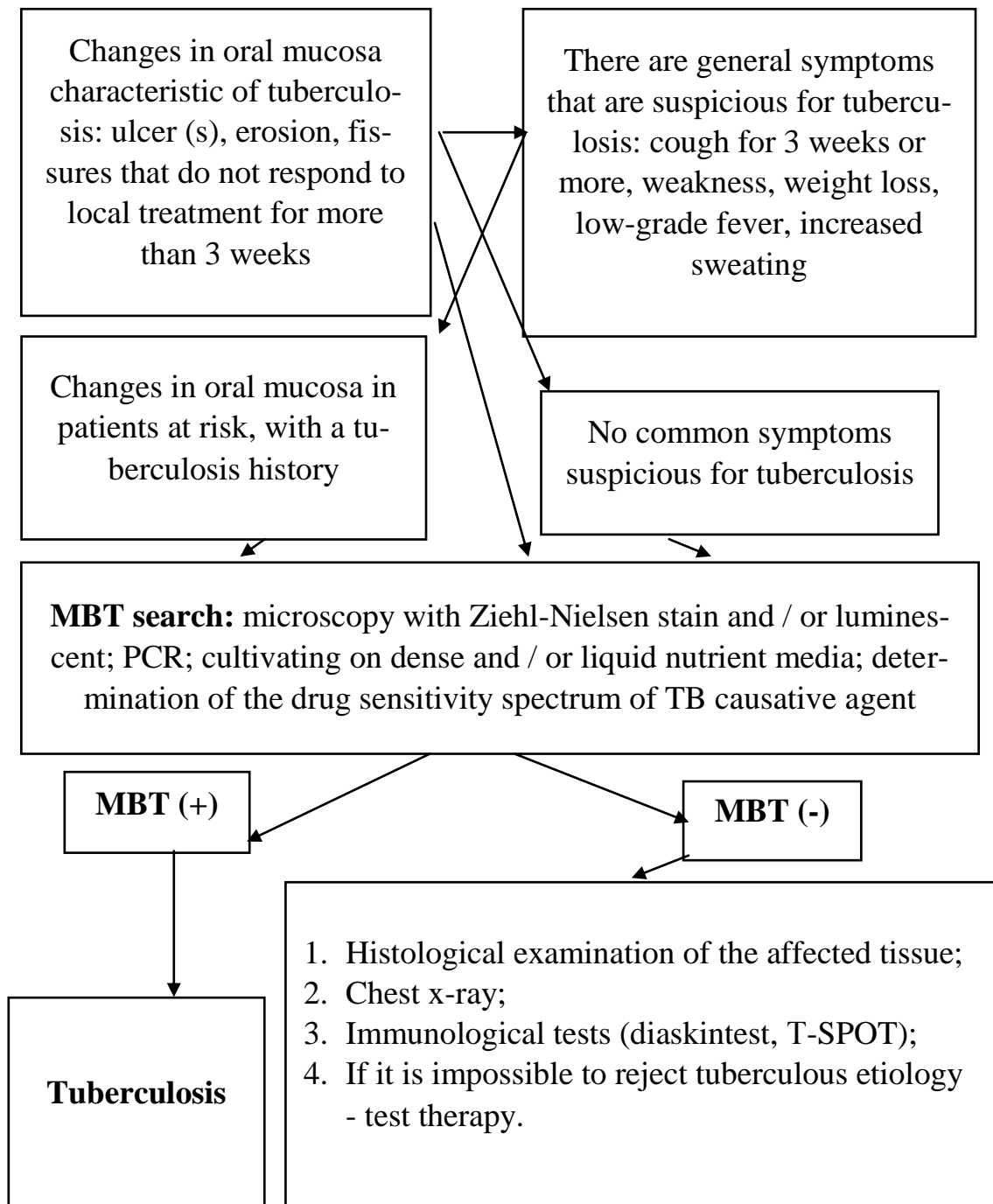
- patients with recurrent or chronic diseases of the bronchopulmonary system, patients with pneumoconiosis;
- patients with diabetes mellitus, gastric ulcer or duodenal ulcer, diseases of the genitourinary system;
- patients suffering from alcoholism, drug addiction;
- HIV-infected patients;
- patients receiving long-term corticosteroid, radiation, cytostatic and immunosuppressive therapy;
- women during pregnancy and in the postpartum period;
- people under investigation held in places of serving a sentence of imprisonment, in places of detention, as well as released from custody, during 2 years of observation;
- people released from the dispensary observation in specialized anti-tuberculosis medical facilities due to recovery from tuberculosis, during the first 3 years;
- people who contact patients with tuberculosis (during household contacts – those living in the site of tuberculosis infection, and professional contacts – medical workers).

In patients from biomedical risk groups, due to a decrease in the body's resistance, tuberculosis can develop very quickly, therefore, they must undergo preventive examinations (fluorography once a year, from the age of 15, and immunodiagnostics for those under 15). The HIV-infected, people with tuberculosis, those who were in contact with TB patients, as well as those under investigation and serving sentences must undergo fluorography twice a year.

### **Algorithm for the diagnosis of orofacial tuberculosis**

Orofacial tuberculosis does not have specific symptomatology and is characterized by various clinical manifestations, which creates a serious problem for the timely diagnosis of this localization of a specific process. Thus, it is necessary:

1. To study a patient's complaints - ulcerations in the oral cavity or on the skin, prolonged cough, low-grade fever of unclear etiology for 3 weeks or more, hemoptysis, pain in the chest during breathing, toxic-allergic reactions on the skin and mucous membranes (phlyctena, keratoconjunctivitis, blepharitis, erythema nodosum), intoxication syndrome.
2. To take a patient's anamnesis - past tuberculosis, tuberculous contact, biomedical and social risk factors, ineffective treatment with conventional methods.
3. To physically examine a patient's oral cavity - palpation, dioscopy, sounding.
4. To do X-ray examination of the chest organs, if required of the skull bones; to do CT and MRI.
5. To do three-fold microbiological examination of sputum or pathological material (ulcer discharge, node aspirate, skin scratch, etc.) for AFB, culture and MGM to determine the drug resistance test.
6. To do an immunological test with a tuberculous recombinant allergen (diaskintest).
7. To do morphological and cytological examination of available pathological material (pleural exudate; bronchoscopy material, ulcer biopsy sample, peripheral lymph node biopsy sample, etc.).
8. To conduct test therapy if it is impossible to reject the tuberculous etiology of the disease, as well as if there is a high risk of an unfavorable outcome (1-2 months) (Fig. 5).



**Figure 5. Algorithm for the for the diagnosis of maxillofacial tuberculosis**

## CHAPTER 3

### TUBERCULOSIS OF THE ORAL MUCOSA

The primary tuberculosis process in OM occurs extremely rarely, it can be detected in about 1% of adult patients with pulmonary tuberculosis.

The inflammatory manifestations of the tuberculosis process may be the appearance of hyperemia, edema, cracks and / or ulcers on the oral mucosa. In this regard, there are two morphological forms of OM tuberculosis – infiltrative and ulcerative. The specific inflammatory process in the form of an ulcer is detected most often.

The infiltrative form is characterized by local or widespread inflammation of the tissues. On examination, a roundish, dense or doughy palpation formation with an uneven surface is determined, often brightly hyperemic, but sometimes it can also have a gray-pink hue.

With an ulcerative form of the OM tuberculosis, either small cracks located in the folds or ulcers (from superficial to deep) are found. An obligatory companion of erosive and ulcerative manifestations of the inflammatory process is a pronounced surrounding edema. The edges of the ulcers are uneven, soft, but can sometimes be dense. The bottom is covered with granulations, which often bleed; there may be gray-yellow miliary rashes (nodules) around.

The pain with an ulcerative form of OM tuberculosis is moderate and may appear when chewing or be constant and disturb the patient regardless of food intake. Regional lymphadenitis is characteristic (with primary tuberculosis), submandibular and cervical lymph nodes are mainly affected, they are painful on palpation and dense.

Specific ulcerative changes must be differentiated from a fixed drug enanthema, secondary recurrent syphilis of OM, lichen planus, candidomycosis, chronic recurrent aphthous stomatitis, Wegener's granulomatosis, viral lesions, trophic ulcers in endocrine and cardiovascular diseases, precancerous and cancerous (table 2).



**Table 2****Differential diagnostic criteria for the defeat of OM**

<b>Signs</b>	<b>Tuberculosis</b>	<b>Wegener's granulomatosis</b>	<b>Candidiasis</b>	<b>Syphilis</b>
Intoxication syndrome	Subfebrile condition	Yes	Yes	Not
Characterization of inflammatory elements in OM	Ulcers, cracks with underlined soft edges on the background of hyperremission and edema	Ulcers, hyperplastic gingivitis, often - perforation of the palate	Erosions with jagged, poorly differentiating edges	A round, oval ulcer with dense, roll-shaped edges
Soreness	Not	Yes	Yes	Not
Consistency	Varies	Varies	Test	The base is dense
Coloring	Varies from pink to red	Pale red	Bright red	Red
Bleeding	Yes	Yes	Yes	Not
Soreness	Yes	Yes	Yes	Not
Discharge	Bloody yellow, gray	Purulent or bloody	White grains, caseous pellicle	No, sometimes transudate
Lymphadenitis	Yes	Not	Yes	Yes
Necessary research	Bacteriological and cytological	Definition CACA*, histological	Bacteriological and cytological	Bacteriological and cytological

CACA\* - classic antineutrophil cytoplasmic antibodies

Extremely rarely scrofulotuberculosis, or scrofuloderma is observed, when nodes are formed in the deep layers merged with the mucous membrane, without a pronounced inflammatory reaction. The nodes gradually increase, soften and open. Irregularly shaped, slightly painful ulcers with underlined edges are formed. The bottom of the ulcers is covered with flaccid granulations and a grayish-yellow coating. After ulcer healing, retracted, disfiguring scars form.

## **Tuberculosis of the tongue, buccal mucosa, gingivae, lips**

The disease can develop both primary and secondary, for example, in a patient with pulmonary tuberculosis, when infected sputum enters the damaged tongue mucous or when the process is localized on the oral mucosa, tonsils, or hematogenously, with dissemination of the causative agent of tuberculosis.

Tuberculosis inflammation can affect the tip of the tongue, its lateral edges, back, midline and base of the tongue. The lateral surface and the tip of the tongue are affected more often than its upper part. In a common process, inflammation can cover the entire tongue, passing to the root. With tuberculosis of the base of the tongue, inflammation can go to the mucous membrane of the buccal mucosa and gums.

First, a dense infiltrate is formed, which subsequently turns into an ulcer. Ulcers, as a rule, are single, less often there is extensive ulceration with severe swelling of the oral mucosa and enlargement of the regional lymph nodes. Miliary-ulcerative nodules and micro abscesses may appear next to the ulcer. If the process is productive, ulcers can be with granulations, with clear boundaries, and less painful. In addition, tuberculomas can form in the tongue. They occur more often on the lateral surface of the tongue, but can be found both in its thickness and on the surface of the tongue.

Similarly, a specific process in the lips and buccal mucosa can occur in patients with pulmonary tuberculosis when infected sputum gets on damaged mucous membranes or skin; less often - hematogenously, or when the process spreads from the mucous membrane of the palate, tonsils, that is, from adjacent regions of the oral cavity. Most often, there are ulcerations, the favorite localization of which is the mucous membrane of the lips. At first, there is a single dense formation of irregular shape, somewhat rising above the epithelium. Then the process ulcerates and can spread to the mucous membrane of the oral cavity. As a result, erosion transforms into typical tuberculous ulcers.



Symptoms, as a rule, will depend on the area of the lesion. Rarely, the process proceeds without pain. If the ulcers are not deep and are in the folds of the tongue, painful sensations will hardly be expressed. In common processes, acute pain is characteristic, which occurs during both chewing, tongue movement, and persists, albeit of less intensity, at rest. Also, characteristic are hypersalivation, restriction of tongue mobility, and the appearance of an unpleasant aftertaste. Pronounced pain syndrome and

swelling of the tongue prevents its mobility, and this, in turn, distorts speech, the pronunciation of sounds becomes incorrect. Dysarthria is characteristic.

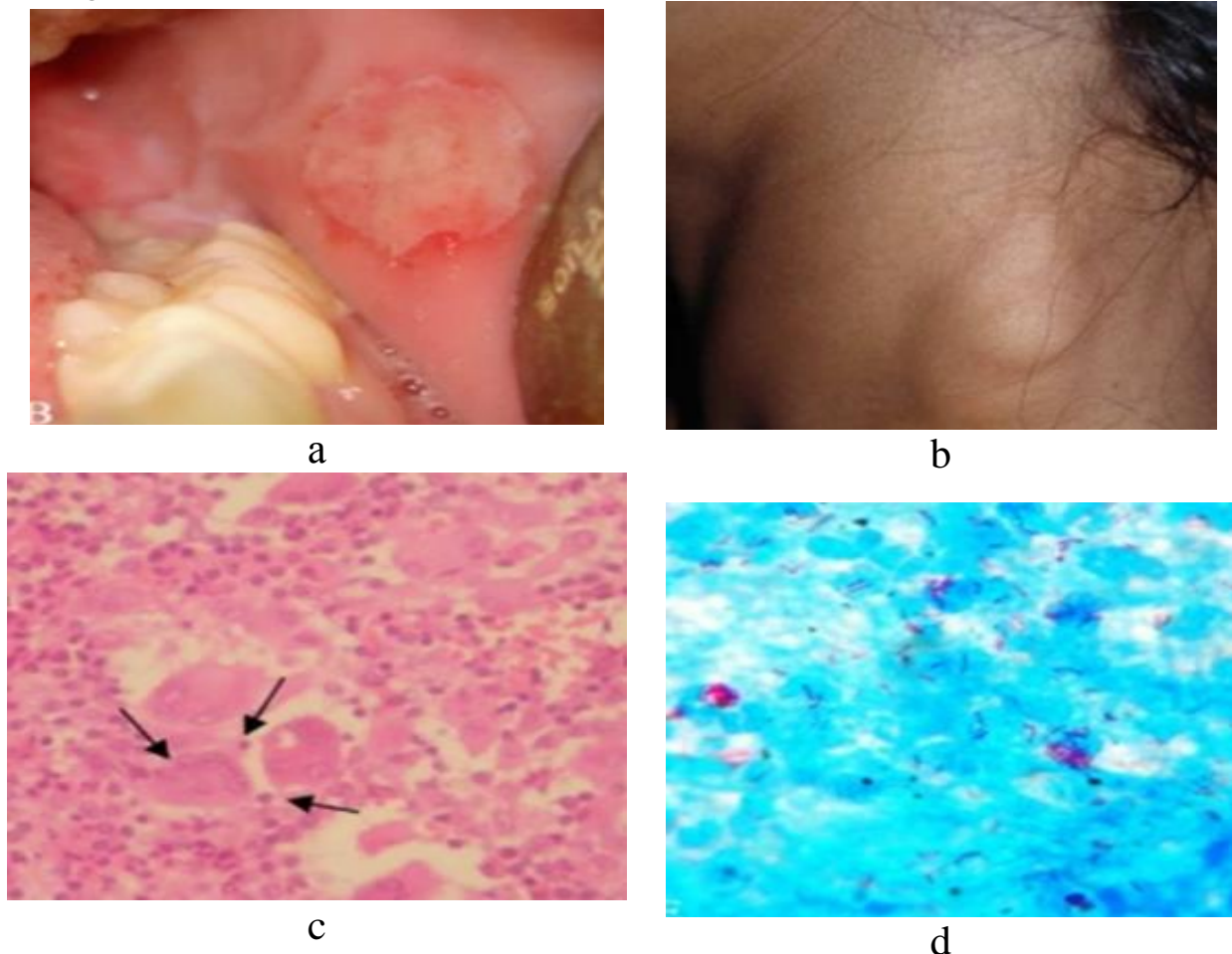
Anamnestic data (contact with a patient with tuberculosis, a previous illness) and detailed clinical, laboratory and instrumental examination suggest the correct diagnosis (table 3).

**Table 3**

**Differential diagnostic characteristic of  
oral mucosa tuberculosis and aphthous stomatitis**

<b>Signs</b>	<b>Tuberculous ulcer</b>	<b>Aphthous ulcer</b>
Anamnesis	Past tuberculosis, contact with a patient with tuberculosis	Viral infections, mechanical trauma, poor hygiene, lack of B vitamins, allergies, foci of chronic infection, heredity
Age, gender	35-50 years old, men more often than women	20 to 40 years old, women more often than men
Incubation period	from 1 to 4-6 weeks	from 4 to 8 days
Inflammatory elements	Ulcer - 1-1.5 cm with uneven edges, a friable bottom, with easily bleeding granulations, small abscesses (Trel grains) around, painful, a tendency to peripheral growth, do not respond to conventional treatment 	Aphthae are single (1-3) oval or round in shape, have clear boundaries in the form of a narrow red border with a grayish-yellow bloom in the center, are painful, respond to local treatment 
Cytology	Caseous necrosis, epithelioid infiltration with the inclusion of Langhans cells	Leukocyte infiltration, intercellular edema, epithelial necrosis
Diaskin test	Positive, doubtful	Negative

The final diagnosis can be made on the basis of a set of examinations with the clarification of risk factors, radiography data (for example, in the case of a combination of a specific process for oral mucosa and pulmonary tissue) and histological / microbiological examination of pathological material (Fig. 6).



**Figure 6. Verified (histology (c) with the stain of biopsy material according to Ziehl-Nielsen (d)) primary tuberculosis of buccal mucosa: tuberculosis ulcer of the left cheek (a), enlarged cervical lymph node on the left (b) [3]**

Thus, a tissue biopsy followed by morphological examination remains the «gold» standard for the diagnosis of oral mucosa tuberculosis.

If the patient has a dense, painless, gray-pink dense formation with a wide and dense base, medium or coarse, with clear boundaries, significantly protruding above the level of the unchanged mucosa, then there is a need for differential diagnostics in order to exclude, first of all, malignant neoplasms. This requires a biopsy of the affected tissue, followed by histological examination.

**Malignant neoplasms of the oral cavity** are a neoplastic process of tissues of the oral cavity that occurs primarily or secondarily (as a result of

metastasis), or as a result of the spread of a tumor process located in neighboring areas, such as the nasal cavity or sinus.

The risk factors for developing malignant neoplasms of OM are chronic traumatic effects on the oral mucosa (sharp edges of the fillings, uncomfortable dentures), eating certain food additives with food, or frequent contact with chemicals (pesticides, asbestos), infection with the human sixteenth-type human papilloma virus, presence of lichen planus of the oral mucosa, genetic predisposition, and smoking (tobacco contains about 20 identified carcinogens). Smoking also contributes to the irritation of the mucous membranes with smoke and heat from cigarettes, cigars or pipes, especially if it is combined with increased alcohol consumption. Chewing tobacco also contributes to chronic irritation of the oral mucosa.

Pretumor processes are Bo-Wen's disease, Verrucous leukoplakia, papillomatosis, leukocerosis.

Oral cancer can occur in various parts of the oral cavity and have different forms (ulcerative, papillary and nodular) and histological types. The following options are identified predominantly:

- epithelioid carcinoma (usually squamous cell carcinoma);
- teratoma;
- salivary gland adenocarcinoma;
- lymphoma;
- melanoma of oral mucosa pigment cells.

The neoplastic process in the oral cavity is most often localized on the lips, tongue, and, somewhat less often, at the base of the oral cavity, on the inner surface of the lips, gums, as well as the salivary gland, hard or soft palate. Malignant neoplasms go through three phases of development: the initial (unclear pains, tightening of the mucosa), the developed stage (ulcers over the tightening, constant pain), advanced (destruction of surrounding tissues).



### **Symptoms Suspicious for Oral Cancer:**

- non-healing ulcers or infiltration with ulceration, often painless and long lasting;
- pain in the oral cavity, which becomes chronic;
- restraint of the tongue movements (violation of the tongue mobility);
- reflex otalgia (earache);
- lack of sensitivity in the innervation zone of the mandibular nerve, unexplained numbness of the gums and some teeth, bleeding of the gums;
- difficulty swallowing (dysphagia and odnofagiya);

- an increase in cervical lymph nodes (table 4).

**Table 4**

**Differential diagnostic characteristics of tuberculosis of the tongue and squamous cell carcinoma**

Signs	Tuberculosis of the tongue	Squamous cell carcinoma of the tongue
Age, gender, localization	35-50 years old, men more often than women, more often dorsal surface	Elderly, men more often than women, more often lateral surface
Pain syndrome	Sharply painful	Painless in the beginning, there may be numbness of the tongue, then constant dull pain
Inflammatory elements	At the beginning of the process, there is usually a dense infiltrate, which later, decaying, forms an ulcer with underlined edges	Initially, a painless nodule that grows rapidly, forming a node or papillary dense growths with viscous bloody decaying masses
		
Cytology	Epithelioid cell granulomas with inclusion of Langhans cells	Atypical epithelial cells, pronounced keratinization of individual cells with the formation of horny "pearls"
Ziel-Nielsen biopsy stain	AFB+*	AFB -

\*AFB – Acid Fast Bacteria



Cancer of the mucous membrane of the buccal mucosa and alveolar processes of the lower jaw metastasizes to the area of the submandibular lymph nodes. Formations that arose in the distal regions give metastases to the nodes near the jugular vein. The tongue cancer progresses to the lymph nodes of the neck, and can capture the submandibular nodes. Distant metastases spread to the internal organs: liver, lungs, brain, heart, and to bone tissue.

### **Tuberculosis of hard and soft palate**

Tuberculosis of hard and soft palate is a rare disease, but nevertheless it is necessary to know its clinical manifestations in order to differentiate them from other chronic inflammations of this localization. When examining the oral cavity, you can find a polymorphic picture, which depends on how long the disease has developed. More often than not, ulcers (from one to three) are formed on the border of the hard and soft palate in the form of scattered roundish whitish small elements surrounded by a zone of hyperemia.

In this case, you can find both superficial and deep ulcers that can necrotize and destroy the underlying bone tissue, forming tuberculous osteomyelitis. If the former look like surface defects on the mucosa, the latter, deep, with uneven edges with a granular bottom, are clearly demarcated from healthy tissue by indurative hyperemic edema (Fig. 7).



**Figure 7. Verified perforating tuberculosis ulcer of the palate. CT scan in axial projection with 3D reconstruction, visualizes erosion, and a bone defect in the back of the hard palate to the right [4]**

With hematogenous dissemination, miliary ulcerative tuberculosis is formed, most often generalization comes from the lungs with a severe progressive course of the disease. Characteristic tuberculous tubercles devel-

op, after the collapse of which ulcers form in the centers of the foci. Manifestations can be very diverse – from superficial, limited in the form of fissured ulcers with slight infiltration, especially in the soft palate, to extensive inflammation that can cross the midline, with the transition to the alveolar processes, upper trigons and tongue (Fig. 8). There are also tuberculous papillomatous ulcerative infiltrates.



**Figure 8. Verified tuberculosis of the hard and soft palate with the transition to the alveolar processes, upper trigons and tongue [5]**

It is necessary to differentiate a tuberculous ulcer on the mucosa of the hard and soft palate from chronic inflammation of the mucous glands of the palate, epidermal carcinoma, primary chancre (syphilis), fungal infection of the oral cavity.

**Chronic inflammation of the mucous glands of the palate** is manifested by local changes without general manifestations of the disease. Intoxication syndrome is uncharacteristic. On examination, sizable softly hyperemic papules are found on a hard and / or soft palate, on which, upon a detailed examination, the excretory ducts of the mucous glands can be seen. The main reason for the occurrence of this disease is the improper wearing of the upper jaw prosthesis (the anatomical features of the jaw are not observed, a special solution for treating the prosthesis, etc. is not used). Respectively, removing the prosthesis alone without any pharmacological therapy leads to the disease regression.



## **Tuberculous gingivitis**

Tuberculous gingivitis can occur both in chronic and in acute forms. The disease in a chronic form is sluggish, slightly painful, characterized by diffuse swelling of the gingival papillae, forming lobules, from right to left fangs. During an exacerbation, the symptoms of gingivitis become more pronounced and are similar to the symptoms of acute gingivitis.

Acute tuberculous gingivitis is generalized (inflammation on the entire surface of the gums) or local (a process in a certain group of teeth) and has classic signs of specific inflammation:

- initially, a painful, brightly punctured condensation with a smooth, shiny mucous surface appears on the gum, then gum swelling; on palpation of this formation with a probe, the latter easily “falls” down due to the loss of elasticity by the gingival tissue; when pressed, it bleeds easily, subsequently an ulcer forms with expanding granulations;
- pain syndrome;
- bleeding gums;
- the presence of false periodontal pockets;
- deposits in the form of tartar or plaque.

By its localization tuberculous gingivitis is classified into:

- papillary gingivitis (swelling of the gingival papillae);
- marginal gingivitis (inflammatory process of the marginal gum);
- diffuse gingivitis (attached gums).

The process usually looks like ulceration on the gum of the lunar shape in the form of a “claw strike”, painful, with thin edges, red, easily bleeding (Fig. 9).



**Figure 9. Verified tuberculous gingivitis, ulcerative form [6]**

The severity of the general manifestations of tuberculous gingivitis will be characterized by a complex of general changes in the body (intoxication syndrome), as well as the prevalence of the inflammatory process in the mucous membrane. Mild gingivitis is characterized by a lesion of predominantly interdental papillae; the process of moderate severity extends to the free (marginal) gum; severe gingivitis is characterized by inflammation of the entire gum, including the attached (alveolar) part.

Often, the disease is accompanied by regional lymphadenopathy of the submandibular, sometimes of the chin area. Lymph nodes increase in size, become soft, elastic, can be painless for a long time. Over time, fluctuation with the formation of fistulas may appear. In a laboratory study of their contents, MBT are detected, in a histological examination caseous necrosis is detected. The process ends with the formation of gross scars.

Tuberculous gingivitis is usually combined with specific lesions of any other parts of the oral cavity, spreading from the tonsils, mucous membrane of the buccal mucosa, palate, etc.

## CHAPTER 4

### LUPUS VULGARIS

The damage of the oral mucosa in the form of a specific lupus process can be combined with the damage of the face skin, or precede it, or, conversely, skin rashes can precede a mucosal lesion and then serve as the initial site of the spread of tuberculous inflammation to the oral mucous. In almost all cases, this disease occurs when the infection spreads from the skin of the facial part of the skull, mainly the paraorbital and perirhinal area. Specific inflammatory elements are localized on the skin of the face, the mucous membrane of the oral cavity (red border of the lips, gums, hard and soft palate) and the nose. The tongue is extremely rarely affected. Mostly affected are middle-aged women. The combination with tuberculosis of the upper airway and lungs is possible.

At the onset of the disease, red or yellow soft tubercles, the size of a pinhead, painless, appear on the face and / or mucous skin, with a tendency for merging with each other and for peripheral growth. As the result of the merging, lupomas are formed - slightly protruding above the surface, inelastic, having different size and outlines of formation, yellowish in color, of soft consistency, malleable when pressed on with a glass cover (Fig. 9). As it progresses, the inflammatory process develops eccentric, while the center becomes atrophic and ulcerates. In the process of inflammatory elements formation, the general condition of patients changes dramatically: weakness, malaise, emaciation, excessive sweating, hypersalivation, and a rise in body temperature are noted.

The typical local symptoms of lupus vulgaris are the “apple jelly” symptom and the Pospelov symptom, based on the ability of the lupoma to change shape and color when pressed on with a glass slide (during dioscopy) or with a button probe:

- pressing on the lupoma with the a glass slide causes a temporary blanching of the entire inflammatory complex, consisting of either one large formation (maybe up to 1 cm), or several merged due to the perifocal expansion of blood vessels. Due to this blanching, elements of yellowish-red necrosis are visible in its central parts (“apple jelly” symptom) (Fig. 10);

- when probing the surface of the lupoma, the button-like probe, when pressed, easily falls inward, confirming necrosis of the epidermis with the destruction of lupoma elastic and collagen fibers (Pospelov symptom).



**Figure 10. Lupomas and «apple jelly» symptom with lupus vulgaris [7]**

In the clinical course of lupus vulgaris of oral mucosa, there are distinguished four stages: infiltrative, tubercular, ulcerative and cicatricial. Lupus lesions of the oral cavity can be combined.

The clinical picture of lupus inflammation of the oral mucosa includes four types of lesions:

- marginal, covering the gingival margin first in the form of a common infiltration and then turning into a tubercle-erosive (ulcerative) form. In this case, the gingival margin and interdental papillae swell sharply, the gingival margin is smoothed, and the mucous membrane of the gums acquires a bright red color. The gums seem to be poked with pins, painless, dull, slightly bleeding;
- supramarginal: infiltrative or tubercle-ulcerative lesions do not affect the gingival border;
- total, when the process extends to the entire outer surface of the gums as an infiltrative, often erosive, and sometimes ulcerative lupus. In this form, the bone tissue of the alveoli is often affected and hypertrophic lupose gingivitis may develop;
- bilateral, proceeding as ulcer lupus.

A specific inflammatory process in the form of lupus vulgaris with lesions of the upper lip develops gradually and does not tend to spontaneous healing. Lesions of the lips mucous membrane occur in an ulcerative form, accompanied by significant swelling and pain during movement. The dis-

ease begins with the appearance of multiple papular elements of red color, which then take a yellowish tint. They merge, forming ulcers with irregular-shaped edges, the bottom of which is covered with a dirty gray coating or papillomatous overgrowing granulations, which sometimes resemble bright juicy raspberries. On the surface of the ulcer of the lip red border, crusts are often formed, sometimes quite thick. Subsequently, superficial cicatricial atrophy remains at the site of ulcerative lesions, with the formation of coarse cicatricial tissue together with the formation of so-called wedge-shaped deformity leading to the contraction of the lateral parts of the upper lip, which complicates the process of eating, speaking, and disfigures the face. The reappearance of new lupomas on the scar is characteristic. In places of secondary ulceration, connective tissue scars, even more disfiguring and rough, can form. Sometimes fistulous passages form in the labial area or at the level of the gums.

The development of pathological mobility of the teeth during the destruction of the interdental septa due to the destruction of the jaw alveolar tissue is possible. In the absence of treatment, the process takes a chronic character and can take several years, leading to the formation of more pronounced deforming changes. With damage to both lips, a microstomy can develop. Regional lymphadenopathy is characteristic. Lymph nodes are enlarged, dense.

Lupus erythematosus can affect the hard and soft palate. Inflammation occurs mainly in contact, the process, likewise, is ulcerous. There is no typical localization; inflammatory elements can be found separately on a hard and soft palate or have a common character. The initial forms look like a limited hyperemic portion of the mucous membrane. Subsequently, on the hyperemic and infiltrated palate appear yellowish lupomas, which merge to form ulcers, in the center of which yellowish-white contents resembling apple jelly are observed.

On the tongue, the tuberculosis process is localized in the region of its root or back. Both scattered small superficial lupomas prone to decay, destructing the surface of the tongue with small abscesses, and verrucous and papillomatous growths, which subsequently form erosions, cracks, or ulcers, are observed.

## CHAPTER 5

### TUBERCULOUS TONSILLITIS AND PHARYNGITIS

Primary pharyngeal tuberculosis practically does not occur (rarely in childhood), secondary pharyngeal tuberculosis mainly occurs as a result of the progression of a chronic specific process in the lung tissue, sputagenously or hematogenously affecting the pharyngeal mucosa and palatine tonsils. Other variants of an isolated process with this localization are identified in single cases. The following forms are distinguished: an infiltrative form, where the mucous membrane of the tonsils and pharynx is diffusely edematous with follicular hypertrophy; an ulcerative form (superficial ulcers with gray-pink granulations), mixed infiltrative-ulcerative and tuberculous lupus (typical lupomas of gray-pink color). Basically, patients are diagnosed with the first two types of inflammation.

Depending on the localization of the lesion, the symptoms of pharyngeal tuberculosis will be varied. So, if the process is localized in the nasopharynx, the patient will be bothered by nasal congestion; with the damage of the oropharynx there will be sore throat when swallowing, dry mouth, an unpleasant aftertaste. If tuberculosis affects the larynx, the patients will have complaints of hypersalivation, nausea, aggravated by eating, choking on swallowing, pain when swallowing, dysarthria, hoarseness, coughing and hemoptysis. For a pharyngeal abscess that complicate pharyngeal tuberculosis, stenotic respiration and severe dysphagia are characteristic.

The severity of the pain syndrome directly depends on the involvement of the sensory nerves that innervate the pharynx. If a specific lesion is localized in the lateral wall of the pharynx, the pain usually radiates to the ear.

According to the clinical course, acute and chronic forms of pharyngeal tuberculosis are distinguished. Acute tuberculosis of the pharyngeal mucosa is extremely rare, more often in people aged 20 to 40 years. The process is accompanied by general symptoms of intoxication with an increase in body temperature, initially from subfebrile, weakness, sore throat, and a sense of perspiration. Further, intoxication increases, the temperature becomes febrile, sore throat becomes constant, dysphagia and dysarthria appear. As a rule, the attachment of a secondary infection leads

to an unpleasant, putrid odor from the mouth. These symptoms are caused by the formation of ulcers on the mucous membrane of the posterior pharyngeal wall. Swallowing food becomes so painful that the patient prefers to refuse food altogether than endure severe pain, which leads to a sharp loss in the patient's body weight. Ulcers quickly increase in size, capture more and more areas of the mucous membrane spreading in depth.

With pharyngoscopy, swelling and hyperemia of the mucous membranes of the oropharynx, small gray-yellow tubercles, merging with each other with ulceration, are noted. The bottom of the ulcers is more often with granulations of a grayish tint, the edges are uneven, slightly raised (Fig. 11).

Chronic pharyngeal tuberculosis can occur slowly with less severe pain. It develops, as a rule, in patients with fibro-cavernous pulmonary tuberculosis. It is significantly less common as a result of the spread of the process from the tonsils, palate or gums. Often the lymph glands of the neck are involved in the process, which enlarge and become painful. General symptoms of intoxication (low-grade fever, weakness, night sweats, loss of appetite and weight loss), as well as local symptoms indicating the development of a chronic pathological process in the nasopharynx, oropharynx and / or larynx are characteristic.



**Figure 11. Verified tuberculosis of the palatine arches, tongue and posterior pharyngeal wall, infiltrative-ulcerative form [8]**

With laryngoscopy, against the background of cicatricial deformity, indicating a chronic inflammatory process, dense, painful papular rashes of yellow-red color and ulcers with uneven edges (can be raised or, on the contrary, “sag”) are revealed, at the bottom of which there are gray-yellow granulations.

The diagnosis is made taking into account the anamnesis, on the basis of morphological and bacteriological studies, clinical data, the results of X-ray and immunological examinations.

Differential diagnosis is mainly carried out with pharyngeal abscess, malignant neoplasms, pharyngeal syphilis.

**A pharyngeal abscess** occurs when a bacterial infection from the tonsils, sinuses, middle ear spreads to the lymph nodes and fiber of the pharyngeal space. A gradual increase in intoxication symptoms is characteristic - an increase in body temperature to febrile, weakness, weight loss, loss of appetite. Eating is difficult due to choking; the lump of food is swallowed with difficulty, accompanied by increasing soreness. With the development of an abscess at the level of the larynxopharynx, dysarthria occurs, and the breathing rhythm also changes - it becomes intermittent, stenotic, swelling of the neck and face is observed behind the angle of the lower jaw. Patients take the forced position of the head - it is tilted to the side on which the abscess is localized and slightly laid back. The process can lead to asphyxiation due to pus entering the larynx.

With pharyngoscopy, a fluctuating formation of a bright red color is detected. In a laboratory study of pus, nonspecific microorganisms are detected.

**Pharyngeal syphilis** is characterized by the formation of a hard pharyngeal chancre and can take three forms: erythematous, erosive, and ulcerative, localizing, as a rule, at the level of the larynx. In any form, the chancre is painless, accompanied by lymphadenitis, often unilateral. In the absence of therapy, after 1.5-2 months, papular necrosis rashes of a grayish-white color and with a hyperemic rim appear on the mucosa. Then they ulcerate, merge with each other, increasing in size. During bacterioscopy of discharge from ulcers, pale treponemas appear.

**A malignant tumor of the pharynx** is primarily manifested by a single papule, which begins to grow, resembling cauliflower, thus, it becomes difficult to swallow first solid and then liquid food. Symptomatic depends on the stage of the process. Initially, the patient is concerned about mild discomfort when swallowing and hypersalivation; an unpleasant aftertaste appears in the mouth. Subsequently, the tumor grows into the surrounding tissue and disintegrates. In metastasizing of the process, regional lymph nodes are primarily affected. The diagnosis is determined by biopsy of the altered area, followed by its cytological and immunohistochemical examination.



## CHAPTER 6

### TUBERCULOSIS OF THE TEMPOROMANDIBULAR JOINT

Tuberculous arthritis of the temporomandibular joint (TMJ) is extremely rare. The disease is considered as a bone-articular form of tuberculosis, since the spongy part of the condyles of the lower jaw is affected.

#### **TMJ tuberculous arthritis develops as:**

- bone-articular tuberculosis inflammation that occurs in the head of the joint with a transition to its synovial membrane (more often);
- a metastatic process in which MBT enter the TMJ synovial membrane by hematogenous dissemination from the primary focus of tuberculosis infection in the lymph nodes, lungs, intestines, kidneys, etc., and then into the joint cavity (rarely);
- reactive - due to the high sensitization of the body to MBT antigens, in the absence of a specific morphological reaction in the joint cavity (Poncet's disease) (rarely).

#### **Three pathogenetic forms of the disease are distinguished:**

- primary bone;
- primary synovial;
- infectious and allergic.

Cases of the spread of the tuberculosis process in localized and disseminated forms of tuberculosis of the skin or lymph nodes to the TMJ capsule are described.

During a specific inflammatory process in the TMJ, as with any localization of osteoarticular tuberculosis, three stages are distinguished:

- 1 — pre-arthritis;
- 2 — arthritis;
- 3 — postarthritis.

In the first phase of tuberculous inflammation (pre-arthritis) in the articular head of the lower jaw, as well as its branches, a specific granulation inflammation (tuberculous osteomyelitis) develops, leading to the formation of granulomas and, for a limited extent, to the destruction of bone beams. Clinically, the disease is asymptomatic and can only be diagnosed

accidentally, as the focus of inflammation is located inside the bone, and, since the bone does not have pain receptors, it does not cause pain.

The second phase, arthritic, corresponds to the spread of the process to the closing plates of the subchondral bone, the joint capsule. Destructive inflammation approaches the periosteum, a joint, or spreads into soft tissues; local and general signs of the inflammatory process appear. In the temporomandibular joint, severe pain with limited function is noted, swelling of the joint and hyperemia of the skin in this area appear.

As the process grows, especially with the prevalence of exudative inflammation, the bone beams in the area of the lesion completely collapse, as a result of which the tuberculous lesion turns into a cavity. Destruction foci, both reaching 3-4 mm, and larger bone caverns, are well visualized with radiation methods of examination (radiography, CT, ultrasound of the TMJ). The spread of the tuberculosis process to the soft tissues leads to the formation of “cold” abscesses, the autopsy of which ends with the formation of fistulas on the skin of the face and external auditory canal.

A pathogenetic feature of tuberculous lesion of bones and joints is pronounced dystrophic processes in the tissues surrounding the tuberculous lesion, which are radiologically determined as osteoporosis. The proliferation of connective tissue in the structures of the joint is manifested by bone deformation and persistent dysfunctions in the form of contractures and ankyloses. Tuberculous abscesses in the thickness of the articular head and joint cavity during “attenuation” of the main pathological process can be calcified (post-arthritic phase).

**Diagnosis of the disease comes down:**

- to a carefully collected history (past tuberculosis of any localization, the presence of risk factors with an emphasis on immunodeficiency formed due to various reasons),
- to analyzing the results of radiation survey methods;
- to analyzing the data of the main verification signs of tuberculosis - detection of mycobacterium tuberculosis in joint fluid by any methods (microscopy, cultivating on culture media, PCR) or characteristic tuberculosis granulomas in biopsy material obtained by joint arthroscopy.

**X-ray signs of TMJ tuberculosis (Fig. 12):**

- resorption of articular surfaces;
- narrowing of the joint space;
- focal or diffuse osteoporosis of the articular head;

- destruction of cortical closure plates,
- weak periosteal reaction;
- destructive cavity;
- development of fibrotic adhesions in the joint.



**Figure 12. Orthopantomogram of teeth and jaw. Verified tuberculosis of the right temporomandibular joint. The articular surface of the right condyle of the lower jaw is erosively destroyed, the joint space narrowed (arrow) [9]**

Differential diagnosis is carried out with inflammatory arthropathies (TMJ arthritis, traumatic arthritis) and deforming arthrosis.

In the comparison of different arthritis types, pronounced clinical symptoms in a non-specific process are noteworthy:

- severe unilateral pain in the joint, which intensifies with the slightest movements of the lower jaw, and decreases only in the resting state of the lower jaw;

- limited opening of the mouth to 10-15 mm (between the central incisors), the lower jaw is shifted to the side of the affected joint (deviation of the lower jaw);

- a large area of irradiation, possibly in the temporal region of the head, sometimes the neck;

- swelling, edema, or soft tissue infiltration in front of the ear tragus may occur;

- sharp pain during palpation, hyperemia and tension of the skin of the parotid region.

With TMJ arthrosis, some patients note a constant aching, dull pain, aggravated by a load on the joint, while others complain only of the appearance of pathological noises, crunching, crepitus, clicks. There may also be complaints about the need to chew food on only one side, as chewing on the opposite side causes pain and inconvenience.

On examination, asymmetry of the face is observed due to the displacement of the lower jaw towards the affected joint. Palpation and auscultation reveal crunching, crepitus in the joint. Palpation of the lateral pterygoid muscle is usually painless. When observing the movement of the incisal point while opening and closing the mouth, its displacement to the side is observed.

A careful medical history (e.g. trauma), laboratory data (rheumatoid factor) and radiation methods of examination help in differential diagnosis.

**In non-specific arthritis**, with an X-ray examination of the temporomandibular joint, a slight narrowing of the joint gap and limited osteoporosis of the bone parts of the articular surfaces can be found only 10-14 days after the onset of the disease.

**With deforming arthrosis**, a sharp deformation of the articular head and tubercle is determined due to marginal bone growths, osteophytes, hyperostoses.

## CHAPTER 7

### TUBERCULOSIS OF THE FACIAL BONES

Tuberculosis can affect the frontal and zygomatic bones, upper and lower jaws. The alveolar form of tuberculosis of the bones of the facial skull and paradont affects the bone alveoli. As a result of hematogenous or lymphogenous introduction of MBT from the primary lesion, tuberculous osteitis develops, which is a typical tuberculous granuloma, consisting of an accumulation of giant Pirogov-Langans cells and epithelioid cells, in the center of which there is caseous necrosis. The formed focus can exist for a long time in the bone, progressively evolving, without any clinical manifestations. On radiation examination, the primary osteitis is determined by the picture of melting sugar. Gradually, the tuberculosis process, growing in the bone, leads to the formation of a bone cavity.

**Tuberculosis of the frontal bone** develops painlessly but slowly progresses, forming limited or widespread destruction of bone tissue. General condition does not suffer. As the disease develops, a local swelling appears at the site of the lesion, with the pressure on which pain occurs. Then the intensity of the pain begins to increase, dull headaches appear, mainly in the frontal region, the swelling begins to fluctuate. Sometimes bone perforation occurs; with a sufficiently large size, a defect formed in the frontal bone can form a skin retraction in the area.

**Tuberculosis of the zygomatic bone** proceeds without pronounced signs of general intoxication, manifests itself in the form of a local swelling in the region of the zygomatic bone, resulting from the destruction of bone tissue and the accumulation of caseous pus under the skin. It is possible that, against the background of a satisfactory condition, the patient has complaints about swelling in the periorbital region on the one side. The skin in the projection of the zygomatic bone and above it acquires a reddish tint, is stretched, and looks “glossy”. Subsequently, the bone tissue is destroyed, which, with a long-existing process, leads to the formation of a fistula, from which a scanty grayish-white discharge appears.

**Tuberculosis of the temporal bone** also often proceeds against the background of a general satisfactory condition of the patient, being detected by chance upon palpation of a local swelling in the temporal region that

occurred during bone destruction. In the patient, as the abscess forms in the temporal bone, the opening of the mouth is sharply limited, which complicates not only eating, but also communication, as it leads to defects in the pronunciation of words and sounds.

**Tuberculosis of the lower jaw** can develop in the actual bone tissue of the lower jaw, mainly in its corner (central form) or in the region of the alveolar process (alveolar form) when the MBT penetrates through the root canal or periodontal pocket of the damaged tooth (there may be a spread of the process from the temporal bone, middle ear). The disease begins gradually with the appearance of mild soreness or, rather, increased sensitivity of the lower jaw during chewing, which patients often interpret as exacerbated chronic periodontitis. The general condition does not change. In the bone tissue in the affected area, first inflammatory and then destructive changes increase. This is expressed in the appearance in the area of local sore swelling, which soon begins to fluctuate, and then opens. Along with it, problems with eating are intensified, as the chewing process becomes sharply painful, which leads to masticatory muscles contracture.

**Periodontal tuberculosis** is a pathological process that affects the gums, periodontal tissues located at the level of the tooth root, and the alveolar bone.

For patients with pulmonary tuberculosis and / or tuberculosis of maxillofacial region, common, often deep caries and periodontitis, as well as various related complications, are characteristic.

The likelihood of developing periodontal tuberculosis directly correlates with the prevalence and duration of the process in the lung tissue, and, maybe, with an isolated course of the disease. As a rule, chronic pulpitis and apical granulomas occur.

The overwhelming majority of cases of **apical granulomas** are detected accidentally during the reorganization of the oral cavity, since, due to the disturbed innervation of periodontal tissue (the myelin sheath of nerve fibers is destroyed), the process is asymptomatic.

Symptoms occur with the progression of the disease and abscess formation. Mild symptoms of intoxication appear (subfebrile or, rarely, febrile temperature, weakness, loss of appetite, headache of various intensities - as the disease develops, it intensifies and becomes almost constant), as well as local symptoms associated with periodontal tissue disease - moderate pain in the tooth, worse when biting. Periodontal mucosa is swollen, loose, bleeds easily. The gum "sags" when pressed on in the affected area due to destructive changes in the alveolar bone. There is a

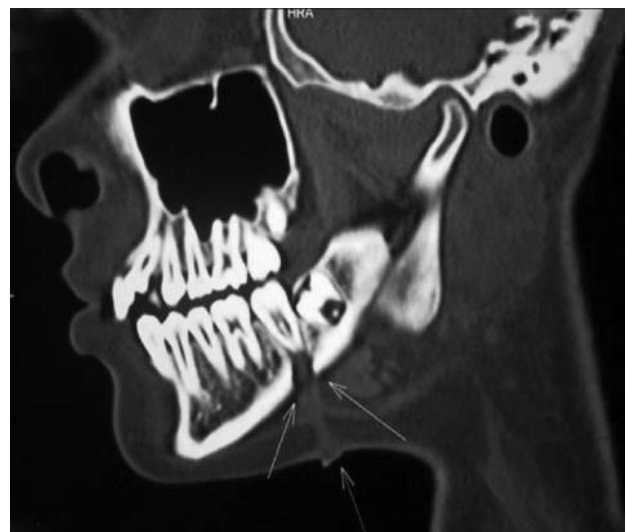
"loosening" of the teeth in the affected area, the mechanical density of the tooth decreases, which leads to their destruction. Peripheral lymph nodes (submandibular, cervical) increase in size and become dense to the touch and painful. Long-lasting inflammation leads to the deterioration in the general condition of the patient and an increase in symptoms of intoxication.

When radiography is carried out at the level of the tooth root, more often in the region of its apex, medium and large foci are visualized, possibly with destruction of bone tissue having indistinct boundaries, up to the formation of fistula, which are well visualized by MRI examination (Fig. 13).

The diagnosis of tuberculous periodontitis is established when a pathogen (MBT) is detected in a fistula discharge, or if a typical tuberculosis granuloma is detected during histological examination of a periodontal granuloma after a tooth extraction (macrophages, epithelioid cells and giant Pirogov-Langhans multinuclear cells are found around the caseous necrosis zone).



a



b

**Figure 13. Verified tuberculosis of the lower jaw (alveolar form). On the orthopantomogram (a), an osteolytic lesion is visualized around the right permanent second molar; on an MRI of the bones of the skull (b) in the sagittal plane, a bone defect of the lower jaw is determined (arrow) [10]**

Periodontal tuberculosis must be differentiated from fibroma, gum fibromatosis, epulis, etc.

*Fibroma* is a benign neoplasm, which is characterized by the accumulation of mature elements of the connective tissue, blood and lymph

vessels. There is no intoxication syndrome. A local examination of the oral cavity reveals a mobile formation that is clearly circumscribed from healthy tissue and painless on palpation. When chewing, it is often injured by teeth and inflamed, which causes complaints about bleeding gums, ulceration, etc. Decay is not characteristic. Peripheral regional lymph nodes do not reactively inflame.

The neoplasm biopsy with its subsequent morphohistological examination is significant in establishing the diagnosis.

***Gum fibromatosis.*** There are no symptoms of intoxication. On palpation in the gingival region of the upper and / or lower jaw, dense, painless, not bleeding formations with clear boundaries are found. They can be localized in a separate area, scattered diffusely in the oral cavity or completely replace the alveolar tissue with fibrous growths. Destruction and / or decomposition of tissue is not characteristic. Regional lymph nodes are not enlarged. Total fibromatosis leads to the deformation of the lower face and makes it difficult to close the lips.

Diagnostically significant method that allows you to establish a diagnosis is a biopsy of the formation with its subsequent morphological examination.

***Epulis*** also refers to benign neoplasms, occurs in places of chronic irritation of the oral cavity. General symptoms of intoxication are not characteristic. It is detected, as a rule, during the oral cavity debridement, during a routine examination by a dentist, or when consulting a dentist about caries of another tooth. It looks like limited growth on a wide or narrow stalk, mushroom-shaped or rounded on the gum, more often in its anterior region in the dentition. As the tumor grows in periodontium and bone, foci of destruction appear in the alveolar process, especially in the interalveolar septa, and pathological tooth mobility develops. It is extremely rare that unilateral regional lymphadenitis develops. Tumor biopsy followed by morphological examination is a verification criterion.

Osteolytic tuberculous lesion of periodontium must be differentiated from a non-specific inflammatory process. Osteomyelitis of the jaw is an infectious and inflammatory process in the bones of the jaw, leading to its destruction.

***Odontogenic osteomyelitis*** occurs against the background of neglected forms of caries, pulpitis, periodontitis, alveolitis, etc. The penetration of bacteria into the bone tissue of the jaw occurs through an infected pulp or tooth root.



Osteomyelitis can develop secondarily, with the progression of the process and the spread of microorganisms by the hematogenous route from furuncles and carbuncles of the maxillofacial zone, or the middle ear, tonsils. A variant is possible when primary inflammation develops in the jawbone, and tooth tissues undergo a purulent-inflammatory lesion already secondarily. In case of a jaw fracture or damage to the mucous membrane of the nasal cavity, infection penetrates into the bone tissue from the environment.

**Stages of osteomyelitis:**

- acute;
- subacute;
- chronic (sequestering and rarefying forms).

Depending on the length of the process, osteomyelitis may be:

- limited;
- focal;
- spilled (diffuse)

The disease begins with a sharp rise in body temperature to febrile, chills, general weakness, loss of appetite, and sleep disorders.

The patient is concerned about pain in the pathological process area. As the disease progresses, the pain from the local becomes diffuse, radiating to the ear, eye socket, temple. A tooth in the area of a purulent focus and adjacent teeth acquire a pathological mobility. Gingival mucosa becomes edematous. Purulent secretion may occur from the gingival pockets. A fetid, putrid odor is released from the patient's mouth. When adjacent soft tissues are involved in the pathological process, a limitation of jaw mobility, pain when swallowing, opening the mouth and difficulty breathing appear. A violation of the sensitivity of the lower lip, mucous membrane of the oral vestibule and chin skin may occur. Fistulas with purulent discharge form.

It may be complicated by the development of odontogenic sinusitis or thrombophlebitis of the facial vein branches, as well as a pathological fracture of the jaw.

In a general blood test, signs of an acute inflammatory process with pronounced leukocytosis, neutrophilia with a shift to the left, up to metamyelocytes are detected. In a biochemical blood test, C-reactive protein, sialic acids, fibrinogen are sharply increased.

On radiography, with the first symptoms of the disease in the periodontium of individual teeth or their roots, signs of chronic periodontitis are revealed, then, as the process develops, one or several cavities with sequestration are determined against the background of thickening of the bone.

## CHAPTER 8

### TUBERCULOSIS OF THE SALIVARY GLANDS

There are labial, buccal, lingual, root, incisal, palatine, parotid, submandibular and sublingual salivary glands. Some of them are located outside the oral cavity, but all their excretory ducts open precisely in it. Tuberculosis develops mainly in the parotid gland, less often in the mandibular and sublingual glands, and can spread to the lymph nodes of the neck. The process is usually one-sided, asymmetrical, but can be total. Cold abscesses may form, which open and form fistulas.

**Parotid tuberculosis** is the rarest clinical manifestation. A little more than a hundred cases are described. Tuberculosis of the salivary glands is diagnosed in the vast majority of cases in patients with pulmonary tuberculosis, there are also cases of primary damage. The diagnosis is complicated, since there are no specific clinical and radiation signs of this disease. Only bacteriological and histological data allow us to correctly diagnose.

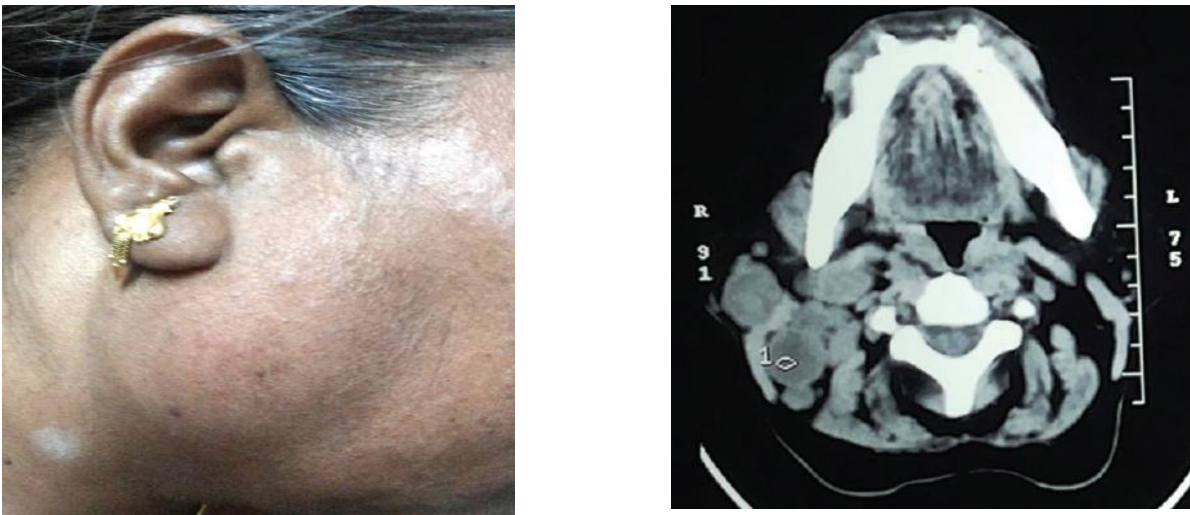
Clinically, tuberculosis of the parotid gland usually manifests itself as progressive unilateral edema in the parotid region, of diffuse or nodular (pseudotumour) character. As a rule, edema is soft, mobile, spreads in the anteroposterior direction from the submandibular angle to the earlobe. Common signs of the disease with this localization of the process are manifested by a moderately severe intoxication syndrome. In addition to swelling in the parotid gland, patients are concerned about both localized pain and swallowing and opening the mouth. Rarely, facial paralysis and trismus occur. Examination of the oral cavity and the mouth of the tooth canal does not reveal any signs of inflammation (rarely a tiny discharge can appear at the mouth). During the formation of the decay cavity, softening areas occur in the swollen gland, and when fistula is formed, a purulent discharge of a grayish color, odorless, can ooze. During the examination of the neck, enlarged lymph nodes from one to several groups are often palpated.

An ultrasound examination of the parotid gland plays a primary role in the diagnosis of the parotid gland tuberculosis, and is not specific. Due to its surface location, high-resolution ultrasound determines the localization of the process in the parotid gland or in the periparotid region, differ-

entiates the disease, especially from inflammatory processes and malignant neoplasms. Sonographically, parotid tuberculosis mumps is classified into two types: parenchymal and periparotid. The parenchymal type is the most common and manifests itself in the form of a diffuse increase in the parotid gland of the hypoechoic structure. The periparotid type is manifested by the heterogeneity of visualization, where zones of a hyperechoic structure are observed in the peripheral zone of the parotid gland, which corresponds to enlarged periglandular lymph nodes.

On radiography with contrast (contrast sialography), areas of destruction are observed in the salivary glands, it is possible to detect sequestries, calcifications and fistulas of various shapes and sizes. The gland lobules are uneven, asymmetrical due to sclerotic tissue changes. The salivary ducts deformation, calcifications and fistulas make it possible to suspect a tuberculous etiology of the disease.

On the CT of the skull in the salivary gland, an irregularly shaped heterogeneous intra-parotid formation is observed, surrounded by edema on the periphery (Fig. 14). The presence of the cavity in its central part is reinforced by suspicions for a tuberculous etiology of the process. In an MRI study of the parotid gland, tuberculous lesions usually appear hypointensive (on T1 weighted) and hyperintensive (on T2 images) changes with homogeneous contrast enhancement.



**Figure 14. Verified tuberculosis of the right parotid gland. Edema and CT image of the enlarged right parotid gland with hypoechoic softening [11]**

Thus, non-invasive research methods, such as ultrasound, CT and MRI of the parotid gland, are sensitive, but not specific for the detection of intraparotid tuberculosis lesions. A diagnosis can be confirmed by detect-

ing the causative agent of tuberculosis (MBT) in a discharge from the fistula or typical tuberculous granuloma by histological examination of the material obtained by puncture of the gland or histological examination of the affected tissue after paratectomy. The identification of specific granulomas with caseous necrosis in the center is irrefutable evidence of the tuberculous etiology of the disease. The study of the material obtained by puncturing of the affected area, by cultivating on culture media or MGM, in case of a positive result, confirm the nature of the disease.

## CHAPTER 9

### TUBERCULOSIS OF PERIPHERAL LYMPHATIC NODULES

Peripheral lymph node tuberculosis is characterized by the formation of specific granulomatous inflammation of the lymphoid tissue. First, the lymph nodes involved in the inflammation are soft and elastic, and subsequently, due to the intensification of exudative necrotic processes, their tissue will disintegrate with the formation of abscesses and fistulas.

Submandibular, supraclavicular, axillary and inguinal peripheral lymph nodes are affected. About 70% of cases of tuberculosis of the peripheral lymph nodes are localized in the neck. In 20% of cases, the process develops in several groups.

Women suffer 3-5 times more often than men do. There are three forms of the disease: infiltrative, caseous (purulent-caseous, ulcerative necrotic) and inductive (fibrous).

The infiltrative form is characterized by inflammatory infiltration of the lymph node (one or more) with the formation of tuberculous granulomas. The clinical course is variable. The disease can begin acutely with an increase in body temperature to 38–39 °C and a rapid increase in lymph nodes. On palpation, they are only slightly painful, their consistency dense or densely elastic. Often, the lymph nodes merge into conglomerates fused to the subcutaneous tissue due to the involvement of surrounding tissues in the process – periadenitis. The skin over the nodes is not changed. An increase in peripheral nodes is possible without pronounced perifocal phenomena and symptoms of intoxication. With progression, the lymphoid tissue is caseified (caseous form). Symptoms of intoxication increase, the affected lymph nodes become sharply painful, the skin above them is hyperemic, thinned, fluctuations appear, abscesses form, melt the surrounding tissue and form fistulas with purulent discharge, usually grayish-white, odorless. After the lymph nodes empty, body temperature decreases, pain decreases, fistulas slowly heal with the formation of characteristic scars in the form of frenulum or papillae. In the absence of emptying of the nodes, the disease acquires a chronic course with periodic exacerbations (inductive form). Inflammatory changes subside, caseous masses calcify. Lymph nodes decrease in size, become dense, the disease acquires a tendency to a wave-like course.

The most reliable diagnostic method is a puncture or operative biopsy with cytological, microbiological and histological examination of pathological material.

Differential diagnosis is often carried out with nonspecific lymphadenitis, a tumor process. Lymphadenitis occurs, as a rule, against the background of acute respiratory viral infections, as a complication of tonsillitis, chronic tonsillitis, etc. The peripheral lymphadenopathy is often one-sided, mainly cervical, supraclavicular, subclavian, chin or axillary. An increase in intoxication symptoms is observed – low-grade fever, weakness. Lymph nodes enlarge, become painful. The skin above them is hyperemic, swollen. On palpation, soreness intensifies. In the absence of antibiotic therapy, fluctuation appears, a fistula with a greenish-yellow discharge forms. To clarify the diagnosis, it is necessary to culture pathological material on a nutrient medium with a determination of sensitivity to antibiotics.

**Lymphoma** is a malignant lesion of the lymphatic system. It occurs at any age, but more often at a young age. The worrying symptoms are weakness, fever, often the wrong type, night sweats, arthralgia, skin itching. A rash of a papular nature may appear, mainly in the periarticular region. Almost all groups of peripheral lymph nodes are affected. They become dense, merge together, and are painless. The skin above them is swollen, without pronounced erythema. The same process also occurs alongside in the intrathoracic and / or mesenteric lymph nodes. The symmetry of the lesion is characteristic.

If malignancy is suspected, a biopsy of the affected lymph node is performed, followed by a histological examination. The pathognomonic sign of lymphoma is the detection of multinucleated Berezovsky-Sternberg cells.

## CHAPTER 10

### FEATURES OF THE OROFACIAL TUBERCULOSIS TREATMENT

After the verification of the diagnosis, the treatment of patients with maxillofacial tuberculosis is carried out in specialized anti-TB institutions (dispensaries, hospitals, centers, sanatoriums). Confirmation of the diagnosis of "tuberculosis", determination of treatment tactics and clinical follow-up are carried out by the medical commission of the head TB facility of the Russian Federation territorial entity.

The TB facility where the diagnosis is made, within three days, informs the patient in written form about the established diagnosis and the registration with the dispensary. The terms of observation and the amount of necessary treatment, diagnostic and anti-epidemic measures are determined by the clinical form of tuberculosis, the presence of drug resistance of the tuberculosis causative agent, complications, background and concomitant diseases. Since the day the diagnosis of tuberculosis is established, patients are subject to the follow-up by a TB specialist in a TB facility in accordance with the established procedure for the TB patient follow-up.

Tuberculosis treatment is carried out by TB specialists, dental care is provided by the dentists of a specialized facility.

Drug treatment includes tuberculosis chemotherapy proper, pathogenetic therapy, treatment of concomitant diseases and their complications. Both non-invasive and invasive local methods are used.

#### **General goals of treatment for tuberculosis patients:**

- elimination of tuberculosis clinical manifestations;
- achieving persistent regression of specific inflammation with the formation of minimal residual changes in the affected organ;
- full restoration of functionality and work ability;
- patients' social adaptation.

#### **Basic principles for treating a patient with tuberculosis:**

- treatment should be early and timely;
- treatment of a patient with tuberculosis should be long and continuous, step-by-step and successive: according to indications, the patient



with tuberculosis is provided with any medical care (primary, outpatient, inpatient, sanatorium-resort, high-tech and emergency). Hospitalization of a patient with tuberculosis is carried out if the patient has bacterial excretion, moderate and severe concomitant diseases and adverse reactions to anti-TB drugs, requiring constant medical supervision; after inpatient treatment, the patient is treated in a tuberculosis dispensary and / or tuberculosis sanatorium;

- treatment of tuberculosis patients is carried out comprehensively. It includes chemotherapy (etiotropic anti-tuberculosis therapy), if necessary, surgical treatment and collapse therapy for pulmonary tuberculosis to heal decay cavities (air injection into the pleural or abdominal cavities, valve bronchial block), as well as pathogenetic therapy and treatment of concomitant diseases.
- treatment of tuberculosis patients is carried out under strict control of taking anti-TB drugs (prevention of the development of secondary drug resistance of MBT). All anti-TB drugs are taken by patients with tuberculosis only in the presence of the medical personnel, who in a special form record the intake of the corresponding anti-TB drugs.

### **Hygiene and diet**

The daily routine for tuberculosis patients should be relaxed. Physical activity should be limited. A patient needs a regular 8-hour sleep and preferably a two-hour rest in the afternoon, walks in the fresh air. The rejection of bad habits is important.

The nutrition of a tuberculosis patient is an essential component of their routine. The diet is characterized by high calorie content (total calorie content 2800-3500 cal.), high in protein and vitamins.

Proper nutrition is of great importance in the treatment of tuberculosis. The use of meat and dairy products, fresh fruits and vegetables is recommended. There should be at least four meals a day.

A patient must neither overeat nor be malnourished. Some patients are prescribed with high-calorie nutrition, but not more than one third higher than the daily allowance.

In addition, treatment of tuberculosis of the oral cavity and maxillofacial area include mandatory oral hygiene, and foods that irritate the oral mucosa (hot, spicy, alcohol, smoking) must be excluded from the diet. According to indications, general treatment should be supplemented with local measures: oral sanitation, ulcers cleaning, anti-inflammatory therapy of periodontitis, treatment of caries and preventive antibacterial measures.

Examination of the oral cavity in patients with pulmonary tuberculosis with bacterial excretion and the provision of dental care should be carried out no earlier than 2-4 months after the start of anti-tuberculosis therapy (in the absence of bacterial excretion) after the removal of intoxication symptoms and at normal body temperature. Surgical interventions are carried out strictly according to the indications, namely, with the clinical effect of anti-TB treatment and the limitation of the local process in the oral cavity, in bone tissue. Teeth with periodontal tuberculosis must be removed.

**Chemotherapy** is the main component of the treatment of tuberculosis and consists of the long-term use of a combination of drugs that inhibit the MBT multiplication (bacteriostatic effect) or destroy them in the patient's body (bactericidal effect).

A chemotherapy mode is a combination of anti-tuberculosis and anti-bacterial drugs, the duration and frequency of their administration, the timing and content of control studies, as well as organizational forms of treatment. The chemotherapy mode is established according to the results of determining the drug sensitivity of MBT, isolated from pathological material, or the history of their absence (mainly an assessment of the risk of MDR-TB).

Chemotherapy is carried out in two phases:

1. intensive care phase is aimed at eliminating the disease clinical manifestations, maximizing the effect on the MBT population in order to stop bacterial excretion and prevent the development of drug resistance, reducing infiltrative and destructive changes in organs; it may be part of preparation for surgery;

2. continued treatment phase is aimed at suppressing the persisting mycobacterial population; provides a further reduction in inflammatory changes and involution of the tuberculosis process, as well as restoration of the body's functional capabilities.

Medicines used in chemotherapy for tuberculosis are divided into:

1. **first-line** anti-TB drugs (basic drugs for the treatment of tuberculosis caused by drug-sensitive mycobacteria): isoniazid, rifampicin, rifabutin, rifapentin, pyrazinamide, ethambutol, streptomycin;

2. **second-line** drugs (reserve, drugs for treating tuberculosis MDR MBT): levofloxacin, moxifloxacin, sparfloxacin, kanamycin, amikacin, capreomycin, bedakvilin, cycloserine, terizidone, prothionamide, ethionamide, aminosalicylic acid, thioureido- iminomethylpyridinium perchlorate (perchlozone);

3. **third-line** anti-TB drugs (other anti-TB and anti-bacterial drugs recommended for the treatment of highly drug-resistant tuberculosis) - linezolid, imipenem with cilastatin (Imp), meropenem, amoxicillin clavulanate, thiouredoiminomethylpyridinium perchlorate (Tpp).

WHO recommends dividing anti-TB drugs into 3 groups for the treatment of MDR-TB patients, depending on the priority of use:

Group **A**: fluoroquinolones (levofloxacin and moxifloxacin), bedaquiline and linezolid are highly effective and are highly recommended for inclusion in all modes in the absence of contraindications;

Group **B**: clofazimine (not used in the Russian Federation) and cycloserine or terizidone are conditionally recommended as second-choice drugs;

Group **C**: it includes all other drugs that can be used while the MBT sensitivity to them is preserved if the mode cannot be composed of drugs from groups A and B.

The choice of chemotherapy mode for a patient with maxillofacial tuberculosis is not different from the treatment of tuberculosis of other localizations, which will be based on the spectrum of drug sensitivity of MBT to anti-TB drugs.

The chemotherapy modes for tuberculosis patients are defined in the guideline for improving the diagnosis and treatment of respiratory tuberculosis [12].

**Mode I** is prescribed for patients with active tuberculosis with bacterial excretion, when the MBT is still sensitive to anti-TB drugs, including extrapulmonary tuberculosis patients without bacterial excretion in the absence of the risk of multiple drug resistance of the pathogen.

In the intensive care phase, four main anti-TB drugs are prescribed: isoniazid, rifampicin, pyrazinamide and ethambutol. The duration of the chemotherapy intensive phase is at least 60 daily doses (2 months). In the phase of continuing therapy, two or three main drugs are prescribed with the mandatory inclusion of isoniazid and rifampicin, with the duration of at least 120 doses (4 months). Thus, **the total treatment period for mode I is at least 6 months.**

**Mode II** is prescribed for patients with MBT resistance to isoniazid, or isoniazid resistance in combination with other drugs, but not to the combination of isoniazid and rifampicin. The mode consists of five drugs with obligatory inclusion: rifampicin, pyrazinamide, levo-phloxacin or moxifloxacin or sparfloxacin, aminoglycoside (kanamycin or amikacin) or polypeptide (capreomycin). The duration of the intensive phase is not less

than 90 daily doses (three months of treatment); in the phase of continuing therapy, the patient is prescribed four anti-TB drugs with mandatory inclusion of rifampicin, levofloxacin, and pyrazinamide into the mode. The duration of the phase of continuing therapy is at least 180 daily doses (6 months). Thus, **the total duration of treatment according to Mode II is at least 9 months.**

**Mode III** is prescribed for patients suffering from tuberculosis without bacterial excretion and the risk of MDR. In the phase of intensive care, four main drugs are prescribed: iso-niazide, rifampicin, pyrazinamide, and ethambutol. The duration of the intensive care phase is at least 60 daily doses (2 months); in the phase of continuing therapy, two or three main drugs are prescribed with the mandatory inclusion of isoniazid and rifampicin or pyrazinamide for at least 120 doses (4 months), **the total duration of treatment for Mode III is at least 6 months.**

**Mode IV** is prescribed for patients with established drug resistance to at least isoniazid and rifampicin (MDR-TB) at the same time or only to rifampicin.

Mode IV can be standardized and individualized.

A standard chemotherapy mode is prescribed:

1. for patients with known drug resistance to rifampicin and isoniazid or only rifampicin according to MGM and with unknown drug sensitivity of the pathogen to the rest of the main and reserve anti-TB drugs;
2. for patients at high risk of MDR-TB in the absence of bacterial excretion or until getting the results of identification of the pathogen selected culture and studying its drug sensitivity.

An individualized chemotherapy mode involves the selection of drugs based on the results of qualitative studies of the drug sensitivity of MBT strains selected from patients and the history of the disease.

The standard chemotherapy mode includes a combination of anti-TB drugs: capreomycin, levofloxacin, pyrazinamide, protionamide or ethionamide, cycloserine or terizidone, aminosalicylic acid. The duration of the intensive phase should be at least 240 doses (8 months). At least four anti-TB drugs are prescribed in the continuation phase: levofloxacin, pyrazinamide, cycloserine / terisidone, aminosalicylic acid or protionamide / ethionamide or ethambutol while maintaining sensitivity to it. The duration of the treatment of the continuation phase is at least 310 doses (12 months); **the total duration of chemotherapy for tuberculosis patients with MDR MBT in Mode IV is at least 20 months.**

In the intensive phase, Mode IV should include the six most effective drugs with the primary prescription of aminoglycoside or polypeptide, fluoroquinolone, pyrazinamide.

**MDR TB can be traced in:**

- patients contracting disease from a reliable contact with a patient suffering from MDR-TB (MDR-TB at a probable source of infection should be documented);
- patients who previously received two or more ineffective courses of tuberculosis chemotherapy;
- patients with recurrence of tuberculosis and in other cases of repeated treatment, if patients had previously been diagnosed with drug resistance to one of the main drugs - isoniazid or rifampicin;
- patients with negative clinical and radiological dynamics of the process, as well as when bacterial excretion preserves or appears of after a controlled intake of 90 daily doses;
- tuberculosis patients with persistent or reappeared bacterial excretion after a controlled intake of at least 60 daily doses, after controlled treatment according to chemotherapy Modes I, II or III and not having the results of determining the drug sensitivity of the pathogen, in the absence of other causes of treatment failure and ensuring patient commitment to treatment;
- patients with tuberculosis and HIV infection with negative clinical and radiological dynamics of the process during controlled treatment according to Modes I, II or III in the absence of results of determining the drug sensitivity of the pathogen to anti-TB drugs, regardless of the number of doses taken.

**Mode V** is prescribed for tuberculosis patients with established drug resistance of the pathogen to isoniazid and rifampicin in combination with established or suspected resistance to ofloxacin fluoroquinolone.

The intensive phase includes a combination of six anti-TB drugs: moxifloxacin / levofloxacin, cycloserine / terizidone, bedaquiline, linezolid, capreomycin, pyrazinamide / ethambutol, protionamide or ethionamide, aminosalicic acid, imipenem + cilastatin, perimeromenidemenide.

The duration of the intensive phase in XDR-TB is at least 240 daily doses (8 months); at least four anti-TB drugs are used in the continuation phase with the mandatory inclusion of moxifloxacin / levofloxacin, cycloserine / terizidone, linezolid. The phase duration is not less than at least

310 daily doses (12 months); **total treatment duration is of at least 20 months.**

During chemotherapy for patients with tuberculosis, concomitant therapy is prescribed to prevent and correct side effects of drugs, as well as symptomatic and pathogenetic drugs.

The most common adverse reactions to anti-TB drugs are hepatotoxic reactions associated with toxic effects on the liver. A number of chemotherapy drugs can cause damage to the peripheral and central nervous system (isoniazid, cycloserine, terizidone), cause an increase in uric acid with manifestations of arthralgia (pyrazinamide). Side effects of the use of aminoglycosides (amikacin, kanamycin) can occur in the form of nephro- and ototoxic reactions. Ophthalmic (ethambutol) and cardiotoxic (bedaquiline) adverse reactions rarely occur. Allergic reactions may occur, especially when using antibiotics (capreomycin, kanamycin, amikacin). In the treatment of MDR-TB, a number of drugs prescribed in the form of tablets cause irritation of the gastric mucosa with the development of nausea and vomiting (aminosalicylic acid, protionamide / ethionamide).

The frequency of adverse reactions depends on the concomitant pathology of the patient (chronic alcoholism, chronic persistent hepatitis, diabetes mellitus, cardiovascular pathology, gastrointestinal tract diseases, central nervous system, etc.). Adverse reactions are manifested, as a rule, in the first month of chemotherapy and, extremely rarely, in the further continuation of complex treatment after temporary withdrawal and adequate pathogenetic support.

**Pathogenetic therapy** includes the use of nonspecific agents aimed at normalizing the pathological changes caused in the body by the tuberculous process.

The objectives of pathogenetic therapy are:

- acceleration of the reverse development of inflammation;
- prevention of the formation of pronounced fibrotic and residual changes;
- prevention of the development of adverse reactions to the introduction of antibacterial drugs,
- stimulation of reparative processes in the body.

The choice of a means (method) of pathogenetic therapy should be justified taking into account the mechanisms of tuberculosis pathogenesis, the use of diagnostic methods to assess the existing relevant disorders, possible interactions with other drugs (methods) and pharmacoeconomic efficiency.

Correction of the systemic inflammatory response syndrome, suppression of severe inflammatory reactions includes anti-inflammatory (glucocorticosteroid and non-steroidal) drugs, antikinin drugs, detoxification therapy.

Correction of secondary immunodeficiency states: immune preparations, including those of microbial, plant, fungal, animal origin, as well as synthetic and semi-synthetic. According to the main pharmacodynamic effects, they predominantly affect nonspecific protection factors, B and T lymphocytes, monocytes / macrophages, cytotoxic cells, including interferon preparations, interferon inducers, thymic hormones, immunoregulatory peptides.

Correction of adaptive reactions: adaptogens of plant, animal origin, nootropics, immunomodulators, dietary supplements, physiotherapy, motor mode, lymphotropic therapy.

Normalization of metabolic processes, including fibrosis formation processes, collagen metabolism, antioxidant defense systems: hyaluronidase preparations, antioxidants (sodium thiosulfate,  $\alpha$ -tocopherol according to the scheme), ozone therapy.

Strengthening sluggish inflammatory reactions: immunostimulants, physiotherapeutic methods.

### **Local symptomatic therapy for erosive and ulcerative lesions of oral mucosa**

1. The patient is trained in gentle sanitation of the oral cavity, for this purpose it is possible to use the Bass method, which suggests the location of the toothbrush (a "soft" brush is used) during cleaning at an angle of 45 ° relative to the axis of the tooth. First, the external and internal surfaces of the teeth are processed with vibrating movements (the toothbrush itself does not move), and then the chewing surfaces are processed with back and forth movements.
2. To relieve mucus and food debris, rinse the mouth with aqueous solutions of antiseptics (1.5% hydrogen peroxide solution, 0.05% chlorhexidine solution, etc.).
3. The disinfecting and cauterizing effect is obtained by treating the oral mucosa with lactic acid solutions, initially with a 50% concentrate, and then with 75-100%.
4. In case of pain, anesthesia is carried out by irrigation with lidocaine aerosol 10%, applications of 10% suspension of anestezin in peach, sunflower oil; 2% lidocaine solution, as well as gels and benzocaine solu-

tions (Zi-lactin, Ziladent Orajel, Mouth-Aid; Orajel Baby; Orajel Maximum strength; Anbesol).

5. It is possible to use isoniazid or rifamycin in the form of irrigation or applications. The duration of local treatment is from 10 to 20 days. The dose of the drug taken systemically decreases accordingly.
6. To improve the removal of necrotic plaque in the acute period, proteolytic enzymes are used (0.1% solution of trypsin, terrilithin).
7. During the period of periodontal tissues regeneration, it is necessary to use locally accelerating healing drugs: preparations based on bien, solcoseryl, panthenol, methyluracil ointment, actovegin gel.
8. Physiotherapy is carried out at the stage of regeneration after the resolution of the acute period. UV, laser therapy are possible.

Thus, correctly prescribed treatment, taking into account the combination of specific and non-specific therapy, provides a cure for tuberculosis, most often with the formation of a superficial scar (Fig. 14).



before treatment



after 4 months of treatment

**Figure 14. The dynamics of the complex treatment of verified tuberculous ulcers in the mucosa of the upper lip [13]**

### **Features of the treatment of tuberculosis of bones and joints of the facial skull**

Treatment is carried out in a specialized institution in the department of osteoarticular tuberculosis. At the initial stage, conservative anti-TB treatment is carried out. Etiotropic therapy, similarly, is determined by the spectrum of drug sensitivity of the causative agent of tuberculosis (if MBT is detected in the analysis of synovial fluid, pus, osteolytic fragments).

If the process is complicated by an abscess, fistula or the formation of an osteolytic cavity, surgical intervention is recommended. Surgical



treatment is carried out by phthisiosteologists together with maxillofacial surgeons, the timing and methods are determined individually, depending on the stage of the disease, the area of the lesion, the development of complications.

**Surgical treatment includes:**

- radical preventive operations (surgical treatment of the inflammatory surface, necrectomy, opening an abscess, thorough curettage);
- radical recovery operations (removal of intraarticular tissues affected by the tuberculosis process, with the replacement of the defect using alloplasty or endoprostheses).

When perforating the bones of the skull, trepanation and curettage of granulations on the dura mater are recommended. In this case, the bone defect is replaced by a prosthesis or graft. With tuberculosis of the jaw (alveolar bone), subperiosteal resection and removal of affected teeth are performed. Treatment of mumps depends on the activity of the inflammatory process. In the acute period, local use of isoniazid and rifampicin in the form of instillations with their oral or parenteral administration with appropriate dose adjustment can be combined. Physiotherapy with this form of tuberculosis is possible during the period of subsidence of the clinical manifestations of the disease in the form of electrophoresis of the parotid glands with a solution of galantamine or potassium iodide. With the development of an extensive abscess in the salivary gland, resection or removal is necessary.

During chemotherapy and other methods of conservative treatment, immobilization of the lower jaw with joint unloading, followed by a set of physiotherapy exercises, therapeutic massage of the face and neck are indicated for patients.

## TESTS FOR KNOWLEDGE CONTROL

**Choose one correct answer.**

Question № 1

**The method used to verify tuberculosis of the oral mucosa is**

- 1) fluorography
- 2) lung radiography
- 3) computed tomography of the skull bones
- 4) endoscopy of the mucosa
- 5) histology

Question № 2

**One of the risk factors for the development of tuberculosis of the oral mucosa is**

- 1) age under 7 years
- 2) senile age
- 3) permanent trauma to the mucosa
- 4) the presence of tuberculosis in the past
- 5) protein fasting

Question № 3

**The causative agents of tuberculosis are**

- 1) bacteria
- 2) mushrooms
- 3) protozoa
- 4) viruses
- 5) rickettsia

Question № 4

**MBT stained by the Ziehl-Nielsen method are visible under a microscope as**

- 1) raspberry sticks on a blue background
- 2) blue sticks on a red background
- 3) green chains on a black background
- 4) purple-crimson on an orange background
- 5) yellow on a green background

Question № 5

**Non-existent kind of MBT is**

- 1) human
- 2) bull
- 3) canine
- 4) bird
- 5) African

Question № 6

**Signs of the specificity of tuberculous granuloma include**

- 1) epithelioid granuloma with the presence around lymphocytes
- 2) the presence of epithelioid cells around caseous necrosis
- 3) epithelioid granuloma with central necrosis and Pirogov-Langhans cells
- 4) lymphoid infiltration
- 5) lymphoid necrotic granuloma

Question № 7

**The basis of cellular immunity is formed by**

- 1) neutrophils
- 2) B lymphocytes
- 3) T lymphocytes
- 4) basophils
- 5) monocytes

Question № 8

**To the tuberculous pathology of the maxillofacial region refers**

- 1) scrofuloderma
- 2) ulcerative stomatitis
- 3) gingivitis
- 4) cancerous ulcer
- 5) periodontitis

Question № 9

**The main morphological substrate of lupus tuberculosis is**

- 1) ulcer
- 2) vesicle
- 3) lupoma
- 4) papulo-necrotic changes
- 5) petechiae

Question № 10

**Papilomatous growing granulations of lupus vulgaris foci resemble**

- 1) apple fruit
- 2) raspberries
- 3) cherry berries
- 4) rowan berries
- 5) sea buckthorn berries

Question № 11

**For lupomas diagnosis is used**

- 1) only dioscopy
- 2) only sounding
- 3) smear imprint
- 4) dioscopy and sounding
- 5) microscopy

Question № 12

**The main histological sign of lupus tuberculosis is**

- 1) the presence of ordinary white blood cells
- 2) the abundance of red blood cells
- 3) the presence of fibroblasts
- 4) the abundance of lymphocytes
- 5) the presence of giant Pirogov-Langhans cells

Question № 13

**On the tongue, tuberculous lupus erythematosus is localized in the region of**

- 1) root and back
- 2) root and top surface
- 3) root and edges
- 4) root and tip
- 5) the tip of the tongue

Question № 14

**There are four stages in the clinical course of lupus erythematosus**

- 1) infiltrative, tubercular, ulcerative and calcifications
- 2) infiltrative, tubercular, cicatricial and calcifications
- 3) infiltrative, tubercular, ulcerative and cicatricial
- 4) infiltrative, tubercular, compaction and calcification
- 5) infiltrative, tubercular, ulcerative and compaction

Question № 15

**Scrofuloderm is characterized by the presence of**

- 1) painless nodes of pink or brown color, which can ulcerate with subsequent scarring or resorption
- 2) tubercles (lupomas)
- 3) erosion and ulcers, prone to fusion
- 4) small intradermal nodes surrounded by perifocal infiltrates
- 5) infiltrates

Question № 16

**Miliary ulcerative tuberculosis is often localized in the oral cavity**

- 1) in the area of the gums and buccal mucosa
- 2) in the palate and on the tongue
- 3) in the palate and on the gums
- 4) on the tongue and buccal mucosa
- 5) in the cheek area

Question № 17

**Tuberculosis of tonsils and pharynx is more often combined with**

- 1) disseminated pulmonary tuberculosis and caseous pneumonia
- 2) tuberculoma and fibro-cavernous tuberculosis
- 3) primary tuberculosis complex
- 4) disseminated and fibro-cavernous pulmonary tuberculosis
- 5) focal and infiltrative pulmonary tuberculosis

Question № 18

**The main symptoms of tuberculous lesions of the tonsils and pharynx are**

- 1) difficulty in nasal breathing, pain when swallowing, dysphagia
- 2) difficulty in nasal breathing, cough, dysphagia
- 3) pain when swallowing, dysphagia, vomiting
- 4) difficulty in nasal breathing, cough, pain when swallowing, dysphagia, vomiting
- 5) cough, vomiting, shortness of breath

Question № 19

**Most often, tuberculosis affects**

- 1) all salivary glands simultaneously
- 2) parotid salivary gland

- 3) submandibular salivary gland
- 4) sublingual salivary gland
- 5) sublingual and submandibular salivary glands

Question № 20

**Clinical options for tuberculous lesions of the salivary glands are**

- 1) exudative - sclerosing and productive - caseous
- 2) exudative - productive and caseous - sclerosing
- 3) caseous - sclerosing
- 4) exudative - sclerosing
- 5) exudative - caseous and productive - sclerosing

Question № 21

**In case of tuberculosis lesions, from the ducts of the salivary gland, can ooze**

- 1) ichorous fluid, color of meat slops
- 2) crumb-like pus
- 3) scanty transparent discharge
- 4) no discharge
- 5) muddy jelly-like secret

Question № 22

**Miliary ulcerative tuberculosis develops**

- 1) in a sputogenic way
- 2) in a hematogenous way
- 3) in a lymphogenous way
- 4) in a lymphohematogenous way
- 5) in a lymphobronchogenic way

Question № 23

**The characteristic manifestations of miliary ulcerative tuberculosis are**

- 1) small nodules of a grayish-reddish color in the mouth, mucous membrane of the cheek, back and lateral surfaces of the tongue
- 2) yellow "nodules" at the bottom of the ulcer - Trel grains
- 3) dense, movable nodes of a spherical shape in the deep layers of the skin
- 4) small tubercles on the infiltrated surface of the mucous membrane
- 5) dense motionless painful nodules on the mucous membrane of the oral cavity

Question № 24

**The main pathway for the entry of MBT into the human body is**

- 1) aerogenic
- 2) alimentary
- 3) contact
- 4) transmission
- 5) intrauterine

Question № 25

**Secondary tuberculosis develops in**

- 1) children whose parents are sick with tuberculosis
- 2) adults under 30 years old with a negative Mantoux reaction
- 3) adolescents from foci of tuberculosis
- 4) persons who have had any form of tuberculosis infection (infection, disease)
- 5) persons over 70 years old

Question № 26

**The main source of tuberculosis infection is**

- 1) a patient with respiratory tuberculosis excreting MBT
- 2) cattle with tuberculosis
- 3) a patient infected with mycobacteria
- 4) a child with chronic tuberculosis intoxication
- 5) a patient with focal pulmonary tuberculosis, not excreting MBT

Question № 27

**The purpose of the use of recombinant tuberculosis allergen is**

- 1) tuberculosis prevention
- 2) clarification of the localization of the tuberculosis process
- 3) determination of the dispensary group
- 4) diagnosis of tuberculosis and assessment of its activity
- 5) treatment of tuberculosis

Question № 28

**A recombinant tuberculosis allergen test is performed**

- 1) intramuscularly
- 2) intradermally
- 3) cutaneously
- 4) subcutaneously
- 5) intravenously

Question № 29

**Exudative-caseous form of tuberculosis of the salivary glands is characterized by**

- 1) the appearance in one of the salivary glands area, swelling in the form of a separate painless node, which slowly increases, against the background of normal body temperature
- 2) a slow onset, cough, weight loss, shortness of breath, swelling in the salivary glands, an increase in the lymph nodes of the submandibular, anteroposterior, with their compaction, soreness, and an increase in local temperature
- 3) a slow onset, mild symptoms of intoxication, neurological pain in the affected half of the face, redness of the skin in the affected gland, one or more painful swellings are palpated, which gradually soften to fluctuation
- 4) an acute onset, sharp pain in the affected gland, high body temperature, cough, sudden weight loss
- 5) an acute onset, high body temperature, severe intoxication, marked increase in the salivary glands symmetrically on both sides, with a sharp pain on palpation

Question № 30

**The productive-sclerosing form of salivary gland tuberculosis is characterized by**

- 1) the appearance in the area of one of the salivary glands, swelling in the form of a separate painless node, which slowly increases, against the background of normal body temperature
- 2) a slow onset, mild symptoms of intoxication, neurological pain in the affected half of the face, redness of the skin in the affected gland, one or more painful swellings are palpated, which gradually soften to fluctuation
- 3) an acute onset, severe pain in the affected gland, high body temperature, cough, sharp weight loss
- 4) a slow onset, cough, weight loss, shortness of breath, swelling in the salivary glands, an increase in the lymph nodes of the submandibular, anteroposterior, with their compaction, soreness, and an increase in local temperature
- 5) an acute onset, high body temperature, severe intoxication, expressed by an increase in the salivary glands symmetrically on both sides, with a sharp pain on palpation



Question № 31

**A tongue non-healing wound, infiltrate or ulceration, existing for more than two weeks**

- 1) may be a sign of the tongue tuberculosis
- 2) may be a sign of oral cancer
- 3) the answers 1, 2 are correct
- 4) may be a sign of a fungal infection of the oral cavity

Question № 32

**Painless erosion in the oral cavity is characteristic**

- 1) only of primary syphilis with the development of chancre in the oral cavity
- 2) of oral cancer and primary syphilis
- 3) of oral cancer and tuberculosis
- 4) of tuberculosis and primary syphilis

Question № 33

**Peripheral lymphadenopathy is**

- 1) an obligatory sign of oral tuberculosis
- 2) a mandatory sign of primary syphilis of the oral cavity
- 3) a mandatory sign of fungal infection of the oral cavity
- 4) an obligatory sign of oral cancer

Question № 34

**Extensive ulceration with severe swelling of the mucous membrane of the oral cavity and an increase in regional lymph nodes are characteristic of**

- 1) tuberculosis
- 2) primary syphilis
- 3) cancer
- 4) tuberculosis and syphilis
- 5) tuberculosis and cancer

Question № 35

**Signs of the tuberculosis process are**

- 1) severe soreness and swelling in the lips, combined with small papular rashes in the perioral region
- 2) severe soreness and swelling in the area of the lips, combined with bright red, diffused spotted-papular rashes in the perioral region

- 3) small papular rashes in the perioral region, mainly in the corners of the mouth
- 4) swelling in the lips, not giving pain

Question № 36

**Yellow-red in color and with clear borders, a nodule, painless on palpation, from 1 to 3 cm in diameter, found on the skin in the corner of the mouth, this is**

- 1) lupoma
- 2) primary chancre
- 3) melanoma

Question № 37

**The phenomenon of "apple jelly" occurs with**

- 1) fungal infection
- 2) pyoderma
- 3) lupus tuberculosis
- 4) syphilis
- 5) osteomyelitis of the jaw

Question № 38

**The most characteristic clinical symptom of a disease with tuberculous lesions of oral mucosa is / are**

- 1) pain and ulcer
- 2) hypersalivation
- 3) feeling of pressure and fullness
- 4) hyperemia of oral mucosa

Question № 39

**Difficult breathing through the nose, hoarseness, pain when swallowing, followed by the development of dysphagia occur with the development of the inflammatory process in the area of**

- 1) pharynx
- 2) hard and / or soft palate
- 3) palatine tonsils
- 4) tongue

Question № 40

**Frontal tuberculosis is detected**

- 1) when patients appeal due to high fever and sharp pains in the affected area
- 2) when patients appeal due to a painless swelling in the affected area, of 2-3 cm or more in diameter
- 3) when patients appeal in connection with a sudden sharply painful swelling in the affected area, of 2-3 cm or more in diameter
- 4) during a routine examination by a dentist

Question № 41

**The symptom of “melting sugar” is found on**

- 1) x-ray of bones in patients with acute hematogenous osteomyelitis
- 2) an ultrasonogram of the salivary glands in patients with tuberculosis
- 3) x-ray of bones in patients with tuberculosis
- 4) sialogram with destruction of gland tissue of any etiology

Question № 42

**Bone tissue destruction always develops with**

- 1) tuberculosis of bones and joints
- 2) sarcoma
- 3) osteomyelitis
- 4) all answers are correct

Question № 43

**Tuberculous periodontitis in 90% of patients is asymptomatic,**

- 1) as the process is always limited and superficial
- 2) as the nerve fibers innervating this area are destroyed by the toxins of the MBT
- 3) due to the anatomical features of periodontal innervation
- 4) as they often form periodontal granulomas.

Question № 44

**Depression on the gum, appearing with palpation of the soft tissues surrounding the diseased tooth**

- 1) proves that the tooth alveolus is destroyed
- 2) is an indirect sign of the alveoli destruction
- 3) characteristic of tuberculous gingivitis
- 4) does not occur with tuberculous periodontitis

Question № 45

**Periodontal granuloma complicated by odontogenic abscess must be differentiated from**

- 1) epulis
- 2) primary chancre
- 3) Buruli ulcer
- 4) sarcoma

Question № 46

**Fetid, putrid breath occurs in patients with**

- 1) tuberculous periodontitis
- 2) acute hematogenous osteomyelitis
- 3) cancer of the oral mucosa and tongue
- 4) true 1 and 2
- 5) true 2 and 3

Question № 47

**Sialography with contrast**

- 1) allows you to clearly establish the tuberculous etiology of the process
- 2) allows you to suspect a tuberculous etiology of the process
- 3) eliminates the tuberculous etiology of the process

Question № 48

**An immunological reaction based on the determination of free IFN in serum is**

- 1) Mantoux test 2TE
- 2) Diaskintest
- 3) QuantiFERON-TB Gold
- 4) T-Spot.TB

Question № 49

**Positive in vitro immunological laboratory test result (T-Spot.TB, QuantiFERON-TB Gold)**

- 1) indicates active tuberculosis
- 2) indicates a high risk of developing tuberculosis
- 3) occurs both in active tuberculosis and in latent tuberculosis infection
- 4) indicates latent tuberculosis infection

Question № 50

**Physiotherapy for maxillofacial tuberculosis**

- 1) is not used
- 2) is used in the acute period
- 3) is used during the period of subsiding of clinical manifestations (darsonvalization)
- 4) is used during the period of subsiding of clinical manifestations (UHF)
- 5) is used during the period of subsiding of clinical manifestations (electrophoresis with potassium iodide)

Question № 51

**As instillations for oral tuberculosis, you can use a solution of**

- 1) prednisone
- 2) isoniazid
- 3) streptomycin
- 4) spirit

Question № 52

**For topical treatment of the tongue tuberculosis, it is recommended to use**

- 1) 50% lactic acid
- 2) 3% boric acid
- 3) fucorcin

Question № 53

**A negative result of immunological laboratory tests (T-Spot.TB, QuantiFERON-TB Gold, "Tu-Binferon")**

- 1) allows to exclude tuberculous etiology of the process
- 2) does not allow to exclude tuberculous etiology of the process
- 3) is possible against the background of effective treatment of the disease
- 4) true "1" and "3"
- 5) true "2" and "3"

Question № 54

**Oral tuberculosis develops:**

- 1) rarely
- 2) slowly
- 3) fast
- 4) often

Question № 55

**Primary infection of the oral cavity is presented as**

- 1) an ulcer, accompanied by unilateral satellite lymphadenopathy most often in the submandibular region
- 2) an ulcer combined with bilateral lymphadenopathy most often in the maxillary region
- 3) an ulcer not accompanied by regional lymphadenopathy

Question № 56

**In patients with tuberculosis of the oral cavity can occur on the tonsils and / or in the salivary glands**

- 1) ulcers
- 2) tubercles
- 3) erosion
- 4) granulomas
- 5) everything is right

Question № 57

**If laryngeal tuberculosis is suspected, it is necessary to perform**

- 1) chest x-ray
- 2) laryngoscopy
- 3) biopsy of regional lymph nodes
- 4) general blood test
- 5) other

Question № 58

**Clinical signs of tonsil tuberculosis**

- 1) are very specific and allow you to diagnose a disease
- 2) do not have specificity and do not allow to diagnose the disease
- 3) allow you to suspect a disease

**Choose some correct answer options**

Question № 1

**The secondary forms of tuberculosis of the oral mucosa are:**

- 1) lupus tuberculosis
- 2) inductive tuberculosis
- 3) scrofuloderma (collicative tuberculosis)

- 4) miliary ulcerative tuberculosis
- 5) infiltrative tuberculosis
- 6) tuberculosis complex
- 7) papillomatous tuberculosis

Answer options:

- 1) 1, 3, 6
- 2) 1, 2, 5
- 3) 4, 6, 7
- 4) 2, 5, 7

Question № 2

**The stages of the clinical course of lupus erythematosus include**

- 1) infiltrative
- 2) tubercular
- 3) stenosing
- 4) cicatricial
- 5) fibrosing
- 6) ulcerative
- 7) obliterating

Answer Options:

- 1) 2, 3, 6, 7
- 2) 1, 2, 4, 6
- 3) 1, 4, 6, 7
- 4) 1, 2, 3, 5

Question № 3

**Types of damage to the oral mucosa with lupus tuberculosis, depending on the localization of the process are**

- 1) marginal
- 2) medial
- 3) bilateral
- 4) lateral
- 5) total
- 6) supramedial
- 7) supramarginal

Answer Options:

- 1) 1, 5, 6, 7
- 2) 3, 4, 5, 6
- 3) 2, 3, 5, 6
- 4) 1, 3, 5, 7

Question № 4

**Pathomorphological stages of salivary gland tuberculosis are**

- 1) calcination
- 2) hyperplasia
- 3) caseous lesion
- 4) fibrosis,
- 5) exudation
- 6) atrophy
- 7) alteration

Answer Options:

- 1) 4, 5, 6, 7
- 2) 2, 3, 6, 7
- 3) 2, 3, 4, 6
- 4) 1, 2, 5, 6

Question № 5

**Differential diagnosis of salivary gland tuberculosis is carried out with**

- 1) chronic lymphadenitis
- 2) tumors of the salivary glands
- 3) infectious mumps
- 4) thymomegaly
- 5) actinomycosis
- 6) acute otitis media
- 7) oral candidiasis

Answer Options:

- 1) 1, 2, 5
- 2) 2, 4, 5
- 3) 1, 5, 7
- 4) 3, 4, 6



Question № 6

**The penetration of MBT in the bones of the facial skull occurs**

- 1) sputogenically
- 2) hematogenously
- 3) lymphogenously
- 4) bronchogenically
- 5) by contact, in case of the damage to the oral mucosa
- 6) transplacentally
- 7) by an alimentary route in case of violation of the integrity of the oral mucosa

Answer Options:

- 1) 1, 4, 5
- 2) 2, 3, 5
- 3) 1, 5, 7
- 4) 3, 4, 6

Question № 7

**It has a detrimental effect on MBT**

- 1) ultraviolet radiation
- 2) halogens
- 3) infrared radiation
- 4) high temperature
- 5) ultrasound
- 6) x-ray radiation
- 7) electromagnetic field

Answer Options:

- 1) 2, 3, 6
- 2) 5, 6, 7
- 3) 1, 2, 4
- 4) 2, 3, 4

Question № 8

**The accelerated highly sensitive methods for detecting MBT include**

- 1) cultivation on Levenshtein-Jensen medium
- 2) cultivation in a liquid nutrient medium in the BACTEC system
- 3) GeneXpert MTB / RIF
- 4) microscopy with staining of the smear according to Ziehl-Nielsen

- 5) LED microscopy
- 6) biological test in guinea pigs
- 7) real-time PCR

Answer Options:

- 1) 2, 3, 7
- 2) 2, 5, 7
- 3) 1, 5, 6
- 4) 4, 5, 7

Question № 9

**The most common symptoms of tuberculosis periodontitis include**

- 1) constant pain in the tooth, worse when biting
- 2) shortness of breath
- 3) headache
- 4) cough
- 5) fever to febrile
- 6) thirst
- 7) lacrimation

Answer Options:

- 1) 1, 2, 6
- 2) 2, 3, 4
- 3) 3, 5, 7
- 4) 1, 3, 5

Question № 10

**With the progression of exudative-caseous form of the submaxillary gland tuberculosis is noted**

- 1) redness of the skin, merging with underlying tissues
- 2) cough
- 3) increase in body temperature
- 4) speech impairment
- 5) heartbeat
- 6) the appearance of several painful tumor with gradual softening and fluctuation
- 7) increase in blood pressure

Answer Options:

- 1) 1, 3, 6
- 2) 1, 2, 3
- 3) 2, 3, 5
- 4) 3, 5, 7

Question № 11

**The main manifestations of tuberculosis of the tonsils and pharynx are**

- 1) difficulty in nasal breathing
- 2) headache
- 3) malaise
- 4) tonsil enlargement without discharge in crypts
- 5) tachycardia
- 6) pain when swallowing
- 7) weakness

Answer Options:

- 1) 1, 2, 7
- 2) 2, 3, 4
- 3) 1, 4, 6
- 4) 3, 5, 6

Question № 12

**Medical risk factors for tuberculosis include**

- 1) lack of BCG vaccination in children
- 2) HIV infection, therapy with biologically active drugs
- 3) asocial lifestyle, tobacco smoking
- 4) complicated course of BCG vaccination in children
- 5) diabetes, OM
- 6) head injury, chicken pox
- 7) contact with a patient with tuberculosis excreting MBT

Answer Options:

- 1) 2, 4, 7
- 2) 1, 2, 5
- 3) 3, 5, 6
- 4) 1, 4, 7

Question № 13

**The epidemiological risk factors for tuberculosis include**

- 1) lack of vaccination in children
- 2) family contact with a tuberculosis patient
- 3) HIV infection, biologically active drug therapy
- 4) asocial lifestyle, tobacco smoking
- 5) complicated course of BCG vaccination in children
- 6) work contact with a patient with tuberculosis
- 7) contact with a patient with tuberculosis secreting MBT

Answer Options:

- 1) 2, 6, 7
- 2) 2, 5, 7
- 3) 3, 5, 6
- 4) 1, 4, 7

Question № 14

**Mycobacterium tuberculosis are**

- 1) prokaryotes, have acid resistance
- 2) optional aerobes, have pronounced hydrophobicity
- 3) optional aerobes, have alcohol resistance
- 4) anaerobes, have pronounced hydrophobicity
- 5) eukaryotes, have alkali resistance
- 6) obligate aerobes, motionless, do not form a dispute
- 7) prokaryotes, have alkali resistance

Answer Options:

- 1) 2, 5, 6
- 2) 1, 5, 6
- 3) 4, 5, 7
- 4) 1, 3, 7

Question № 15

**Chest X-rays for the early detection of tuberculosis in the adult population are carried out annually to**

- 1) homeless people, refugees and internally displaced persons
- 2) patients with diabetes
- 3) patients with chronic nonspecific diseases of the respiratory system, gastrointestinal tract and genitourinary system

- 4) people with HIV
- 5) patients who are registered at drug rehabilitation and psychiatric institutions
- 6) persons who contact patients with tuberculosis

Answer Options:

- 1) 2, 4, 7
- 2) 1, 2, 3
- 3) 3, 5, 6
- 4) 1, 6, 7

Question № 16

**Oral tuberculosis symptoms are**

- 1) chest pain
- 2) glossalgia
- 3) yellowing on the tonsils
- 4) mandatory skin lesion in perioral area
- 5) oral mucosa ulceration
- 6) tongue erythema
- 7) night fever
- 8) gingival edema

Answer Options:

- 1) 2, 5, 6, 7, 8
- 2) 1, 2, 4, 7, 8
- 3) 2, 3, 5, 6, 7
- 4) 1, 2, 3, 6, 7

**Match each element of the left set with the corresponding element of the right set**

**Question № 1**

- |  |   |
|--|---|
| <p>A. Marginal damage to the oral mucosa with lupus tuberculosis</p>                             | <p>A. infiltrative or tubercle-ulcerative lesion does not affect the gingival border</p>  |
| <p>B. supramarginal lesion of the mucous membrane of the oral cavity with lupus tuberculosis</p> | <p>B. covering the gingival margin first in the form of a common infiltration and then turning into a tubercle-erosive (ulcerative)</p> |

form. In this case, the gingival margin and interdental papillae swell sharply, the figure of the gingival margin is smoothed out, the mucous membrane of gums becomes bright red

В. total damage to the oral mucosa with lupus tuberculosus

В. proceeding as a type of lupus erythematosus

Г. bilateral lesion of the oral mucosa with lupus tuberculosus

Г. the process extends to the entire outer surface of the gums as an infiltrative, often erosive, and sometimes ulcerative lupus. With this form, the bone tissue of the alveoli is often affected and the picture of “hypertrophic lupose gingivitis” may develop”

Answer Options:

- 1) А – Г, Б – Б, В – А, Г – Г.
- 2) А – Б, Б – А, В – Г, Г – В.
- 3) А – В, Б – Г, В – Б, Г – А.
- 4) А – А, Б – Б, В – Г, Г – В.

## Question № 2

А. Diaskintest result, papule 4 mm

А. hyperergic

Б. Diaskintest result, papule 15 mm

Б. positive

В. Diaskintest result, hyperemia 10 mm

В. doubtful

Г. Diaskintest result, papule 1 mm

Г. negative

Answer Options:

- 1) А-Б; Б-А; В-В; Г-Г.
- 2) А-Г; Б-В; В-А; Г-Б
- 3) А-А; Б-Г; В-В; Г-Б
- 4) А-В; Б-Б; В-Г; Г-А

### Question № 3

A. Scrofuloderma

Б. Lupus tuberculosis

В. Tonsil tuberculosis

Г. Salivary Gland Tuberculosis

A. Tonsil enlargement, without crypt secretion

Б. The presence of lupomas

В. Painful salivary glands

Г. Dense knot coming from subcutaneous tissue

Answer Options:

1) A – Б, Б – Г, В – А, Г – В

2) A – В, Б – Г, В – А, Г – Б

3) A – Г, Б – Б, В – А, Г – В

4) A – А, Б – В, В – Г, Г – Б

### Question № 4

A. swelling of the neck and face behind the corner of the lower jaw against the background of the forced position of the head (tilt outward and slightly back)

Б. pain in opening the mouth and swallowing, tumor formation in the parotid or submandibular region

В. dense tuberous tumor formation in the parotid or submandibular region, accompanied by hypersalivation and an unpleasant aftertaste

Г. tumor-like, moderately painful formation in the parotid or submandibular region

A. peripheral lymph node tuberculosis

Б. pharyngeal cancer

В. salivary gland tuberculosis

Г. pharyngeal abscess

Answer Options:

1) A – Б, Б – Г, В – А, Г – В

2) A – В, Б – Г, В – А, Г – В

3) A – В, Б – Г, В – А, Г – Б

4) A – Г, Б – В, В – Б, Г – А

### Question № 5

- A. Signs of damage to the oropharynx      A. hypersalivation, cough
- B. Signs of damage to the larynx      B. nasal voice, shortness of breath
- B. Signs of a nasopharyngeal lesion      B. dry mouth, bad mouth

#### Answer Options:

- 1) A – Г, Б – Б, В – А
- 2) A – Г, Б – Б, В – А
- 3) A – Б, Б – А, В – Б

### Question № 6

- A. superficial, less often – deep, painless erosion on the mucosa with sharp, rounded or oval edges with a diameter of 0.5 to 1 cm      A. chronic inflammation of the mucous glands of the palate
- B. painful formation on the mucosa of a bright red color with uneven, poorly differentiating edges      B. syphilitic chancre
- B. large sizes softly hyperemic papules on a hard and / or soft palate, on the surface of which there are holes      B. candidiasis
- Г. ulcer on the gum of the lunar shape, slightly painful, with thin edges, red, easily bleeding      Г. Tuberculous gingivitis

#### Answer Options:

- 1) A – Б, Б – Б, В – А, Г – Г
- 2) A – Б, Б – Г, В – А, Г – Б
- 3) A – Б, Б – Г, В – А, Г – Б
- 4) A – Г, Б – Б, В – А, Г – Б



## ANSWERS TO TEST TASKS WITH ONE RIGHT ANSWER

1-5	2-4	3-1	4-1	5-3	6-3
7-3	8-1	9-3	10-2	11-4	12-5
13-1	14-3	15-1	16-2	17-4	18-1
19-2	20-5	21-2	22-1	23-2	24-1
25-4	26-1	27-4	28-2	29-3	30-1
31-3	32-2	33-2	34-5	35-1	36-1
37-3	38-1	39-1	40-2	41-3	42-3
43-2	44-2	45-4	46-5	47-2	48-3
49-3	50-5	51-2	52-1	53-5	54-1
55-1	56-5	57-2	58-3		

## ANSWERS TO TEST TASKS WITH A MULTI-TASK RESPONSE CHOICE

1-1	2-2	3-4	4-3	5-1	6-2
7-3	8-1	9-4	10-1	11-3	12-2
13-1	14-4	15-2	16-1		

## ANSWERS TO TEST TASKS WITH MULTIPLE MATCHING

1-2	2-1	3-3	4-4	5-3	6-1
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## **SITUATIONAL TASKS (PRACTICAL SKILLS TRAINING)**

### **Situational task №1**

Male, 47 years old. When questioned over the past three months, he is worried by weakness, decreased appetite, unproductive cough, fatigue, and an increase in body temperature up to 38.2 °C. He went on an outpatient basis to a therapist at the place of residence; non-specific antibiotic therapy (amoxiclav) was performed. In addition, it is noted that in the oral cavity on the mucous membrane of the right cheek, about two months ago, an unhealed ulcer appeared, which in time increased in size. Socially well-received, working in harsh climatic conditions (oil field shifts). Of the past diseases, OM is noted with exacerbations 2 times a year, frequent infections of the upper respiratory tract, and over the past two years, he suffered from pneumonia three times. He does not abuse alcohol, he has smoked for 1.5 packs a day for a long time.

The condition is satisfactory. A patient with low nutrition (height – 185 cm, weight - 53 kg). Respiratory rate up to 22 in 1 minute. Percussion in the projection of the upper lobe of the left lung detects blunting percussion sound. Auscultation in this area against the background of bronchial breathing, determine multiple wet rales of various sizes; breathing on the right with a hard tint. Heart sounds are rhythmic, heart rate 109 per minute, blood pressure - 112/65 mm Hg. Abdomen without features.

Complete Blood Count (CBC): red blood cells -  $3.58 \times 10^{12}$  / l, hemoglobin - 149 g / l, white blood cells –  $10.4 \times 10^9$  / l, band neutrophils - 3%, neutrophils - 78%, 1 - 15%, lymphocytes – 15%, monocytes - 4%, erythrocyte sedimentation rate (ESR or sed rate) - 39 mm / h.

On the survey X-ray of the lungs in the upper lobe of the left lung, a non-uniform darkening area is defined subpleurally, in which a decay cavity up to 2.5 cm in size with indistinct external boundaries and a path to the root of the lung is visualized. In the surrounding tissue, single small focal shadows. The root is structural, not increased. The shadow of the mediastinum is normal. Sines are free, the diaphragm is spherical.

When examining the oral cavity on the mucous membrane of the right cheek, against the background of hyperemia and edema, a painful ulcer is determined, measuring up to 0.6 cm in diameter with underlined soft edges and a yellowish-gray bottom, which bleeds when pressed. Regional lymph nodes are not enlarged.

**The task:**

1. Indicate the leading radiological syndrome in the lungs. Assume the most likely diagnosis.
2. What anamnesis data, risk factors, and clinical manifestations of tuberculosis are observed in the patient.
3. Identify the methods of the patient's further examination to verify pulmonary tuberculosis.
4. Identify the differential diagnostic series for infiltrative ulcerative lesions in the oral cavity.
5. Identify the methods for verifying tuberculosis of the oral mucosa.
6. Treatment tactics, prognosis.

**Answer:**

1. The main radiological syndrome is the syndrome of the area of compaction / darkening of the lung tissue, the cavity syndrome, which may correspond to non-specific destructive pneumonia and, taking into account the upper-lobe localization, infiltrative pulmonary tuberculosis in the decay phase.
2. It is necessary to collect an epidemiological history of tuberculosis (past disease, tuberculous contact); to clarify when the last time before the illness fluorography was made, its result. Risk factors - often recurring in the last two years of pneumonia, OM, hard physical work in extreme weather conditions, smoking; clinical manifestations - cough for more than 3 weeks, intoxication syndrome for more than 2 weeks, weight loss, lack of the effect of the antibacterial therapy. The ineffectiveness of nonspecific therapy always makes one doubt the diagnosis of pneumonia. Therefore, in primary health care institutions, a minimum standard for examining tuberculosis patients with this clinical symptom is performed. In addition to an X-ray examination, a 3-fold sputum examination by light microscopy with a Ziehl-Nelsen stain for acid-resistant mycobacteria and a diagnostic test with a tuberculosis recombinant allergen in standard dilution (diaskintest) are required. If the AFB is detected, the patient is redirected to a TB hospital by a specialized trans-port. With a negative microscopic result, but persisting suspicions about a specific process in the lungs (treatment inefficiency, dubious / positive diaskintest), the patient is thoroughly examined in a specialized facility (anti-tuberculosis dispensaries, centers, hospitals).
3. For verification of pulmonary tuberculosis, mandatory studies are: microbiological studies, including the study of two samples of diagnostic material by luminescence microscopy, molecular genetic tests for the presence of MBT DNA markers, cultured when the material is inoculated on a liquid and solid nutrient medium with a species identification of the select-

ed cultures and determination of the drug sensitivity of the MBT to anti-TB drugs by cultural or molecular genetics methods. A diagnostic test with a recombinant tuberculosis allergen in standard dilution and chest x-ray (if performed at the initial stage) are indicated. And if it is medically required (HIV-infected, mandatory), multispiral computed tomography of the lungs and mediastinum is performed.

4. Differential diagnosis: aphthous / traumatic ulcer, infections (bacterial, fungal and viral), drug reaction to antibiotic therapy, malignant neoplasm.

5. In cases of suspected OM tuberculosis, the study of an ulcer purulent discharge or an ulcer smear imprint for the detection of MBT (microscopy, culture, PCR) and a biopsy of the ulcer edge for morphological verification of the diagnosis are indicated.

6. Comprehensive treatment with the inclusion of chemotherapy for tuberculosis according to the spectrum of drug resistance of MBT to PTP, pathogenetic and symptomatic treatment of ulcers on the mucous membrane of the left cheek: rinsing or mouth baths with chamomile, stomatophyte, or miramistin in the morning and before going to bed. To accelerate epithelization after rinsing, it is necessary to apply salcoseryl or metrogyl-dent. The prognosis for pulmonary tuberculosis and OM, as well as for future life after treatment, is favorable.

### **Situational task №2**

Boy, 8 years old. Complaints of pain when swallowing solid food, weakness, sweating, a rare dry cough, subfebrile temperature and weight loss over the past half a month. He considers himself sick for 3-4 weeks. He had contact with a mother, a tuberculosis patient, who was treated irregularly in a tuberculosis hospital in a unit for a multidrug-resistant pathogen. From the anamnesis: vaccination in the maternity hospital, revaccination at 7 years old. The dynamics of tuberculin tests: from 1 year of life to 7 years old - corresponds to post-vaccination allergy. An objective examination: on the left shoulder, there are two post-vaccination scars. The skin is pale, moist. Low painful cervical and submandibular lymph nodes from 1.0 cm in diameter, soft elastic in consistency, are palpated on both sides, the largest (up to 1.5 cm) is located in the submandibular region on the right. In the lungs on the right, in the interscapular space, shortening of the pulmonary sound, isolated dry rales are detected. Heart - tachycardia up to 112 beats / s, tones are muffled. The abdomen is soft, painless. The liver protrudes 1.0 cm below the costal arch.

An examination of the oral cavity revealed an ulcer up to 3.0 cm in diameter at the border of the hard and soft palate, with irregular, torn edges, a dense texture and necrotic contents. On the X-ray of the lungs in direct projection, the shadow of the right lung root is widened, deformed; the external boundary is blurred, uneven; a focal shadow of  $1.5 \times 2.3$  cm in diameter, medium intensity, uniform, with blurry boundaries, is determined in the upper lobe of the right lung.

CBC: hemoglobin - 105 g / l, red blood cells -  $3.05 \times 10^{12}$  / l, white blood cells -  $8.6 \times 10^9$  / l, ESR - 51 mm / h. Mantoux reaction with 2 TE PPD-L - 21 mm papule, diaskintest - papula with 18 mm vesicle. Microscopy of sputum stained by Ziehl-Nielsen - AFB negative.

**The task:**

1. Indicate the risk factors for tuberculosis in the child. Determine the pathogenesis of the development of the tuberculosis process.
2. Justification of the diagnosis of pulmonary tuberculosis in the absence of AFB.
3. What methods of additional examination are necessary to verify the etiology of an ulcer in the palate?
4. Describe the result of immunological research.
5. The tactics of treatment.

**Answer:**

1. A risk factor for the development of tuberculosis in a child is family contact with a mother, a tuberculosis patient. The pathogenesis of the development of the disease is primary, since according to the Mantoux test, a child under 7 years old was not infected with the MBT.
2. Diagnosis justification:
  - contact with a patient suffering from tuberculosis;
  - childhood;
  - data from an objective examination (increased body temperature, sweating, coughing, an increase in several groups of peripheral lymph nodes, changes in auscultation of the lungs, changes in the hemogram, indicating inflammation);
  - results of immunological tests;
  - X-ray data (determined by the expansion of the right root of the lung with focal lung tissue infiltration, which indicates the localization of the inflammatory process);
  - Sputum microscopy with Ziehl-Nielsen staining is an insensitive method and, therefore, a more sensitive laboratory diagnosis is used to verify the diagnosis: sputum analysis on MBT DNA by polymer-

ase chain reaction, culture on culture media with determination of drug resistance of MBT to anti-TB drugs.

3. The "gold standard" for the diagnosis of specific oral ulcers is morphological verification with the detection of tuberculous inflammation, as well as the study of the biopsy of the affected area by microbiological methods. In case of refusal to carry out a diagnostic operation, you can perform a puncture of the lymph node. Taking into account the anamnesis (the contact), clinical and radiological manifestations of the disease and in the presence of caseous necrosis in the lymph nodes, it is highly likely that the formation of an ulcer in the palate occurred, similarly, due to tuberculosis. To exclude deep destructive inflammatory processes in the hard palate, it is necessary to conduct an MRI of the bones of the facial skull with 3D reconstruction.
4. Reactions to the Mantoux test 2 TE PPD-L and diaskintest are hyperergic, which confirms the presence of active tuberculosis infection in the child's body.
5. Comprehensive treatment, chemotherapy according to the spectrum of drug resistance (in the absence of the MBT, the child should be guided by the mother's bacteriogram). If a defect in the bone is detected according to the indications, surgical treatment with subsequent plastic surgery and regenerative procedures.

## CONCLUSION

Orofacial tuberculosis of the area is difficult to diagnose, and this should be an important factor in the differential diagnosis of lesions that appear in the oral cavity. The most important diagnostic tools remain a thorough clinical / anamnestic assessment, biopsy of changes for histological examination, as well as finding acid-resistant mycobacteria when staining the material according to Ziel – Nielson, cultural and molecular genetic laboratory methods, as well as immunodiagnosics.

This manual defines the clinical course, diagnosis, differential diagnosis, as well as the goals and basic principles of treatment of patients with orofacial tuberculosis, including the features of the therapy for this extrapulmonary localization. In addition to chemotherapy, the issues of pathogenetic, symptomatic and surgical treatment of maxillofacial tuberculosis are highlighted.

## LIST OF ABBREVIATIONS

AFB	– Acid Fast Bacteria
RTA	– The recombinant tuberculosis allergen (diaskintest)
TMJ	– The temporomandibular joint
WHO	– World health organization
ELISA	– Enzyme-linked immunosorbent assay
ESR	– erythrocyte sedimentation rate
LTB	– Latent tuberculosis infection
DR TB	– Drug resistant tuberculosis
MBT	– Mycobacterium tuberculosis
NTM	– Nontuberculous mycobacteria
MDR	– Multidrug resistance
ATD	– Antituberculosis drugs
PCR	– Polymerase chain reaction
OM	– Oral mucosa
TB	– Tuberculosis
XDR TB	– Extensively drug-resistant tuberculosis
ESAT-6	– early secretory antigen target-6kDa
CFP-10	– culture filtrate antigen-10kDa
CBC	– Complete Blood Count



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L.G. TARASOVA, O.V. FILINYUK

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clinic, diagnosis, differential diagnosis**

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Editorial and publishing department of Siberian State Medical University  
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