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PHARMACOTHERAPY IN DENTISTRY

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The authors of the book made recommendations to students of dental faculties and practicing dentists on the effective use of pharmacotherapy in dental practice. The book describes the pharmacological characteristics of the main groups of drugs used in dentistry.

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FOREWORD

In recent years, the pharmaceutical market of Ukraine has significantly replenished with new drugs, which rational use improves the possibilities of effective pharmacotherapy. An important component in formation of clinical thinking of a future dentist is knowledge of rational pharmacotherapy. However, this task is difficult for a young specialist who needs science-based recommendations in his professional activities.

The authors of the textbook "Pharmacotherapy in Dentistry" set a goal to expand future dentists' knowledge in pharmacotherapy, to develop clinical thinking, skills and confidence in prescribing medicines. The presented book contains recommendations on drug prescribing for specific nosological forms, including dosage regimens, methods of a drug administration and the duration of the course of treatment.

The book contains 3 sections. The first section sequentially presents material on the modern principles of anesthesia in dentistry, an effective use of drugs in therapeutic and surgical dental practice. The second section presents material important for practice of a dentist on pharmacotherapy in emergency conditions. The third section is devoted to the pharmacological characteristics of drugs used in the professional activity of a dentist. The manual discusses the medicines that are necessary for preparation of a patient for medical manipulations (general anesthetics, sedatives, analgesics, local anesthetics), for the treatment of certain nosological forms (antiseptics, antibiotics, antifungal, antiviral, anti-inflammatory drugs, immunostimulants and probiotics) and drugs aimed at enhancing the body's resistance (biostimulants, vitamins, antioxidants, etc.).

The training material was prepared by a team of qualified clinical pharmacologists of the Ukrainian Medical Stomatological Academy (T. A. Petrova, G. Yu. Ostrovska, N. N. Ryabushko, A. A. Kapustianska), who have experience in the proper use of pharmacotherapy in dental practice. The book can be useful for students of dental faculties and for dental practice.

LIST OF CONDITIONAL ABBREVIATIONS

ABD	antibacterial drug
ACTH	adrenocorticotropic hormone
AG	aminoglycoside
AIDS	acquired immune deficiency syndrome
AS	anaphylactic shock
ATC	average therapeutic concentration
ATP	adenosine triphosphate
BBB	blood-brain barrier
BP	blood pressure
BT	biliary tract
c-AMP	cyclic 3,5-adenosine monophosphate
CBV	circulating blood volume
CCF	chronic circulatory failure
CHD	coronary heart disease
CIS	commonwealth of independent states
CNS	central nervous system
COX	cyclooxygenase
CS	cephalosporins
CVS	cardiovascular system
DNA	deoxyribonucleic acid
EA	epidural anesthesia
ESR	erythrocyte sedimentation rate
FQ	fluoroquinolones
GABA	gamma-aminobutyric acid
GCS	glucocorticosteroids (corticosteroids)
GHBA	gamma-hydroxybutyric acid
GIT	gastrointestinal tract
HC	hypertensive crisis
HIV	human immunodeficiency virus
HPAS	hypothalamic-pituitary-adrenal system
HR	heart rate
IFN	interferon

IM	immunomodulators
i.v.	itravenous
i.m.	intramuscular
IST	immunostimulants
ISU	immunosuppressants
ITD	immunotropic drugs
IU	international unit
LA	local anesthetic
LPO	lipid peroxidation
LRT	lower respiratory tract
MAO	monoamine oxidase
MCS	mineralocorticosteroids
MFA	maxillofacial area
MIC	minimum inhibitory concentration
MLV	mechanical lung ventilation
MRSA	methicillin resistant staphylococcus aureus
MVB	minute volume of blood
NA	narcotic analgesics
NAD	nicotinamide adenine dinucleotide
NADP	nicotinamide adenine dinucleotide phosphate
NLA	neuroleptanalgesia
NNA	non-narcotic analgesics
NSAIDs	non-steroidal anti-inflammatory drugs
PABA	para-aminobenzoic acid
PBP	penicillin binding protein
PCA	patient-controlled analgesia
PG	prostaglandins
PRSA	penicillin-resistant staphylococcus aureus
RNA	ribonucleic acid
SA	sulfonamides
s.c.	subcutaneous
SET	systemic enzyme therapy
TMJ	temporomandibular joint
UA	unit of action
URT	upper respiratory tract
UT	urinary tract
WHO	World Health Organization

Section 1

PHARMACOTHERAPY IN DENTISTRY

1.1 ANESTHESIA IN DENTISTRY

Pain refers to the most common complaint doctors of all specialties deal with in their practice. According to WHO, in developed countries, pain is compared in scale with a pandemic. It is a complex and insufficiently studied problem of medicine. The phenomenon of pain is due to the versatility and individuality of the mechanisms of its occurrence.

The scientific foundations for studying pain and anesthesia were laid in the 19th century, when the use of chloroform anesthesia and the release of morphine from opium poppy first began. At the end of the first half of the 20th century the science of pain (algology) has been identified as an independent industry. During this period (the beginning of the 40s), pain clinics began to be created in the USA and Europe, which specialized in the treatment of various types of pain. In 1984, a flight therapy colloquium was organized, which develops science, streamlines the principles of prescribing painkillers. In 1990, the European Union for international cooperation in the field of pain research (Euro Pain) was created. The scientists of the CIS countries Veyn A. M., Avrutsky M. Ya., Krizhanovsky G. M., Shtok V. M. made a great contribution to the development of the problem in the study of pain, and the analgesic properties of individual drugs and specific pain syndromes – Antonov I. P., Anisimova E. N., Lebedeva R. M., Golikov A. P., Bukhtiarova T. A., Zoryan E. V., etc.

The occurrence of pain is primarily associated with the activation of special pain receptors (nociceptors), which perceive pain irritation and transmit it to the central links of the nervous system, corresponding to the sensation of pain. The flow of pain impulses along the nerve pathways enters the brain and is perceived if it exceeds a critical threshold level. Pain mediators are considered to be: substance P (plasmokine), cholecystokinin, somatostatin, etc. In the genesis of this process, an imbalance in the opioid system or its deficiency, which is accompanied by autonomic disorders and poor health, plays an important role. The final perception of

pain is a psychological process and is a combination of sensations, their assessment based on a combination of factors of the body and its previous experience.

Pain, which is associated with the pathology of the formations of the oral cavity, especially teeth, is considered the most frequent. In therapeutic and surgical dentistry, there are a large number of diseases (caries, pulpitis, periodontitis, tooth and jaw injuries, inflammatory processes of soft tissues, osteomyelitis, tumor processes, etc.), which are accompanied by the occurrence of pain. Features of localization and blood supply to dental pathology determine the occurrence of severe pain with impaired function of the damaged area.

The occurrence of pain indicates a violation of the vital functions of the person and indicates the affected area. The positive role of pain as a signal of trouble and warning on the one hand, an independent pathological phenomenon and a stressful obstacle to the normal functioning of the body, on the other, were revealed. At present, such a definition has become classic: "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".

The quality of the dentist's work is based on the painless implementation of the dental interventions necessary to treat the disease and the adequate use of therapeutic measures. The rational use of anesthetic and analgesic agents ensures the effectiveness of treatment, making a significant impact on the outcome of the disease. Taking into account the specifics of the anatomical and functional signs of the MFA associated with its rich innervation, the rapid spread of inflammatory processes, severe pain symptoms, it is clear that dentistry needs high-quality analgesia.

In dental practice, acute and chronic pain is distinguished by clinical characteristics. Acute pain is a new, recent pain that is inextricably linked to damage to superficial or deep tissues and, as a rule, is a symptom of a disease. Acute pain is a danger signal. It is well determined. You can determine the nature of pain irritation, as well as its localization. Now an idea of acute pain has formed as a sensory reaction with the further inclusion of emotional-motivational, vegetative-endocrine, behavioral factors that arise as a result of impaired body integrity. As a result of severe irritation of pain receptors (trauma, burn, ulcer), pain is perceived as temporary, but

it can be life threatening. Its duration is determined by the duration of the damaging factor. The individual nature of the pain is largely determined by the emotional component. Severe acute pain can be unbearable or vary depending on its intensity. It can cause passivity, depression and even lead to suicide. Adaptation to acute pain occurs faster.

Chronic pain often acquires the status of an independent disease, lasts a long time, and the cause of it can not often be determined. This type of pain is more consistent with the concept of a syndrome – a complex of symptoms and signs typical for a particular condition. Chronic pain can not depend on the underlying disease or a damaging factor and develops according to its own laws. The International Association for the Study of Pain (IASP) defines chronic pain as "pain that lasts longer than the normal healing period", for more than three months. However, the main difference between chronic pain is not a temporary factor, but qualitatively different neurophysiological, biochemical, psychological and clinical relationships. In dentistry, taking into account different parameters, the following types of pain are distinguished: phantom, post-traumatic, caused by damage to the nervous system and chronic process in the bone and muscle systems, oncological, etc.

Each type of chronic pain has its own clinical features, predetermined by the origin and mechanism of its occurrence, localization, individual characteristics of the patient's personality, the influence of cognitive and social factors, and the existing "pain experience". The main clinical characteristics of this type of pain are its duration, monotony, diffuse nature. The concepts of "chronic pain syndrome" are used for relatively long pain, when the disease that caused it has already been eliminated, for example, after surgical or therapeutic treatment of a pathological lesion, etc. Such pain does not sufficiently respond to conventional NNA, which are widely used.

Particular attention is paid to practical medicine in the treatment of chronic pain, which accompanies almost all forms of malignant neoplasms. The patient's constant sensation of pain manifests itself in particular autonomic, affective, and behavioral responses. Fear of the future, reactive depression, insomnia, suicide attempts and aggressive reactions regarding medical personnel develop. Long-term pain exposure is characterized by an increase in the influence of psychological factors on pain mechanisms.

The formation of the latter depends more on a complex of psychological factors than on the nature and intensity of peripheral influence. A variant of chronic pain is psychogenic pain, when there is no peripheral effect or it plays the role of a triggering factor. Chronic pain is also a favorite mask of latent depression, and is built on the lack of monoaminergic mechanisms (especially seratonergic). The variety of mechanisms and manifestations of prolonged pain syndromes suggests that this type of pain is especially severe with respect to the choice of pharmacotherapeutic approaches.

Thus, the choice of optimal methods for treating pain and certain analgesic drugs in the context of dental practice is a fundamentally important component that provides a faster healing process for the patient. The rational use of analgesics should be grounded on evidence-based methods for the consistent use of painkillers, their appropriate dosage and combination.

1.1.1. Use of general anesthetics

General anesthesia (narcosis) is one of the most effective methods of anesthesia, as it provides for the "exclusion" of consciousness, sensitivity, physical activity, conditioned and some unconditioned reflexes with moderate inhibition of the vital centers of the extended brain. Narcosis is a state of reversible inhibition of the central nervous system, which is achieved using pharmacological agents. For operations in dentistry, inhalation and non-inhalation anesthetics are used.

For modern general inhalation analgesia, volatile liquids (enflurane, isoflurane, etc.) and gaseous substances (fluorotane, nitric oxide, xenon, etc.) are used. Certain requirements are imposed on anesthetics: high anesthetic activity, good controllability of anesthesia and elimination from it, a wide range of effects and low toxicity. Inhalation analgesia is well regulated by changing the ratio of the components of the mixtures that are inhaled. It is represented by: a) facemask narcosis (oropharyngeal, nasopharyngeal), which is used to remove teeth, dissection of the focus of inflammation; b) intubation narcosis (a tube is inserted through the nose, mouth, tracheostoma), which is used to carry out the most traumatic and long-term surgical interventions on the MFA tissues. This type of anesthesia is one of the most expensive, including both the cost of drugs and means of delivery (anesthesia machines).

Mononarcosis is rarely used, for a faster introduction to anesthesia and to reduce complications from the use of general anesthetics, it is used in combined methods of anesthesia. To quickly reach the stage of surgical anesthesia, as a rule, thiopental sodium is first introduced, and then analgesia is maintained with low toxicity drugs with a wide range of effects (nitric oxide, etc.). In mixed anesthesia, separate drugs are combined, which allows to reduce the dose of each of them, and, consequently, its toxicity.

When prepared for surgery, premedication is performed – a drug preparations complex aimed at ensuring anesthesia and surgery, which include sedative and analgesic effects, decrease in saliva secretion, and prevention of vagal reflexes. It is used when preparing a patient for general anesthesia using the following groups of drugs: antipsychotics (droperidol, chlorpromazine), tranquilizers (diazepam, tazepam, gidazepam, phenazepam, tenoten), sleeping pills hypnotic (imovane, donormyl), NA (fentanyl, promedol, morphine) – cholinoblockers (atropine sulfate, metacin). Premedication is prescribed by an anesthetist. The characteristics of drugs for general anesthesia are described in detail in the section "Local anesthetics and drugs for anesthesia".

1.1.2. Use of local anesthetics

In dentistry, this type of anesthesia is often performed. It is safe and convenient. A physician conducting the anesthesia must not only perfectly master the skills of its execution, but also know all the properties of anesthetics and vasoconstrictors used. Now in dentistry, the most commonly used are amide anesthetics (articaine, mepivacaine, lidocaine, trimecaine, levobupivacaine, etc.), which satisfy doctors with the duration and strength of anesthesia.

Local anesthesia of MFA tissues:

1) injectable:
- infiltration (soft tissue, hard tissue);
- conduction (peripheral, central).

2) non-injectable:
- application method (chemical, physical).

Infiltration anesthesia provides anesthesia of peripheral nerve endings, due to the introduction of LA directly in the field of surgical intervention. Infiltration anesthesia is used to anesthetize the soft tissues of the upper

limbs, alveolar bone of the jaw, and remove temporary and permanent teeth in children and adults.

Intraligamentary anesthesia (intracircular) is performed by introducing LA into the periodontal tissue, which penetrates the intraosseous space through the hole of lamina cribriformis and then to the periapical region.

Conduction peripheral anesthesia involves the anesthetic to the peripheral branches of the main trunks. In this case, the anesthetic blocks the conduction of nerve impulses, preventing the depolarization of the membrane by blocking the incoming sodium stream.

Central anesthesia involves the anesthesia of the second and third branches of the trigeminal nerve at target points on the base of the skull. It is used for anesthesia on the upper and lower jaws when it is impossible to perform general anesthesia or insufficient effect of peripheral conduction anesthesia.

Even when using the most modern anesthetics of amide anesthetic group, the maximum analgesic effect is not always achieved, especially on the lower jaw. 10–19 % of the population have individual characteristics of pain reactions. LA is not always effective in the following dental interventions:

- treatment of pulpitis of molars and premolars of the lower jaw;
- surgical treatment of inflammatory diseases of MFA (periodontitis, periostitis, abscess, phlegmon), often of the lower jaw;
- preparation of hard tooth tissues with an intact pulp on the upper and lower jaw under unremovable orthopedic constructions.

Improving the methods of LA is accompanied by the introduction into the dental practice of modern NNA, tranquilizers, sleeping pills, sedatives. Drugs are usually prescribed before bedtime or in 30–120 minutes before anesthesia, depending on the state of anxiety of the patient. The choice of the drug and its dosage should preferably be agreed with the therapist or anesthetist.

Anesthesia method, which involves the introduction of one or more medicines in the preoperative period in order to increase the safety of anesthesia and reduce possible complications, is a potential anesthesia. Its main objectives are to reduce psychoemotional stress, increase the effect, prevent unwanted reflexes, and cause vegetative stabilization. In order to potentiate anesthesia, diazepam (seduxen, sibazon) can be prescribed

orally – 0.1–0.3 mg/kg of body weight 30 min. before anesthesia, imovane (zopiclone) 0.0075 g orally at bedtime, donormyl 0.01 g orally at bedtime, phenazepam 0.001 g orally before going to bed. Recently, tenoten tranquilizer of homeopathic origin has been widely used (also in children) (1–2 tablets sublingually 30 minutes before surgery).

Non-injectable pain relief is represented by application or superficial anesthesia, which is based on pain relief of terminal nerve endings.This includes chemical (use of drugs) and physical methods of pain relief. Application pain relief is used for interventions on the oral mucosa, hard tissues and tooth pulp, at the injection site and submucous abscesses on the gums, removal of temporary moving teeth, etc.

There are many painkillers for application anesthesia: amprovizol aerosol, which contains anesthesin, legrazol aerosol, which includes sovcain, lidocaine aerosol (xylocaine spray, xylonor) based on lidocaine, pyrozole aerosol, containing pyromecaine, streptourazole aerosol, which contains trimecaine, perylene ultra, based on tetracaine, pulponest and pulperil, which contains procaine, etc. The characteristics of local anesthetics are described in detail in the section "Local anesthetics and means of anesthesia".

1.1.3. Use of non-narcotic analgesics

Non-narcotic (non-opioid) analgesics are widely used to relieve moderate pain of a predominantly inflammatory genesis that occurs in the MFA with pulpitis, periodontitis, periostitis, pericoronaritis, injuries and other lesions. These drugs have common properties:

- carry out a pronounced effect in relation to pain of an inflammatory nature than intense pain of a different genesis;
- have a dose limit, with a further increase in which the analgesic effect does not increase;
- do not cause the development of tolerance and dependence;
- when using them, additional analgesia is achieved by combinations with adjuvant drugs and opioids;
- available for outpatient treatment.

To provide first aid in dental practice in acute moderate pain, NNAs are used, which are recommended by the WHO: paracetamol, ibuprofen, acetylsalicylic acid. These drugs, blocking COX-2, disrupt the synthesis of PG. The latter take part in the processes of the onset of pain, inflammation

and fever, reduce the sensitivity of pain receptors to bradykinin, reduce local tissue edema and weaken the mechanical path of nociceptors. In severe cases of pain, NNA with a high analgesic potential is used – ketoprofen lysine salt (artrosilene), lornoxicam (xefocam), ketorolac (ketanov), parecoxib (dynastat). Currently, they have also found the use of NNA from the group of selective COX-2 inhibitors (meloxicam, nimesulide, celecoxib, parecoxib, etodolac, aceclofenac).

The dentist needs to have skills in the rational use of NNA for the treatment of postoperative pain. The latter has a complex genesis and is associated with the reaction of all body systems in response to surgical tissue trauma. Surgical manipulation leads to the formation of a primary peripheral focus of acute pain, which, since the moment of injury, serves as the site of active neurohumoral processes that are the source of the upward nociceptive pain flow. Traditional methods of postoperative pain management based on NA do not eliminate the stress response to surgical trauma and related homeostasis disorders (pressor cardiovascular reactions, peripheral vasospasm, decreased tissue and organ blood flow, metabolic acidosis, impaired blood rheology, tendency to to develop thrombosis, hypovolemia, etc.).

An important role has been proved in reducing the severity of postoperative pain syndrome of classical NNA – inhibitors of PG synthesis, as well as agonists of α2-adrenergic receptors (clonidine), antagonists of the synthesis of excitatory amino acids (ketamine). In the NNA group, ketorolac tromethamine (ketanov) is of particular interest, which has a pronounced analgesic activity comparable to morphine and significantly exceeds the analgesic effect of other NNAs. Ketoprofen, which is a non-selective inhibitor of COX-1, COX-2, is widely used in practical medicine, including dentistry. Its central effect is due to a direct effect on the thalamic centers of pain sensitivity, which is associated with inhibition of the synthesis of PG in the central nervous system by the drug. Among the selective COX-2 inhibitors there are dexketoprofen (dexalgin), meloxicam (movalis), nimesulide (nise, mesulid), parecoxib (dynastat), aceclofenac (airtal), which exhibit a pronounced analgesic, anti-inflammatory, antipyretic effect. Recent drugs do not affect the "constitutional" COX-1, which is responsible for the physiological effects of PG, which significantly reduces the risk of side effects.

Co-analgesics (adjuvants, analgesic aids) are used as additional drugs for the prescription of NNA and NA and are prescribed independently to neutralize acute pain (especially neuropathic). Some drugs have an analgesic effect (tricyclic antidepressants, hydroxyzine) or a partial analgesic effect (caffeine, gabapentin, pregabalin). These drugs are described in more detail in the section "Psychotropic drugs".

1.1.4. Use of narcotic analgesics

Narcotic (opioid) analgesics have the most pronounced analgesic properties, which allow them to be used to relieve severe pain. NA rise the threshold of pain perception, prolong the period of its tolerance, and weaken the emotional and behavioral reactions to pain. Unlike anesthetics, their analgesic effect develops while maintaining consciousness. These drugs find overwhelming use in dentistry for intense pain that is associated with traumatic injuries in the MFA. NA are also used for pain relief during planned surgical interventions and in case of oncological diseases.

Taking into account the large number of opioid preparations with various analgesic properties, their rational choice should depend on the severity of pain syndrome and individual characteristics of the patient. In complex clinical cases and severe pain, it is advisable to use strong opioids (morphine, omnopon, dipidolor, etc.), and with less pronounced pain intensity, analgesics with moderate analgesic properties (tramadol, codeine, tilidine, etc.).

When using NA in cancer practice, the following principles should be adhered to:

- prescribe analgesics prophylactically, not expecting severe manifestations of pain;
- take drugs orally, if possible;
- adhere to regular drug taking "with the clock in your hands";
- use the rules for phased drug prescribing: non-opioid analgesic (paracetamol) + adjuvant – weak opioid (codeine, tramadol) + paracetamol + adjuvant – strong opioid (morphine) + paracetamol + adjuvant – long-acting opioid (methadone, morphilong) + NNA;
- prescribe, if necessary, additional doses of drugs;
- use psychotropic drugs, muscle relaxants, clonidine in the treatment of resistant pain syndromes.

The most common method of opioid analgesia in oncology is the systemic administration of NA "according to the scheme" or "on demand", the advantage of which is the ease of use and low cost of the drugs. One of the modern types of pain relief is patient-controlled analgesia. In this case, the need to introduce an additional portion of NA is determined by the patient himself.

Long-term use of NA causes a risk of drug dependence, which is characterized by tolerance, mental and physical dependence, as well as withdrawal symptoms. Tolerance is manifested by a gradual loss of the effectiveness of the drug with repeated administration of the same dose. Physical dependence is associated with the development of withdrawal symptoms, which are characterized by the following manifestations: chills, hyperventilation, hyperthermia, mydriasis, muscle pain, vomiting, anxiety, etc. Physical dependence occurs, as a rule, with drug abuse, and not in medical practice.

In the practice of a dentist, adequate pain relief with NA for a variety of diseases of the MFA and the implementation of dental interventions have a significant impact on the effectiveness of treatment.

1.1.5. Pharmacotherapy of pain in therapeutic dentistry

In the practice of a general practitioner, a moderate or severe pain syndrome is observed in many diseases of traumatic and inflammatory origin. In case of tooth injuries that arise as a result of an impact in a solid substance with a solid object, pain usually occurs. The following types of traumatic injuries are distinguished: bruise, fracture, dislocation.

With a bruise (contusion) of the tooth, significant tissue damage does not occur, but the impact force is transmitted to the periodontal tissue, which may be accompanied by a rupture of the neurovascular bundle of the periodontium, and hemorrhage. In this type of injury, the nature of pain depends on the degree of tooth mobility. It can be moderate or severe, aggravated by biting and percussion. It is necessary to create conditions for the calmness of the damaged tooth (remove from occlusion), to prescribe a sparing diet. If necessary, carry out treatment or tooth extraction. The prescription of NNA is recommended (paracetamol 0.5 g enterally, 3 times a day, ibuprofen 0.4 g enterally, 3 times a day, ketorolac 0.01 g enterally, 3 times a day), as well as antihistamines (suprastin 0.025 g enterally 2–3 times a day, loratadine 0.01 g enterally once a day).

When a dislocation (traumatic dystopia) occurs, the tooth is displaced relatively to the hole due to rupture or stretching of the periodontal fibers and root wall injury. In case of incomplete dislocation, tooth displacement and mobility (I–II degrees) are observed. Jaw closure may be impaired. The root of the tooth leaves the hole partially or completely. If the tooth crown is located below the level of other teeth, then this indicates damage to the alveolar ridge (stick-in dislocation). With a complete dislocation of the tooth, its traumatic removal from the hole occurs. With these types of disorders, tissue edema and hematoma of the oral mucosa at the site of injury are observed. The patient complains of severe pain. In treatment, an important place is taken by orthopedic and surgical methods (reposition, fixation with braces or splint, replantation, extrusion, etc.). Therapeutic therapy is based on the following measures: a) antiseptic treatment of the oral cavity – 0.2 % solution of ethacridine lactate, 0.05 % solution of chlorhexidine, rotocan (1 teaspoon per glass of water) or rinsing with these drugs; b) prescribig ABD – amoxicillin 0.5 g enterally 3 times, lincomycin hydrochloride 0.5 g 2 times a day i.m.; NNA and antihistamines.

A fracture is accompanied by breaking off a part of the crown or the whole crown and tooth root. There are uncomplicated fractures (damage to the enamel, dentin) and complicated fractures of the tooth crown (with pulp injury and root fracture). In these cases, depending on the nature of the injury, soft tissue swelling, tooth crown defect, displacement of root fragments are observed, sometimes a bright red pulp is found at the fracture site. Probing is accompanied by sharp pain. A damaged tooth is usually motionless or barely movable. A variety of dental procedures are performed: elimination of enamel and dentin chips, amputation of the pulp, endodontic treatment, filling, reposition, replantation, splinting, tooth extraction, etc. The lesion site must be treated with an antiseptic, anesthetized with high-quality LA, NNA. If inflammation occurs, it is advisable to prescribe meloxicam, nimesulide and ABD (lincomycin, doxycycline, amoxiclav, etc.).

Pain in acute pulpitis, depending on its clinical form, may be moderate or severe. In acute partial pulpitis, the nature of the pain is arbitrary, in the form of short seizures (10–30 minutes) with long breaks. After 1–2 days, the inflammatory process spreads and acute diffuse pulpitis occurs. The

pain acquires a prolonged nature (several hours) with slight painless periods. Depending on the location of the causative tooth, pain can spread to the ear, temple, neck, etc. An objective examination reveals a deep carious cavity, which is filled with softened dentin. With purulent lesion of the pulp, the pain acquires an almost continuous, "pulsating" character, is significantly enhanced by the action of a thermal stimulus. For chronic forms of pulpitis (simple, hypertrophic, gangrenous), "aching" pain is more typical, it is associated with the influence of temperature and chemical factors and continues for some time after their elimination. The pain syndrome that develops with inflammation of the pulp is insufficiently stopped by conventional NNA (paracetamol, ibuprofen, ketanov, etc.). In these cases, if the pathological process in the pulp is not eliminated, it is important to carry out the necessary dental procedures.

With periodontitis, the nature of the pain depends on the clinical course and the prevalence of the process. First, in acute serous periodontitis, an unexpressed "aching" pain occurs, which corresponds to the area of the affected tooth and intensifies when pressing the tooth or during percussion. In the future, when the process becomes purulent, a constant intense pain occurs (clearly localized, "aching", "tugging", "throbbing", etc.). It is associated with the pressure of inflammatory exudate on the receptors; in most cases it is sharp. An important diagnostic feature is the occurrence of pain with horizontal and vertical percussion. On the mucous membrane in the area of inflammation, a periosteal abscess is sometimes formed, which can spread to the transitional fold and cause its smoothing. As a result, facial asymmetry develops. In the chronic course of periodontitis, the patient has no complaints of pain, but when collecting the anamnesis it turns out that the tooth pain appeared earlier.

To prevent the development of periostitis or phlegmon, the patient should be provided with the qualified assistance of a professional dentist. Depending on the localization of the process, conservative-endodontic or conservative-surgical methods are used. Antiseptic treatment of the canals is carried out using 2 % solution of chloramine, 0.03 % solution of chlorhexidine, 3 % solution of hydrogen peroxide, 1 % solution of decamine, microcide, etericide, chlorophyllipt, etc. In the future, the canals are filled due to modern methods. Effective NNA (ketorolac, ketoprofen, solpadeine, etc.) are used for analgesia, including combined ones.

For prolonged pain, long-acting drugs are indicated (solpaflex, naproxen, nimesulide, celecoxib, etc.).

The nature of the pain in different types of stomatitis depends on their form and clinical course. The most common manifestations are hyperemia and swelling of the mucous membrane, typical subjective sensations (pain, burning, dryness, etc.). The development of erosive and erosive-necrotic lesions is associated with the formation of ulcers of the mucous membrane and is accompanied by severe pain. In accordance with the severity of the disease, local and general treatment is used with the prescription of LA, NSAIDs, NNA and ABD. Sodium mefenaminate salt is used in the form of 0.25–0.5 % aqueous solution for application, mouth baths, instillation. Paracetamol, ibuprofen, nimesulide, etc. are also prescribed internally according to generally accepted schemes.

In acute inflammation of the gums (gingivitis), the clinical picture is characterized by swelling of the gums, bleeding when eating food, halitosis, pain. The latter is due to the phenomena of alteration and exudation. The most severe pain is observed in case of necrotizing ulcerative forms of gingivitis, which is also characterized by a deterioration in the general condition of the patient (fever up to 39 °C, headache, loss of appetite). In severe forms of ulcerative lesions, the process can extend to the entire dentition, as well as the cheeks, tongue, and palate. In complex treatment simultaneously with antibacterial, enzymatic, keratoplastic agents, it is advisable to use NNA (ibuprofen, mefenamic acid, etc.).

With periodontitis, gum disease occurs, which spreads to all periodontal tissues, and progressive destruction of the periodontal and bone tissue of the interdental septum develops. In case of acute focal periodontitis, the patient complains of local "aching" pain, which is associated with a rupture of the gingival joint when moving the crown or filling deep into the periodontal tissues. In accordance with the clinical picture of generalized periodontitis, I, II and III degrees of its development are distinguished. At the initial stages, the gingival pockets are shallow, deposition of supradental calculus is noted on the lingual side of the lower anterior teeth. The progression of the disease is associated with severe atrophy of the gum papillae, deepening of periodontal pockets, deposition of significant calculus, formation of serous-purulent exudate and occurrence of tooth mobility. With severe periodontitis, pain in the gums often occurs. In com-

plex treatment, selective anti-inflammatory drugs (nimesulide, meloxicam, diclofenac, aceclofenac) with effective analgesic properties can be used.

1.1.6. Pharmacotherapy of pain in neurodentistry

During surgery or as a result of spontaneous injuries, mechanical damage to a nerve can occur. This causes painful anesthesia or pain. The latter has a burning character, remissions periodically occur. Pain often occurs after extraction of molars. At first it is local, then more common; it is easily provoked by a temperature stimulus and emotional stress. The treatment of pain of this type is complex, local procedures are ineffective, and neurosurgical intervention is often necessary.

Facial pain mainly occurs due to various lesions of the trigeminal or glossopharyngeal nerve, pterygopalatine ganglion, geniculate ganglion of the facial nerve, as well as in the form of angioneurology or pathological occlusion syndrome.

Trigeminal neuralgia of predominantly central origin is characterized by episodes of excruciating short-term pain localized in the zone of innervation of one or more of its branches. The pain can spread vertically on the face, on both cheeks or take the shape of a circle. Painful paroxysms last from a few seconds to several minutes.

Bilateral trigeminal neuralgia of predominantly central origin – a chronic disease. Pain appears on one side of the face, and after a while on the other. Treatment consists in the prescription of carbamazepine 0.2 g 1–2 times a day daily, with further gradually increase of the dose to 0.4 g 3–4 times a day. Phenytoin, clonazepam, valproic acid also have an analgesic effect for trigeminal neuralgia. To enhance the action of anticonvulsants, antihistamines are prescribed – 2 ml of 2.5 % diprazine solution or 1 ml of 1 % diphenhydramine solution i.m. Intravenous drip introduction of 1 % nicotinic acid solution is used during an exacerbation of trigeminal neuralgia. With concomitant spastic conditions, muscle relaxants (tizanidine) are prescribed. Sedative, antispasmodic or vasodilating agents, vitamins are also prescribed, of which B vitamins and their complexes (neurobeks, neurovitan) are the most effective.

Trigeminal neuralgia of predominantly peripheral origin can occur as a result of exposure (tumors, diseases of the paranasal sinuses, malocclusion, etc.) on various parts of the peripheral trigeminal nerve. These con-

ditions are characterized by a prolonged pain syndrome, which increases paroxysmally. The use of NNA has a noticeable therapeutic effect. Carbamazepine drugs are often ineffective.

Among the trigeminal neuralgia with a predominance of the peripheral component in the pathogenesis, the main forms are: odontogenic trigeminal neuralgia, postherpetic neuralgia, dental psexalgia, neuralgia of different branches of the trigeminal nerve, etc.

Odontogenic trigeminal neuralgia is more often manifested by pain in the innervation zones of the II and III branches of the trigeminal nerve. A feature of odontogenic neuralgia is the severity of pain and autonomic components. Doctors often prescribe NNA, tranquilizers (diazepam 2.5–5 mg enterally 2–3 times a day), antipsychotics (thioridazine 0.05–0.15 mg enterally per day, haloperidol 0.0015 g enterally 3 times a day, etc.). One of the most effective painkillers is ketanov, which is prescribed according to the scheme: 1–2 days – 20 mg (with moderate pain), 30 mg (with severe pain) i.m., 3–4 days – 10–20 mg orally every 8 hour, 5–7 days – 10–20 mg orally in 12 hours. Subsequently, a dose of 5–10 mg is maintained in 12 hours, for 5–6 days. With the development of persistent pain, it is advisable to prescribe narcotic analgesics.

Damage to the trigeminal nuclei is characterized by attacks of extremely sharp pains that are not amenable to treatment with anticonvulsants and sensitivity disorders. The disease occurs against the background of atherosclerosis, hypertension, etc. Prescription of 10 ml of 2.4 % solution of euphyllin i.v., and i.m. – solution of papaverine or dibazol, NNA, and in some cases – NLA.

Dental plexalgia is characterized by constant unbearable dull pain, which is mainly localized in the area of innervation of the dental plexus, sometimes with a transition to the healthy side. It turns out temperature asymmetry in the area of projection of pain, where usually there are disorders of sensitivity. Treatment consists in the use of NNA (ketonal, ketorol, solpaflex), and in the case of severe pain – NA. LA are prescribed to all patients: 5–10 % anesthesin or 10 % lidocaine ointment. To enhance the action of analgesics and anesthetics, tranquilizers and antipsychotics are used. Postherpetic trigeminal neuralgia is manifested by the following forms of pain syndromes: diffuse eye and face pain, acute trigeminal neuralgia, early postherpetic and late postherpetic neuralgia. In this case,

headaches, general malaise appear. After 2–3 days, pain occurs in the zone I or II branches of the trigeminal nerve, sometimes all of them. Pain is burning in nature, extremely unbearable, accompanied by itching and swelling of the face. Ganglioneuritis, which arises as a result of herpetic lesion, lasts about 3–6 weeks and passes without a trace. In the acute stage, LA (an adhesive patch with lidocaine, etc.), antidepressants (amitriptyline, nortriptyline), anticonvulsants (carbamazepine, gabapentin, etc.), classic NNA or NA, capsaicin, etc. are used to influence the pain syndrome effectively.

Glossopharyngeal neuralgia is one of the most severe types of pain in dentistry. Vaginal pharyngeal nerve neuralgia is characterized by severe, paroxysmal pain in the pharynx, tonsils, tongue root, lower jaw angle, and auditory meatus. The onset of pain attacks can be associated with speech or eating and is accompanied by dry mouth, the appearance of thick viscous saliva. The duration of the "lumbago" can be from a fraction to several seconds or last 1–1.5 minutes. Blockade of sites of the carotid sinus is carried out with novocaine or other LA, typical NNAs are prescribed.

With pterygoid neuralgia (Slader's syndrome), paroxysmal pain (within a few hours, and sometimes even a day) appears first in the deep parts of the face, and then spreads to the palate, tongue, skin of the temporal region, and the eyeball. Swelling of the eyelids, conjunctival hyperemia, excessive secretion of saliva, nasal mucus, and tearing are observed. Emergency care for pterygoid neuralgia is to lubricate the distal portion of the middle turbinate with LA solution, which can also be an important diagnostic test. Analgesics, antihistamines, seduxen are prescribed enterally.

The damage of the geniculate ganglion of the facial nerve by the herpes zoster virus is characterized by the appearance of burning, paroxysmal or persistent pain in the ear region, which radiates to the face, occipital region and neck. Herpetic eruptions in the external auditory canal, paresis of facial muscles, dizziness occur. In case of damage to the geniculate ganglion of the facial nerve, specific antiviral therapy, analgesics, anticonvulsants, antihistamines are prescribed enterally.

Nasal nerve neuralgia (Charlin's syndrome) is manifested by paroxysmal intolerable pain in the eyeball and half of the nose. The pain intensifies at night. In case of neuralgia of the nasociliary nerve, the mucous membrane of the anterior nasal cavity is lubricated with LA (2 % lidocaine

solution) with adrenaline in combination with the prescription of NNA, vitamin therapy, and physiotherapeutic methods of treatment.

Neuralgia of the auriculotemporal nerve (Frey's syndrome). The basis of the symptom complex is pain in the temple, inside the ear, the front wall of the external auditory canal, and especially in the TMJ. Pain is usually aching, burning, pulsating in nature, often radiating to the lower jaw. Treatment at the time of the attack is NNA in combination with tranquilizers, in case of severe pain – novocaine blockade of the site of projection of the auriculotemporal nerve. In the future, patients are prescribed sedatives, tranquilizers, anticholinergics, analgesics. It is recommended to use vitamins of group B and vitamin C.

Lingual nerve neuralgia is characterized by attacks of burning pain in the anterior two thirds of the tongue. Often, pain is accompanied by sensitivity disorders in the corresponding half of the tongue. The duration and frequency of pain paroxysms can be different. Therapy: for attacks, patients are prescribed NNA in combination with antihistamines, as well as LA.

Neuritis of the facial nerve is characterized by acute paralysis or paresis of the facial muscles, sensitive and autonomic pathologies. Disturbances of sensitivity are manifested in the form of mild or moderate pain in the ear and mastoid process. Severe pain syndrome is typical for the damage of the facial nerve until the tympanichord moves away from it. Treatment includes using NNA in combination with tranquilizers or antipsychotics, antihistamines.

With angioneurology, against the background of general malaise, there is a paroxysmal "boring" short pain that spreads along the branches of the external carotid artery. Sometimes it is dull, constricting, radiating to the temporoparietal and frontal areas, eyeballs, nose. A pain attack can be triggered by alcohol, ice cream, more often it occurs against the background of mental overwork and emotional stress. For relief of pain attacks in case of angioneurology, novocaine blockades are performed with 1 % novocaine solution along the vessels, locally – Remisid gel, LA.

In case of pathological occlusion syndrome, the pain appears first in the temporal region, the eyeball, in the ear region, and then spreads to the back of the head and face. Emergency care for this type of pain syndrome is to prescribe analgesics and minor tranquilizers in usual doses.

Stomalgia (glossalgia, glossodynia) is characterized by unpleasant sensations in the oral cavity and tongue. If the pain is limited only by the tongue, then in these cases the disease is diagnosed as glossalgia or glossodynia, and if it captures the entire oral cavity – as stomalgia. The main difference of glossalgia is the disappearance of pain when eating food. Clinically paresthesias such as burning, tingling, numbness are more common. Approximately half of patients with paresthesia complain of pain of a "crushing" nature in the tongue, which is common, without a clear localization. Patients associate the occurrence of pain with fatigue, eating meat, a long talk, etc.

Emergency and specialized care consists in the use of psychotherapy for all types of stomalgia. Sedatives, tranquilizers and antipsychotics are prescribed. The most effective is chlordiazepoxide (elenium). The dose is selected individually, starting from 5–10 mg per day, gradually increasing it by 5–10 mg per day (no more than 30–50 mg). Alimemazine (theralen) 2.5–5 mg 3 times per day is also effective. A bath for the tongue with 2 % solution of novocaine, applications of 1–2 % emulsion of anaesthesin in peach oil, pyromecainic or lidocaine ointment are prescribed. Dry mouth can be cured with 1 % solution of pilocarpine hydrochloride. To normalize the tone of the autonomic nervous system, pyroxane, belataminal, electrophoresis of 0.25 % solution of gangleron and andecalin to the site of the upper cervical sympathetic nodes are recommended. Mandatory prescription of vasoactive drugs – cavinton or stugeron (control of blood pressure). Recent studies have shown that orthopedic measures (prosthesis correction, normalization of occlusal height and removal of dissimilar metals) often contribute to recovery.

Dysfunction of the temporomandibular joint. The main symptom is facial neuralgic pain radiating to the temple, occiput and neck. Symptomatic treatment is based on periarticular infiltration of 1 % procaine or xylocaine. Sedatives, tranquilizers are also prescribed. NNA (paracetamol, mefenamic acid, celecoxib, nimesulide, meloxicam, ketorolac) should be prescribed, if necessary.

1.1.7. Pharmacotherapy of pain in surgical dentistry

Alveolitis is a serous or purulent inflammation of the alveolus of an extracted tooth. It arises as a result of trauma by extraction and the devel-

opment of an infectious and inflammatory process. It is characterized by subfebrile condition, severe pain and halitosis. In the alveolus, detritus is dirty gray. Antiseptic treatment is carried out (0.05 % solution of chlorhexidine, 0.2 % solution of ethacridine lactate, 1 % solution of dioxidine), curettage or, in some cases, suturing the edges of the alveolus. The alveolus is swabbed with iodine gauze, which is saturated with propolis tincture. Solcoseryl gel, a sterile bone substitute, etc. are used to fill the alveolus. If necessary, they use ABD (amoxicillin, lincomycin, ciprofloxacin), antihistamines and vitamin preparations for general therapy. In complex treatment, NNA are recommended (ketoprofen, nimesulide, meloxicam, etc.).

Arthritis of TMJ is a disease of inflammatory or inflammatory-dystrophic origin. It manifests itself as severe pain on the joint and jaw, which often radiates. The pain increases during chewing, opening the mouth, jaw movements and are accompanied by irradiation in the ear, lower jaw and lower areas of the face. Palpation of the joint is painful. In complex treatment, physiotherapeutic procedures are used (compresses with a 20 % solution of dimexide with prednisolone), occlusion correction, intraarticular injections of lydase (hyaluronidase). If necessary, individually selected NNA are used. With arthrosis near the joint, injections of rumalon, traumeel-S, etc are prescribed.

Myoarthropathy is characterized by pain that is localized in the TMJ and spreads to the temple area or the corresponding half of the face, m.sternocleidomastoideus area. Pain can be of a different nature and localization. It can be in the form of pressure, drilling or a painful cap on the forehead. To eliminate the pain, the prosthesis and the bite are corrected, the painful muscles are infiltrated with an anesthetic (1 % procaine or xylocaine). Tranquilizers, muscle relaxants, NNA are prescribed.

Maxillary sinusitis is an inflammation of the maxillary sinus of odontogenic origin. It occurs when the bottom of the maxillary sinus is perforated or the tooth root is pushed into it (5, 6, 7). The pain is moderate or severe, depending on the degree of damage. They draw the edges of the alveoli together, fix with catgut sutures or suture the defect. In complex treatment, NNA can be recommended depending on the severity of pain.

Pericoronaritis develops with inflammation in the soft tissues that surround the unexplored third molar (wisdom tooth) of the lower jaw. Gum inflammation occurs over the tooth and a “hood” is formed. Opening the

mouth and swallowing is limited due to contracture. For pericoronaritis, moderate and localized pain is typical. With increased inflammation, the pain can radiate. In complex treatment, antiseptic treatment of the oral cavity, tamponade of the site with iodoform gauze are used. If necessary, the "hood" is dissect and drainage of the wound is performed. It is advisable to use local antibacterial therapy and effective analgesics.

Periostitis is an acute inflammation of the periosteum in the area affected by periodontitis tooth. The process is manifested by severe pulsating and bursting pain, swelling of the transitional fold is observed. The alveolar process of the jaw is deformed from the vestibular side, where the subperiosteal abscess is located. Collateral edema develops, the face become asymmetric. Periostotomy is performed, anti-inflammatory (analgesic) and desensitizing agents are prescribed enterally. Rinsing and irrigation of the oral cavity with antiseptics are also prescribed.

Osteomyelitis is an acute or chronic inflammatory process of the bone that occurs under the influence of exogenous and endogenous factors. There are hematogenous, post-traumatic, odontogenic types of osteomyelitis. 80 % of diseases are of odontogenic origin.

Acute odontogenic osteomyelitis begins with fever, pain in a certain area of the jaw, sleep disturbance, impaired appetite. In the area of the alveolar ridge, deformation on both sides, puffiness of the transitional fold, hyperemia, tooth mobility, destruction of the "causative" tooth, and the release of pus from the gingival pockets are observed. The disease is accompanied by the formation of maxillary abscesses and phlegmons. The high rate of clinical course of osteomyelitis is more typical for the upper jaw than the lower jaw, due to the difference in their anatomical structure.

The principles of treatment are based on the removal of the "causative" tooth, periostotomy of the alveolar ridge, drainage of wounds, lancing of abscesses and phlegmons, as well as drug therapy. For antiseptic treatment, chlorhexidine, hydrogen peroxide, furacilin, lysozyme are used, enzymes (trypsin, chymotrypsin, DNase) are used. For general treatment, antimicrobials (lincomycin, clindamycin, tobramycin, ciprofloxacin), antifungals (fluconazole, terbinafine), immunostimulants (cycloferon, polyoxidonium, methyluracil, imudon), detoxification agents (Ringer's solution, rheopolyglucin) are prescribed. The differentiated use of modern NNA takes an important place.

Acute hematogenous osteomyelitis is associated with the hematogenous spread of infection (for example, with sepsis). This form is characterized by an instant increase of intoxication and the development of local manifestations of the disease. Primary infiltration and fistulas, high body temperature are observed. For treatment, intensive surgical and drug therapy using modern effective antibacterial, anti-inflammatory, analgesic agents are used.

Acute post-traumatic osteomyelitis is associated with the development of purulent-necrotic bone process as a result of trauma. The clinical course of the disease and treatment principles are similar to other acute forms of osteomyelitis. If a jaw fracture or an ineffective approximation of fragments is detected, immobilization and reimmobilization must be carried out.

Chronic odontogenic osteomyelitis of the jaw is the result of an ineffective treatment of an acute process. The disease lasts for years. Under the influence of provoking factors (infection process, hypothermia), an exacerbation occurs, which is characterized by an increase in resorptive changes in the bone and periosteum. There are clinical forms of chronic osteomyelitis such as destructive, resorptive and destructive-resorptive.

Sialoadenitis is an acute inflammation of the salivary gland of various localization. Acute inflammation of the parotid salivary gland is treated as mumps. Acute inflammation of the salivary glands most often has a viral etiology. In the affected area there is a painful deformation of the face, swelling, fever. Inflammation of the parotid gland causes prolonged, compressive pain of moderate intensity (painful "points") in front of the tragus of the ear, behind the auricle and in the section of the mandibular branch. The amount of saliva that is secreted from the duct of the gland is reduced, and the viscosity is increased. The patient has symptoms of intoxication, fever. The development of simultaneous damages to the pancreas, mammary glands, testicles, prostate is expectable. Treatment is carried out in a specialized infectious department, and if necessary, lancing of abscesses or phlegmon is performed. Conservative therapy is prescribed (antibacterials, anti-inflammatory drugs, detox medications, immunostimulants, antihistamines, vitamin preparations). In the complex treatment, attention should be paid to analgesic therapy (ibuprofen, ketoprofen, meloxicam, etc.).

Boil (furuncle) is a purulent-necrotic inflammation of the hair follicle, surrounding tissues and a skin infiltrate. This lesion is characterized by the occurrence of a bluish-crimson inflammatory infiltrate in the form of a cone in the skin areas where the hair follicles are located. There is a necrosis cell (rod) in the center. A marked swelling of the surrounding tissues and acute soreness are noted. The patient's condition is of moderate severity: moderately elevated temperature, headache, decreased appetite. A threatening prognosis occurs when the focus of inflammation is localized in the nasolabial triangle, which creates the conditions for its spreading to the meningeal membranes, etc.

Carbuncle is a simultaneous purulent-necrotic inflammation of several hair follicles. It is characterized by a sharp violation of the general condition, intoxication, fever (up to 40 °C), an increase of regional lymph nodes, phlebitis. Several "rods" of significant size can be observed in the focus of inflammation. Treatment is carried out in a hospital. In the case of boil or carbuncle abscess, the inflammation focus is lanced under anesthesia. If necessary, the wound is drained. In complex therapy, antimicrobials (cefotaxime, augmentin), detox medications (neogemodez, reopoliglykin), immunostimulants (echinacea compositum S, sodium nucleinate, polyoxidonium) are used. For local treatment of wounds, antiseptics (chlorhexidine, miramistin, dioxidine, etc.) and enzymes (trypsin, chymotrypsin) are used. The surrounding skin is treated with salicylic alcohol, zinc and salicylic acid or ichthyol ointments. Adequate analgesia is important. For its implementation, highly effective analgesics are prescribed (ketorolac, ketoprofen, solpadeine, etc.).

An abscess is a limited purulent infectious inflammation of soft tissues of subcutaneous fat. Phlegmonis a diffuse inflammation of soft tissues. The cause may be teeth affected by periodontitis, pathological gingival pockets, osteomyelitis of the facial bones, etc. By their localization, abscesses and phlegmons may be submaxillary, zygomatic, buccal, parotid chewing, chin. The local picture is characterized by a marked edema, deformation of soft tissues, flushing of the skin over the inflammation focus, painful infiltrate when palpating. In most cases, fluctuation occurs. In certain forms, a violation when opening the mouth and pain when swallowing may occur. The general condition of the patient gets worse; there is an elevation of temperature, headache, sleep disturbance, food refusal.

The clinical course of the disease is more pronounced with phlegmons of anaerobic origin.

The following algorithm is recommended for the treatment of these inflammations: the abscess and phlegmon are lanced under anesthesia, the "causative" tooth is removed, the inflammation cell is drained, intensive antibacterial therapy is prescribed (tienam, cefotaxime, cefoperazone, etc.), and anaesthetization with ketanov according to the scheme (20 mg 3 times a day 1–2 days and 20 mg 3–7 days orally), if necessary, anti-inflammatory drugs, antifungals, immunostimulants, vitamin preparations, detox medications.

TMJ dislocation is associated with a displacement of the articular head of the lower jaw from the articular fossa. Distinguish between acute and habitual dislocations. The causes of acute dislocations can be: excessive opening of the mouth, yawning, biting, a trauma. Common dislocations are associated with malocclusion, chronic arthritis and arthrosis. According to the localization, anterior dislocations occur most often. In this case, the patient complains of inability to close (frontal dislocation) or open (posterior dislocation) teeth. Pain is severe due to reflex contraction of the masticatory muscles. After reduction of the dislocation, the jaw is immobilized and analgesics are prescribed (ibuprofen, ketoprofen, nimesulide). The most effective analgesic is ketanov (ketorolac) – 10 mg enterally 3–4 times a day. For a more rapid resumption of joint function, it is advisable to use physiotherapeutic procedures.

A common dislocation or subluxation of TMJ is associated with overextension of the ligaments of the joint. There is a slight asymmetry of the face, increased excursions and the maximum lowering of the articular head of the lower jaw (50–70 mm between the central incisors of the upper and lower jaw). There is articular noise and lateral displacement of the lower jaw at its maximum omission. The treatment is aimed at renewing the function of the joint by strengthening the tone of the muscular-ligamentous apparatus. Anti-inflammatory therapy is carried out using NSAIDs (diclofenac sodium, aceclofenac, meloxicam, celecoxib). Ointments based on ibuprofen, ketoprofen, indomethacin, etc are used locally. It is advisable to prescribe physiotherapeutic procedures.

Damage to the soft tissues of the MFA, as a rule, is accompanied by a violation of the integrity of the tissues of certain areas (wounds, excori-

ation), whereas a bruise is a mechanical damage to the soft tissues without violating their integrity. There are gunshot and non-gunshot causes of damage. In these cases, congestive hyperemia, tissue edema, hematoma, paresthesia, pain syndrome quickly develop. A bruise is accompanied by pain in the area of the injury, and can also lead to a violation of the function of mouth opening and chewing.

Wound injuries by the nature can be cut, stab, bite, etc. Contused and lacerated wounds of the face occur most often. The clinical picture is characterized by impaired tissue integrity, edema, bleeding, infection, and formation of hematoma. Injuries to this area can be combined with lesions of the teeth and other organs.

In the treatment of excoriation, antiseptic treatment with aniline dyes is used (0.1 % solution of ethacridine lactate, 1 % solution of methylene blue, 3 % solution of brilliant green). Antiseptics such as 0.05 % solution of chlohexidine, 1–2 % alcohol solution of iodine, 1 % solution of iodinol and 3 % solution of hydrogen peroxide are used to treat wounds. It is advisable to apply local hypothermia, a pressure dressing, ultraviolet radiation or UHF to the bruised area. Heparin, troxevasin ointments or indovasn ointment are also used. If necessary, face wounds are sutured in layers. In complex therapy, anti-inflammatory drugs, antihistamines, vitamin preparations, enzymes, regenerative drugs are prescribed. Painkillers are used differentially depending on the severity of pain (ibuprofen, ketoprofen, ketorolac).

Fractures of bones of the facial area of the skull represent a partial or complete violation of the integrity of the bone that occurs under the influence of mechanical factors. By their nature, there are open and closed, full and incomplete, uni- and bilateral fractures. By localization, there are such fractures of the MFA: alveolar process, nasal bone, zygomatic complex, upper and lower jaw. Most fractures are distinguished by the appearance of pathological mobility of bone fragments, malocclusion, presence of bruises or wounds at the site of injury, swelling, violation of facial symmetry and the occlusal harmony. Pain syndrome is characterized by a positive "load syndrome", that is, pain occurs in the area of the injury when you press the chin. A peculiar clinical picture is observed with fractures of different locations: the alveolar process – the mobility of the affected area, swelling, hematomas, ruptures of the mucous membrane; nasal

bone – nosebleed, swelling of the tissues of the nose, shortness of breath and crepitation of bone fragments during palpation; zygomatic complex – swelling of the zygomatic area, limited opening of the mouth, paresthesia of the infraorbital and nasolabial area, sometimes the separation of the alveolar process or maxillary bones; mandibular bone – violation of the integrity of the mucous membrane, soft tissue wounds, painful opening of the mouth, occurrence of fragments with pathological mobility, malocclusion.

Fractures of the MFA are treated with comprehensive surgical, drug and orthopedic therapy. Important areas of drug therapy are the use of antibiotics, anti-inflammatory drugs, desensitizing drugs, vitamin preparations and agents for stimulation of reparative regeneration. Reposition and fixation of fragments of the jaw with metal tooth splints does not eliminate pain in the injured area, therefore, it is advisable to prescribe ketanov in the complex of therapeutic measures according to the previously described scheme. Diclofenac sodium, aceclofenac, ketoprofen, meloxicam, etc. can also be used for anesthesia.

After surgery, it is too hard to relieve pain syndrome effectively. This type of pain is complex in its genesis; its severity depends on the duration of the operation and its invasiveness. The central mechanism of this type of pain is associated with surgical intervention, which leads to the activation of upward pain flow. The peripheral effect on the formation of pain is predetermined by the release of mediators-algogens (PG, leukotrienes, kinins, etc.) from the injured tissues. Well-known pathological effects of pain cause: emotional and physical suffering of patient, adverse reactions from the CVS, respiratory system and gastrointestinal tract, sleep disturbance and a decrease in the patient's physical activity.

Modern pharmacology allows to a certain extent to cope with pain that occurs in the postoperative period. To date, near 20 NSAIDs with common therapeutic and side effects are most often used to treat postoperative pain. Selective and specific COX-2 inhibitors are widely used. A stereoisomeric form of ketoprofen-dexketoprofen (dexalgin) is the representative of this group. The drug effectively blocks pain impulse conduction on the periphery and in the central nervous system and reduces the production of algogens. In the postoperative period, depending on the duration of the intervention, 100–150 mg dexalgin is prescribed for

1–3 days. It is advisable to add 50 mg dexalgin i.v. to decrease manifestations of the intraoperative stress reaction. Spinal anesthesia in combination with pre- and postoperative administration of dexalgin prevents pain syndrome more effectively than general anesthesia. The use of dexalgin monotherapy may be ineffective in certain patients, thus requires an additional single-dose administration of morphine. This combined use of analgesics helps to achieve synergy between both drugs and helps to reduce their doses.

Positive experience was also gained by using the selective COX-2 inhibitor rheumaticam (meloxicam) for pain relief in the postoperative period. The latter is administered deeply intramuscularly 7.5–15 mg once a day, depending on the intensity of the pain. When receiving the effect after 2–3 days, it is advisable to switch to taking the drug enterally (7.5–15 mg once a day). In the postoperative period, nimesulide is used (100 mg enterally 2 times per day or 200 mg suppositories rectally once a day), ketorol (30 mg i.m. every 4–6 hours, solpadeine 2 tablets 3 times a day), tramadol (300 mg per day for 3–4 times i.v. or i.m. or 50–100 mg enterally 3–4 times a day).

An effective method of protecting patients from operational stress is central analgesia using nalbuphine opioid receptor antagonist-antagonist. Unlike other drugs of this group, nalbuphine does not increase blood pressure and heart rate, what is especially important during surgery for patients with CVS pathology. The drug prevents postoperative nausea and vomiting, its analgesic effect persists for 6–8 hours after general anesthesia.

The most effective attempts to improve the quality of postoperative analgesia are based on the optimization of drug administration methods. A modern method of pain relief is the PCA, aimed at the individual needs of the patient. If necessary, the patient can receive an analgesic bolus through a remote device, which creates confidence in timely pain relief. An effective drug for PCA is morphine, which, however, is associated with the most common complications. Fentanyl and remifentanil, which do not have active metabolites, can be promising and induce postoperative hyperalgesia delayed for 5–6 hours. The disadvantage of this method is the high cost of equipment, which makes it inaccessible to most domestic clinics. An effective method of postoperative analgesia is EA using opioid

analgesics. The latter provides modulation of pain impulses at the level of the posterior horns of the spinal cord. Morphine, pethidine are used for bolus administration, and fentanyl is used for prolonged epidural infusion. A single 4–5 mg morphine injection provides a high analgesic effect for 12–14 hours. A modern LA – ropivacaine is also used

1.1.8. Pharmacotherapy of pain in neoplasms

Benign neoplasms of MFA by its origin are divided into odontogenic, cystic, vascular, non-vascular, osteogenic neoplasms, and neoplasms of nervous tissues. For benign tumors, a slow, limited growth (with the exception of hemangiomas) and the absence of metastases are inherent. The clinical picture of a tumor depends on its localization: painless deformation of soft tissues or bones in the neoplasm site, a change in skin color and temperature, tooth mobility, etc. can occur. An X-ray examination reveals signs of a benign tumor. The general condition of the patient is usually satisfactory.

The principles of treatment are based on surgical methods of tumor removing. In case of hemangiomas, diathermocoagulation, sclerotherapy with cytotoxic poisons are used, in the presence of a hard-to-reach tumor – X-ray therapy. For medical postoperative treatment, antibacterials, antihistamines, vitamin A, NNA, etc. are used. For adequate analgesia, it is advisable to prescribe ketoprofen, xefocam, ketanov.

According to the localization, malignant neoplasms of MFA are divided into tumors of the face, scalp, salivary glands, jaw, oral cavity, and tongue. The etiology and pathogenesis of tumor growth has not been fully elucidated, but contributing factors may include: smoking, alcohol abuse, poor oral hygiene, the use of improperly selected dentures, etc.

The early stages of the tumor process are characterized by minor symptoms (weakness, malaise, decreased immunity, painless neoplasm). As the tumor develops, the clinical picture of the disease becomes more pronounced (anemia, leukemia, intercurrent diseases, cachexia). In its intensity, pain in oncological practice can be mild, moderate, severe and very severe. The severity of pain depends on the location of the tumor and metastasis, the stage of the disease, the involvement of other organs in the process. Pain is especially pronounced in the terminal stages (III and IV) of the disease.

More often, tumors cause pain during secondary infection, squeezing a tooth or nerve, and bone erosion by a malignant tumor. Next to neuralgic pain, anesthesia occurs in the area of the compressed nerve. Paresthesia is usually accompanied by neuralgic, intense pain. Lip cancer is a painless ulcer with a dense bottom and edges. Following the process of inflammation, pus is released from the ulcer, and soreness appears. Pain in cancer of the tongue is more pronounced at the last stage of development, which is associated with its spread to the soft tissues, lower jaw and the bottom of the oral cavity. Jaw cancer is characterized by its enlargement and deformation, the occurrence of prolonged pain, sometimes there is numbness in the teeth. Salivary carcinoma can cause pain as a result of compression of the tongue nerve. A cardinal symptom of jaw sarcoma is severe neuralgic pain in one of the branches of the trigeminal nerve, and often this is the only symptom.

Currently, the most common combination treatment of malignant tumors include X-ray, surgical intervention and therapeutic therapy (cytostatics, detox medications, sedatives, local anesthetics). The classic algorithm for analgesic therapy is represented by the phased use of analgesics:

- prescription of paracetamol or other modern NNA;
- addition of a weak opioid (codeine, dihydrocodeine);
- addition of a strong opioid (promedol, morphine, omnopon).

A way to increase the effectiveness of anesthesia is the simultaneous administration of adjuvants – auxiliary drugs that potentiate the effect of analgesics. In oncological practice, tranquilizers, antidepressants, sedatives, anticonvulsants, antihistamines, etc. are widely used for this purpose.

1.1.9. Physical methods of anesthesia

In dental practice, cryotherapy as a physical method of anesthesia is used. This is cooling anesthesia – applying a drug with a low boiling point to tissues. In this case, the nerve endings lose their sensitivity, and anesthesia of the chilled area occurs. Chloroethyl has a freezing effect, it is used to anesthetize submucosal and subcutaneous abscesses, to remove moving teeth, and to prevent the spread of hematoma (in case of injuries to the soft tissues of the face). An overdose of chloroethyl is dangerous due to the general toxic effect when the drug is inhaled and the local

side effect is burns. Pharmaethyl, which does not cause burns, is also used. Cryotherapy can reduce the local inflammatory response by slowing the release of inflammatory mediators.

Physical methods of treating chronic pain also include heat therapy, electrotherapy, percutaneous electroneurostimulation, central electroneurostimulation, and acupuncture.

The method of anscutaneous electrical nerve stimulation stimulation is based on stimulation of the affected area with the specified parameters of the electric current. It is highly effective in acute post-traumatic and postoperative local pains, etc.

Acupuncture refers to a long-standing effective method of treatment, which is used in various branches of medicine. It consists in the introduction of special thin needles at strictly defined points on the body. Varieties of this method are electro-puncture (influence of electric current on biologically active points), electro-acupuncture (influence of electric current of very low strength) and auriculopuncture (stimulation of the biologically active points of the auricle).

1.2

PHARMACOTHERAPY OF DISEASES OF HARD TOOTH TISSUES

Disease of the hard tissues of the tooth can be of carious and non-carious etiology. One of the most common diseases of hard tooth tissues is caries (lat. – caries dentis). Caries develops after teething and is accompanied by demineralization and softening of the hard tissues of the tooth with the subsequent formation of a defect in the form of a cavity. Non-carious lesions of the hard tissues of the tooth that occur during their development include hypoplasia, hyperplasia, fluorosis and hereditary lesions (imperfect amelo- and dentinogenesis). Fluorosis is the most common disease of this group. Non-carious lesions that occur after teething are manifested by abnormal tooth wear, wedge-shaped defects, necrosis, erosion of hard tissues, etc. Lesions of teeth of non-carious origin often have an unclear origin, which impede their effective prevention and treatment.

1.2.1. Caries

A number of factors contribute to the occurrence of the carious process: pathogenic microflora of the oral cavity, irrational nutrition, changes in the properties of saliva, a decrease in the fluoride content in drinking water, hereditary factors, concomitant diseases, etc. The most important risk factors for caries are plaque bacteria, which produce organic acids, which in turn cause the development of foci of demineralization. The leading role is played by the fluoride content in drinking water. The sensitivity of the human body to fluorides and the ability to metabolize them are individual. The data on the occurrence of caries in regions with optimal fluoride content in drinking water evidences this. Therefore, caries is a disease multifactorial in its etiology and pathogenesis, the development of which can be partially prevented if preventive measures are used.

Prevention of caries is usually carried out in two directions: eliminating the cariogenic situation in the oral cavity and increasing the resistance of tooth tissues. During the period of intrauterine development, caries prevention is aimed at ensuring a full nutrition of the fetus and the intake of vitamins, eliminating factors that violate the metabolism in the body. In infancy, proper feeding of the child is the basis for ensuring resistance to caries. Then, in childhood, a balanced diet promotes the intake of fluoride, calcium, phosphorus, iodine, vitamins, which is also important for prevention of caries.

An important component in the prevention of caries in children and adults is constant hygiene, which is aimed at weakening the action of exogenous and endogenous factors. Currently, mouthwashes that contain antiseptic agents are used to ensure effective oral hygiene. The latter complement the action of a toothbrush, toothpaste, dental floss. The most effective antiseptic that is used in rinses is chlorhexidine bigluconate. Unfortunately, prolonged uncontrolled use of the drug (more than 7–14 days) leads to the appearance of undesirable manifestations (staining of the surface of the teeth, formation of tartar, dysbiosis, desquamation of the epithelium). Rinsing agents, which include 0.075 % cetylpyridinium chloride, have more positive properties. The drug has bactericidal and bacteriostatic activity, acts on most gram-negative and many gram-positive microorganisms, is effective against fungi, including the genus Candida. It is highly active in preventing the formation of plaque. In its activity, it can be compared with triclosan, but to a lesser extent it causes dysbiosis, the formation of resistant forms of microorganisms, does not possess pronounced irritating properties and does not stain tooth tissue.

The measures to improve the condition of the oral cavity include the elimination of gingival deformities, the closure of fissures and blind fossae of the tooth and the healing the whole body.

Pharmacological measures that help to reduce the intensity of caries growth and increase the tooth tissue resistance include the use of fluoride preparations and remineralizing agents. When prescribing fluorides, the following data should be considered:

1) the fluoride content in drinking water should not exceed 0.3–0.5 mg/l;

2) calcium compounds can bind fluoride preparations and reduce their effectiveness;

3) the optimal fluoride concentration for local caries prophylaxis is 1–2 % (based on fluoride ion), and an increase in concentration is not accompanied by an increase in their anticariogenic effect.

Fluoride preparations are the most common means of caries prophylaxis, due to their mechanism of action: a) the formation of hydroxyapatite under the influence of fluoride hydroxyfluoroapatite prevents an increase in the permeability of enamel; b) fluorides block anaerobic glycolysis in microorganisms and reduce the content of lactic acid, which can damage the tooth tissue; c) fluorides contribute to the retention of calcium and phosphorus, stimulate the processes of remineralization.

General prevention is carried out using fluoridation of water, salt and milk. A known method is the fluorination of drinking water with a fluoride content of up to 1 mg/l. An alternative method is the use of oral sodium fluoride in children, which has a protective effect on teeth that have erupted or will erupt. Dosing is carried out taking into account the age of children and the content of fluorides in drinking water. When the concentration of fluoride in water is 0.1–0.3 mg/l, 2–6 year-old children take 1.1 mg, older than 6 years – 2.2 mg daily after breakfast (at least 250 days a year up to 12–14 years). Calcium preparations that interact with fluorides should not be used simultaneously.

Another drug for the general prevention of caries is Vitaflor – a combined preparation containing sodium fluoride, vitamins A, D and C. 1–6 year-old children are prescribed 1/2 teaspoon or 1 tablet, 7–14 year-old children – 1 teaspoon or 2 tablets. Vitaflor is used orally during or after meals 1 time per day (4–6 courses per year for 1 month with 2-week breaks).

Local prevention is carried out by applying fluorides in the form of solutions, pastes, gels, varnishes, cements on the surface of the tooth, which contributes to their secondary mineralization.

"Ftorlak" is a combined preparation containing sodium fluoride, resins, chloroform and alcohol. When applied to the teeth, the drug forms a film that provides long-term diffusion of fluoride into the enamel. Fluoride has antimicrobial activity and reduces tooth sensitivity to pain. Sodium fluoride is used in the form of 0.1–0.2 % solution for rinsing the oral cavity once

every 1–2 weeks. 1–2 % of the solution or gel based on agar is applied with a swab to the dried tooth surface for 10–12 minutes (2–3 applications with intervals of 2–3 days, 2–3 courses per year). Applications of calcium gluconate and sodium fluoride are also used. Pre-brush your teeth, wipe them with cotton swabs with a solution of hydrogen peroxide, dry and apply a swab moistened with 10 % calcium gluconate solution for 15–20 minutes, which is then replaced with 2 % sodium fluoride solution for 1–2 minutes. The procedure is repeated 3 times every other day every six months. 8 % solution of tin fluoride has more activity than sodium fluoride.

For primary prevention of caries, application products based on a polyelectrolyte complex of polyacrylic acid and polyethyleneimine are proposed, containing calcium, fluoride, phosphorus and a hydrophobic varnish based on a natural resin with a fluoride-containing polymer that is easily hydrolyzed.

Caries can be effectively prevented by using toothpastes that contain fluoride compounds. Popular effective pastes include Colgate, Colgate Total (USA), Aquafresh (GlaxoSmithKline, UK), Macleons (SKB, UK), Signal (Unilever, UK). Widely used pastes also include Fluorodent (Freedom, Russia), Lacalut (Germany), Pepsodent (Unilever, UK), Fluodent (Pharmachim, Bulgaria), etc. Gel pastes are represented by Fluodent (Pharmachim, Bulgaria), Fluocaril (France), Helios (Russia), etc. R.O.C.S. toothpaste (Switzerland) incorporates the most effective fluoride source – aminofluoride. The technology for the production of pastes should provide for the presence of fluoride ion in the toothpastes in a free ionized state, while the fluoride content should not exceed 1–2 %.

Taking into account the variety of factors that can contribute to the development of caries, new approaches to its prevention are being developed. It is known that the development of caries is accompanied by a decrease of trace elements (lithium, gold, indium, nickel, titanium, zirconium, tungsten, platinum, cadmium, barium, copper, lead, zinc) in the body. Scientists drew attention to the mineral concentrate, which includes many of the above trace elements, macroelements, as well as lipids, proteins and amino acids. The use of an aqueous solution of kelp can be a promising area for improving primary prevention of dental caries by improving the function of the salivary glands, saturating the oral cavity with mineral components, enhancing self-cleaning of the oral cavity, etc.

Fucus vesiculosus (Fucus) brown algae preparations contain 42 macro- and microelements, polysaccharides and a wide range of vitamins that are easily absorbed in the body and provide a pronounced therapeutic and prophylactic effect. The best results (halving the increase in caries) in 8–10 year-old children were obtained using toothpastes with the specified algae.

Protection against caries is determined by toothpastes, which include the amino acid arginine and calcium carbonate, and, as it turned out, they have a pronounced anti-carious effect no less than that of fluoride compounds.

Treatment of caries is a complex process aimed at ending the destructive process, restoring the shape and function of the tooth. There are various methods of caries treatment: etiotropic and pathogenetic, conservative and surgical, local and general. Methods of pharmacotherapy of the carious process are conservative, which can conditionally be divided into etiotropic (elimination of factors) and pathogenetic (prevention and deceleration of development). The use of a specific technique for the pharmacotherapy of caries depends on the clinical form of the disease (in the stage of "spot" or "deep caries"), course ("acute" or "chronic"), the intensity of the lesion ("single" or "multiple") and the presence of concomitant pathology. To assess the degree of tooth damage with caries, indicators of its prevalence, intensity, etc. are used.

Traditional methods are used to anesthetize manipulations performed on hard tooth tissues: tranquilizers (sibazon, chlozepide) in combination with paracetamol, ibuprofen, and other NNAs. Premedication is carried out in 20–40 minutes before starting treatment. For local anesthesia, application anesthesia is widely used (2.5 % solution of trimecaine, aerosol of 20 % alcohol solution of lidocaine). With very high sensitivity of the teeth, conductive anesthesia with 2 % solution of lidocaine or 4 % solution of articaine can be used.

Antipyretic agents include antiseptics, which are used to remove plaque and treat a carious cavity before filling. Soft plaque is removed with cotton swabs impregnated with 3 % solution of hydrogen peroxide, 4 % solution of chloramine B, alcohol. To increase the antibacterial protection of the oral cavity, reduce dysbiosis and the formation of plaque, it is advisable to use 0.1 % solution of lysozyme in 0.6 % solution of so-

dium chloride in the form of mouth baths after eating. For better adhesion of the filling (at the stage of filling), it is advisable to use 0.1–0.5 % formalin solution, which promotes dehydration of tooth tissues, algipor, triclosan.

General pharmacotherapy of caries consists of the following stages: a) exposure to the underlying cause of the disease; b) elimination of cariogenic factors in the body; c) increasing the resistance of teeth to cariogenic factors; g) increasing the body's immune defense.

Indication for general therapy is multiple tooth damage mainly in children, adolescents and pregnant women.

For general pharmacotherapy, foreign sodium fluoride preparations are used internally: fluosen (15 mg tablets) and coreberon (20 mg tablets). They are prescribed for a long time 2–3 tablets a day after meals. It is advisable to combine this treatment with vitamin D and calcium preparations (not simultaneously). In the prevention of caries, these drugs are not recommended because of their large doses. It is also possible to use sodium fluoride in the form of 1 % solution – 2–5 drops 2–3 times a day. Avoid an overdose of fluorides, to keep the concentration of fluoride within narrow therapeutic boundaries, if you use disodium monofluorophosphate (drug with delayed release).

The main method of treating initial dental caries is remineralizing therapy. There are various types of this treatment: fluorides or calcium phosphate compounds. For the prevention of caries, applications of 1–2 % solution of sodium fluoride, varnish fluoride, sodium fluoride gels are used. For the treatment of initial caries, alternately application of 10 % solution of calcium gluconate and 2 % solution of sodium fluoride. In case of a massive carious lesion, up to 30 procedures are performed daily or every other day. A second course is carried out after six months.

Local pathogenetic therapy includes methods that enhance the enamel remineralization processes, normalize its structure, the ability to recalcify affected dentin and stimulate pulmonary odontoplastic function. To treat caries in the "white and light brown spot" stage, remineralizing therapy is carried out, for which 1–2 % sodium fluoride gel based on 3 % agar is used, which is applied to cleaned teeth (3–5 applications). For remineralizing therapy for initial caries, Dentoria gel containing 2 % fluoride can be used.

Initial caries is treated with calcium phosphate gel (pH 6.5–7.5 and pH5.5), made on the basis of calcium chloride and sodium hydrogen phosphate. The gel contains calcium and phosphate ions in a 1:4 ratio (a similar ratio is observed in saliva). The gel is used for brushing teeth for 1 month 2 times a day. It should be noted that neutral gel is used to treat initial caries, and acid gel (pH 5.5) is used to treat carious spots with softening areas in the center. One of the new directions in the prevention of caries is the coating of intact fissures with composite materials (sealing).

In case of acute caries, the tooth cavity is filled with artificial dentin prepared with 5 % sodium fluoride solution, and phosphate cement containing 5 % calcium glycerophosphate and 2 % (by weight of cement powder) sodium fluoride is used. Cement Fluosit, which contains 11 % sodium monofluorophosphate, can also be used for temporary fillings.

Currently, a new method of prevention and treatment of caries is introduced – deep fluoridation. Effective remineralization of enamel can only be achieved by constantly maintaining an optimal concentration of fluoride in saliva, and the enriched apatite is almost easily dissolved in an acidic environment. The traditional application of fluorides on the enamel surface cannot be an effective method of exposure to hard tissues, the current level of development of medicine allows the use of other original techniques. For deep fluorination, "Enamel-sealing liquid" or "Tiefenfluorid" preparations have been developed, consisting 2 solutions, as a result of successive application of which to the tooth, an alkaline substance is formed in the enamel (a gel of silicic acid with microcrystals of calcium fluoride, magnesium and copper). After treatment with the drug, the concentration of fluoride ions is created on the enamel surface, which is 10 times higher than when applying salts such as sodium fluoride salt. Fluoride is released for a long time, providing reliable remineralization, in particular in problem areas. The use of an enamel-sealing preparation allows children to stop the progression of initial and superficial caries, as well as to keep intact teeth that are in the process of eruption and "maturing".

To increase the resistance of teeth to the carious process, remodent is used in the form of 3 % solution. Teeth are pre-cleaned with hygienic toothpaste. Applications are carried out for 15–20 minutes. (3–5 applications per course). 2–3 courses are prescribed per year. The drug is also used to rinse the oral cavity (15–20 ml for 3–5 minutes).

There is evidence of a close relationship between the development of dental pathology (including caries) with changes in the immune system. Now, experience has been accumulated in the prescription of Imudon simultaneously with 3 % solution of remodent according to the scheme (from 3 to 8 tablets per day sublingually for 3–5 weeks, 1–3 times a year).

With caries in the "brown and black spot" stage, remineralizing therapy is ineffective, therefore, teeth are prepared and filled. 20–30 minutes before the intervention, premedication and anaesthetizationf are carried out (0.2–0.5 g paracetamol, 0.4–0.6 g ibuprofen, 0.01 g ketorolac or LA, enterally). If necessary, you can use mild inhalation anesthesia with nitrous oxide or intravenous anesthesia with propanidid, ketamine. To close the cavity for 1–2 weeks, put a temporary filling of zinc sulfate and zinc oxide (3 : 1) and 5–10 % kaolin, which is prepared before filling, dentin paste, zinc-eugenol paste.

Treatment of deep caries is a complex problem that requires solving a number of issues. First of all, it is a matter of preserving the pulp of the tooth when removing softened dentin. For recalcification and stimulation of odontogenesis use Calcin paste made on the basis of calcium hydroxide. Other pastes based on calcium hydroxide are also used – Calxyl (pH 12), Serocalcium (pH 12, 31), Biopulp (pH 11.1), Vita-pulp, Calxide, Regeneran, Reogan. These drugs have odontotropic anti-inflammatory and bactericidal effects and protect the pulp from irritation with drugs and other substances. After 6 months removing of the dentin residues should be repeated and a final filling performed.

Zinc, zinc-salicylic, iodoform, zinc-eugenol and other pastes, in which zinc oxide serves as a solid base, also have odontotropic properties. Pastes made of zinc oxide with eugenol and white clay, made on a solution of crystalline lysozyme and dimexide (25 ml of crystalline lysozyme contained in 1 ml of 70 % dimexide) also work well. The pastes are applied in a thin layer and insulated with a pad of water dentin from a pad of phosphate cement in order to protect lysozyme from inactivation.

There is evidence of certain effectiveness in the use of pads with calcium hydroxide – varnish based on chlorhexidine (contains 1 % chlorhexidine gluconate and 1 % thymol) and Ledermix paste (contains Demeclocyclin and Triamcinolonacetonid). Used drugs help to remove pathogenic

bacteria and eliminate (due to steroid) pain. For insulating linings, gutta-percha is used, and then – a temporary seal.

An alternative to the treatment of deep caries is the use of linings made of ionomer resins. The latter contribute to the mineralization of dentin and have a thermal conductivity 6 times lower than that of calmecin.

For general prevention and treatment of caries, calcium preparations are widely used, which play an important role in the formation of bone tissue and teeth, regulate the function of cell membranes, increasing the body's resistance. The daily requirement for calcium is 1 g.

Three generations of calcium preparations are used. Until recently, exclusively calcium preparations of the 1st generation were used to treat acute initial caries, namely, simple calcium salts (gluconate, glycerophosphate, carbonate, lactate, citrate, chloride), which are not sufficiently absorbed by the body. In order to improve metabolic processes in the hard tissues of the tooth, calcium gluconate is prescribed (up to 1 year – 0.5 g; 2–4 years – 1 g; 5–6 years – 1.5 g; 7–9 years – 2 g, 10–14 years – 2–3 g), calcium glycerophosphate (adults – 0.25–0.5 g, children – 0.05–0.2 g, depending on age) 3–5 times a day. Calcium chloride is prescribed orally in the form of 5–10 % solution by teaspoon, dessertspoon or tablespoon 3–4 times a day. The drugs should not be introduced s.c. and i.m. because of the probability of necrosis, therefore, use the drop method and i.v. bolus method.

The second generation of calcium preparations includes complex preparations of calcium and vitamin D salts. When they are used, there is a rather high probability of an overdose of vitamin D, a fat-soluble vitamin that has the property of cumulating in the body. The third generation includes complexes of calcium salts, vitamin D (in low doses) and minerals. The latter drugs are well absorbed by the body due to the presence of vitamin D_3 and trace elements, which are activators of a number of enzymes. There is a wide choice of complex preparations of calcium of domestic and foreign production: Marine Calcium D_3 and Zinc, Marine Calcium D_3 and Vitamin C, Calcemid (UNIS, Ukraine), Calcemin (Health Life, USA), Calcium-D_3 Nycomed (Nycomed Pharma, Norway), etc. Calcium is contained in the form of salts of citrates and carbonates in the composition of these drugs, their drawback is the dependence of absorption on

the acidity of gastric juice (under the influence of hydrochloric acid, calcium preparations dissociate into ions). The source of ionic (active) calcium is Sunamol-LDZ – a drug of natural origin, which is easily absorbed. The composition of the drug includes 27 trace elements and Vitamin D_3 in a small dose (20 IU/ml), which eliminates an overdose.

To stimulate the growth of bones, teeth, hematopoiesis, phosphorus seems to be an important macrocell. The daily need for it is 1.5–2 g. Phytin is used, which is a mixture of salts of phosphoric acids. The drug is used for adults – 0.25–0.5 g 3 times a day, for children under 1 year – 0.05–0.1 g; up to 2 years – 0.1 g; 3–4 years – 0.15 g; 5–6 years – 0.2 g; 7–9 years – 0.25 g; 10–14 years – 0.25–0.3 g 3 times a day.

For the prevention and treatment of caries, they use remodent – a preparation made from animal bones that contains macro- and microelements (calcium, phosphorus, magnesium, potassium, sodium, chlorine, and organic substances) necessary for enamel remineralization. It is prescribed to adults and children over 2 years of age for the prevention and treatment of caries in the form of 3 % solution for rinsing and applications. The latter is also a part of some toothpaste.

Vitamins help to improve metabolic processes and increase the body's natural resistance. For the treatment of acute forms of caries, it is advisable to use ascorbic acid (0.1–0.2 g a day), pyridoxine (0.05–0.1 g a day) and ergocalciferol (6–8 year-old children – 3–5 drops of 0.125 % oil solution of the drug per day).

An important role in the protective reactions of the body is played by iron, which contributes to the remineralization of tooth tissues, the synthesis of hemoglobin and respiratory enzymes. The daily need for it is 15 mg. Iron is used for dental diseases associated with malnutrition, exhaustion, anemia, with a general loss of strength after infectious diseases or surgical interventions. Tablets Fitofterolactol contain iron lactate and phytin. 1–2 tablets are prescribed 2–3 times a day after meals. Aloe syrup with iron has an antianemic and biostimulating effect. 0.5–1 teaspoon per 0.25 cup of water 3 times a day should be administered.

With a weakened resistance of the body, sodium nucleinate, potassium orotate, and methyluracil are prescribed. Perhaps the use of anabolic steroids (nerobol, retabolil), as well as adaptogens (preparations of ginseng, golden root, eleutherococcus).

If the process of salivation is disturbed, it is recommended to use bromhexine and tinctures from medicinal herbs (Thermopsis lanceolata and Tussilago farfara). The secretion of salivary glands can be increased by a solution of potassium iodide, a yarrow broth. A positive effect on the restoration of the function of the salivary glands is exerted by the application of solcoseryl gel, emulsion of dibunol, an oil solution of vitamin A.

Thus, for the effective treatment of caries, it is necessary to consider carefully all the links of its development and implement a rational pharmacotherapeutic effect on them.

An important stage of surgical intervention in case of caries is filling, which replaces the tooth tissue defect and restores the anatomical shape of the tooth. Now there is a wide selection of materials for filling, therefore, a rational approach to the selection of a specific material in a particular clinical situation requires deep knowledge. According to the purpose, filling materials (dental restorations) are divided into 5 groups:

- permanent – used to restore the anatomical shape and function of the tooth;
- temporary – used to close the cavity;
- linings – used for laying under permanent filling materials, most often with the aim of treating deep caries;
- cements – used to fill the root canals of the teeth;
- sealants (hermetics) – used to close non-mineralized fissures in order to prevent caries.

Filling materials must meet certain technological, functional, biological, aesthetic requirements and possess such properties: sufficient hardness, chemical resistance, high adhesion to tooth tissues, coefficient of thermal expansion, which approaches the tooth tissues, low thermal conductivity, stable color, pH level, that approaches 7, plasticity and convenience in the formation of fillings, easy introduction into the tooth cavity, antiseptic and anti-inflammatory properties, radio-opacity.

An ideal filling material that meets these requirements has not yet been created. Therefore, they use a material whose qualities are most appropriate for this case.

Dental cements. According to the current classification (DS Smith, 1995), 4 types of dental cements are distinguished:

- phosphate, zinc phosphate, silicophosphate, silicate;

- phenolate – zinc eugenol, $Ca(OH)_2$ salicylate;
- polycarboxylate, zinc polycarboxylate, glass ionomer cement;
- acrylate – polymethyl acrylate, dimethyl acrylate.

Phosphate cements (phosphate cement, Adhesor, phosphate cement containing silver, Argil; dioxivisphate, etc.). The positive properties of these cements are their low toxicity, good heat-insulating qualities, and compliance of the material with the coefficient of thermal expansion of hard tooth tissues. They are easily inserted and adhere well to tooth tissues. Recently, silver salts have been added to the composition of zinc-phosphate cements, giving cements antimicrobial and anticariogenic properties. However, they also have some drawbacks: they can dissolve under the influence of oral fluid, they are easily erased, they shrink when hardened, and they do not satisfy aesthetic needs (porous and not brilliant). Phosphate cement is used for filling cavities under crowns, for primary teeth, as well as for insulating lining, for fixing artificial crowns and bridges. Bactericidal phosphate cement containing silver is used in pediatric dentistry as a permanent filling material for temporary teeth, as well as an insulating lining for amalgam and cement fillings (only in the posterior teeth).

Silicate cements (Silicin, Silicin-2, Fritex) have better physical and mechanical properties compared to previous cements. They are stable in the oral cavity, have a color and shine, i.e. assume the properties of enamel. However, they negatively affect the pulp of the tooth, are quite fragile, poorly withstand chewing load. Silicate cements are used mainly for filling carious cavities of classes I, III, and V both in permanent and milk pulpless teeth. Silicophosphate cement (Silidont) is a mixture of powders of phosphate (20 %) and silicate (80 %) cements. This material is used in pediatric dentistry for filling carious cavities of classes I, II and V in temporary molars, permanent molars and premolars of classes I, II and V.

Phenolate-based cements contain zinc oxide and refined eugenol or clove oil. They positively affect the pulp, have odontotropic and anti-inflammatory properties. However, their high solubility in oral fluid, as well as low mechanical strength, allows the use of such cements only for linings and temporary fillings.

Calcium hydroxide chelate cements (Dycal (Dentsply), Life, etc.) are based on the hardening reaction between calcium hydroxide and other salicylic acid oxides and esters. They are widely used in the treatment of

acute deep caries and for direct coverage of exposed pulp. Their advantages are ease of use, quick hardening, positive effect on the pulp, disadvantages – low strength, gprobable deformation, solubility (with leaky filling).

Polycarboxylate cements (Poly-F-Plus, Carbocement, Adhesor-Carbofine). The advantage of these cements is almost complete safety for hard tissues and tooth pulp, the property of chemically binding to enamel and dentin. They are ideal for filling the temporary teeth, as they do not require insulating lining and have pronounced adhesion to hard tooth tissues. In permanent teeth, they are used for temporary fillings and as a lining material.

Glass-inomer cements are modern filling materials that combine the properties of silicate and polyacrylic systems. They have significant adhesion to hard tooth tissues; they are firmly bound to dentin and composite filling materials, and have high biological compatibility with tooth tissues. They are used for filling cavities of classes III, V in permanent teeth and for temporary restorations in permanent teeth with an unformed root. These materials are an ideal filling material for closing carious cavities of all classes in temporary teeth. They can be used as lining material, especially when working with composite materials. The disadvantages of glass-inomer cements are slow hardening, low strength, moisture sensitivity, radioparency and a probable influence on the pulp.

Insulating varnishes are thin pads (liners) that protect the pulp from the toxic effects of filling material. There are such varnishes: Dentin-Protector (Vivadent), Amalgam Liner (VOCO), Thermoline (VOCO), Evicrol (SpofaDental). Their positive properties are high chemical resistance, moisture resistance, bacteriostatic and odontotropic qualities. The main disadvantage is the lack of thermal insulation effect, limiting the use of varnishes in deep carious cavities.

Composite filling materials are modern filling materials with high physical, mechanical and aesthetic properties. Such materials consist of three main components: an organic matrix (polymer matrix), inorganic filler (inorganic particles), and surfactants (silane).

Composite filling materials include:

- macro-filled composite materials (macrophiles), the particle size of the filler is 1–100 microns. They include the first generation of mate-

rials: Evicrol (SpofaDental), Consize (3M), Visio-Fill, Visio-Molar and others;

- micro-filled composite materials (microfiles), the particle size of the filler is 0.04–0.4 microns. They include Isopast (Vivadent), Durafill (Kulzer), Helio-Molar (Vivadent), Silux Plus (3M);
- hybrid composite materials, the particle size of which is from 0.04 to 100 microns. Today, the most common are: Prisma (Dentsply), Herculite XRV (Kerr), Charisma (Kulzer), Tetric (Vivadent), Arabesk (VOCO), etc.

Hybrid composite materials are universal; therefore, they can be used for filling carious cavities of all classes, as well as for complete restoration of the crown of the tooth and reconstruction of the dentition. These materials have several advantages: maximum mechanical strength, chemical resistance, high aesthetics and lightfastness, minimal shrinkage and high adhesion.

Compomers – a new class of filling composite materials. They combine the qualities of composites and glass ionomer cements. The most famous are: Dyract (Dentsply), Dyract XP (Dentsply), F-2000 (3M), Elan (Kerr), Hytac (ESPE), etc. They are used to fill in the carious cavities of all classes in temporary teeth and classes III, V cavities in permanent teeth.

1.2.2. Non-carious lesions of the teeth

The most common of non-carious lesions of hard tooth tissues that occur during their development is fluorosis. Tooth fluorosis is a genesis complex enamel hypoplasia that is complex due to the influence of excess fluoride ions in drinking water, food or the atmosphere. Fluorosis is an endemic disease. More often this violation occurs in the areas where the amount of fluoride in natural sources of wateris much higher than the recommended norm (1–1.2 mg/l).

Fluorosis appears on the teeth immediately after their eruption by changing the color of the enamel, which loses its transparency, becomes yellowish-brown. For fluorosis, unlike caries, bilateral and symmetrical focuses are typical, which are located mainly closer to the cutting edge of the tooth and the occlusal surface. Further, enamel demineralization progresses.

The choice of pharmacotherapy in the practice of a dentist depends on the stage of fluorosis. Those forms of the disease that are not accom-

panied by the loss of hard tooth tissue does not require such treatment. 5-minute whitening with 30 % solution of hydrochloric acid is carried out on pigmented sites, and also with 33 % solution of hydrogen peroxide. Recently, a new concept and technology for removing pigmented enamel using microabrasion and a laser have appeared.

To improve the condition of tooth hard tissues, it is recommended to carry out local saturation of tooth tissues with calcium phosphate preparations, vitamins of group C, P, PP. Also 10 % solution of calcium gluconate and 6 % solution of vitamin B_1 are used for electrophoresis. With erosive and destructive forms of fluorosis, the anatomical shape of the tooth can be restored using composite materials. In case of significant destruction of the crown of the tooth, orthopedic treatment methods should be used. For brushing teeth affected by fluorosis, we recommend pastes with remineralizing effect that does not contain fluoride (Pearl, Remodent). It is advisable to remove excess fluoride from drinking water or other sources.

Non-carious lesions that occur after teething include the following diseases: abnormal tooth wear, wedge-shaped deffects, necrosis, erosion of hard tissues, hyperesthesia, and injuries. In practice, the most common hyperesthesia of the teeth happens in a limited and generalizable form. Pharmacotherapy includes the local use of 30 % solution of silver nitrate, which is reconstituted after applying to the teeth of 10 % formalin solution or 4 % eugenol solution. Pastes with alkaline properties (sodium bicarbonate, potassium carbonate, magnesium carbonate, etc.) are to be applicated.

To increase the stability of hard tissues, sthey use odium fluoride, strontium chloride, calcium glycerophosphate, calcium gluconate, etc. 75 % fluoride paste is rubbed into the tooth surface, 75 % paste of strontium chloride and calcium glycerophosphate, 1–2 % aqueous solution of sodium fluoride is used in in the form of applications or by electrophoresis. Applications of 3 % remodent solution, 5 % thiamine chloride solution with 2 % novocaine solution for electrophoresis are also used (10–15 procedures). For pain relief, an anesthetic mixture is used (Platonov's liquid No.1, No.2), electrophoresis with anesthetics. For general pharmacotherapy, 0.5–0.75 g calcium glycerophosphate, 0.5 g calcium gluconate 2–3 times a day for 3–4 weeks are administerd.

1.3 PHARMACOTHERAPY OF PULPITIS

Pulpitis is an inflammatory process of the pulp, characterized by a complex of functional and structural changes that occur during the progression of the carious process. The etiological factors of pulpitis can be divided into the following categories: bacterial, traumatic, allergic, chemical, iatrogenic and idiopathic. A common cause of pulpitis is considered biological agents (microbes and their toxins) that come from the carious cavity. After filling a tooth for tooth decay, pulpitis or periodontitis occurs in 10 % of cases a year later. And after 2–3 years there is an increase in cases of complications up to 50–60 %. There are other possible routes of infection (with pathological tooth wear, cracks, wedge-shaped defects, periodontitis, osteomyelitis). Among the microorganisms that cause pulpitis, associations of highly virulent pyogenic cocci, putrefactive microbes, fusospirochete flora, fungi, and gram-positive rods predominate. The most common are associations of streptococci and lactobacilli.

The following is the microflora of the root canal according to the frequency index in patients with various types of pulpitis. Characterization of potential causative agents of pulpitis is important in the treatment of immunocompromised individuals and in the case of complications of pulpitis with acute purulent periodontitis or periosteal reactions.

With a small lesion and a slow development of the carious process, a reparative layer of dentin is formed at the border of the pulp and dentin, which protects the pulp from inflammation for a while. Next, there is a lesion of odontoblasts, the appearance of enzymes and the development of inflammatory vascular changes, the creation of cellular infiltrates from lymphocytes, macrophages, and plasma cells. The initial inflammatory reaction of the pulp is considered delayed-type hypersensitivity. When eliminating the carious process, these phenomena are reversible and the pulp tissue can recover.

Table 1

Characteristics of the microflora of the root canal in patients with pulpitis (frequency index)

Bacterial species	Acute serous	Acute purulent	Chronical
Peptostreptococcus spp.	0.22	0.9	0.69
Streptococcus intermedius	0.27	0.6	0.75
Streptococcus sanguis	0.33	0.45	0.75
Streptococcus mutans	0.27	0.35	–
Streptococcus millers	0.13	0.3	0.50
Streptococcus mitis	0.07	0.3	0.56
Eubacterium spp.	–	0.55	–
Actinomyces naeslundii	0.22	0.35	–
Actinomyces odontolyticus	0.33	0.2	–
Actinomyces israelii	0.13	–	–
Actinomyces spp.	–	–	0.63
Propionibacterium spp.	0.07	0.1	0.25
Prevotella melaninogenica	–	0.45	–
Prevotella intermeia	–	–	0.75
Prevotella oralis	–	0.3	0.43
Fusobacterium necroforum	–	0.35	–
Fusobacterium spp.	0.27	–	0.31
Veillonella spp.	–	–	0.25
Corinebacterium spp.	–	–	0.19
Staphylococcus anaerobius	–	0.1	–
Staphylococcus spp.	–	–	0.13
Candida albicans	–	0.1	0.19
Rothia dentocariosa	0.22	–	0.13
Lack of growth	0.22	–	–

With further acute development of inflammation of the pulp, its volume increases, nerve elements experience significant irritation, a paroxysmal pain syndrome appears with irradiation along the trigeminal nerve. If the bacterial onset continues, the inflammatory process progresses and suppuration or pulp necrosis may develop.

According to the classification of E. M. Gofung, acute (partial, general, purulent) and chronic (simple, gangrenous and hypertrophic) forms of pulpitis are distinguished. In acute pulpitis, as a rule, a large carious cavity is determined, the bottom of which is painful when probed. There is a significantly expressed reaction to temperature stimuli (especially cold). Percussion becomes painful with diffuse inflammation of the pulp, as well as with pulpitis complicated by periodontitis.

The intensity of the pain syndrome depends on the severity of the process (paroxysmal pain is typical for acute pulpitis, aching – for chronic). Temperature and mechanical stimuli enhance the pain response; however, it can occur without exposure to irritants.

In the treatment of pulpitis, the sequence of actions of the doctor is aimed at eliminating pain syndrome and inflammatory process, stimulating reparative processes and restoring the shape and function of the tooth. Depending on the indications, conservative (biological) and surgical (amputation of part or all of the pulp) methods are used.

When treating pulpitis, all food residues are carefully removed from the carious cavity, and then solutions of acetylsalicylic acid or analgin, lidocaine, novocaine, Dent drops are introduced into it on a cotton swab. Cauterizing agents (3 % carbolic acid with anesthesin, camphorophenol, alcohol tinctures) can be used cautiously and in exceptional cases. However, it should be remembered that cauterizing agents cause a superficial burn of the pulp, which further complicates the surgical treatment of pulpitis with the devital method. Enteral anesthetics are prescribed (paracetamol, ibuprofen, nimesulide, pentalgin).

At the beginning of treatment in a dental clinic, premedication with tranquilizers, antipsychotics and analgesics, as well as local anesthesia are used to prevent an inadequate response of the patient to medical manipulations. Effective anesthesia is carried out by means of conduction, intraligamentary, intrapulpal or "druck"-anesthesia.

A biological (conservative) method of treating pulpitis is aimed at stopping the further development of the carious process, eliminating infected dentin, preserving pulp viability with the help of drugs, which can stop the inflammatory process and stimulate the formation of irregular dentin. Partial preservation of pulp viability in the root canals with removal of its coronal part is called the vital pulp amputation method. Treatment, which is carried out with the removal of coronal and root pulp (pulpectomy, extirpation), can be vital or devital (with preliminary necrotization).

Conservative treatment is carried out after opening of the cavity and removing softened dentin. This method consists in direct coating of the pulp with a drug or indirectly through the dentin of the carious cavity. Following the preparation of the tooth cavity, it is treated medically with solutions of anesthetics (3 % solution of hydrogen peroxide, alcohol), antibiotics (gentamicin, chloramphenicol, etc.), enzymes (trypsin, chymotrypsin), drying the cavity and applying medical paste to its bottom.

Modern methods include the use of various anti-inflammatory and antimicrobial agents, as well as stimulating dentinogenesis and enhancing the barrier function of mineralized dentin between the carious cavity and the pulp cavity. Positive results in the conservative treatment of pulpitis were obtained using calcium-based pads that are superior in quality to medical pads made of antibiotics and sulfonamides. Under the action of calcium hydroxide, softened dentin is remineralized, and the pulp forms a barrier to irregular, tertiary dentin. In the exposed pulp, compaction of the main substance is formed, fibrous structures and odontoblasts appear, with which the construction of the dentin bridge is associated. Next, an insulating pad and a permanent seal are applied. The following medicinal pastes are left at the bottom of the cavity: calcin, calmecin, calxyl, biopulp, serocalcium, regeneran, which have pronounced odontotropic properties. The application of calcium hydroxide may be preceded by topical application of pastes containing antibacterial agents. In the cavity, antibiotics exhibit antimicrobial properties, and after penetration into the pulp they have anti-inflammatory and analgesic effects, without causing significant morphological changes.

For dental practice, the problem of the resistance of microorganisms to ABD remains important, and therefore, when choosing a treatment, it is important to take into account the sensitivity of microflora to a specif-

ic antibacterial drug. Analysis of the bacterial flora of the inflamed pulp showed the presence of a large number of staphylococci, hemolytic and non-hemolytic streptococci, enterococci. Microflora may be sensitive to gentamicin, amoxiclav, clarithromycin, chloramphenicol. Resistance to penicillin, tetracycline is found. The following simple and combined pastes can be used to relieve acute phenomena usually associated with infection: zinc-eugenol, norsulfazol, chloramphenicol-norsulfazol, lysozyme-vitamin (also contains dimexide), microcide-norsulfazol.

The complex use of ABD increases the effectiveness of the conservative method of treating pulpitis. However, when using antibiotics, there is a risk of developing a chronic course in pulpitis due to the suppression of local immunity.

Due to the lack of blood circulation in the middle of the necrotic pulp, therapeutic concentrations of antibiotics are not created there. Their systemic use is not required. However, patients with hypersensitivity to infection (immunocompromised individuals with transplanted bone marrow and other immunosuppressive conditions) need to be given prophylactic antibiotics. Antibiotic prophylaxis is carried out an hour before the treatment of the canal. The drugs of choice are modern drugs amoxicillin/clavulanate – 1.2 g i.v. ampicillin/sulbactam – 1.5 g i.v.; clarithromycin – 500 mg i.v.; ciprofloxacin – 0.2 g i.v.

For conservative treatment of the inflammatory process in the pulp, hormonal drugs that are characterized by anti-inflammatory, analgesic, hyposensitizing properties gave a good account of themselves. But after the termination of their effect, changes in the pulp undergo a reverse development, reparative processes are disturbed, the layer of odontoblasts is disorganized. To eliminate pulp inflammation, the use of drug combinations (prednisolone or hydrocortisone and tetracycline) is pathogenetically justified. In the practice, dentists use pastes that contain antibacterial and hormonal drugs, painkillers (for example, pulpomyxine by Septodont). It must be remembered that corticosteroids inhibit dentinogenesis and formation of granulation tissue. Pastes with anti-inflammatory properties are used for temporary application, followed by their replacement with odontogenic agents (calcin, regeneran).

In the treatment of pulpitis, proteolytic enzymes and antiseptics are used. It is known that proteolytic enzymes act only on damaged protein

substances; the pulp is freed from the products of inflammation. For the treatment of pulpitis, 1 % trypsin solution is used, as well as pastes containing enzyme preparations (for example, a paste containing lysozyme, vitamin A, zinc oxide). The use of antienzyme preparations (contrykal, trasylol) for the treatment of pulpitis consists in an excessive increase in the activity of the proteolysis system enzymes in the inflammation site.

For the pharmacotherapy of pulpitis, various drugs are also used that have anti-inflammatory, regenerating, analgesic, hyposensitizing effects. They contain biologically active substances and trace minerals made from therapeutic mud. For the conservative treatment of pulpitis, heparin, furazolidone and a fraction of the therapeutic mud are effectively used. For traumatic pulp injuries, positive results were obtained using paste based on sterilized bone meal, heparin ointment, as well as sorbents.

After the inflammatory phenomena subside, it is recommended to use biomaterials containing collagen and hydroxyapatite (Ostim-100, KP-2, Collapan-1, etc.). Densply developed a material Pro ROOT MTA – a mineral trioxide aggregate, with direct coating which provides reliable sealing and enhances repair. A positive result was achieved in the treatment of pulpitis with ointment from sterile bone meal and heparin.

A universal method that is used in all cases when the use of conservative treatment is excluded is vital pulpotomy. It involves the removal of coronal pulp and the application of a drug on the stump of the root pulp that can provide a seal, a long anti-inflammatory and antiseptic effect.

Often with vital pulpotomy, there are used preparations based on calcium hydroxide, which, due to alkaline pH, have a pronounced bactericidal effect. This action is of short duration due to the rather rapid neutralization of the drug. In addition, it has been proven that calcium hydroxide stimulates the process of resorption of temporary teeth. Preparations used during pulpotomy, such as eugenol paste, glutaraldehyde, pastes with ABD and GCS, as well as calcium hydroxide, are not able to provide long-term anti-inflammatory and antiseptic effects, hermetic closure of the pulp stump and preservation of its vital activity.

The best results in the treatment of pulpitis by vital amputation were obtained using a collagen sponge with tetracycline and oletetrin. The feasibility of using this method may be due to obstruction of the root canal. Situations with obstruction of the root canals are found in inflammatory

periodontal diseases in the elderly, when canal calcification occurs in 90 % of cases.

In pediatric dentistry, if possible, vital amputation of the coronal part of the pulp and the creation of favorable conditions for the preservation and functioning of the root pulp are recommended. In the presence of vital pulp in the root canals of temporary teeth and permanent teeth with unformed roots, internal resorption of the root is practically not observed, and physiological resorption occurs at the appropriate time. When applying vital pulpotomy in pediatric practice, in order to prevent negative results of the method, it is necessary to take into account many factors: the presence of a general somatic pathology, the nature of the child's behavior, X-ray data, the absence of diffuse pulp damage, the rate of stopping bleeding from the pulp stump after amputation of its crown part.

In this regard, widespread drug Pulpotec is of considerable interest. It contains a powder (polyoxymethylene, iodoform, zinc oxide) and a liquid (dexamethasone acetate, formaldehyde, phenol, guaiacol), which are mixed immediately before application to the pulp stump. Pulpotec is used to treat pulpitis in temporary and permanent molars in children and adults, while maintaining the viability of the root pulp. A portion of the Pulpotec preparation mixed up to a creamy consistency is applied to the pulp stump. The tooth cavity is closed with temporary cement. After mixing the ingredients, the paste hardens quickly, does not stick to a tool, creates optimal conditions for linings and seals, and allows to isolate the pulp hermetically.

After amputation of the coronal part of the pulp, mummifying agents are applied to the root canal cells (resorcinol-formalin, camphor-phenol paste, Gysi's paraform paste, Foredent, Rezoform, Ribler's paste, etc.). The paste polymerizes in the presence of a catalyst (10 % sodium hydroxide solution). The disadvantage is staining the teeth in pink.

A common treatment for pulpitis is pulpectomy. The method of vital extirpation is to remove the entire pulp (crown and root) with the mandatory use of painkillers. Root canals are treated with antiseptic agents (10 % solution of iodinol, 10–15 % solution of dimexide, 1–2 % solution of chloramine, 3 % solution of hydrogen peroxide). After preliminary drying, the root canals are filled with paste prepared on the basis of calcium hy-

droxide (Calcin, Calxyl, Reogan), as well as containing eugenol (Radiocal, Caryosan). After this, a permanent seal is applied.

Pulp devitalization increases the number of visits, arsenic analgesia is imperfect and patients experience discomfort, fear and tension during the manipulation. In addition, there remains a risk of developing arsenic periodontitis. When choosing a devital method for the treatment of pulpitis, preference should be given to paraformaldehyde-based preparations that do not contain arsenic anhydride. For pulp necrotization, pastes prepared on the basis of paraformaldehyde can be used (Paraformaldehyde, Trioxymethylene, Sinarsen, Pulpatoxin, Devipulp, Falin). After necrotization of the pulp, depending on the indications, the doctor performs its amputation or extirpation.

If formalin-containing preparations are introduced into the root canals after a pulpectomy, formaldehyde (formalin) is deposited in crystalline form on the surface of the residual pulp with the formation of an aseptic mummified strand that covers the lumen of the root canal of the tooth. However, formaldehyde vapors can cause the development of a toxic effect when it penetrates into the periapical regions, and the result is a systemic spread. Attempts to replace formaldehyde with other drugs, for example, glutaraldehyde, were ineffective and led to an increase in the number of adverse outcomes in the treatment of pulpitis by vital pulpotomy.

Sometimes the pulp devitalization method is also used using arsenic paste, which includes arsenic anhydride, thymol, cocaine and dicain. The necrotic effect of arsenic, accompanied by pain, is to some extent eliminated by cocaine, dicain, and thymol has an antiseptic effect. For pulp necrotization, the paste is applied in an amount of 0.006–0.008 g, covered with a swab soaked in 5 % solution of dicain or phenol, and closed tightly with dentin paste or aqueous dentin. Some preparations contain a strictly defined amount of arsenic anhydride (Mukarsen, Devitalizin, Necronerv, Arsonerv). Arsenic paste is left in the tooth cavity for 24–48 hours. In case of violation of the indicated period, intoxication of the apical periodontium of arsenous acid and pulp decomposition products is observed. In this case, it is necessary to treat the canal with unithiol (arsenic antidote).

1.4 PHARMACOTHERAPY OF PERIODONTITIS

Periodontitis is called inflammation of the connective tissue between the compact plate of the tooth cell and the cement of the root of the tooth. Periodontitis is of infectious and non-infectious origin. By localization, it can be apical, when the process is concentrated at the apex of the tooth root or marginal – the process is located at the gingival margin. Pathogenic microorganisms (most likely streptococci) penetrate the periodontium through the apical hole from the infected root canal or other inflammatory foci (osteomyelitis, etc.). Infection can be caused by hematogenous route. The reasons for the development of periodontitis can also be trauma, the mechanical effect of a high filling, the toxic effect of a drug (arsenic, formalin) or filling material that extends beyond the apex of the root.

The nature of the inflammatory process in the periodontium can be acute with a predominance of alternative-exudative changes or chronic – with the development of proliferative-regenerative processes, a long course, less pronounced symptoms. Depending on the clinical course, degree and nature of periodontal damage, the following types of periodontitis are distinguished: acute (serous and purulent), chronic (fibrous, granulating, granulomatous) and chronic during the period of exacerbation. The severity of the clinical manifestations of the disease depends on the nature of the pathological process, the intensity of its course.

The development of chronic focal infection in the posterior tissues and its effect on the body is a complex problem of dentistry. In the case of a prolonged action of the infection on cement, dentin of the tooth root, periodontium and bone tissue, destructive changes can develop in them. The anatomical proximity of the foci of microbes to the bloodstream of the periodontal can contribute to the development of bacteremia. In pa-

tients at risk of CVS pathology, the latter can lead to the development of infectious endocarditis, myocarditis, acute myocardial infarction, etc. A close relationship has also been established between odontogenic infection foci and respiratory system diseases, rheumatoid arthritis, immunity indicators, etc.

The leading symptom of acute periodontitis and the chronic process during exacerbation is sharp pain due to exudate pressure on the tissues and nerve receptors, which increases with touch and percussion. The progression of the disease can cause hyperemia, swelling of soft tissues, asymmetry of the face, soreness of the regional lymph nodes, mastication disorders and, rarely, worsening of the general condition.

Taking into account the fundamentally complex mechanism for the development of periodontal inflammation, especially chronic, it is necessary to use an integrated approach to its treatment, which is based on the atomic, physiological, morphological, etiopathogenetic features of a certain form of the disease.

Now the basis of the treatment of any form of periodontitis is the principle of triple exposure, known in dentistry, on the system of macrocanals, microcanals and periapical sections. Its principles are to eliminate the inflammatory process by creating an outflow of exudate, treating infected root canals, drug treatment of apical inflammation and preventing its spread to surrounding tissues. The stages of pharmacotherapy of periodontitis are as follows:

- the stage of providing the patient with emergency care by prescribing pain medications (ibuprofen, paracetamol, pentalgin, solpadeine);
- root canal treatment.

There are three standard principles for root canal therapy: cleaning, sterilization and three-dimensional obstruction. High-quality rehabilitation, formation and homogeneous filling of the root canal system allow to expect a favorable outcome.

To carry out the outflow of exudate through the root canal, the carious cavity is cleaned and rinsed with solutions of antiseptics (iodinol, chlorhexidine, potassium permanganate, rivanol), as well as hypertonic solutions. A special role is given to the machining of the canals with endodontic instruments. For root canal treatment, antiseptics are often chosen that do not irritate the periapical site (0.5–1-2 % solution of chloramine,

0.1–0.2 % solution of chlorhexidine bigluconate, 0.1–0,5 % solution of decamine, 0.1–0.2 % solution of decamethoxin, 0.01 % solution of miramistin, 1 % solution of iodinol, Lugol's solution). Antibacterial agents are also used to flush the canals (ectericide, chlorophyllipt, microcid, metronidazole, nitroxoline, etc.).

To suppress the microflora of periapical foci, ABD are recommended to be applied topically or for the general treatment of. In particular, lincomycin, clindamycin, amoxiclav, clarithromycin, doxycycline, FQ are prescribed. Locally it is possible to use 10–20 % of sulfacyl sodium solution or 1 % streptocide solution, etc.). Due to the wide spread of antibiotic-resistant forms of microbes, combinations of 2–3 drugs are used, taking into account their interaction. Combinations of broad-spectrum antibiotics (macrolides, AG, ampicillin, piperacillin, etc.) with proteolytic enzymes (trypsin, chymotrypsin, etc.) are used. A mixture of antibiotics and an enzyme in rosehip oil, sea buckthorn oil or 30 % tocopherol acetate oil solution are introduced into the root canal. Data on the effectiveness of antibiotics are controversial. The development of their differentiated application is relevant. In recent years, macrolides, CS, FQ, inhibitor-protected penicillins and lincosamides have been recognized as the most effective.

In the treatment of root canals, a special role is given to enzymes (trypsin, chymotrypsin, lysozyme, deoxyribonuclease, terylitin, lysoamidase). Enzymes are used in the form of 0.1–0.2 % solutions independently or in combination with antibiotics (neomycin, gentamicin, microcide). For the treatment of insufficiently passable canals, electrophoresis of trypsin, lysozyme, trypsin-penicillin mixture, iodine and trypsin, Lugol's solution, 10–20 % potassium iodide solution or 5–10 % iodide solution, silver nitrate are prescribed. Microbial enzyme terrilytin with the plant-derived antibiotic novimanin is also used.

To wash the root canals of the teeth with periodontitis, GCS (hydrocortisone, prednisolone, dexamethasone) are used. To prevent complications after filling the canal, it is recommended to introduce 0.2–0.5 ml of hydrocortisone into the transitional fold in the area of the projection of the root apex.

Medication on the root canal system and periapical canals is an important component of endodontic treatment. Due to the presence of deltoid branching in the region of the apex of the root and additional tu-

bules, the term "complete removal of the pulp" is very arbitrary. Therefore, the disinfection of residual pulp, parietal dentin, and sections of the canal inaccessible for instrumental treatment is of great importance for the success of endodontic treatment and the prevention of the development of inflammatory complications.

Highly effective commercial preparations are currently being used. Such an antiseptic is Osomol-4 (Pierre Rolland, France), which includes formaldehyde and guaiacol, as well as aromatic substances (geranium oil, extracts of tea rose and jasmine). The high antimicrobial effectiveness of formaldehyde is of great importance in the endodontic treatment of upper jaw teeth. Guaiacol has a local analgesic effect.

Another antiseptic and anti-inflammatory drug Mepacyl (Pierre Rolland, France) consists of parachlorophenol, methacrylate acetate, camphor, as well as dexamethasone. These substances are able to penetrate not only into the macrocanal of the tooth root, but also into the dentinal tubules and deltoid branches. The use of Osomol 4 and Mepacyl is advisable for the conservative treatment of acute purulent and exacerbations of chronic forms of periodontitis.

Destruction of pathogenic microflora located in the root canal, deltoid branches and dentinal tubules, relief of inflammatory phenomena in the periapical tissues, stimulation of reparative processes in the periodontium and bone tissue of the periapical region is achieved by applying an antiseptic dressing. Preference is usually given to ready-made complex preparations that have a multifaceted therapeutic effect. In clinical practice, drugs for antiseptic dressings Mepacyl and Osomol-4 are widely used.

The therapeutic effect of Mepacyl is achieved due to the high bactericidal activity of parachlorofenol and methacryl. Camphor has an antiseptic and analgesic effect. Dexamethasone contributes to the rapid relief of inflammatory and allergic phenomena, reduces the irritating effect of antiseptics. Mepacyl is used in particular with insufficiently passable canals. The drug is injected into the root canals on paper points or applied to the tooth cavity on a cotton swab. Then the tooth is closed with an airtight dressing. The optimal application period is 1–2 days, if necessary, re-manipulation is done. Balanced concentrations of antiseptics in the Osomol 4 preparation provide, on the one hand, high antibacterial activity, and on the other, minimal irritating effect on periapical tissues.

The absence of hormonal drugs allows to maintain a normal level of local protective reactions and regenerative capabilities of the periodontium. In addition, it allows mummification of pulp in the deltoid branches and dentinal tubules after application of arsenic anhydride.

For the introduction of drugs into hard-to-reach root canals, the method of electrophoresis from the cathode is used, especially 5–10 % of alcoholic solution of iodine, potassium iodide, a mixture of trypsin with iodine preparations and antibiotics. UHF currents, ultrasound, phonophoresis of 2 % iodine solution and fluctophoresis of 2 % potassium iodide solution are also used.

Among the reasons for unsuccessful endodontic treatment, first of all, it is worth mentioning the so-called micro-penetration or violation of hermetic obstruction in any part of the root canal. Violation of the tightness promotes the penetration of microorganisms into the root canal and their spread into the periapical tissues. For quality obturation of root canals, endometasone, forfenan, gutta-percha points with sealant are used. The best result is achieved by using a combination of baseline with gutta-percha. To improve the quality of filling, it is recommended to use fillers – points in combination with plastic hardening pastes (sealers). In economic and practical terms, sealants such as tiedent, sildent, viedent should be used.

Well-known impregnating methods resorcinol-formalin, silvering gave a good account of themselves in case of insufficiently passable canals. The liquid is introduced into the mouth of the root canals and injected into them. To speed up the polymerization process, 1 drop of 7 % alcoholic solution of sodium hydroxide is added. The canal is filled with resorcinol-formalin paste, which is obtained by adding zinc oxide to the resorcinol-formalin mixture.

When carrying out silvering, 30 % silver nitrate solution is used, injected into the root canal, then 1–2 drops of 25–30 % ammonia solution are introduced into the root canal and 1–2 drops of 10 % formalin solution are added, then the cavity is closed by bandage. Both methods, in connection with tooth discoloration, are used only for filling molars.

Traditionally, canal filling is carried out using hardening, non-hardening and solid materials. Non-hardening materials are based on zinc oxide or white clay, mixed with glycerin (vaseline). To give antiseptic prop-

erties to pastes, thymol, formalin, phenol, antibiotics, etc. are added. Due to the rapid resorption, it is advisable to use these materials for filling milk teeth. Plastic hardening materials include cements, pastes on natural and synthetic components, amalgam. They use phosphate, zinc-eugenol (Caryosan, Calcimol) cements, guaiaquil, etc. Resins (endodent, epoxide, intradont, etc.) are referred to solid filling materials. The literature provides indications of the temporary filling of canals with calcium hydroxide preparations (metapex, calasept, biocalex).

It is possible to improve the results of pharmacotherapy of periodontitis if NSAIDs are used (diclofenac sodium, nimesulide, meloxicam, etc.) enterally, which, as you know, significantly potentiates the effect of ABD.

To stimulate reparative processes in bone tissue, methyluracil, thyrocalcitonin, lysozyme, retabolil, sea buckthorn, rosehip, tea tree oil, lysozyme-vitamin and calciotonin paste are used. Sometimes, in order to improve regeneration, bone meal, collagen, solcoseryl gel, osteoplastic materials (biolant, colapol, ostim-100 with metronidazole) are used. Collapan in the form of a gel containing hydroxyapatite, collagen, gentamicin sulfate, metronidazole, dioxicin, claforan, etc. appeared on the dental market.

The modern treatment methods in dentistry include the prescription of drugs to correct the immune system. Quite often for this purpose, they use Imudon (contains a mixture of microorganisms of the oral cavity) and Milife (contains a monoculture of fungus Fuzarium sambienium), which have a stimulating effect on the immune system.

There are some features of treatment methods that are different in origin and clinical manifestations of periodontitis. With the most common acute apical periodontitis, treatment depends on the stage of inflammation. In the stage of intoxication, after removal of the contents of the root canal, antiseptic solutions are introduced into it and the tooth is closed with an airtight dressing for 1–2 days. In the stage of exudation – the apical hole of the tooth root is expanded and an outflow of its contents is provided. In advance, it is necessary to ensure the painlessness of the performed manipulations (local anesthesia with lidocaine or ultracaine). With symptoms of general intoxication, antibacterial, anti-inflammatory and desensitizing agents are prescribed orally or i.m. to suppress the infectious process.

Acute medical periodontitis often occurs in case of intoxication with arsenic paste. After the quick removal of the necrotic pulp, the root canal is washed with 3 % solution of hydrogen peroxide, 1–2 % solution of chloramine; solution of trypsin and wads moistened with 5 % solution of unithiol or 1 % solution of iodinol are left in the canal for 1–2 days. In order to reduce inflammation and exudation, NSAIDs or GCS are prescribed. After pain disappears, an antiseptic treatment is repeated and the tooth canal is filled. If the effect is not achieved, electrophoresis with 5 % solution of iodine (for molars) or saturated solution of potassium iodide (for incisors, canines, premolars) is performed. The cavity is closed with artificial dentin and filled in 1–2 days.

In acute apical traumatic periodontitis, first of all, it is necessary to eliminate the cause of the damage and conduct symptomatic therapy with analgesics, anti-inflammatory and desensitizing drugs.

Methods of treatment of chronic apical periodontitis are divided into: conservative, conservative-surgical and surgical. In single-rooted teeth, drug treatment is carried out in three stages. At the first stage of therapy, antiseptic treatment is performed and necrotic pulp is removed. Antiseptic treatment with a proteolytic enzyme can be performed before and after these manipulations. The narrow canals that are obliterated before mechanically removing the pulp are dilated mechanically or with 20 % solution of Ethylenediaminetetraacetic acid disodium salt (EDTA). The latter binds calcium in dentin and puts it into a soluble state. The drug is left in the canal for 24 hours. Then the pulp is removed, treated with an antiseptic, the decalcified dentin is removed, washed with alcohol and dried. A swab with an antiseptic or lysozyme solution is left in the canal. At the second stage, it is treated with an antiseptic and an enzyme. In case of insufficiently passable canal, its processing is repeated and the canal is plugged. In the third stage of therapy, if the swab is clean, the tooth canal is washed with alcohol, ether, and filled. To stimulate reparative processes before filling, a paste containing anabolic agents, vitamins, and lysozyme is place into the top of the root.

Chronic apical periodontitis of multi-rooted teeth requires greater attention. After mechanical processing of the root canals, they are also washed with an antiseptic, a solution of a proteolytic enzyme and lysozyme. Wads with phenol-formalin or camphorophenol under an airtight

dressing are applied to canals that are insufficiently passable. Wads are removed after 2–3 days, the canals are treated with an antiseptic and an enzyme, the decayed pulp is removed and treated with resorcinol-formalin, electrophoresis is carried out with an alcoholic solution of iodine and trypsin. However, caution should be exercised when applying high concentrations of formalin, phenol, and resorcinol, which can cause periodontal toxicity and pain. Drugs with antibacterial and anti-inflammatory properties (eugenol, clove, sea buckthorn oil, hydrocortisone, furacilin) permittedto be left in the canals. In chronic apical periodontitis, pastes containing calcium glycerophosphate, calcium hydroxide, nitrofuran derivatives, anabolic agents and anesthetics prepared with karatolin, camphor, peach oil or vitamin A concentrate can be used.

In cases of inefficiency of conservative treatment, surgical interventions are performed – resection of the apex of the root, tooth extraction, etc. For example, in case of acute purulent periodontitis complicated by acute purulent periostitis, surgical treatment is necessary to prevent the development of osteomyelitis. An incision is made along the transitional fold to the bone 2–3 cm long in the area of the causative tooth under appropriate anesthesia. Rubber drainage is introduced into the incision, the patient is prescribed NNA (ibuprofen, ketanov, nimesulide) and ABD (clindamycin, FQ, CS, macrolides of the second generation, combined penicillins in combination with metronidazole, doxycycline) enterally. If the creation of an outflow of purulent exudate through the root canal or an incision along the transitional fold is impossible, then it is necessary to carry out tooth extraction under anesthesia. After the operation, if necessary, analgesics, antiseptics, broad-spectrum antibiotics, proteolytic enzymes, etc. are prescribed.

1.5 PHARMACOTHERAPY OF PERIODONTAL DISEASES

Periodontium is a complex of tissues (peridental membrane, alveoli bone, gums with periosteum, root cement), which are connected by a genetic and functional community. According to the WHO classification, periodontal diseases include gingivitis, periodontitis, parodontosis, idiopathic processes in periodontium and parodontome.

Periodontal disease occurs under the influence of a variety of local and general factors. A significant role in their occurrence is played by local factors – presence of dental plaques, microbial toxins, autoimmune processes, injuries, and functional insufficiency of periodontal tissues. Among the common factors, it is worth noting a deficiency of vitamins, atherosclerotic vascular damage, disorders of the nervous trophism, endocrine changes, defects in the body's immune system, gastrointestinal diseases, increased lipid peroxidation, etc. For example, the accumulation of toxic lipid peroxidation products leads to damage to periodontal structures and protein matrix of the alveolar bone due to sclerotic vascular lesions.

In the complex treatment of periodontal diseases, an impact on the etiological links of the process is provided – elimination of local irritants and pathogenetic links – repair of the structural and functional elements of periodontal disease. The elimination of causative factors is mainly carried out at the expense of local therapy and professional hygiene. Surgical, orthopedic, drug and physiotherapeutic methods of treatment are used to influence the pathogenetic links of inflammation.

Local therapies imply:

- elimination of local causes;
- impact on the inflammatory and destructive process in periodontium;
- normalization of microcirculation;

- stimulation of reparative processes;
- increased local immunity.

The main links of general treatment are: stimulation of the body's reactivity, anti-inflammatory and desensitizing therapy, general health-improving and immune therapy. The complex of therapeutic measures should include special drug and non-drug methods. An individual approach to the choice of treatment methods is important. In the structure of periodontal diseases, the most common is the pathology of inflammatory genesis (gingivitis, periodontitis).

Typical signs for gingivitis: plaque, gingival inflammation (with pain symptoms), bleeding on probing, lack of gingival margin and signs of periodontal destruction. There are acute and chronic catarrhal gingivitis, necrotizing ulcerative gingivitis and hypertrophic gingivitis. The main principles of treatment are as follows:

- removal of plaque with the help of 0.06 % chlorhexidine solution (in the form of rinses);
- prescription of NSAIDs applications – 5 % butadiene ointment or 3 % indomethacin ointment, 1 % sodium mefeminate solution or 0.2 % alcohol solution sanguirytrin, 2 % thiotriazoline ointment;
- reducing proteolysis and bleeding – 5 % solution of aminocaproic acid;
- improving microcirculation – applications of 1 % solution of nicotinic acid or 2 % solution of pentoxifylline.

Individualization of treatment primarily depends on the nature of the course of gingivitis and its prevalence. Acute catarrhal gingivitis is most often a symptom of an acute respiratory infection. Its clinical picture usually does not differ in rich symptoms (pain on palpation, swelling, bleeding when probing the gums are typical). Sometimes gum abscess may form.

In the chronic course of gingivitis, the symptoms are more pronounced (swelling and tension of the gums, pain, bleeding when eating).

With catarrhal gingivitis, hygiene measures and the use of NSAIDs are usually sufficient. They also prescribe rinsing of the oral cavity with 2 % sodium hydrogencarbonate solution, chamomile (romazulan), sage tinctures, lysozyme solution, 1 % citral solution, use gum application with halosorbin, karatolin, rosehip oil, sea buckthorn oil, baths with 0.06 % chlorhexidine solution for 2–3 minutes. It is possible to conduct electrophoresis

of 1 % galascorbin solution, 5 % ascorbic acid solution or phonophoresis of aloe (10 sessions).

Necrotizing ulcerative gingivitis can occur independently or be a complication of other forms. This type of gingivitis is especially characterized by damage to the integrity of the gums with the development of necrosis, bad breath, the release of a large amount of saliva, pain during conversation, eating. There is an amount of soft deposits, bleeding when plaque is removed. Often the general manifestations of the disease join (fever, loss of appetite, increased heart rate). The process may be acute or chronic.

Treatment of necrotizing ulcerative gingivitis includes the following measures:

- plentiful irrigation with antiseptics (0.02 % solution of potassium permanganate, 0.02 % solution of furacilin, 0.5 % solution of decamethoxin, 0.2 % solution of ethacridine lactate, 0.2 % solution of chlorhexidine, 2 % solution of sodium bicarbonate, 1–2 % solution of metronidazole);
- anesthesia (emulsion or 5 % anaesthesin ointment, 5–10 % novocaine ointment, aerosols lidocaine, amprovizol, etc.);
- removal of necrotic films using proteolytic enzymes (trypsin, chymopsin, iruksol, deoxyribonuclease);
- rinsing with astringent anti-inflammatory drugs (1 % solution of tannin, tinctures of sage, chamomile, decoction of oak bark, etc.);
- applications of biogenic stimulants (bioseed, Kalanchoe sap), etc.;
- the use of keratoplastic agents – karatolin, sea buckthorn oil, retinol, vinylin, solcoseryl;
- general anti-inflammatory therapy using NSAIDs and corticosteroids;
- if necessary, antibiotic therapy according to generally accepted principles due to the sensitivity of microflora to antibiotics. Ampicillin (1 g 4 times a day intramuscularly) in combination with metronidazole (500 mg enterally 3 times a day), clarithromycin (500 mg per day i.v. 2–3 days), and also azithromycin (in the first 500 mg per day, then 250 mg enterally).

Hypertrophic gingivitis is characterized by local or generalized gum hypertrophy. There is bad breath, swelling, soreness and bleeding. More often this form is associated with hormonal disorders or is a consequence

of the use of antiepileptic drugs. With hypertrophic gingivitis, sclerotherapy is performed: injections of 50–60 % glucose solutions into the gum; 0.1–0.2 ml of a solution of novembikhine, cyclophosphamide or embitol (3–8 injections in each papilla); solution of lydase. Cauterizing therapy is carried out with 20–30 % solution of resorcinol, 10–25 % solution of zinc chloride, 25 % solution of dimexide.

Periodontitis is a disease in which gum disease spreads to other periodontal tissues. In accordance with the severity of clinical manifestations, initial degree, degrees I, II, III of generalized periodontitis are distinguished.

In the chronic course of generalized periodontitis of the degree I, patients complain of bleeding gums, halitosis. The gingiva is cyanotic; a moderate supra- and subgingival calculus is formed. Interdental papillae may be swollen or hyperplastic. Periodontal pockets with a depth of 2–3 mm with moderate serous-purulent discharge are found in the areas of the periodontal teeth. There may be degree I tooth mobility, more often – in the area of the lower frontal teeth.

Degree II of generalized periodontitis is characterized by symptomatic diffuse gingivitis with severe atrophy of the gingival papillae, gaping of the interdental spaces. Periodontal pockets reach a depth of 3–5 mm or more. The necks of the teeth are exposed by 2–3 mm. The teeth become mobile. Between the teeth free spaces are formed – diastema.

With degree III of periodontitis, periodontal pockets reach a depth of 8 mm or more, tooth mobility – II–III degree, resorption of the alveolar bone reaches 2/3 of the root length and more. Due to significant resorption of the alveolar bone and pathological tooth mobility, their displacement is observed in different directions: vestibular, oral, distal, etc.

Activation of the course is accompanied by an exacerbation of symptomatic gingivitis, significant suppuration from periodontal pockets, and significant mobility of the teeth reaching degree II or III, noticeable resorption of the alveolar bone.

Treatment of the inflammatory process in the periodontium begins with the removal of defects in fillings or orthopedic structures, the removal of dental plaques and stone, etc.

The effectiveness of pharmacotherapy depends largely on the local use of ABD, which must meet certain requirements: to be in a periodon-

tal pocket for a long time in a concentration that is "fatal" to periodontal bacteria. Drugs for washing periodontal pockets, ointments and gels have only a limited effect.

Among the causes, inflammatory and dystrophic-inflammatory processes in periodontal microorganisms occupy a special place. In 80 % of patients, aerobic-anaerobic-fungal associations are sowed, in 17 % – anaerobic-fungal associations, in 3 % – aerobic-anaerobic associations. On average, associations of 3–6 types of microorganisms are distinguished in the contents of the periodontal pocket in one patient, while staphylococci predominate among aerobic and facultative bacteria, enterobacteria – Escherichia coli and Klebsiella; among anaerobes – fusobacteria, Prevotella and peptostreptococci, etc. Significant contamination of periodontal pockets by pathogenic yeast fungi was established. Pathogenic fungi of the genus Cryptococcus neoformans, as a rule, are found in patients with AIDS. The obtained data on the role of anaerobic and mixed bacterial flora in the development of periodontal diseases made it possible to single out a group of periodontopathogenic bacteria, including representatives of the genera peptostreptococci, actinomycetes, fusobacteria, some bacteroides, hemophilic actinobacilli, and convoluted forms.

In the presence of an abundant gram-negative and gram-positive anaerobic and microaerobic flora (typical for most patients with suppuration), the main drugs of choice should be macrolides or antibiotics of the lincomycin series. In addition to the spectrum of action adequate to this microflora, they are distinguished by a convenient oral form, rapid absorption in the blood and accumulation in the focus of inflammation, good tolerance by most patients.

In case of intolerance to macrolides and lincosamides, as well as in persistent processes, in particular, abscess formation and necrotic gingivitis, which is associated with fusobacteria, broad-spectrum antibiotics are indicated: FQ (levofloxacin, gatifloxacin or ciprofloxacin in combination with metronidazole), CS (oral cefadoxil – cefuroxime axetil, cefpodoxime proxetil or parenterally – cefotaxime, cefuroxime, etc.).

When isolating predominantly gram-positive coccal flora, the use of such drugs as cefazolin, augmentin, vancomycin is microbiologically justified. It is advisable to combine these drugs with metronidazole or nitazole.

For exposure to microflora of dental plaques in inflammatory periodontal diseases, local antimicrobial therapy using 0.06 % chlorhexidine is a priority. Chlorhexidine is used in the form of rinses (Peridex, Corsodyl, etc.). It has been proven that gels containing chlorhexidine (Elugel, Corsodyl) have more advantages than solutions. Studies have shown the effectiveness of cetylpyridinium chloride at a concentration of 0.045–0.05 %. An example of a preparation based on cetylpyridinium chloride is the commercial agent Cepacol. Removal of plaque is facilitated by 0.05 % solution of catamine, a drug that is less toxic than chlorhexidine.

Of great importance in the prevention of periodontal disease is oral hygiene, which depends on the choice of toothpaste. With exacerbation of inflammation use toothpastes containing antiseptics (chlorhexidine or triclosan, or cetylpyridinium chloride) within 2–3 weeks. These toothpastes are: Parodontol triclosan, which includes sodium fluoride, triclosan, plantain and nettle extract. New Pearl Total toothpaste contains triclosan and sodium fluoride, has anti-carious and anti-inflammatory effects. Aquafresh toothpaste has a significant cleansing activity, anti-inflammatory and refreshing effects, low abrasiveness, slightly increases the enamel's resistance to demineralization, and does not have an irritating effect. The most widespread solution is chlorhexidine bigluconate, that is a part of the Corsodyl mouthwash. It is recommended to use during an exacerbation of periodontitis (no more than 2 weeks). Another ABD is 0.05 % cetylpyridinium chloride, which is used to prevent inflammatory periodontal diseases in mouthwashes Oral-B Tooth and Gum Care, Reach. When prescribing the listed oral hygiene products containing strong antiseptics, it must be remembered that their prolonged and in many cases unreasonable use contributes not only to the violation of the barrier function of the epithelium, but also to the chronicity of inflammatory processes.

Miramistin in the form of 0.01 % solution or 0.5 % ointment is one of the most famous cationic detergents, which has a pronounced bactericidal and fungicidal effect, increases immunity and reduces the resistance of microorganisms to ABD. An important feature of miramistin is its low absorption capacity, due to which it practically does not enter the bloodstream and has only a local effect. In periodontics, triclosan, a chlorine derivative of phenol, is widely used. The drug is active against most bacteria, fungi, has low toxicity, high activity against tartar, and delays the forma-

tion of collagen. Betadine (an iodine-based drug) has been used successfully to flush periodontal pockets. The drug has a pronounced bactericidal effect against fungi, viruses, protozoa, is effective for removing dental deposits (especially when using it as an irrigation solution in ultrasound machines). It is similar to betadine in pharmacological properties and method of use – iodine-containing drug "Wocadine".

For antiseptic treatment of the oral cavity and periodontal pockets they also use 1 % alcohol solution of citral, 0.01–0.1 % solution of potassium permanganate, solution of rivanol (1:500, 1:10000), 0.02 %-0.05 % solutions of decamethoxin, 1 % solution of dioxidine, 1 % aqueous solution of iodinol, 0.25 % alcohol solution of chlorophyllipt, solution of furacilin, maraslavin, tinctures of calendula, celandine, etc. All preparations are used as instillations in periodontal pockets, applications, irrigation, baths, as a part of periodontal medical dressings.

Other drugs are also used depending on the type and severity of the pathological process. So, with the edematous form of hypertrophic gingivitis, decongestants and cauterizing agents are used in the form of installations and applications (20 % solution of resorcinol, 10–30 % solution of zinc chloride, plantain sap, vagothyl, 25 % solution of dimexide).

For local therapy of generalized periodontitis, it is advisable to use multicomponent preparations of plant origin, which have a complex therapeutic effect. Such products include herbal preparation Stomatofit (Poland). The latter is an alcoholic extract of medicinal plants: oak bark, chamomile flowers, sage leaves, thyme, peppermint, calamus rhizomes. The drug has pronounced antiseptic, anti-inflammatory, epithelizing and astringent effects.

After the classic local treatment – removal of soft plaque, supra- and subgingival deposits, hemostasis with 3 % solution of hydrogen peroxide, irrigation of periodontal pockets with 0.1 % solution of chlorhexidine bigluconate, Stomatofit is used. The latter is used on loose turundas for the gums for 15 minutes (50 ml of warm water for 7.5 ml of the drug). The course of treatment is 7 days.

Synthetic preparations are widely used for treatment of periodontitis. Gel for gums Metrogyl Denta is a combination of 1 % solution of metronidazole and 0.25 % solution of chlorhexidine. In case of periodontitis after dental plaque removal, periodontal pockets are treated with Metrogyl

Denta gel – a doctor can use a special syringe for this. Metrogyl Denta gel can also be used in the form of applications on the gum area. It is applied 2 times a day after hygienic brushing, then for 30 minutes you can not rinse your mouth and eat. The course of treatment averages 10 days. After professional therapy, patients can continue treatment on their own: the gel is applied to the gums 2 times a day for 10 days.

Nitrofuran series drugs (furacilin, furazolidone) are used, which, in addition to the antimicrobial effect, can reduce the manifestations of exudation. Nitrofurans are prescribed in the form of rinses, applications for washing gingival pockets, dressings and more.

Studies have also shown that subgingival applications of 1.64 % sodium fluoride solution within two days without the use of other methods of treatment completely eliminated microorganisms from the periodontal pocket after 4 days.

Recently, due to an increase in the level of slagging of the body, antiseptic agents of natural origin have attracted attention. They are less likely to cause unwanted side reactions, have antiseptic properties. So, a decoction of Icelandic moss (sodium usnitat) has an antimicrobial effect. Alcoholic and oil solutions of usnic acid sodium salt, which has significant antiseptic properties, are used as external agents for purulent wounds, burns, stomatitis and inflammatory periodontal diseases. Sodium usninat is a part of Fitosept preparation, which provides an antimicrobial effect against gram-positive bacteria in the oral cavity, promotes reparative processes in the mucous membrane, and has a deodorizing effect.

The anti-inflammatory properties of eucalyptus are well known due to the rich content of essential oil in the plant. Chlorophyllipt – a drug from eucalyptus leaves is prescribed for diseases caused by staphylococci resistant to antibiotics. Eucalymin is an herbal medicine containing eucalyptus extract, which is used for periodontitis, stomatitis. Increased plaque formation on hard tooth tissues decreases after topical application of various vegetable oils (cinnamon, clove, eucalyptus, mint).

For topical treatment of inflammation of the oral mucosa, chamomile extract is used. Chamomile and chamomile oil contain a number of components that have pronounced anti-inflammatory activity. In vitro aqueous extracts from chamomile flowers inhibit the development of Staphylococcus aureus and alpha hemolytic streptococci. Chamomile tincture is

used to rinse in case of inflammatory diseases of the oral cavity (stomatitis, gingivitis, candidiasis).

Tincture of sage leaves is used as anti-inflammatory and disinfectant rinses for diseases of the mucous membrane, periodontal disease, etc. The drug Salvia obtained from sage has an astringent, antimicrobial, anti-inflammatory effect, stimulates the regeneration of soft tissues. In its antibacterial activity, the latter is superior to rivanol and furacilin.

From the herbaceous perennial plant – macleaya microcarpa – the drug Sanguiritrinum was produced. The drug has antimicrobial activity against gram-positive and gram-negative bacteria, yeast-like fungi, Trichomonas. It is used in the treatment of inflammatory periodontal diseases and ulcerative lesions of the oral mucosa.

The effect of plant extracts (basil, linden, larkspur) has been clinically studied in the treatment of inflammatory diseases of the periodontium and oral mucosa. The action of these preparations was most pronounced with respect to Staphylococcus aureus and Candida albicans. In the clinic, these plants are successfully used to treat periodontitis of moderate severity, decubitus ulcers, etc.

The clinical condition of periodontal disease improves with the use of an aqueous solution of Fucus extract – preparations of brown algae Fucus vesiculosus. At the same time, the number of periodontopathogenic microorganisms and the indicators of periodontal and hygienic indices are reduced. Fucoids are also effective in increasing immunity in diseases of the blood, gastrointestinal tract, endocrine system.

In connection with the use of many drugs in the treatment of generalized periodontitis, doctors have questions about their interaction, toxic and irritating effects, and especially sensitization of the body and the occurrence of allergic reactions. This explains the interest of periodontists in herbal preparations of multivalent action. The proposed phytopreparations are Stomatofit (for rinsing and irrigation) and Stomatofit A (for instillation in periodontal pockets). They contain medicinal raw materials of natural origin (chamomile flowers, peppermint leaves, arnica grass, sage leaves, oak bark, thyme grass, calamus rhizome). The drugs act multilaterally on the various links of the etiopathogenesis of periodontal diseases, simultaneously carry out anti-inflammatory, decongestant, bactericidal, antifungal, analgesic, tannic, wound healing effects.

New drugs of prolonged action are of great interest for dental practice. This group includes medicinal substances immobilized on silica. It also includes calendula, which is located on the polysorb (a sorbent with high adsorption capacity, the ability to desorb biogenic products, microorganisms, various toxic agents). The drug is recommended for local use in chronic catarrhal gingivitis, periodontitis, as a highly effective tool.

In local anti-inflammatory therapy, metronidazole is often used, taking into account not only the role of anaerobic microorganisms in the occurrence of periodontal tissue diseases, but also that the drug is for the treatment for pseudomembranous colitis. The latter is a serious complication caused by use of lincomycin and clindamycin in periodontics. Forms of this drug with sustained and controlled release are being developed and produced: metronidozole benzoate in the form of a 25 % gel (elyzol). It is administered using cannulas twice with an interval of 1 week; the drug hardens under the influence of gingival fluid. Minocycline hydrochloride is used in the form of a 2 % ointment, and 25 % of tetracycline hydrochloride is impregnated with ethylene-vinyl acetate fiber (actisite). This fiber, which is not resorbed, is wrapped around the subgingival part of the root. The drug provides a high concentration of tetracycline in the gingival fluid, as well as its long-term contact with tissues. 10 % doxycycline in the carrier (atridox) is introduced into the pocket with a special syringe and resorbed in it for 6–8 days, while exerting a pronounced antimicrobial effect.

In more complex cases, ABD is used for additional systemic antibiotic therapy. Indications for systemic use of antibiotics are:

- severe generalized periodontitis (multiple periodontal abscesses);
- atypical forms of periodontitis – early progressive, etc.;
- generalized juvenile, rapidly progressive periodontitis;
- symptomatic necrotizing ulcerative gingivitis;
- preparation for periodontal surgery;
- cardiovascular disorders, diabetes mellitus, immunodeficiency in patients at risk;
- after surgical treatment.

Before starting treatment, antibiotic tolerance is determined. To prevent possible allergic reactions. At the same time, prescribe antifungal, multivitamin, antienzyme therapy may be prescribed.

ABD, which is used in periodontics, must meet the following requirements:

- to influence the maximum spectrum of microorganisms of the odontogenic focus (including periodontal species);
- to accumulate in restored tissues, including bone and other periodontal tissues;
- to carry out the necessary effect when taken orally;
- to have low toxicity;
- to be suitable for prolonged use without pronounced selection of antibiotic-resistant strains.

The most widely used in periodontics are preparations of metronidazole, a classic antianerobic drug. At present, about 50 % of the strains of Prevotella spp., Fusobacterium spp., Capnocytophaga spp. and Bacteroides spp. show stability against it. The latter position does not allow to consider it as the drug of choice for various forms of periodontitis. This drug can be used in combination with others if the contents of the periodontal pocket of the protozoa – the oral trichomonas, gingival amoeba. So, improvement of clinical indicators in the treatment of rapidly progressive periodontitis can be achieved by the use of such schemes: metronidazole (500 mg 2 times a day, 8 days) and doxycycline (200 mg 1 time per day), metronidazole (250 mg) and amoxiclav (375 mg) 3 times a day for 8–14 days, amoxicillin and sulbactam in combination with metronidazole.

When assessing the sensitivity of microflora to lincomycin, its low antimicrobial effectiveness was also revealed for the entire spectrum of 50–70 % of the isolated strains of Bactepoides spp., Staphylococcus aureus, Porphyromonas gingivalis, Fusobacterium spp. were resistant to this antibiotic.

High therapeutic efficacy in periodontics Dalacin C (clindamycin) in patients with generalized periodontitis has been established. After a course of antibiotic therapy with this drug, after 5–7 days, the gingival margin consolidation, the absence of purulent discharge from periodontal pockets, a significant decrease in the average depth indicator of periodontal pockets, and a decrease in tooth mobility were determined.

The combined preparation Cifran CT, which includes ciprofloxacin hydrochloride and tinidazole, is intended for the treatment of infec-

tions caused by aerobic and anaerobic microorganisms. The spectrum of antibacterial action of ciprofloxacin includes most gram-negative and gram-positive microorganisms. Tinidazole is a newer representative of imidazole, similar in spectrum of antibacterial action to metronidazole. "Cifran CT" is used for empirical therapy of generalized periodontitis, chronic osteomyelitis, and other infections of the MFA.

Positive results on the use of the drug Vilprafen (josamycin) are obtained, active against gram-positive aerobic microorganisms – staphylococci, streptococci, aerobic cocci, non-spore-forming bacteria, gram-negative microorganisms and bacteria. Vilprafen is prescribed 2 times a day for 12–14 days. After the treatment, more than 80 % of patients stopped purulent discharge, hyperemia and swelling of the gingival mucosa disappeared, and abscess formation did not occur. No adverse reactions have been observed.

It is advisable to use antibacterial films with the prolonged action of Diplen-Denta C (based on clindamycin phosphate) and Collapan-C (based on cefotaxime), which provide antibacterial and osteostimulating effects, contribute to the high efficiency of treatment of periodontitis.

For medical treatment of gingival pockets, SA is sometimes used (bactrim syrup, inhalypt, etc.). Usually they are introduced into the composition of medical pastes or dressings in order to expand the spectrum of antimicrobial action.

Periodontal bacterial factors are causes of the development of immunosuppression, both in general and local immunity systems, as well as autoimmune disorders. Therefore, in periodontics, it is advisable to use imudon, which is a multivalent complex of antigens that cause an increase in the number of immunocompetent cells responsible for the production of antibodies and enhance phagocytic activity, increase the content of lysozyme in saliva, and stimulate it. Immunocorrecting drug Licopid is of interest. It is used in the treatment of patients with chronic generalized periodontitis, the active substance of which is glucosaminylmuramyl dipeptide – a universal fragment of the bacterial cell wall. Licopid increases the activity of phagocytes, positively affects local and humoral immunity. The anti-inflammatory, anti-infectious effect is associated with the stimulating effect of Licopid on cell populations of the immune system. The effectiveness of the drug was noted in the treatment of a number of in-

flammatory diseases of the oral cavity: lichen planus, recurrent herpetic stomatitis, etc. Licopid is prescribed 1 mg sublingually 2 times a day 30 minutes before meals for 10 days.

Pathogenetic treatment of periodontal inflammation is of great importance. To this end, in periodontics, NSAIDs are primarily used. So, to fill in periodontal pockets, gel that contains diclofenac sodium is used. The drug has analgesic and anti-inflammatory effects due to inhibition of PG synthesis. A pronounced anti-inflammatory effect is possessed by 3 % indomethacin, 5 % butadionic, 2.5 % ketoprofen ointment, as well as 3 % sodium salicylate ointment, 1 % sodium mefenaminate solution, a paste based on sodium mefenamine. NSAIDs reduce manifestations of exudation, pain; inhibit the formation and release of biologically active substances that inhibit the activity of lysosomal enzymes.

Sometimes, in severe cases of the disease, GCS are used in periodontal disease – more powerful anti-inflammatory drugs that have anti-edematous, desensitizing, anti-allergic, antiproliferative and immunosuppressive effects. In dental practice, various official preparations are used: 1 % hydrocortisone ointment, a suspension of hydrocortisone, 0.5 % prednisolone ointment, as well as ointments and creams containing triamcinolone (fluorocort, ledercort, kenalog), flucinolone acetonide (synalar, flucinar), flumetazone pivalate (locacorten, lorinden), ointments depersolon, dermosolon, etc. GCS have a good effect in combination with ABD (neomycin, gentamicin, clotrimazole or for example, triderm, triacutan, etc.). However, it should be remembered that the use of corticosteroids for the treatment of inflammation does not create conditions for fixing the effect, because they suppress immunity and delay osteosynthesis. Indication for the use of corticosteroids is also the strengthening of proliferative processes in periodontal disease.

An anti-inflammatory effect is exerted by a number of other drugs. So, the effect of heparin is associated with its ability to suppress the activity of hyaluronidase, reduce vascular permeability, stabilize cell membranes, and improve regeneration processes. Heparin is used as an ointment, administered by iontophoresis, injection along the transitional fold in case of hypertrophic gingivitis, periodontitis, periodontal disease.

In periodontal practice, enzyme preparations are widely used. They break down necrotic tissues, have an anti-inflammatory effect and im-

prove metabolic processes. For local processing of gingival pockets, trypsin, chymotrypsin, ribonuclease, deoxyribonuclease, chymopsin, lysozyme, and terylitin are used. Preparations are prepared immediately before use and injected into the gingival pockets on turundas. The most pronounced anti-inflammatory effect is observed with a combination of enzymes with antibiotics, sulfonamides. 25000–50000 IU of antibiotics (neomycin, streptomycin, microcide) is taken per 1 ml of enzyme solution. Sulfanilamides are prescribed at the rate of 0.1 g per 5 mg of enzyme. The widely used drug Iruxol contains antibiotic chloramphenicol and enzyme clostridiopeptidase. Enzymes for injection into the transition fold or intramuscularly can also be used.

Currently, the experience of using SET, which relates to innovative methods in periodontics, is widely represented in the literature. Among the drugs, the pathogenetic substantiation in the complex treatment of periodontitis belongs to phlogenzyme, which has practically no side effects and has many positive qualities. Wobenzym and Lysobact are also used.

To achieve a local anti-inflammatory and anti-edematous effect, the methyluracil derivative (metacil) is used. The drug alone or in combination with ABD is administered in the form of a suspension prepared in an oil solution of vitamins A, E, carotolin, put into gear gums and covered with paraffin or wax. Widely used are agents that improve tissue regeneration (carotolin, sea buckthorn oil, vinylin, Shostakovsky's balm, solcoseryl jelly and ointment, thiatriazolin ointment, etc.).

The development of the concept of the role of LPO in periodontogenesis attracted the attention of specialists to antioxidant preparations as potential treatment options. At the first stage, dental deposits are removed by conventional methods, and periodontal pockets are treated with antiseptics. Then paste is applied under the paraffin dressing containing the osteotropic antibiotic lincomycin (2–4 procedures, depending on the severity of the process), after which applications with antioxidant paste containing water and fat-soluble antioxidant vitamins (tocopherol, ascorbic acid, bioflavonoids, thiol antioxidants) are used. To enhance the effect, patients are directly and indirectly prescribed directly acting antioxidants (tocopherol acetate, rutin, ascorbic acid) in winter and spring, and indirectly acting preparations (glutamic and lipoic acid, etc.) in summer

and autumn. Analysis of the results of the application of the proposed method indicates that it is more effective than traditional methods.

To enhance and normalize metabolic processes in periodontics:

- biostimulants (aloe extract 1 ml s.c., bioseed 1–2 ml s.c. i.m., peloidodistiuatum 1 ml s.c., humisol 1–2 ml i.m., etc.);
- ATP in 1 ml of 1 % solution i.m.;
- leukopoiesis stimulants (methyluracil and pentoxyl – enterally);
- protein-polysaccharide preparations (honsonide in the form of applications, the vitreous body 2 ml s.c. for 8–10 days, solcoseryl 2 ml i.m. or topically in the form of a 20 % gel, proposol aerosol, etc.);
- immunostimulants (prodigiosin, levamisole, licopid, imudon, etc.);
- anabolic drugs (nerobol, retabolil, calcitrin);
- haemostimulants (ferroceronum, etc.). hyposensitizers are used antihistamines, calcium chloride, calcium gluconate, phytin, sodium thiosulfate, vitamins C, P.

It is obvious that successfully resolving the treatment of periodontal diseases, especially the problem of securing the achieved results, is impossible without the active participation of surgeons and orthopedic surgeons. At the same time, the development of new methods of orthopedic interventions is necessary.

Prevention of periodontal disease with a certain development of its methods really still remains a weak link. The efforts of hygienists have only recently made it possible to count on results, since right now, on a large scale; the emphasis is on hygienic training and hygienic motivation in preschool and school groups. The most significant at present is professional oral hygiene, including local therapeutic intervention, training in the rules for its use, control of implementation, etc.

1.6

PHARMACOTHERAPY OF DISEASES OF THE ORAL MUCOSA

Diseases of the oral mucosa occupy an important place in the practice of a dentist. They can be caused by various etiological factors, both exogenous and endogenous (physical, chemical, allergic, toxic, infectious, stress, immune). The pathology of the oral mucosa is often the result of the development of common diseases (diabetes mellitus, thyrotoxicosis, leukemia, agranulocytosis, anemia, pemphigus, etc.) or the result of the use of certain drugs.

Diseases of the oral mucosa are divided into infectious (viral, bacterial, fungal), allergic, traumatic, drug, toxic, caused by somatic diseases, dermatoses, immunodependent chronic diseases, etc.

The main directions in the treatment of diseases of the oral mucosa are:

- elimination of etiological factors: removal of an allergen, elimination of a chemical or physical irritant, inhibition of an infectious agent, etc.
- elimination of pathological manifestations on the mucous membrane (inflammation, pain, allergies, necrosis, hypertrophy, etc.).
- restoration of functions of the mucous membrane (stimulation of epithelialization and immunity, saliva, etc.).
- normalization of the functional state of the body (treatment of concomitant pathology, normalization of immunity, general strengthening measures).

Today, despite the successes of modern dentistry, the diagnostics and pharmacotherapy of lesions of the oral mucosa, which are represented by a large number of nosological forms similar in clinical picture, remains a difficult task.

1.6.1. Xerostomia

Xerostomia develops with impaired salivation, is usually chronic in nature and is manifested by a disorder of a number of functions. Xerostomia is divided into: a) true (primary), associated with damage to the salivary glands; b) secondary (symptomatic), which occurs when taking sedatives, antihypertensives, antihistamines, anticholinergics, diuretics. Xerostomia develops with diseases of the gastrointestinal tract, endocrine system and mental sphere. At a dentist, every tenth patient complains of dry lips and oral cavity.

In supporting dental health, the quantitative and qualitative composition of saliva plays an important role. It contains minerals, microelements, vitamin D, fluoride, which are necessary for the "maturing" of enamel after teething and remineralization of dentin. Parotin, which has a hormone-like property, is isolated from saliva. Saliva glycoproteins form a protective organic film on the tooth surface – pellicula, which prevents the action of acids on enamel. Saliva removes food residues from the oral cavity, protects against infection due to the content of lysozyme, beta-lysines, white blood cells.

The presence of saliva in the oral cavity helps the free movement of the tongue and lips during conversation, the perception of taste, water-salt balance, the excretion of salts of certain metals (silver, mercury, lead, bismuth), drugs (penicillin, SA, salicylic acid, strychnine, quinine, alkaloids), viruses (rabies, poliomyelitis, mumps, hepatitis), halogens, arsenic, etc. Thanks to the enzyme amylase, which is located in saliva, the digestion process begins already in the oral cavity.

Decreased saliva secretion in a number of diseases can lead to the development of xerostomia and rapidly progressive caries, marginal periodontitis, candidiasis, etc. Symptoms of xerostomia are most pronounced in Sjögren's disease, which is a systemic autoimmune disease characterized by lesions of the exocrine glands (mostly salivary, lacrimal) manifestations, with immune disorders, etc.

The reasons for the development of Sjögren's disease are not fully understood. It is characterized by dry mouth, mumps, and tooth decay. It is difficult for patients to speak and take dry food; bad breath, burning and soreness in different parts of the mucous membrane appear. Often a secondary infection joins with the development of fungal or viral sto-

matitis. Lesions of the lacrimal, gastrointestinal, bronchial, skin exocrine glands are sometimes noted with a significant decrease in their secretion; dry keratoconjunctivitis, arthritis, increased erythrocyte sedimentation rate (ESR), fever, etc. The disease can cause prolonged disability and early incapacity of patients.

Xerostomia treatment is carried out comprehensively by dentists, rheumatologists and other specialists. For the pathogenetic treatment of xerostomia in case of Sjögren's disease, encad was proposed, which has an anti-inflammatory, immunomodulating effect and promotes the regeneration of the oral mucosa. Drugs or herbs that increase the secretion of the salivary glands, for example, a solution of potassium iodide, a yarrow broth are prescribed. A good effect is given by the application of solcoseryl gel, emulsion of dibunol, coenzyme Q10, oil solution of vitamin A.

To increase the antibacterial protection of the oral cavity, to reduce dysbiosis and plaque formation, it is advisable to use mouth baths with 0.1 % lysozyme solution in 0.6 % sodium chloride solution after meals. To reduce burning sensation and pain when eating food, novocaine solution, 0.25 % diphenhydramine solution can be used. In case of complete absence of saliva in the cavity, "artificial saliva" can be used, for example, bensilol. To increase the acid resistance of the enamel, remineralization terapy is carried out. When filling cavities, it is recommended to use light-hardening composite filling materials, glass ionomer cements, and compomers. To stimulate salivation, aceclidine is used – 1–2 ml of 2 % solution administered s.c. For this purpose, acidic products, chewing gum Orbit or indifferent components (wax), etc. are also used.

1.6.2. Mucosal damage

The clinical picture of traumatic injuries of the mucous membrane (wound, bite, etc.) is characterized by the formation of hematomas, ulcers and the occurrence of pain. For effective treatment, it is necessary to eliminate the irritant, conduct antiseptic treatment. Rinsing, irrigation or application of the oral cavity are administered with the following drugs: 0.25 % solution of hydrogen peroxide, 0.01–0.1 % solution of potassium permanganate, 0.25–0.5 % solution of ethonium, etc. Applications of LA are used to remove necrotic masses and severe soreness. To accelerate the regeneration, applications of keratoplastic drugs are prescribed (haloscorbin,

karatolin, solcoseryl, metacil, rosehip oil, sea buckthorn oil, vitamins A, E, etc.). In the treatment of postoperative mucosal injuries, the effectiveness of the use of a two-layer adhesive dental film Diplen-Denta C was found. The use of this new prolonged dosage form in comparison with traditional application means can significantly reduce the healing time.

With significant traumatic injury, catarrhal stomatitis can occur, which is characterized by hyperemia, swelling of the oral mucosa, decreased salivation, halitosis, etc. The use of a hypertonic solution of sodium bicarbonate, enveloping (decoction of marshmallow root or flax seed) and anti-inflammatory (sodium mefenaminate) is indicated) drugs. It is advisable to prescribe vitamins A, E, C, P, ascorutin, calcium chloride, which reduce the permeability of the vascular wall.

When pathogenic microflora is attached, traumatic erosive or ulcerative stomatitis can occur. Depending on the type of stomatitis, antiseptic treatment of the oral cavity, anesthesia, necrectomy and stimulation of reparative regeneration are performed. Solcoseryl, methyluracil, pentoxyl, anabolics, and vitamins are used to stimulate the regeneration. At the last stages of treatment, it is advisable to apply keratoplastic agents (rosehip oil, sea buckthorn oil, vitamin A preparations, etc.).

In case of physical damage to the oral mucosa (thermal burns, galvanic current, ionizing radiation), after eliminating the cause, the treatment is carried out, as in non-specific acute inflammatory processes.

The primary reaction of the oral cavity to radiation is characterized by hyperemia, dry mouth, a metallic taste, swelling, punctate hemorrhage and decreased sensitivity. Radial stomatitis can occur during radiation therapy of malignant neoplasms. This type of damage is characterized by changes in the oral cavity: hyperemia, dryness, anemia, burning, soreness, hemorrhagic syndrome, increased keratinization of the epithelium of the mucous membrane, which is rejected in places, erosion. Putrid breath is typical. Ulcerative gingivostomatitis or necrotic tonsillitis may develop. Typically, these changes are reversible. In treatment, it is important to carry out sanitation of the oral cavity, to eliminate the focus of chronic infection. At the initial manifestations of radiation stomatitis, the mucous membrane should be treated with 1 % solution of hydrogen peroxide, furacilin 1:5000, 1 % solution of dimexide, 1 % solution of chlorhexedine, etericide. If necessary, that area should be anesthetized with 1 % solution

of novacaine, trimecaine, 10 % anaesthesin emulsion. The mucous membrane and periodontal pockets are washed with antiseptic solutions and enzyme applications with antibiotics are performed. In order to stimulate regeneration, the mucous membrane is treated with 1 % citral solution in peach oil, rosehip or sea buckthorn oil, karatolin, actovegin, kalanchoe ointment, ethonia, 10 % methyluracil, etc.

For the treatment of local radiation injuries, especially ulcerative, it is advisable to use irrigation with an immunomodulator gepon (0.04 % solution). The latter has established itself as a drug that has anti-inflammatory effects and promotes regeneration processes.

In diseases of the mucous membrane caused by chronic radiation sickness, general and local therapy is carried out. General pharmacotherapy includes the use of radioprotectors (cystamine, cysteine, etc.), hematopoiesis stimulants (cyanocobalamin, folic acid, sodium nucleinate, pentoxyl, etc.), vitamins, vikasol, calcium, GCS, antihistamines and ABD.

Local treatment is carried out when ulceration occurs. Antiseptic ulcer treatment daily; under local anesthesia, necrotic tissues are removed using solutions of proteolytic enzymes; for a long time (1–2 months), keratoplastic agents are applied daily (propolis ointment, carotolin paste, halascorbin, vitamin B_{12} solutions, sea buckthorn oil, etc.).

Chemical damage can be acute or chronic. The clinical picture of acute acid damage is characterized by hyperemia, edema, coagulation necrosis in the form of a dense film. However, with a burn with sulfate acid, a brown film appears, with nitrate acid – yellow, with other acids – grayish white. A dense film is not typical of the collication necrosis that occurs when an alkali burns and damage to all layers of the mucous membrane is observed. Healing is very slow.

In acute chemical damage to the mucous membrane, it is necessary to remove quickly and neutralize the chemical agent by washing the oral cavity with weak solutions of neutralizing substances or water. In case of acid burn – 2 % sodium bicarbonate solution, magnesium oxide, 0.1 % ammonia solution; alkaline burn – 5–1 % solution of citric, acetic acid, 0.1 % solution of hydrochloric acid; burn with silver nitrate solution – 3 % sodium chloride solution, Lugol's solution; burn with arsenic anhydride –5 % solution of unithiol, 1–3 % solution of hydrogen peroxide, magnesium oxide (dusting). If necrosis occurs, LA, antiseptics (vinylin, cygerol,

Shostakovsky's balm, etc.), keratoplastic drugs (1 % citral, actovegin, oil solutions of retinol or tocopherol) are used. If necessary, NNA are prescribed.

1.6.3. Leukoplakia

Leukoplakia is a chronic inflammatory disease with increased keratinization of the epithelium (hyperkeratosis), the main cause of which is the action of local irritants (smoking, overhanging fillings, sharp edges of carious teeth, hot and spicy foods, etc.). Leukoplakia is considered a precancerous condition.

The most frequent localization of leukoplakia is the mucous membrane of the cheeks in the area of the corner of the mouth. The main clinical sign is a plaque – a hyperkeratous formation of pearly white or chalky color. As a rule, the plaque rises above the level of the mucous membrane, has clear or blurry edges with a dense surface. The lesion, usually does not cause subjective sensations in patient, sometimes patients indicate the presence of discomfort.

Treatment depends on the form of the disease, the size of the lesion site and the rate of development of the process. Elimination of the cause of the disease (for example, smoking) with flat leukoplakia (clouding of the epithelium in the form of a spot), usually leads to its disappearance within 1–2 months.

General pharmacotherapy includes vitamins of groups A, B, C. 3.44 % retinol acetate oil solution (5–10 drops 3 times a day) or enteral palmitate retinol solution is prescribed. Ascorbic acid is prescribed 0.2 g 3 times a day for 3 weeks, nicotinic acid – 0.5 g 3 times a day for 1 month. In case of ulcerative form of leukoplakia, GCS allowed to be used (in the first week – prednisolone 5 mg 4 times a day, in the second – 5 mg 3 times, in the third – 5 mg 2 times, in the fourth – 5 mg 1 time).

The choice of local treatment also depends on the form of leukoplakia. If sanitation of the oral cavity does not lead to the elimination of keratinization, then keratolytic agents should be used (3–5–10 % salicylic acid solution, linseed infusion, celandine). Electrophoresis or applications of benzotef, thiotef have has a good effect.

In case of varicose leukoplakia, which develops from a flat form and is characterized by the formation of white plaques or warty growths, a sim-

ilar pharmacotherapy is carried out for 1 month in order to transfer it to a flat form. If this fails, surgical method is used. After surgery, application of oil solutions of vitamins A and E, in case of pain – local anesthetics are prescribed. In the presence of candida-type fungi, antifungal drugs are used.

In the presence of erosion and ulcers (erosive form of leukoplakia), necrotic tissues are removed and the surface of the ulcer is cleaned using proteolytic enzymes. Mefenamine sodium salt, ointments with GCS (synalar, fluorocort, lorinden) are locally used. To stimulate the regeneration processes, metacyl, solcoseryl, calendula ointment, Kalanchoe extract are used. The treatment is completed with the prescription of keratoplastic agents (karatolin, vitamins A, E, rosehip oil, sea buckthorn oil, etc.). If after 2 weeks epithelization does not occur, tissue excision is performed for histological examination.

1.6.4. Acute herpetic stomatitis

Infectious diseases of the oral cavity are often of viral origin (herpes infection, foot and mouth disease, influenza, parainfluenza, etc.). One of the most common diseases is herpetic stomatitis caused by herpes simplex virus. The infection rate of the population with this herpes virus is approximately 100 %, and according to the WHO, it ranks second among viral diseases (the first place is influenza). Primary herpetic infection can often be observed in children under the age of 3 years (80 %). There is a tendency to increase of this type of morbidity and torpidity to therapy.

During the development of the disease, the mucous membrane of the oral cavity becomes hyperemic, swollen, with small (2–20) blisters (with millet grain) or their groups appear on the lips and cheeks. After 2–3 days, the blisters burst and very painful red erosion forms. The general condition of the body depends on the course of the disease (from mild to severe).

A dentist in his practice can also observe herpetic cheilitis. Similarly with stomatitis, the primary element of the lesion is a vesicle. The course of primary herpetic infection is 3–5 days (sometimes up to 14 days).

The treatment is carried out with mandatory anesthesia. For this 1 % solution of pyromecain or trimecain, anaesthesin in peach or sunflower oil

(5–10 % suspension), 1 % solution of dicain applications are used. Then antiseptic treatment is carried out with 0.5 % solution of hydrogen peroxide or solution of potassium permanganate and furacilin (1:5000), 1 % miramistin solution.

An integrated approach is used in the treatment of herpetic stomatitis. It is based on the use of antiviral drugs that neutralize the virus and prevent new rashes. For general treatment, antiviral drugs are used: bonaphton (0.1 g 3–5 times a day), acyclovir (0.2 g 5 times a day for 10 days), herpetic multivirus vaccine (each 0.1–0.2 ml i.m.), DNA-ase (0.01–0.05 g s.c. 2 times a week). During the height of the disease, local antiviral drugs are used: 0.25–1 % oxolinic and 1–2 % florenal ointments or 5 % acyclovir cream, 3 % gossypol liniment, IFN in the form of solution or ointment.

In severe cases, in addition to standard therapy with acyclovir, it is advisable to use antihomotoxic drugs (engystol, lymphomyosot, mucosa compositum) according to generally accepted schemes. It was found that the use of these drugs significantly reduces the duration of treatment, reduces the dose of acyclovir, and increases the effectiveness of therapy. Side effects with this treatment were not observed.

It is important to increase the level of immunity of the body and mucous membrane. Therefore, it is advisable to prescribe immunomodulators (imudon, levomizole, sodium nucleinate, licopid). So, imudon is prescribed 1 tablet for resorption 4–6 times a day for a week. For this purpose, interferogens (proteflazide, cycloferon), parenteral gammaglobulin, methyluracil, pentoxyl, lysozyme are also prescribed, and the affected area of the mucous membrane is treated with interferons.

To accelerate the cleansing of erosions, applications with proteolytic enzymes (trypsin, chymotrypsin, terylitin) are carried out. Hyposensitizing agents (diphenhydramine, diazolin, suprastin), rinsing with decoctions of sage, chamomile, calendula tincture, etc. are used. Then, after 3–4 days, agents that accelerate epithelization (oil solution of vitamin A, rosehip oil and sea buckthorn oil, carotolin, Shostakovsky's balm, methyluracil ointment, aerosols livian, vinisol) are used. During this period, the use of antiviral ointments is limited, and then they are completely canceled. In case of severe course and the occurrence of concomitant infection, antibiotics should be prescribed. The following is the algorithm for the treatment of acute herpetic stomatitis in children:

- in the prodromal period: IFN – 3–4 drops in the nostrils and under the tongue every 4 hours;
- before meals, 5–10 % anaesthesin solution in peach oil, lidocaine gel are used for pain relief;
- means for treating the oral cavity after each meal (potassium permanganate solution 1:5000, furacilin solution 1:5000; strong solution of freshly brewed tea; enzyme solution of trypsin or chymotrypsin);
- during the rash, antiviral drugs are prescribed: florenal, tebrophen, bonaphton. They are applied to the mucous membrane of the oral cavity after its hygienic treatment 3–4 times a day;
- imudon is prescribed up to 8 tablets per day sublingually. Solutions of neoferon, IFN are also used;
- during the extinction of the disease, keratoplastic agents are used: rosehip oil, carotolin, sea buckthorn oil;
- for general treatment antihistamines, antipyretic, analgesic and immunomodulating agents are used;
- a balanced diet, sparing food, adequate fluid intake, and oral hygiene.

1.6.5. Chronic recurrent herpetic stomatitis

Relapsed stomatitis may occur in people infected with the herpes virus. The virus remains in the body throughout life. Recurrent herpes is often localized at the border of the skin and mucous membrane of the lips, cheeks, gums, and the bottom of the oral cavity. Then there are rashes of the type of isolated blisters or their groups. Subjective sensations manifest themselves in the form of itching and burning, pain rarely occurs. After 2–5 days, the blisters burst and erosion forms, which are covered with crusts. General manifestations of recurrent herpes are usually less pronounced than with primary herpetic stomatitis. Depending on the recurrence rate, the clinical course can be mild, moderate, and severe.

The main goal of treatment is the prevention of relapse, that is, the elimination of inflammatory processes in the oral cavity (periodontitis, tonsillitis). Between relapses, an antiherpetic vaccine is used (0.2 ml s.c. 5–10 times every 1–3 days), revaccination is carried out after 3–6 months.

During remission, immunotropic drugs (gammaglobulin, cycloferon, proteflazide, etc.), antioxidants and multivitamins are prescribed.

1.6.6. Shingles

Shingles occurs as an independent disease or complicates the course of other diseases against the background of immunodeficiency (HIV infection, cancer, etc.). Caused by Varicella herpetiformis. Ther appears erythema on the skin (chin, cheek, neck) or the mucous membrane of the mouth (cheek, lip, tongue, hard palate), on which a group of blisters filled with serous exudate appears. Subsequently, the blisters burst and erosion forms, which is covered with fibrinous deposits. In debilitated patients, the latter can transform into necrotic ulcers. Severe burning pain and regional lymphadenitis are observed.

General pharmacotherapy is based on antiviral drugs. Acyclovir is prescribed (4 tablets for 5 days), bonaphton or metisazon. It is advisable to use DNase (0.03–0.05 g i.m.), non-narcotic analgesics, and vitamins of group B. For the anti-inflammatory effect, 0.25–0.5 % aqueous solution of mefenamine sodium salt is topically applied, 1 % solution of citral (rinses), 4–20 % alcohol solution of propolis in combination with oils (applications, irrigation).

1.6.7. Influenza stomatitis

Influenza is a common respiratory infection that is caused by the influenza A, B, and C virus. The disease is characterized by the development of catarrhal phenomena of URT with intoxication.

This infection causes the development of catarrhal stomatitis, which is manifested by hyperemia, heartburn, paresthesia, etc. Against the background of catarrhal changes, red (millet-like) rashes are observed, which more affect the palate, pharynx, and tongue. Further, a desquamative or destructive necrotic process develops, hemorrhagic syndrome with hemorrhages. Blisters with hemorrhagic exudate burst and painful erosion is formed. The mucous membrane is restored on the 7–8th day of the disease.

Antiviral therapy of the underlying disease and influenza stomatitis is carried out using antiviral drugs – oseltamivir (0.075 g 2 times a day for 5 days), arbidol (100 mg 3 times a day), rimantadine (0.05 g once a

day for 7 days). IFN are also used: human leukocyte interferon (CHLI) or laferon – in the nostrils, viferon – rectally. IFN inducers (amixin, lavomax, aflubin, mefenamic acid, amizon) are highly effective. NSAIDs (ibuprofen, nimesulide) are used for symptomatic therapy. Antiseptics for local oral hygiene are recommended. Also antiviral ointments (0.25–0.5 % oxolinic, 0.25–0.5 % florenal, 5 % acyclic), multivitamins, antioxidants, etc. are used.

1.6.8. Damage to the mucous membrane in chickenpox

As in shingles, Varicella herpetiformis causes chicken pox. Along with rashes on the skin, single vesicles (blisters) appear on the mucous membrane, hard palate, tongue. Blisters quickly burst and erosion (aphthae) is formed, similar to the manifestations of herpetic stomatitis. Due to the fact that the blisters do not appear simultaneously, they are characterized by fake polymorphism (papules, vesicles, crusts). The general condition of the patient depends on the course of the disease (from mild to severe).

In severe cases, antiviral drugs are prescribed (acyclovir – 0.2 g 3 times a day, bonaphton – 0.1 g 3 times a day). With a mild to moderate degree, it is impractical to prescribe the latter. Antiseptic treatment of rashes with solution of ethacridine lactate (1:1000), 1 % solution of miramistin and stomatidine is locally prescribed.

Specific prophylaxis is carried out using herpetic immunoglobulin 5 ml i.m., not later than 3 days after contact.

1.6.9. Damage to the mucous membrane in measles

A specific sign of measles is the appearance in the oral cavity and in the area of large molars of typical whitish-yellow spots that protrude slightly above the level of the mucous membrane. These spots usually do not merge with each other (Belsky – Filatov symptom). At the same time, rashes appear on the skin of the face and behind the ears.

This type of stomatitis does not require special medical treatment. It is recommended to use rinses and irrigations at home with mild vegetable solutions, a solution of sodium bicarbonate or furacilin.

1.6.10. Damage to the mucous membrane in AIDS

AIDS is caused by two lymphotropic retroviruses, HIV-1 and HIV-2. The latter affect lymphocytes (T helpers), monocytes and other macro-

phages. Progressive lesions of the immune and nervous system slowly develop. HIV infection may be slightly symptomatic for a long time (from 2 to 15 years). The transition to the AIDS stage can last up to 5–7 years. At this stage, there are three main clinical forms: onco-AIDS, neuro-AIDS, infection-AIDS, which can lead to death of the patient in several months.

In patients with AIDS, a variety of oral lesions are observed. A classification of the manifestations of HIV infection of the oral cavity was put forward in 1990.

The first group is the lesions that are most closely associated with HIV:

- candidiasis;
- hair leukoplakia;
- HIV gingivitis;
- necrotizing ulcerative gingivitis;
- HIV periodontitis;
- Kaposi's sarcoma;
- non-Hodgkin lymphoma.

The second and third groups include diseases that are least associated with the infection or possibly associated with it (xerostomia, cytomegalovirus or herpetic infection, bacterial periodontitis, osteomyelitis, etc.).

Scientists' views on the sequence of clinical manifestations of AIDS are mixed. According to most authors, mucosal lesions are the first manifestation of AIDS, but some scientists believe that these lesions are associated with the terminal stages of the disease and a decrease in blood lymphocytes.

It is believed that such dental disorders as rapidly progressive periodontitis, necrotizing ulcerative gingivostomatitis, angular cheilitis, desquamative glossitis, candidiasis, herpes, hairy leukoplakia can reflect AIDS. Most often there is candidiasis (88 %), hairy leukoplakia (83 %), gingivitis (80 %), periodontitis (60 %). Dental disorders are characterized by rapid progress in inflammatory and dystrophic-inflammatory processes, refractory state, atypical clinical manifestations and resistance to the applied treatment methods or their low efficiency.

Taking into account the characteristics of the etiology, pathogenesis and clinic of HIV infection, its treatment should be comprehensive and based on:

- antiviral therapy (antiretroviral therapy);
- immunomodulatory therapy;

- treatment of opportunistic diseases;
- treatment of tumor diseases.

The use of antiviral and immunomodulating agents is aimed at inhibiting the reproduction of the causative agent of HIV infection, the resumption of impaired functions of the immune system and stopping the further transmission of this infection to healthy people.

Today, three groups of modern medicines are used:

- nucleoside reverse transcriptase inhibitors (didanosine, zalcitabine, zidavudin);
- non-nucleoside reverse transcriptase inhibitors (delavirdine, viramune);
- protease inhibitors (indinavir, ritonavir).

In Ukraine, in clinical practice, azidothymidine (didanosine, retrovir), which has a direct etiotropic effect, is more widely used. A new method for its synthesis is being developed. This drug increases the lifespan of AIDS patients and reduces the frequency and severity of opportunistic infections. Triapten (foscarnet) and cycloferon are also used. The latter is close to azidothymidine for effectiveness, but is less toxic.

Correction of immunity disorders is aimed at increasing T lymphocytes and is carried out using immunotropic drugs (thymus hormones – tyrosine, thymopectin, humoral immunity correctors – gammaglobulin, interleukin-2). For the treatment of opportunistic infections (herpes, cytomegaly), acyclovir, ganciclovir, ribavirin are used. The treatment of malignant neoplasms is carried out according to well-known methods (surgical treatment, chemotherapy).

Dental care for AIDS patients consists in the rehabilitation of the oral cavity (antiseptics, antibiotics, etc.) and the use of symptomatic treatment (local anesthetics, painkillers). For the complex treatment of candidiasis, antifungal and immunostimulating agents are used. In the treatment of hair leukoplakia, the overall effect on the immunodeficiency virus is effective. Treatment of gum and periodontal lesions is carried out in accordance with generally accepted schemes.

1.6.11. Vincent's necrotizing ulcerative stomatitis

Vincent's necrotizing ulcerative stomatitis is caused by the symbiosis of Bacillus fusiformis and Vincent's spirochete (Borellia vincenti). Under ordinary conditions, these microbes are saprophytes of the oral cavity, but in the case

of a decrease in the reactivity of the body and oral mucosa, they acquire aggressive properties. The disease causes adverse conditions in the oral cavity, hypothermia, stress, and trauma. Necrotizing ulcerative stomatitis can be a manifestation of a general illness of the body, immunodeficiency states, intoxications, etc. The nature of the process is seasonal (spring and autumn).

Vincent's necrotizing ulcerative stomatitis begins with symptoms typical of an infectious disease: fever, heaviness in the head, lethargy, aching joints, dry mouth, and work decrement.

First, catarrhal phenomena develop – the oral mucosa is hyperemic. Over time, the process becomes ulcerative. Single or multiple ulcers with uneven soft edges appear in the oral cavity on the gums and different parts of the mucous membrane They are covered with a grayish coating and have a putrid odor. Ulcers are often localized in the cheek area, in the retromolar space, on the tongue, on the mucous membrane of the lips. At this time, the general condition of the patient worsens, who notes pain during conversation, bleeding gums, increased salivation.

Local anesthesia is performed (1 % solution of dicain, 5–10 % solution of anaesthesin in oil, lidocaine in aerosol), as well as conductive anesthesia with 1 % solution of novocaine. For the treatment of affected areas, 1–2 % solution of hydrogen peroxide, solution of potassium permanganate (1:5000), solution of chloramine (0.25–1 %), solution of chlorhexidine (0.06 %), solution of citral (0.01 %), solution of propolis (25 drops per glass of water) are used. Necrotic sites are removed using the enzymes of trypsin, chymotrypsin, ribonuclease. Enzymes and oxidizing agents should never be prescribed at the same time. Ulcers are treated with bioparox (fusafungin), microcide, 4 % alcohol solution of propolis, 1 % solution of galascorbin, solcoseryl, sea buckthorn oil, etc.

General treatment is based on modern antibacterial agents that adversely affect anaerobic microorganisms. Metronidazole 0.25–0.5 g is effective 2–3 times a day for 7–10 days, ampicillin (1 g 4 times a day i.m.) in combination with metronidazole (500 mg 3 times a day), clarithromycin (first 500 mg, then 250 mg), cefotaxime 1–4 g i.m., clindamycin (150 mg every 6 hours). It is advisable to use simultaneously anti-inflammatory drugs (sodium mefenaminate, ibuprofen, nimesulide). The complex of therapeutic agents includes hyposensitizing drugs (diphenhydramine, suprastin, tavegyl, etc.). Vitamins (ascorbic acid, rutin, multivitamin prepa-

rations) and a balanced diet are also prescribed. Complete epithelization occurs after 3–6 days. In the future, it is advisable to carry out sanitation of the oral cavity. However, the process is capable of recurrence and transition to the chronic form.

1.6.12. Vincent's angina

Vincent's angina is a fusospiral infection, can develop independently or simultaneously with Vincent's necrotizing ulcerative stomatitis. There are unilateral lesions of the tonsils in the form of a yellowish-white coating (ulcerative form) or a yellowish-black film (diphtheroid form). When the plaque and film are removed or rejected, an erosive surface is formed. Pain and bad breath are characteristic. Regional lymph nodes are enlarged, the general condition, as a rule, is not disturbed.

Pharmacotherapy is based on the use of antibacterial agents. Local treatment is similar to that for necrotizing ulcerative stomatitis. A diet, heavy drinking are recommended.

1.6.13. Gangrenous stomatitis

Gangrenous stomatitis is manifested by necrotic lesion of the mucous membrane, which is caused by anaerobic-clostridial infection against the background of general infections, intoxications, hypovitaminosis, etc.

This severe form of dental pathology is characterized by the development of specific lesions (necrosis) of all layers of the mucous membrane with severe intoxication. Necrotic lesions in the form of a gray-brown or gray-green mass cover the cheeks, tongue, lips, and soft palate. Skin necrosis may also occur. It is characterized by severe pain and a significant deterioration in the general condition of the patient.

Treatment is based on detoxification methods (reopoliglykin, rheosorbilact), sorbents (enterosgel). An important role is played by antibacterial therapy (metronidazole, lincomycin, clindamycin, penicillins, CS). Local treatment is similar to the principles that are used for necrotizing ulcerative stomatitis.

1.6.14. Lichen planus

Lichen planus is a disease of the oral mucosa, which is characterized by a recurring persistent course and a variety of clinical forms. The causes

of lichen planus are diverse (dental pathology, infection, toxins, stress, allergens, autoimmune disorders, etc.). The most popular theory of etiology is neurogenic, according to which the main role in the occurrence of the disease belongs to emotional stress, neuropsychiatric and diencephalic disorders. Immunological theory is based on the emergence of a late immunological reaction with a cytotoxic effect. Thus, lichen planus is considered as a multifactorial process that is associated with impaired neuroendocrine, metabolic and immune regulation mechanisms. It is believed that the duration of the course of the disease and resistance to therapeutic influences largely depend on the presence of immunologically dependent chronic diseases in patients.

In all cases of clinical manifestations, the main element of the lesion is a papule. Papules are usually opaque, then become reddish, rounded or elongated in shape. Single papules on the mucous membrane (especially the distal cheek and retromolar space) and the red border of the lips join together and form a tree-like pattern. At the same time, rashes are observed in the lumbar region and on the flexion surfaces.

Typical, hyperkeratotic, exudative-hyperemic, erosive-ulcerative, bullous and atypical forms of the disease are distinguished. Depending on the form of the disease, patients may complain of itching, a feeling of tightness of the cheeks, burning in the mouth, soreness when taking hot, spicy food, the presence of erosion and vesicles. One form of lichen planus can transform into another.

The treatment of this pathology is a complex task, which is associated with insufficient knowledge of the etiology and pathogenesis of the disease. Modern views on treatment are based on an integrated approach and depend on the form and severity of the disease.

In all forms, rational prosthetics and oral sanitation are recommended. Antihistamines, calcium preparations, histoglobulin are used. Baths with solution of haloscorbin, decoctions of hypericum, chamomile, eucalyptus, sage, 0.5 % solution of chlohexidine, 0.02 % solution of furacilin, application of ointments that contain GCS, dibunol, solcoseryl or dental adhesive paste are locally prescribed.

In typical and exudative-hyperemic forms, sedative therapy (valerian extract, persen, novopassit, minor tranquilizers, antidepressants, etc.) is definitely recommended. Vitamin therapy has a positive effect on meta-

bolic processes. It is advisable to prescribe a vitamin A concentrate (daily dose for adults – 100.000 IU). Vitamin A – 10 drops 3 times a day with meals, for 1.5–2 months or aevit 1 drop 1 time a day – 30–40 days is prescribed. Derivatives of vitamin A (tigason, etretinate) and its analogues – carotenoids (phenoro) are also used. Vitamins B_1, B_6, B_{12} are also used for a long time.

With erosive-ulcerative and bullous forms, in addition to sedative and vitamin therapy, in a hospital, treatment with prednisolone (20–25 mg per day every other day) or triamcinolone (16–20 mg per day), or dexamethasone (3–3.5 mg) is prescribed together with chingamin (0.25 mg 1–2 times a day for 4–6 weeks) and nicotinic acid (0.05 g 3 times a day after meals). It should be remembered that the dose of prednisolone is reduced by 5 mg every 7–10 days. The course of delagil (0.25–0.5 g per day) with methyluracil (0.5 g 3 times a day) and antiviral agents are also effective.

If corticosteroids are contraindicated, hyposensitizing histaglobin therapy is recommended (several courses with a break for 2 months; 2 ml s.c. 2 times a week, 8–10 injections per course). Chonsurid is also used in the form of applications 2–3 times a day or 1 ml under the lesion element every other day.

With limited erosive and ulcerative lesions, they are chipped with a suspension of hydrocortisone (or solution of prednisolone) and 5–10 % chingamin solution. Injections are carried out 1 time in 3 days, 1–1.5 ml for each erosion, 8–10 injections per course. The course is repeated after 3–4 months.

In connection with the identification of patients with dysbiotic disorders of the intestinal microflora, some authors include bifilis, lactusan and sodium nucleate into the complex treatment.

With exudative-hyperemic and erosive-ulcerative form, it is recommended to use a course of treatment (10 days) with antioxidant mexidol. The drug has a rich spectrum of pharmacological action (anxiolytic, antioxidant, membrane-protective, nootropic, antistress, etc.). In the first form, mexidol is administered orally, and in the second, injections of 5 % solution of mexidol under the lesion element are additionally administered.

In severe clinical forms, therapy is used with agents that affect the immune system (referron, interlock, neovir, ridostin). 12.5 % neovir is prescribed – 2 ml i.m. once every 2–3 days, 5 injections per course, ridos-

tin – 2 ml every 2 days, only 4 injections. Immunocorrective therapy with licopid and polyoxidonium is also carried out.

In the complex treatment of lichen planus, physical methods of treatment are of great importance: electrophoresis with vitamins and enzymes, laser therapy, electrosleep, etc. However, the treatment of this pathology is complicated and the use of various pharmacological effects does not prevent relapse.

1.6.15. Candidosis

Candidosis (candidiasis) – acute or chronic infectious disease of the mucous membranes caused by fungi of the genus Candida, which, with a decrease in the body's defenses and barrier function of tissues, contribute to the development of dysbiosis and become pathogenic. Favorable conditions for the development of candidosis are created with the failure of the immune system after infections or prolonged use of drugs (broad-spectrum antibiotics, cytostatics, GCS). Local factors play a role in the development of the disease: lack of oral and dental hygiene, prosthetic trauma, carious teeth, periodontal pockets, chronic diseases, carbohydrate abuse, etc.

According to clinical forms and localization of foci of candidal infection, a lesion is distinguished: lips – cheilitis and seizure, tongue – glossitis, oral mucosa. Acute and chronic forms of the disease are distinguished. The acute form has a course of pseudomembranous and atrophic candidiasis. The clinical manifestations of different forms of candidiasis differ from each other.

Acute membranous candidiasis can occur in infants due to infectious diseases. At the same time, a film appears on the mucous membrane of the cheeks, tongue, and palate (looks like a white clotted plaque), which consists of dead epithelial tissues and accumulations of fungal filaments. In children, the occurrence of candidiasis is promoted by hypovitaminosis, exudative diathesis, rickets.

In a mild course, after removal of the films, hyperemic spots remain in their place. In severe cases of the disease, common membranous surfaces are observed in the oral cavity that is difficult to remove. After scraping the lesions, bleeding erosion that can be noted. Plaque, edema, hypertrophy are observed on the tongue. Similarly, the red border is affected,

which is hyperemic and covered with yellow-white films. In the corners of the mouth – erosion cracks that make eating and conversation difficult. With the spread of the process to the pharynx, larynx, esophagus, the further prognosis worsens significantly.

In acute atrophic candidiasis, the lesions of the mucous membrane are bright red, dry, similar to erythema. Atrophy of the mucous membrane and papillae of the tongue is noted, patients complain of heartburn and intolerable pain. The absence of plaque is typical.

Hyperplastic candidiasis is accompanied by the formation of white papules or plaques that resemble leukoplakia.

Candidiasis treatment should be comprehensive, individualized, etiopathogenetic and symptomatic. Depending on the severity of candidiasis, general and local treatment are used. It is very important to establish the cause of the disease. If the disease is caused by drugs, then it must be withheld, except in cases where the drugs are prescribed for vital indications. Pharmacotherapy for all forms of candidiasis includes drugs that affect the pathogen, pathogenesis, immune defense, and concomitant diseases.

Antifungal antibiotics are more effective treatment for candidiasis, which is designed to decontaminate this infection. Fluconazole is the most widely used representative of triazoles with selective action. In the treatment of candidiasis, it is prescribed orally 50–100 mg per day (maximum daily dose – 400 mg) for 7–14 days. Itraconazole, which belongs to the same group of drugs, has more pronounced toxicity, and it is prescribed 100 mg once a day for 7–14 days.

For general therapy, if there is a sensitivity of the fungus, nystatin should be used (1.500.000–2.000.000 IU per day for 10–15 days), 1 buccal tablet (500.000 IU), mycoheptin 0.25 g 2 times a day, amphoglucamine 0.2–0.5 g 2 times a day.

To increase the effectiveness of general treatment, or as an alternative to it, local use of the following drugs is recommended: 1 % clotrimazole solution or cream, nitazole aerosol, amphotericin B ointment, mycoheptin, levorin and nystatin. Local treatment is carried out until the clinical manifestations are eliminated, plus 7–10 days.

For local treatment of candidiasis, antiseptics with fungicidal and fungistatic effects allowed: 0.1 % chlorhexidine solution or 1 % miramistin

solution, 1 % iodinol solution, Lugol's solution, 3 % alcohol iodine solution, 2–3 % solution of sodium tetraborate and sodium bicarbonate, 1 % solution of gentian violet, 0.5–1 % solution of resorcinol, stomatidine, givalex. Propolis ointment or its 1 % tincture, 0.5 % decamine ointment or its 1 % emulsion, decamine, caramel for resorption are also effective.

In chronic hyperplastic candidiasis, antifungals (clotrimazole, nystatin, levorin, decamine, etc.), antiseptics and antibacterials (etonium, sanguirytrin, quinosole, nitroxoline, propolis, yuglon, methylene blue, Castellani liquid, benzoic acid) are locally used. Teeth should be treated by boroglycerin paste. Laminar dentures are washed after each meal and stored in 1–2 % sodium bicarbonate solution. To support the alkaline environment in the oral cavity, you can use 20 % solution of sodium tetraborate in glycerin, which is used to treat the mucous membrane.

For the treatment of candidal lesions of the red border and skin, it is more convenient to use the dosage forms of antifungal drugs in the form of creams, ointments and liniments (myfungar, exoderil, loceryl, sanguirytrin, nystatin, mycoheptin, clotrimazole, decamine, levorin, riodoxol, dermazolone, amphotericin B). The preparations are applied in a thin layer 3–4 times a day on a skin surface or mucous membrane that is cleansed from exfoliation. The course of treatment is 6–14 days with further bacteriological control.

Fungal lesions require persistent treatment, so even highly effective drugs should not be prescribed as monotherapy. To increase the body's immune forces, immunotropic drugs are prescribed (imudon, cycloferon, licopid, gammaglobulins). It should be remembered that immunotropic drugs that are used in the oral cavity (imudon) show their properties only under conditions of sanitization, in other cases they do not work. A dentist can use drugs in the form of nasal drops (derinat, thymogen, vilosen, IRS-19). In the complex therapy of candidiasis, reparants (methyluracil, pentoxyl), biological stimulants (fibs, aloe preparations), multivitamins, antihistamines, plant hypersalivants (coltsfoot, yarrow, thermopsis) are also used. Recently, to restore the balance of microflora in the oral cavity, probiotics (bifiform, linex, etc.) are used.

For the completeness of treatment, it is very important to conduct a rational prosthetics and follow a complete diet with a limited amount of carbohydrates.

1.6.16. Actinomycosis

Actinomycosis is a chronic infectious process that is caused by an anaerobic radiant fungus – actinomycetes. The disease is characterized by the appearance of specific granulomatous foci in the tissues affected by it, and drusen in the purulent cells. In children, damage to the bone and periosteum may occur.

Actinomycosis occurs as a result of auto-infectious inflammatory processes (odonto-, dental-, tonsilogenic). The place of penetration can be a dead pulp, pathological gingival pockets, affected mucous membrane. The process spreads slowly along interfascial subcutaneous adipose tissue or more quickly from lesion sites. The most threatening complication is the spread of the process to the brain and chest.

The clinical picture of actinomycosis can be varied. There are skin, subcutaneous, submucous, subcutaneous-muscular forms of lesions, as well as actinomycosis of the lymph nodes, bones, etc. With a submucous form in the submucosal layer, hazy white infiltrate occurs, which thickens and merges with the mucous membrane. In the oral cavity, isolated areas of the lesion can be observed. In the depths of the tongue, a dense infiltrate forms, which can be abscessed and disintegrate.

The disease is difficult to treat, therefore it must be complex (surgical, conservative, physiotherapeutic) and sufficiently long in time. In order to influence the causative agent of the disease, penicillin (18–24 million IU i.v. per day for 3–6 weeks) is used, with positive dynamics, phenoxymethylpenicillin (2 g per day) or amoxicillin (3–4 g per day). For alternative therapy, doxycycline (0.2 g per day) and oral medications – tetracycline (3 g per day) or erythromycin (2 g per day) for 6–12 months are suitable.

With the growth of connective tissue, antibiotic therapy is usually not effective enough; therefore, surgical intervention is required – emptying and curettage of granulomatous growths. The abscess cavities are washed with solutions of nitrofuran preparations and 1–5 % alcohol solutions of iodine are introduced. Physiotherapeutic methods: electrophoresis of iodine and lydase, fluctuating currents, treating with ultraviolet light and laser illumination are used.

For the treatment of all forms of the disease, especially in children, 2 ml of actinolizate s.c. 2 times a day, with a course of 20 injections, is administered. Effective use of actinomycete multivalent vaccine (i.c. or s.c.,

starting with 0.1 ml and increasing the dose with each further injection by 0.1 ml to 1 ml, then 1 ml for 10–15 injections).

The following methods are combined in the systemic treatment of actinomycosis: general strengthening – blood transfusion (1 time per day, 4–5 procedures), stimulating (fibs, vitreous, prodigiosin, etc.), vitamins B_1, B_6, B_{12}, C, multivitamins.

The early start of treatment and the use of modern effective methods can lead to the eradication of this complex disease and prevent its spread with the occurrence of threatening complications.

1.6.17. Allergic lesions

Allergy is a manifestation of an increased sensitivity of the body's immune system to an allergen (antigen) upon repeated contact with it. In this case, a whole complex of disorders develops at different levels of the body. Allergic reactions that are diverse in clinical manifestations are united by common pathogenetic mechanisms and develop in three stages: immunological, pathochemical and pathophysiological. The immunological stage is based on sensitization, that is, the formation of antibodies to an allergen that has entered the body. The pathochemical stage occurs as a result of repeated contact of the immune system with the antigen and is characterized by the release of a large number of biologically active substances (histamine, bradykinin). The latter contribute to the development of the pathophysiological stage – the appearance of the main clinical signs of allergies (hyperemia, edema, pain, inflammation, itching, necrosis, drop in blood pressure, shock, etc.).

In dental practice, there are allergic reactions caused by various agents: drugs; dental materials, hygiene products and cosmetics, microbial toxins, household dust. The most common allergic reaction is the reaction of the oral cavity caused by drugs. Reactions can develop with all methods of drug use; however, a less dangerous method is their ingestion. Quite often, after drug treatment (0.5–25 %), allergic diseases of the oral mucosa are observed. They can also occur as a result of sensitization in chronic diseases (periodontitis, recurrent aphthous stomatitis, candidiasis, etc.).

Manifestations of allergies are divided by localization (cheilitis, gingivitis, glossitis, stomatitis); the nature of inflammation (catarrhal, hemor-

rhagic, papular, erosive, etc.). Allergic reactions of the oral mucosa are often combined with skin lesions.

The basic principles of the treatment of allergic diseases are as follows: etiotropic treatment – identification and elimination of the allergen; pathogenetic treatment – specific hyposensitization; non-specific hyposensitization and detoxification – autohemotherapy, hemo-, enterosorption, immunostimulants, calcium preparations, antihistamines, GCS); symptomatic treatment – stabilizers, proteolysis inhibitors, antihistamines, etc.

Treatment of patients with drug allergy and damage to the oral mucosa should be comprehensive. A drug that has become an antigen is canceled or contact with it is eliminated. If a sensitizing drug was used topically (applications, sublingual tablets, etc.), the mouth sould be then rinsed with 0.5–1 % sodium hydrogen carbonate solution, weak (1:2000) potassium permanganate solution. If the drug was administered subcutaneously or intravenously (in the area of the limb), then a tourniquet is applied above the injection point, where 0.2–0.5 ml of 0.1 % adrenaline solution is injected. If necessary, antihistamines (diphenhydramine, cetirizine, etc.) or corticosteroids (prednisolone, etc.) are used.

Inactivation of allergic antibodies is carried out using specific hyposensitization in small doses with the same drug that caused drug allergy. To alleviate the effects of biologically active mediators (histamine, serotonin, etc.) and nonspecific desensitization, antihistamines are prescribed (diphenhydramine, suprastin, ceterizine, clarithin, etc.).

The most common clinical forms are catarrhal and catarrhal-hemorrhagic stomatitis. The mucous membrane becomes bright red, swollen, hemorrhagic spots appear, salivation decreases and dry mouth develops. Their treatment is not difficult. It is necessary to cancel the drug that caused the allergy, prescribe vitamins C, P, B_2, B_6, antihistamines, non-irritating diet, and if necessary, GCS applications (prednicarb ointment, synalar ointment, etc.). For the treatment of stomatitis, herbal preparations are recommended: novimanin, rotocan, tincture of calendula for rinsing the mouth, corticosteroid ointments.

With the development of erosive lesions of the oral mucosa, painful erosions of various sizes, covered with fibrous plaque, are observed. A violation of the general condition develops – fever, malaise, etc. After discontinuing the allergenic drug, desensitizing therapy and antihistamines

are prescribed. In the lesion site, local anesthetics, ointments containing GCS, LPO, stimulating epithelization (vitamins A and E, sea buckthorn oil, rosehip oil, etc.) are used.

Necrotizing ulcerative lesions are manifested by ulcers, which are covered with necrotic decay of a white-gray color. Around the ulcer, signs of inflammation of the mucous membrane are observed. Pain syndrome is typical. The general position of the patient depends on the manifestations of intoxication. Necrotizing ulcerative cheilitis, stomatitis and glossitis are difficult and require more energetic and prolonged therapy. Antihistamines, GCS, vitamins are used enterally, 5–10 ml of 30 % sodium thiosulfate, rheopolyglucin are administered intravenously. Anesthetics, proteolytic enzymes, and keratoplastic drugs are prescribed locally. Irritating and sensitizing products (eggs, coffee, spicy dishes, etc.) should be excluded from the diet.

Allergic diseases of the oral mucosa can be the result of complications of systemic allergic reactions. These include Lyell's disease, which is characterized by volumetric necrotic damage to the skin, mucous membrane and severe general condition of the body. Previously, the drug that caused the allergy must be cancelled. General pharmacotherapy includes corticosteroids intravenously or orally, rheopolyglukin or rheosorbilact, sodium thiosulfate intravenously. Symptomatic pharmacotherapy is also carried out. The oral cavity is locally treated with antiseptic agents.

When the causes of allergic diseases of the oral cavity are different dental materials used in prosthetics, the treatment is carried out according to general rules (antihistamines and NSAIDs, calcium preparations, glucocorticosteroids, etc.).

1.6.18. Chronic recurrent aphthous stomatitis

The development of this disease is promoted by neuroendocrine disorders, gastrointestinal pathology, local and general immune status disorders, allergic diseases, as well as various harmful factors (material of dentures, cement, phenol, etc.). The causes may be staphylococci and adenoviruses.

The disease is manifested by a prolonged recurrent aphthous rash on the mucous membrane, which is very painful. Afta (erosion) is usually small in size, round or oval, singly located. It has a red frame. Over

time, the afta takes nature of an ulcer, which is covered with a yellowish or grayish-white coating. The cycle of its existence is 5–10 days, after which it heals, but after a while a new rash appears.

When carrying out therapeutic measures, it is very important to conduct a clinical and immunological examination, identify a specific allergen and prescribe hypersensitizing therapy. For the purpose of non-specific hypersensitivity, sodium thiosulfate is prescribed. Prodigiosin, levamisole, tactivin, which are prescribed i.m. once every 5 days, contribute to an increase in nonspecific and specific resistance of the body. Levamisole (decaris) acts directly on T-cells or their functions, on macrophages and neutrophilic granulocytes. T-activin normalizes the quantitative and functional parameters of the T-system of immunity, stimulates the production of lymphokines, and the functional activity of stem hematopoietic cells. Hyposensitizing agents (tavegyl, diazolin) are also prescribed to patients. With a long course, it is possible to prescribe GCS (methylprednisolone, prednisolone). Vitamin preparations (ascorbic acid, riboflavin, pyridoxine), tranquilizers and sedatives are indicated.

Local exposure is carried out according to the principles of treatment of necrotizing ulcerative processes. Anesthesia is carried out with an oily suspension of anaesthesin in glycerin, solution or aerosol of lidocaine, solution of pyromecain. Antiseptic treatment is prescribed; irrigation and applications are administerd: with trypsin or chymotrypsin, trasylol, heparin, hydrocortisone in solution of novocaine, to accelerate epithelization – application with solution of sodium usninat in fir oil, carotolin, aloe liniment, citral, and propolis ointment.

In the treatment of this type of stomatitis, the experience of using kamistad combined gel preparation (lidocaine hydrochloride, tincture of chamomile flowers) has been studied. It has several advantages according to the results of the clinical picture and clinical and laboratory parameters. The drug optimizes the regeneration process of the epithelium of the oral mucosa, speeds up the patient's recovery time, has analgesic, anti-inflammatory, antiseptic and wound healing effects.

1.6.19. Exudative erythema multiforme

Exudative erythema multiforme is a recurrent inflammatory lesion of the skin and mucous membrane of an allergic genesis. It is characterized

by the polymorphism of the rashes. In etiology and pathogenesis, an important role is played by autoimmune mechanisms. Infectious-allergic (idiopathic) and toxic-allergic (symptomatic) forms of the disease are distinguished.

The infectious-allergic form begins with an increase in body temperature (39 °C), weakness, pain in the joints, sore throat, etc. Rashes on the mucous membrane appear after 1–2 days, they are polymorphic and very painful. First, erythema appears, and then – blisters with serous or serous-hemorrhagic exudate. The named elements exist for 2–3 days, then crack, and in their place drain erosions are formed, covered with a yellowish-gray bloom. Erosive surfaces of the mucous membrane are infected with microflora of the oral cavity. The process is often localized on the lips, the bottom of the oral cavity, cheeks and palate. Hemorrhagic crusts form on the red frame of the lips, which crack and cause severe pain and bleeding. The progression of the disease is accompanied by difficulty speaking, eating and worsening the general condition of the patient (for Ukrainian book).

The development of a toxic-allergic form is associated with increased sensitivity to drugs. The nature of the rashes corresponds to these in the previous form, but lesions of the mucous membrane are observed more often and are more common. The relapse process is characterized by fixed rashes, that is, they are localized in their previous places.

Treatment should be aimed at identifying and eliminating the cause of the disease, eliminating inflammatory manifestations and pain, accelerating the healing process. The drug load depends on the form of the disease and the general condition of the patient.

In the mild course of the disease, NSAIDs (ibuprofen, mefenamic acid, nimesulide), multivitamins, calcium gluconate, hypersensitizing drugs and antihistamines are prescribed. With moderate severity of manifestations, antibiotics are additionally prescribed enterally (clarithromycin, azithromycin, doxycycline, etc.). In severe form, GCS is prescribed (20–30 mg prednisolone per day or dexamethasone in appropriate doses), antienzyme agents (trasylol, contrykal), detoxification therapy (neohaemodez, rheopolyglucin, rheosorbilact, sodium thiosulfate, i.v. glucose solution). Antistaphylococcal gammaglobulin is administered in oil – 25 units per day for 3–7 days. If necessary, the patient is hospitalized.

Painkillers are used locally (1–2 % solution of lidocaine or trimecaine), antiseptics, proteolytic enzymes, ointments containing antibiotics and corticosteroids, keratoplastic substances.

Prevention of the mentioned disease consists in sanitation of the oral cavity and the whole organism, conducting fortifying therapy, as well as prescribing gammaglobulin, histoglobin and staphylococcal toxoid according to the indications.

One of the severe manifestations of erythema multiforme exudative is Stevens – Johnson syndrome. This syndrome is considered as an allergic drug lesion, which is often caused by refineries and SA. It is characterized by generalized polymorphic damage to the mucous membrane (erythema, papules, blisters). When the disease spreads to the border of the lips, tongue, palate, widespread painful erosions appear, covered with purulent hemorrhagic crusts. In addition to the oral mucosa, the mucous membranes of the eyes, nose, and genitals are affected. Lesions of visceral organs (pneumonia, encephalomyelitis, myocarditis, glomerulonephritis, etc.) may also develop.

For treatment, detoxification therapy, antihistamines, anti-inflammatory drugs, broad-spectrum antibiotics are used. It is advisable to prescribe a massive corticosteroid therapy (60–80 mg of prednisolone per 1 injection). Painkillers, antiseptics, corticosteroid drugs, immunomodulators, enzymes are used locally.

The most severe manifestation of drug-induced immune damage is Lyell's syndrome (toxic epidermal necrolysis), which occuirs after the use of NSAIDs (pyrazolones, salicylates), sulfonamides (biseptol), antibiotics, etc. The disease' pathogenesis has not been adequately studied. The syndrome occurs most often in women and is approximately 1 case per 1 million inhabitants. It is characterized by an acute onset, a rapid increase in temperature (39–40 °C). Erosive lesions with the remains of a grayish-white epithelium of the blisters appear on the mucous membrane of the entire oral cavity. On the skin of the face, trunk, limbs, meerging erythema and spots are formed, that quickly turn into epidermal necrolysis. At the same time, blisters and common erosive lesions can be observed on the skin. Desquamation of fleshy colour epidermis and dermis occurs throughout the skin. The general condition of the patient worsens, severe violations of the respiratory, cardiovascular system, water-salt balance, and sepsis are observed. Mortality is 20–70 %.

Intensive treatment is carried out in a hospital using detoxification, desensitizing (up to 80 mg of prednisolone per 1 injection), anti-inflammatory drugs. The normalization of the water-salt balance is carried out. Local treatment is carried out according to the principles of multiforme exudative erythema.

1.7

ANTIBACTERIAL THERAPY OF ACUTE INFLAMMATORY PROCESSES OF THE MAXILLOFACIAL AREA

Purulent-inflammatory diseases and postoperative purulent complications are an urgent problem of modern dental practice. In surgical practice, adequate antibacterial therapy of abscess, phlegmon, and osteomyelitis is of great importance in the elimination of the inflammatory process. A dentist with a therapeutic profile needs to solve the issues of rational treatment of pulpitis, periodontitis, periodontitis, and infectious lesions of the mucous membrane.

Modern views on the treatment of purulent processes of the MFA are based on uniform biological laws and ideas about the essence of the mechanisms of development of the wound process and its staging. Therefore, the principles for the treatment of these states should be fundamentally united, aimed at creating conditions for the rapid healing of wounds (surgical treatment, local drug treatment, an active effect on macroorganism).

Modern approaches to the treatment of purulent-inflammatory processes can be represented as follows:

1. Active etiotropic treatment in order to reduce the antigenic load in the focus of inflammation and improve the functioning of systemic and local immunity:
   - surgical removal of devitalized tissues;
   - adequate drainage, application sorption in order to remove antigenic material;
   - the use of various means of chemical, physical and biological antiseptics and antibiotic therapy.

2. Conducting pathogenetic treatment in order to restore homeostasis disturbed by the pathogen and stimulate biological defense mechanisms:

- systemic detoxification measures (infusion therapy, forced diuresis, entero-and hemosorption, plasmapheresis);
- adequate analgesia and sedation during operations or dressings;
- immunostimulation.

At the heart of the treatment of purulent wounds of the MFA is the concept of a fundamentally different essence of the inflammatory reaction in the stages I and II of the wound process. Difficulties in the treatment of such patients are associated, firstly, with the constant increase in the resistance of modern microflora to ABD, an increase in the frequency of seeding of microbial associations, including anaerobic pathogens, from the focus of inflammation. Secondly, the nature of the response of the macroorganism is of great importance.

From the point of view on the etiology, the infectious and inflammatory diseases of the MFA can be divided into:

- odontogenic – associated with damage to the pulp of the tooth, periodontium and the spread of infection to the bone, soft tissues of the face and neck, maxillary sinus, etc.;
- periodontal – associated with periodontal lesions;
- stomatogenic – associated with infection of tissues by the microflora of the oral cavity;
- nonodontogenic – rhinogenic sinusitis, boil, carbuncle, erysipelas, hematogenous osteomyelitis of the jaw, a manifestation of a common infectious pathology in the oral cavity;
- specific processes – actinomycosis, tuberculosis, syphilis, etc.

First of all, odontogenic processes can be the cause of serious, life-threatening complications from the cranial cavity, mediastinal region, as well as disseminated lesions of the valvular apparatus of the heart, sepsis.

In determining the role of microorganisms in inflammatory diseases of the MFA, it should be noted that the resident microflora of the oral cavity plays a great role in their occurrence. This creates great difficulties associated primarily with the fact that: firstly, the infection here is always caused by microbes that are in the oral cavity of a healthy person, and secondly, the process in the absence of a specific pathogen can be caused by the action of several species simultaneously, thirdly, the same microorganism

can, under a certain state of factors, cause various pathological processes, or two different pathogens can cause similar pathological processes.

The general effect on the main links of the infectious-inflammatory process of the MFA consists of: a) active etiotropic treatment (destruction of the pathogen); b) pathogenetic treatment (restoration of homeostasis and stimulation of biological protective mechanisms, adequate analgesia and sedation, stimulation of protective and reparative mechanisms, immunocorrection).

Treatment of the inflammatory process of the MFA can be effective only if the purulent lesion is surgically eliminated and wound drainage is subsequently ensured. This allows not only to localize the infection and create conditions for an adequate outflow of the contents from the abscess, but also to prevent the development of complications. However, the standard method of surgical treatment of a purulent wound cannot provide sufficient removal of the microbial flora; therefore postoperative therapy is fundamentally important. One of the main links in this treatment is the rational use of ABD, the effective concentration of which in the blood is ensured by the dose and method of administration.

Advanced requirements are put forward modern ABD. In addition to a wide spectrum of antibacterial activity, the relatively dominant etiopathogens in our time, they must be able to penetrate quickly and selectively the outer cell membrane of bacteria, be resistant to destructive enzymes (β-lactamase, etc.), exhibit a pronounced post-antibiotic effect and not cause immunosuppression.

In most cases, doctors prescribe antibacterial therapy empirically, i.e. not having information about the pathogen and its antibacterial sensitivity. In conditions of a decrease in the activity of almost all traditional ABD in the hospital, combined antibacterial therapy is prescribed with 2–3 drugs of different groups, or new drugs with the widest possible spectrum of action (for example, carbapenems) are used. In the treatment, the route of administration of ABD is of great importance. The effectiveness of systemic therapy can be improved by using intraarterial, intraosseous, or endolymphatic routes of administration of drugs.

Now, in general medical practice, the most optimal empirical schemes of antibacterial treatment of acute inflammations of infectious genesis have been developed, which can rightfully be used also in the MFA.

The antibiotic therapy algorithm can be represented as follows: the initial therapy is oral penicillins (amoxicillin, phenoxymethylpenicillin, etc.), CS I (cefalexin, cefazolin, cefadroxil, etc.) or CS II (cefuroxime axetil, cefaclor). On the day 2–3 of the treatment, the therapeutic effect is assessed and a conclusion is drawn on the effectiveness of the prescribed therapy. The lack of positive dynamics 72 hours after the start of antibiotic therapy indicates the need for correction of the treatment regimen. With the effectiveness of therapy, it is continued until the normalization of clinical and laboratory parameters.

Based on the results of microbiological monitoring, the following antibiotic therapy algorithms are proposed:

1) with the predominance of gram-positive cocci, it is necessary to use preparations of penicillins or cephalosporins of the first generation (cefazolin) or the second generation (cefuroxime, cefoxitin). Recently, glycopeptides (vancomycin, teicoplanin) and a representative of the new group of oxazolidinones – linezolid (an effective synthetic drug for resistant forms of staphylococci and other gram-positive microorganisms) are being used;

2) if gram-negative flora dominates, prescription of 3rd generation cephalosporins (cefotaxime, ceftriaxone, ceftazidime) or additional administration of AG (amikacin, netilmicin), FQ (ciprofloxacin, levofloxacin, gatifloxacin) is required;

3) for the clinical manifestations of the atypical course of diseases, modern macrolides (azithromycin, spiramycin, clarithromycin, roxithromycin) are used.

There are some features of rational antibiotic therapy of individual nosological forms of the MFA. For example, in the treatment of boils and carbuncles, systemic antibiotic therapy is indicated. In mild cases, phenoxymethylpenicillin, amoxicillin or macrolides are prescribed. With recurring boils, it is possible to prescribe bicillin continuously for 1–2 months or macrolides for 1 week every month.

Treatment of acute osteomyelitis, and especially its septic form with simultaneous damage to several bones, is effectively carried out with lincosamide antibiotics. The etiology of the disease is most often associated with Staphylococcus aureus, streptococcus and mixed infection, among which anaerobes are often bacteroides. The effectiveness of lincomycin

or clindamycin in the treatment of acute osteomyelitis is associated with their active influence on the above pathogens. The duration of treatment is 10–14 (21) days, and in chronic course – up to 2–3 months. To increase the effectiveness of the treatment of this nosological form, if necessary, combinations of clindamycin with other ABD (cloxacillin, cefazolin) are used. The combination of clindamycin with AG (amikacin) or FQ (ciprofloxacin) is especially effective. It is important to know that the combination of lincomycin with erythromycin or chloramphenicol is considered antagonistic.

The use of clindamycin is especially justified in cases of osteomyelitis of anaerobic origin. Clindamycin is the drug of choice in the treatment of osteomyelitis and septic arthritis. High efficacy and low toxicity of lincomycin and clindamycin are observed in the treatment of odontogenic infections (acute and chronic periodontitis in the acute stage, periodontal abscess, periodontitis) and damage to the skin, soft tissues and joints.

When using antibiotic therapy, it is important to remember the need for an individual approach to treatment. It should be noted that in elderly patients, the clinical manifestations of inflammatory diseases are often atypical, hypoergic, i.e. without severe clinical symptoms, often there is no fever. The composition of the microflora of both the oral cavity and the purulent-inflammatory foci in such patients differs from the composition of the microflora of young and mature people. In older people, more often than in young people, the pathogens of odontogenic and non-odontogenic infections are resistant to antibiotics. In old age, the risk of developing adverse reactions increases. The pharmacokinetic properties of drugs in such patients may vary due to concomitant diseases, the presence of impaired renal and hepatic function. Therefore, in order to ensure greater safety, prescription of antimicrobial agents enterally prevails in elderly patients or timely switching from the parenteral route of administration to the oral route is carried out for 48–72 hours (stepwise therapy). In such cases, they switch to the oral form of the same antibiotic or close to the spectrum of activity to parenteral.

For the practice of a dentist, it is important to know a number of well-known provisions of antibacterial therapy that are relevant for effective treatment. Recently, among the representatives of microflora, an increase in methicillin-resistant strains of S. aureus has been observed, which can

cause problems when using antibiotics. The arsenal of active antistaphylococcal drugs is limited to inhibitor-protected penicillins (amoxiclav, augmentin), cephalosporins (sulbactomax, sulperazone), glycopeptides (vancomycin), oxazolidinones (linezolid). In case of anaerobic infection, inhibitor-protected penicillins (amoxiclav, ampisulbin), clindamycin, metronidazole, ornidazole are effective. Third-generation CS are ineffective in relation to gram-positive forms; therefore, generation III–IV FQ are used. (levofloxacin, moxifloxacin) or III generation AG (amikacin). In case of detection of fungi in the pathological focus, it is recommended to add fluconazole to the antibiotics. Prescribing modern macrolides (clarithromycin) is recommended for children with a tendency to allergic reactions.

The reasons for the ineffectiveness of antibiotic therapy may be due to inaccuracies in diagnosis or defects in the conservative and surgical treatment that is carried out.

The first group of causes include:

- an infectious process caused by non-bacterial pathogens (viruses, fungi);
- inaccurate diagnosis of the disease (for example, sinusitis of odontogenic or non-odontogenic nature), which is important when prescribing empirical chemotherapy;
- undiagnosed immunodeficiency;
- inadequate choice of ABD (the pathogen is naturally resistant to it or the drug cannot penetrate into the organs or tissues where the focus of infection is located);
- the infection is only a complication of the underlying disease (neoplasm).

The second group of causes include:

- cases of pathogen resistance in vivo with satisfactory in vitro sensitivity;
- development of pathogen resistance during the course of therapy (for infections caused by gram-negative pathogens);
- underestimated single or daily dose;
- superinfection with drug-resistant pathogens.

An ideal option for antibiotic therapy is its appointment and monitoring by a chemotherapist. Unfortunately, this is possible only in a hospital or multidisciplinary association, and not in an outpatient dental service.

In the general treatment of acute inflammatory processes of the MFA drugs from various pharmacotherapeutic groups (GCS, NSAIDs, proteolytic enzyme inhibitors and enzymes, antioxidants, stimulators of reparative processes) are widely used.

It should be noted that immunostimulating therapy plays a particularly important role in the complex treatment of processes with a severe course and in debilitated patients. The use of IST simultaneously with ABD, especially in conditions of pathogen resistance in case of proven secondary immune deficiency (purulent-inflammatory processes or early after surgery), is one of the effective methods to increase the effectiveness of treatment, with an additional blow to the pathogen. The antibiotic suppresses the functional activity of the pathogen and increases its sensitivity to the killer-effect of the phagocyte, and IST significantly stimulates the functional activity of phagocytes and their ability to kill the pathogen. The rational use of drugs should be based on a preliminary examination of the patient's immune status. IST is widely used in diseases that are accompanied by changes in the body's immune system (phlegmon, abscess, carbunculosis, osteomyelitis), in delayed tissue regeneration, including the oral mucosa, in burns, radiation injuries, and in the postoperative state.

The general principles of the use of IST in the treatment of purulent-inflammatory processes are based on the following:

- early prescription – from the first day of the use of ABD, in case of incomplete recovery after an acute infectious disease or postoperative infectious complications;
- careful selection of immunomodulating drugs, determining their dose and treatment regimen, determining contraindications for administration and side effects;
- the use of IST acting on the phagocytic immunity unit (licopid, polyoxidonium, imudon, recombinant cytokines, echinacea preparations) in patients with both detected and undetected immune status disorders, i.e. based on the clinical picture;
- in order to use IST effectively and safely, it is advisable to carry out immunological monitoring.

Thus, at the present stage of development of surgical dentistry, rational treatment provides for the mandatory use of antibiotic therapy using all the rules and recommendations known at this stage of the develop-

ment of medicine. Refusal of antibiotic therapy is impossible, since there is no significant alternative to it now. But it should be borne in mind that modern generations of drugs cannot completely solve the problem of treating acute infections of the MFA, in connection with the development of resistant microflora to them.

Antibacterial therapy in surgical practice is based on the knowledge of the infectious causes of the disease and the severity of its clinical form. The knowledge of potential pathogens of surgical diseases helps to start empirical therapy, and to carry out its correction after bacteriological research, if necessary.

1.7.1. Odontogenic sinusitis

The main reason for the development of odontogenic sinusitis is the microflora of the periapical inflammatory focus in acute or chronic periodontitis of molars and premolars of the upper jaw. In addition, the infection can penetrate from the oral cavity during perforations of the maxillary sinus, as a result of trauma or surgery (tooth extraction, root apex resection). The causative agents of odontogenic sinusitis are: non-sporeforming anaerobic bacteria and microaerophiles – Prevotella intermedia, P. melaninogenica, Porphyromonas spp., Fusobacterium spp., Veillonella spp., Peptostreptococcus sacchococcus, etc. Microbial associations may include microorganisms of the nasal cavity: Staphylococcus aureus, Streptococcus spp.

Systemic antibacterial therapy is carried out in acute sinusitis, exacerbations of chronic sinusitis, before and after surgery of radical maxillary sinusitis.

1.7.2. Odontogenic abscess

In abscesses in adults, mixed flora stands out: Peptostreptococcus spp., Bacteroides spp., Enterobacteriaceae spp., Veillonella spp., Streptococcus spp., Staphylococcus spp., Eikenella spp. In children, Streptococcus spp., Staphylococcus spp. prevail. According to many authors, more than 80 % of species are obligate-anaerobic and microaerophilic in case of MFA abscesses.

With limited purulent-inflammatory diseases of the soft tissues – odontogenic abscesses, antibiotic chemotherapy is usually carried out

Table 2

Empirical antibiotic therapy for odontogenic maxillary sinusitis

Drugs of choice (parenteral)	Oral forms for step therapy (enteral)	Alternative drugs (parenteral)	Oral forms for step therapy (enteral)
Amoxicillin / clavulanate 1 g 3 times a day i.v.	Amoxicillin / clavulanate 500 mg 3 times a day	Cefuroxime 750–1500 mg 3 times aday i.v. or i.m.	Cefuroxime 500 mg 2 times a day
Clindamycin 300 mg 2 times a day i.m.	Clindamycin 150 mg 4 times a day	Ciprofloxacin 0.2 g 2 times a day i.v.	Ciprofloxacin 750 mg 2 times a day
Lincomycin 0.5–0.6 g 2 times a day i.m.	Lincomycin 1 g 2 times a day	Clarithromycin 500 mg i.v. once a day (2–3 days)	Clarithromycin 250 mg 2 times a day
Erythromycin 500 mg 4 times a day i.m. in combination with metronidazole 200–250 mg 3 times a day enteral	Erythromycin 500 mg 4 times a day in combination with metro-nidazole 200–250 mg 3 times a day	Rifamycin 500 mg 2 times a day i.m.	
Oxacillin 1 g 4 times a day, i.m. 2–3 days in combination with metronidazole 200–250 mg 3 times a day enteral	Oxacillin 1 g 4 times a day in combination with metronidazole 200–250 mg 3 times a day	Doxycycline 0.1 g 2 times a day 1 day i.m. and then 0.1 g 1 time per day	As an alternative to metronidazole, tinidazole on the 1st day 1 g 1 time per day, then 500 mg 1 time per day. Ornidazole 500 mg 2 times a day. Nitazole 250 mg 2 times a day
Chemotherapy duration – 7–10 days			

with oral antibiotics. In patients at risk who have defects of the immune system (against diabetes mellitus, after chemo- or radiotherapy, etc.), as well as in cases of threatening localization of an abscess (abscess of the eye fossa, infratemporal, palatine fossa, etc.).p.), it is advisable to carry out stepwise chemotherapy.

Table 3

Empirical antibiotic therapy for odontogenic abscess

Drugs of choice (parenteral)	Oral forms for step therapy (enteral)	Alternative drugs (parenteral)	Oral forms for step therapy (enteral)
Ampicillin 0.5 g 4 times a day enteral in combination with tinidazole 200–250 mg 3 times a day		Clindamycin 150 mg 4 times a day	
Erythromycin 500 mg 4 times a day orally in combination with metronidazole 500 mg 3 times a day		Lincomycin 1 g 2 times a day	
Clarithromycin 500 mg 2 times a day			
Roxithromycin 150 mg 2 times a day			
Risk group			
Lincomycin 0.5–0.6 g 2 times a day i.m.	Lincomycin 1 g 2 times a day	Clindamycin 300 mg 2 times a day i.m.	Clindamycin 150 mg 4 times a day
Erythromycin 500 mg 4 times a day i.m. in combination with metronidazole 500 mg 3 times a day orally 2–3 days	Erythromycin 500 mg 4 times a day in combination with metronidazole 200–250 mg 3 times a day	Clarithromycin 500 mg i.v. once a day (2–3 days)	Clarithromycin 250 mg 2 times a day
Oxacillin 1 g 4 times a day i.m. for 2–3 days in combination with metronidazole 200–250 mg 3 times a day	Oxacillin 1 g 4 times a day in combination with metronidazole 200–250 mg 3 times a day		

1.7.3. Periostitis and osteomyelitis

With the development of odontogenic periostitis and osteomyelitis, anaerobic flora prevails: P. niger, Peptostreptococcus spp., Bacteroi-

des spp., Microaerophilic streptococci. Staphylococcus aureus, Streptococcu pyogenes, and also Streptococcus spp. In chronic odontogenic osteomyelitis, anaerobic Actinomyces israelii, A. naeslundii, A. viscosus and

Table 4

Empirical antibacterial chemotherapy for osteomyelitis of the jaws

Drugs of choice (parenteral)	Oral forms for step therapy (enteral)	Alternative (reserve) drugs (parenteral)	Oral forms for step therapy (enteral)
Oxacillin 1 g 4 times a day, i.m. 2–3 days in combination with metronidazole 200–250 mg 3 times a day. As an alternative to metronidazole – enteral tinidazole 1000 mg once a day, then 500 mg once a day. Ornidazole 500 ml 2 times a day. Nitazole 250 mg 2 times a day	Oxacillin 1 g 4 times a day in combination with metronidazole 200–250 mg 3 times a day	Clindamycin 300 mg 2 times a day i.m.	Clindamycin 150 mg 4 times a day
Amoxicillin / clavulanate 1 (1.2) g 3 times a day i.v. (3–5 days depending on severity)	Amoxicillin / clavulanate 500 (625) mg 3 times a day	Clarithromycin 500 mg i.m. once a day (2–3 days)	Clarithromycin 250 mg 2 times a day or roxythromycin 150 mg 2 times a day
		Lincomycin 0.5–0.6 g 2 times a day i.m.	Lincomycin 0.6–1.2 g 2 times a day
		Fusidin 1000 mg 3 times a day for the first 2 days	Fusidin 500 mg 3 times a day
		Cefuroxime 750–1500 mg 3 times a day i.v. or i.m.	Cefuroxime 500 mg 2 times a day
Therapy duration: 2–4 weeks			

Agachnia propionica (Propionibacterium) and the so-called aerobic actinomycetes R. dentocariosae, B. matruchotii (Corinebacterium) are often found (up to 25–30 % of cases), spp.

Traumatic osteomyelitis, which develops after fractures within the dentition, is more often caused by microflora of the oral cavity; the nature of microflora differs little from odontogenic.

The tactics of antimicrobial chemotherapy for periostitis corresponds to that of a odontogenic abscess. When choosing drugs for the treatment of osteomyelitis, especially chronic (including actinomycotic), one should take into account the high probability of the formation of antibiotic-resistant strains, since such patients, as a rule, have already received various antibiotics for a long time.

The drugs of choice are: imidazoles (metronidazole, ornidazole), lincosamides (lincomycin, clindamycin), amoxicillin/clavulanate, macrolides (roxithromycin, clarithromycin); reserve – CS (cefazolin, cefoxitin), tetracycline, ciprofloxacin. Alternative drugs: lincosamides, cefuroxime, clarithromycin. When P. aeruginosa is excreted, antiseptic drugs (azlocillin, ceftazidime, amikacin, ciprofloxacin) are used. It is advisable to combine the systemic administration of drugs with local antibacterial treatment.

1.7.4. Odontogenic phlegmon of the head and neck

In case of odontogenic phlegmon (fasciitis according to the foreign nomenclature), mixed flora is distinguished in adults: Peptostreptococcus spp., Bacteroides spp., Fusobacterium spp., Veillonella spp., Enterobacteriaceae spp., Streptococcus spp., Staphylococcus spp. In children – Peptostreptococcus spp., Streptococcus spp., Staphylococcus spp. According to many authors, obligate-anaerobic and microaerophilic species account for more than 75 % of phlegmon. With putrid necrotic phlegmon of the bottom of the oral cavity, a polymicrobial flora is released, including Fusobacterium spp., Bacteroides spp., Peptostreptococcus spp., Streptococcus spp., Clostridium spp., Actinomyces spp., Propionibacterium spp. The latter prevail in traumatic, especially gunshot wounds, in association with peptostreptococci.

In addition to these species, in patients with severe course, gram-negative enterobacteria, Pseudomonas aeruginosa and S. aureus (more often in patients with diabetes mellitus and alcoholism) can be isolated.

Taking into account that patients with odontogenic phlegmon are hospitalized in the maxillofacial hospitals, it is advisable for them to carry out stepwise antimicrobial chemotherapy.

In more complex cases of the disease, it is advisable to use the most effective groups of drugs (CS, FQ, glycopeptides, etc.).

1.7.5. Lymphadenitis, adenophlegmon of the head and neck

The source of infection of the lymph nodes with the subsequent development of inflammation can be various organs of the head region. Depending on the primary focus, the composition of the microflora is different. Regional bacterial damage to the lymphatic apparatus can be result

Table 5

Empirical antibiotic therapy for adenophlegmon

Drugs of choice (parenteral)	Oral forms for step therapy (enteral)	Alternative drugs (parenteral)	Oral forms for step therapy (enteral)
Odontogenic, tonsillogenous and dentogenous			
Lincomycin 0.5–0.6 g 2 times a day i.m.	Lincomycin 0.6–1.2 g 2 times a day	Clindamycin 300 mg 2 times a day i.m.	Clindamycin 150 mg 4 times a day
Erythromycin 500 mg 4 times a day i.m. in combination with metronidazole 500 mg 3 times a day, 2–3 days	Erythromycin 500 mg 4 times a day in combination with metronidazole 200–250 mg 3 times a day	Clarithromycin 500 mg i.v. once a day (2–3 days)	Clarithromycin 250 mg 2 times a day
Non-dontogenic			
Amoxicillin / clavulanate 1 g 3 times a day i.v.	Amoxicillin / clavulanate 500 mg 3 times a day	Clindamycin 300 mg 2 times a day i.v. or i.m.	Clindamycin 150 mg 4 times a day
Cefuroxime 750–1500 mg a day i.v. or i.m.	Cefuroxime 500 mg 2 times a day		
Oxacillin 1 g 4 times a day	Oxacillin 1 g 4 times a day		

Table 6

Antibacterial chemotherapy for lymphadenitis

Drugs of choice	Oral forms for step therapy (enteral)
Odontogenic, tonsillogenous and dentogenous (serous). Risk group. The threat of abscess formation	
Amoxicillin/clavulanate enteral 500 mg 3 times a day enteral	Clindamycin 150 mg 4 times a day enteral
Lincomycin 500 mg 2 times a day enteral	
Odontogenic, tonsillogenous and dentogenous (purulent)	
Amoxicillin/clavulanate 500 mg a day enteral	Doxycycline 100 mg 2 times a day enteral, in combination with metronidazole 200–250 mg 3 times a day enteral
Oxacillin 1 g 4 times a day in combination with metronidazole 200–250 mg 3 times a day enteral	Ciprofloxacin 750 mg 2 times a day enteral. Alternative to metronidazole – tinidazole on the 1st day, 1000 mg once a day, then 500 mg once a day enteral. Ornidazole 500 mg 2 times a day enteral. Nitazole – 250 mg 2 times a day enteral
Lincomycin 1000 mg 2 times a day enteral	Clindamycin 150 mg 4 times a day enteral
Non-dontogenic (serous). Risk group. The threat of abscess formation	
Ampicillin 500 mg 4 times a day enteral	Amoxicillin/clavulanate 500 mg 3 times a day enteral
Amoxicillin 500 mg 3 times a day	Clindamycin 150 mg 4 times a day enteral
With intolerance to β-lactams: lincomycin 500 mg 2 times a day, 8 days	Fusidin-sodium 500 mg 3 times a day enteral
Non-dontogenic (purulent)	
Amoxicillin/clavulanate 500 mg 3 times a day	Cefuroxime 500 mg 2 times a day
Cephalexin 250 mg 4 times a day enteral	Clindamycin 150 mg 4 times a day
With intolerance to β-lactams: lincomycin 750–1000 mg 2 times a day	Ciprofloxacin 750 mg 2 times a day
	Levofloxacin 400 mg once a day
	Fusidin 500 mg 3 times a day

of tonsillitis, periodontitis and its complications, damage to the maxillary sinuses, salivary glands, periodontium, oral mucosa, damage to the outer and middle ear, face and scalp, etc. In general, lesions of the lymph nodes can be divided into: odontogenic, tonsillogenous and dentogenous, non-odontogenic.

Lesions of the lymph nodes are distinguished from other odontogenic and non-odontogenic inflammatory diseases of soft tissues by a scanty species composition of microflora and its smaller amount in exudate.

1.7.6. Furuncle, carbuncle

Taking into account the high potential for the spread of infection through the intercellular spaces and veins of the face into the cranial cavity in case of boils and carbuncles, systemic antibiotic therapy is mandatory for all patients. The causative agents of the boil or carbuncle of the face are Streptococcus spp., Staphylococcus spp. (S. aureus, S. pyogenes), as isolated cases, Actinomyces spp.

The drugs of choice are cloxacillin, fluxloxacilin, CS. Lincosamides, macrolides are prescribed in case of allergies to β-lactams.

Table 7

Empirical antibacterial chemotherapy for furuncle, carbuncle

Drugs of choice (parenteral)	Oral forms for step therapy (enteral)	Alternative drugs (parenteral)	Oral forms for step therapy (enteral)
Severe and moderate course (duration depends on severity)			
Amoxicillin / clavulanate 1 g 3 times a day i.v.	Amoxicillin / clavulanate 500 mg 3 times a day	Intolerance to β-lactams – clindamycin 300 mg 2 times a day i.v. or i.m.	Clindamycin 150 mg 4 times a day
Cefuroxime 750–1500 mg 3 times a day i.v. or i.m.	Cefuroxime 500 mg 2 times a day	Clarithromycin 500 mg i.v. once a day (no more than 5 days)	Clarithromycin 250 mg 2 times a day
Cefotaxime i.m. 1 g 3 times a day, i.v. or i.m.	Cefixime 200 mg 2 times a day		Fusidin 500 mg 3 times a day

Drugs of choice (parenteral)	Oral forms for step therapy (enteral)	Alternative drugs (parenteral)	Oral forms for step therapy (enteral)
Ciprofloxacin 400–600 mg 2 times a day i.v.	Ciprofloxacin 750 mg 2 times a day		
Mild clinical course			
Oxacillin 1 g 4 times a day i.m.	Oxacillin 1 g 4 times a day	Clarithromycin 500 mg i.v. once a day	Clarithromycin 250 mg 2 times a day
			Clindamycin 150 mg 4 times a day

1.8

LOCAL MEDICINAL TREATMENT OF WOUND INFECTIONS

For the treatment of purulent wounds, more than 2.000 different substances have been proposed. However, not all of them meet the requirements that are now being put forward drugs for local treatment of purulent-inflammatory processes. The most common is the method of treating a wound under a dressing, which has a significant advantage, since it provides a higher concentration of drugs in the focus of infection.

The state of the wound healing process is often assessed according to three main local criteria:

- type of microbial pathogen and its sensitivity to ABD;
- phase of the wound healing process;
- quality of the radically performed surgical treatment of the purulent foci.

Today, local pathogenetic therapy of purulent wounds in the first phase of the wound process is as follows: relief of pain, inhibition of microflora and stimulation of the immune system, activation of rejection of necrotic tissues and adsorption of toxic wound secretions, normalization of local homeostasis (elimination of acidosis, excessive proteolysis).

In the second phase of the wound healing process, the main principles of treatment are as follows: careful treatment of the wound; ensuring protection of the wound from secondary infection with simultaneous inhibition of "residual" microflora in it; stimulation of reparative processes in the wound; prevention of keloid scar formation.

Local drug treatment of wounds in the third phase of the wound process is carried out according to principles similar to the treatment of wounds in the granulation phase. In the treatment of wounds during this period, there are methods that stimulate the processes of resorption of scar tissue and contribute to the formation of soft scars. To resolve the ke-

loid scar that has formed, biogenic stimulants or physiotherapeutic procedures (mud, phonophoresis, electrophoresis) and corticosteroids are used.

Thus, in the complex local treatment of purulent wounds, many drugs of various pharmacotherapeutic groups can be used: GCS, ABD, enzymes, dehydrating (hyperosmolar) drugs, hydrophobic and hydrophilic draining sorbents (carbon, polyurethane, polymethylsiloxane, etc.), drugs that improve microcirculation, NSAIDs, proteolytic enzyme inhibitors, antioxidants, local hemostatic agents, stimulants of reparative processes.

Traditionally, for complex treatment, the introduction of two groups of drugs into the body is used: antibiotics and antiseptics, the effective concentration of which is provided by the dose and method of administration. The most effective means for the range of dilution and spectrum of action is chlorhexidine. NSAIDs increase the specific activity of ABD and decrease the levels of formation of microorganism resistance to them. Probiotics are used to normalize the composition of the microflora of ecological niches of the body. It is advisable to use drugs with immunostimulating effect and anti-inflammatory properties. As immunocorrections in the complex treatment of patients, in addition to modern IST (licopid, polyoxidonium, immunofan, cycloferon, etc.), local and general ozone therapy, low-frequency ultrasound and hyperbaric oxygenation are used. Recently, non-pharmacological agents and techniques (fetal tissues and cellular elements of the placenta, etc.) are more often used. The natural biopolymer of chitosan (from the shells of sea fish) with a pronounced wound healing effect contributes to an increase in the level of lysozyme in saliva.

To overcome the intoxication syndrome and for anti-inflammatory effect in maxillofacial surgery, modern NSAIDs are widely used (diclofenac, aceclofenac, meloxicam, celecoxib), isolated use of oxidized autoblood, hyaluronic acid-based drug – curiosin, ozone, propolis soft extract, biologically active film, the components of which are methyluracil, hydroxyapatite, ciprofloxacin, metronidazole, etc.

Comprehensive measures have been developed aimed at optimizing the local effect on a purulent wound. For cleaning the local purulent focus, various types of draining sorbents and biologically active compositions based on them are used with efficiency. The use of sorbents contributes to a stable draining effect, reduction of pain in the wound, etc. Sorbents with drugs immobilized on their surface are of great interest. Imosgent is

the brightest representative. Draining sorbents and water-absorbing multifunctional sponges share a common specific quality – pronounced sorption activity. So, teralgin (contains proteolytic enzyme terrilytin), algimaf (contains an antibacterial substance and antioxidant) provide not only a dehydrating effect, but also inhibit the growth of microflora, and have a necrolytic effect.

In the case of infectious complications, along with surgical intervention and systemic therapy, an important role is given to local drug treatment of wounds. This method has significant advantages in connection with the direct impact on the focus of infection. There is a wide selection of drugs that differ in a number of effects: antimicrobial, anti-inflammatory, sorption, wound healing.

Wound treatment should be based on the pharmacological characteristics of the drugs (properties of the active substance, its dosage form, sorption characteristics, etc.), the ability to use differentially both individual drugs, and modern regimens using fundamentally new combined substances. Characteristics of drugs for local treatment of wounds:

1) monopreparations on a fat basis of antimicrobial, wound healing action. These include streptocid, gentamicin, erythromycin, furacilin, methyluracil ointment, synthomycin liniment, etc. These drugs have unidirectional antimicrobial action, slow release of active ingredients, impaired outflow of wound contents and wound sealing. The use of drugs of this group is impractical in the first phase of the wound healing process, which is characterized by a high microbial load and tissue hyperhydration;

2) monopreparations on synthetic hydrophilic water-soluble bases (levomycetin-Darnitsa gel). This group is characterized by the strengthening and potentiation of therapeutic antimicrobial, anti-inflammatory, osmolar action;

3) combination preparations on a fat basis (vaseline, lanolin, oily or balsamic) – algofin ointment, fastin-1 ointment, Vishnevsky's balsamic liniment, etc.;

4) preparations on synthetic bases. The 1st generation includes ointments based on the combination of polyethylene oxide – levomecol and levosin), the 2nd generation includes modern preparations based on improved water-soluble synthetic bases in the composition of propylene glycol, proxanol and polyethylene oxide-400 (dioxizol-Darnitsa solution,

ointments oflokain-Darnitsa, nitacid-Darnitsa, miramistin-Darnitsa, streptonitol-Darnitsa, methyluracil with miramistin, pantestin-Darnitsa gel).

These drugs have a complex effect on the main links of the pathogenesis of the wound process. They regulate the intensity and direction of the diffusion process in the case of their applications on the wound. An osmotic balance sets quickly in between the preparation and the damaged tissue, thus facilitating the penetration of the active substance of the preparation into the deep tissues, prevents their dehydration in various phases of the process and contributes to the effective absorption of wound contents base. Modern multicomponent preparations based on a hydrophilic water-soluble base have low toxicity and pronounced osmotic properties. They are well applied to the wound surface, evenly distributed on it, characterized by slow diffusion into the cells. Molecules of polyethylene oxide-400 penetrate deep into the tissues; create complexes with antimicrobial compounds, reaching the main localization sites of microbes. Drugs also exhibit necrolytic effects. Other components – 1,2-propylene glycol and proxanol-268 – provide a more uniform, long-lasting absorption, create an osmotic balance between the cell cytoplasm and the drug.

Taking into account the phase nature of the wound process, accompanied by certain clinical, functional and morphological changes for effective treatment, drugs should be carefully selected due to dynamics.

So, in the first phase of the wound healing process (purulent-necrotic), drugs with a wide spectrum of antimicrobial action (due to the polymorphism of bacteria and their polyresistance to many antibiotics), anti-inflammatory properties, the ability to absorb wound exudate, and good penetration into the wound cavity should be prescribed.

In the purulent-necrotic phase due to the presence of pain, necrotic tissue and purulent exudate, severe infiltration, significant bacterial contamination, it is advisable to use drugs of a combined composition that can affect all of the listed components of the wound process. The use of drugs on modern hydrophilic bases is recommended (dioxizol-Darnitsa solution or oflokain-Darnitsa ointment). These drugs, due to the introduction of 6 % lidocaine and a polymer hydrophilic base, relieve pain within 24 hours and at the same time preserve analgesic activity in the acidic environment of a purulent wound. Dioxizol-Darnitsa solution with dioxi-

dine also affects effectively gram-negative microorganisms of the Enterobacteriaceae family and the genus Pseudomonas, important pathogens of severe surgical infections. The duration of the action of dioxizol-Darnitsa is three times longer than of dioxidine. The use of this drug (1 time a day) is advisable if it is not possible to conduct a full-fledged revision of a purulent wound with localization of the process in the field of neurovascular bundles, articular bags, etc. The total amount of solution for topical application in case of introduction into the cavity is 50–60 ml (not more than 100 ml). The dressing with the drug does not dry out the wound and does not adhere to it, while most traditional aqueous or alcohol solutions (fucorcin, etericide) do not meet modern requirements because of their unidirectional antimicrobial effect and the absence of an osmolar and analgesic effect.

Oflokain-Darnitsa ointment is indicated in case of moderate pain syndrome against the background of powerful tissue infiltration and severe purulent exudation. Due to the content of ofloxacin, the drug has a wide range of bactericidal effects, in particular on aerobic gram-negative microflora (especially hospital strains with polyresistance to ABD), intracellular microorganisms and microbial associations. Also, lidocaine (3 %) was introduced into its composition.

It should be cautioned in modern surgery that the use of drugs on fatty lanolin-vaseline or emulsion bases (algofin, fastin-1, etc.) with purulent exudation is undesirable, since the vaseline basis has an occlusive effect, and the emulsion basis does not provide a hyperosmolar effect and is not able to absorb purulent exudate.

Levomecol has certain restrictions due to its unbalanced base with predominantly unidirectional diffusion (from the wound to the ointment). The latter can lead to excessive dehydration, overdrying of unaffected tissues, impaired barrier function of cell membranes and the rapid penetration of microbial substances into the systemic circulation. In addition, to chloramphenicol, which is a part of levomecol, there is a high resistance of the main causative agents of surgical infection (70–100 %).

Thus, an important link in the pathogenesis of the wound process in the first 4 days is a pronounced tissue hyperhydration, which in face of inadequate therapeutic tactics can lead to aggravation of tissue trophic disorders with the subsequent development of necrosis. The use of

combined preparations on hydrophilic synthetic base (dioxisol-Darnitsa solution or oflokain-Darnitsa ointment), which exhibit a powerful and long-lasting dehydration effect during the day, will be advisable during this period.

Modern drugs based on advanced principles – nitacid-Darnitsa and miramistin-Darnitsa ointments stop wound and perifocal inflammations very quickly because they absorb purulent exudate and selectively dehydrate the necrotic tissues. They have a pronounced and prolonged hyperosmolar effect (absorbing up to 600 % of the fluid during the day), do not have a damaging effect on viable cells. The optimal combination of nitazole (2.5 %) and streptocide (5.0 %), which are part of nitacid-Darnitsa ointment, allows to consider it the last drug of choice for topical treatment of non-clostridial anaerobic infections (peptococci, peptostreptococci) in associations with aerobes and optional anaerobes (staphylococcus, E. coli, etc.). Due to its properties, the drug should replace low-effective ointments like streptocid, which also exhibit a very limited effect on the microflora. Miramistin-Darnitsa, containing the modern cationic antiseptic miramistin, is indicated for patients with mixed bacterial, fungal and viral infections. It can be indispensable in case of severe and long-lasting purulent-inflammatory wound processes (especially in debilitated patients), as well as with a violation of the body's resistance, etc.

The differentiated use of modern combined preparations dioxizol-Darnitsa or oflokain-Darnitsa provides etiotropic therapy and rapid relief of pain within 1–4 days of treatment, which allows to regulate the use of analgesics and antibiotics. After stopping pain in the exudation subphase, it is advisable to use nitacid-Darnitsa or miramistin-Darnitsa. Knowing the pharmacological properties of modern local drugs provide an opportunity to conduct a differentiated approach to their choice in a dental clinic. At the same time, the time for improving the general condition and laboratory parameters is reduced by 2–5 days, the effectiveness of antimicrobial treatment, the elimination of perifocal edema and tissue infiltration are significantly increased.

In the transition period of the wound process in a state of cleansing the wound from purulent-necrotic contents and reducing microbial contamination, a situation arises when purulent exudation continues or the wound is filled with granulations.

The main tasks of local treatment during this period: a) providing moderate osmotic activity to prevent damage to granulation tissue; b) antimicrobial effects to prevent secondary suppuration; c) inhibition of the activity of proteolytic enzymes; d) maintaining the viability of the damaged tissue; e) immunomodulatory effect; f) creating conditions for a quick transition to the second phase of the wound healing process, etc.

At this time, it is advisable to use streptonitol-Darnitsa, which has moderate osmotic activity (removes excess fluid), which contributes to the complete cleansing of the wound from purulent necrotic residues without damage granulation and a quick transition to the 2nd phase of the wound healing process. Treatment should begin after opening the phlegmon and abscesses.

The second phase of the wound process is characterized by a significant suppression of microflora virulence, extinction of the inflammatory reaction, purification of the wound from purulent-necrotic contents, the appearance of granulation tissue, etc. Surgical closure of wounds (autodermoplasty, etc.) is indicated in the case of large wounds. This timely operation reduces the time of wound healing, improves treatment results.

The main requirements for drugs that need to be applied: reliable protection of granulation tissue from mechanical damage and drying, prevention of secondary infection of the wound, especially with hospital strains of pathogenic microorganisms, moderate drying effect, directed stimulation of reparative processes in the wound, etc. At this phase of the wound process, drugs on hydrophobic, mainly vaseline-lanolin (Vishnevsky's balsamic liniment) or unbalanced synthetic-based (Mefenat ointment) are unreasonably used. The above preparations do not meet modern requirements for optimal wound healing in the second phase of the wound process, since they do not have a bactericidal effect to prevent possible secondary infection, suppress vegetative microflora, and do not have a moderate drying effect.

It is advisable at this time to prescribe the combined preparation – methyluracil with miramistin, which contains cationic methyluracil and synthetic miramistin. This allows to suppress effectively the possible occurrence of foci of purulent inflammation, to ensure adequate release of drugs, strengthen antimicrobial, reparative and have immunomodulating effects. The combined therapeutic effect and high efficiency significantly

distinguishes the preparation methyluracil with miramistin from methyluracil ointment (10 %) on vaseline-lanolin base and allows to reduce the filling time of the wound defect with granulation tissue by almost 1.5–2 times.

The treatment of wounds in the 3rd phase (epithelization and reorganization of the scar) is carried out according to the principles that are largely common with the previous phase: a) necessary effective protection of granulation tissue from the effects of negative factors (mechanical injury, drying, etc.); b) prevention of secondary infection of the wound; c) regulation of reparative processes in the wound with the provision of prevention of the formation of keloid scars. In general, drugs based on dexpanthenol meet these requirements. The latter provides optimization of the regenerative processes of the lesion site with an ordered arrangement of collagen fibers and the formation of the epithelial layer with clear differentiation.

The use of drugs that stimulate the processes of epithelization is especially advisable in the treatment of wound processes with a torpid course (radiation and trophic ulcers in patients with diabetic angiopathy, with burn wounds, patients with significant suppression of immunity). Taking into account the wide range of antimicrobial effects, the use of pantestin-Darnitsa has certain advantages. It is advisable to use it for prevention and treatment of infectious complications in the final phases of the wound process, in cases of rapid maturation of granulation tissue with a violation of the collagen formation process, for the prevention of hypertrophic and keloid scars formation.

Thus, the treatment of wounds requires consistent pathogenetically substantiated use of drugs for topical treatment of wounds, especially combined on modern synthetic hydrophilic bases with improved properties:

- phase I – dioxizol-Darnitsa solution (based on dioxidine and lidocaine) or oflokain-Darnitsa ointment (based on ofloxacin and lidocaine);
- phase II – a preparation based on methyluracil with miramistin;
- phase III – pantestin-Darnitsa (based on dexpanthenol).

Rational local treatment of wounds is an important component of the complex treatment of surgical infection and helps to increase its effectiveness and reduce the duration.

Section 2

PHARMACOTHERAPY OF EMERGENCY CONDITIONS

Knowing the action algorithm for emergency care is necessary for doctors of all specialties, including a dental clinic. The relevance of emergency care is dedicated to the reception of dental patients. First of all, this is a strong psycho-emotional tension of the patient, which leads to increased sensitivity and reactions from the nervous system and HPAS, which often occurs against the background of concomitant pathology. The need for adequate analgesia during surgical interventions and the features of the reflexogenic picture and blood supply of the MFA are characterized by the severity and torpidity of possible adverse reactions when using anesthesia.

This section discusses urgent conditions encountered in the practice of a dentist very often (acute injuries, circulatory disorders, breathing, central nervous system functions, endocrine system, complications of drug treatment, etc.). Most of other acute emergency conditions and their pharmacotherapy are presented in sections 1.1. "Anesthesia in dentistry" and 1.7. "Antibacterial therapy of acute inflammatory processes of the maxillofacial section".

2.1
ACUTE DISORDERS OF BLOOD CIRCULATION

Acute circulatory failure occurs in the event of a mismatch between the metabolic need of the body's cells and blood flow to them. It is the leading syndrome of many pathological conditions (stress, bleeding, trauma, burns, infection, intoxication, allergies, etc.). Depending on the severity and duration of CVS disorders, the patient may develop fainting, collapse or shock.

2.1.1. Faint

Faint is a short-term loss of consciousness that occurs in acute circulatory failure, in which there is cerebral ischemia. It can develop against the background of disturbances in the blood supply to the brain. Stress, pregnancy, vitamin deficiency, overwork.

Among the causes of fainting, one can also name the patient's fear of dental manipulation, which results in expectations regarding the doctor' prescription, the use of antihypertensive drugs, and pain during the administration of anesthetics or a toxic reaction to them.

Fainting can be mild or severe. The main signs of it are the lack of consciousness and active movements. The lack of consciousness at the same time lasts from one to several minutes. Pallor of the skin, a decrease in muscle tone, dilated pupils, a decrease in the conjunctive reflex, cold, sticky sweat, collapse of the veins of the neck, and relaxation of skeletal muscles are typical. The pulse is weak, slowed down to 50 or less beats per minute. The breath is shallow. Arterial systolic pressure is reduced. Deterioration can be manifested by a filiform pulse and a further decrease in blood pressure (up to 50–60 mmHg). Seizures are sometimes observed. Emergency care for faint includes the following steps:

1) giving the patient a horizontal position, providing access to fresh air;

2) an immediate stop of anesthetic;

3) stimulating breathing – the use of 10 % ammonia solution, which is moistened with a cotton swab (put to the nose, rub temples);

4) in more complicated cases – the introduction of 1–2 ml cordiamine, 1 ml of 10 % sodium benzoate solution s.c.;

5) if there is an effect with severe intoxication – the use of 1 ml of 5 % ephedrine solution s.c., 1 % thiopental sodium solution or 1 ml of 1 % mesatone solution s.c.;

6) in case of bradycardia – the introduction of 1 ml of 0.1 % atropine sulfate solution s.c.

When conducting dental interventions, it is necessary to conduct psychological and pharmacological preparation of patients with labile state. To do this, conduct a soothing conversation and an explanation regarding the safety of the intervention, apply sedation. For exhausted patients, it is advisable to drink a glass of sweet tea before the intervention.

2.1.2. Collapse

Collapse is the result of more severe circulatory disorders. The decrease in vascular tone that occurs during collapse leads to a decrease in blood flow to the heart, in cardiac output, and in blood supply to the brain. More often, collapse occurs against the background of cardiovascular disease, diabetes mellitus, adrenal insufficiency.

This condition manifests itself as pallor of the skin, expressed by general weakness, profuse cold sweat, prolonged decrease in blood pressure in diastole to 40 mmHg and below. The patient's facial features are sharpened, the consciousness is suppressed, and he does not respond to external stimuli, the pulse becomes threadlike. Deterioration can lead to toxic shock and death. Collapse can occur when using local anesthetics, ganglionic blockers, sympatholytics, antipsychotics, barbiturates. Providing emergency care for collapse includes the following measures:

- giving the patient a horizontal position;
- cessation of administration or use of drugs that caused collapse;
- the introduction of agents that increase vascular tone (0.2–0.3 ml of 1 % mesatone solution i.v. or s.c.; 0.2 % norepinephrine hydrotar-

trate solution per 250 ml of 5 % glucose solution i.v. dropwise, 1 ml of cordiamine s.c. or i.m.; 1–2 ml of 10 % caffeine-sodium benzoate solution i.m. or i.v.);
- prescription of GCS (hydrocortisone – 3–5 mg/kg, prednisolone – 0.5–1 mg/kg);
- in case of severe bradycardia – the introduction of 0.5–1 ml of 0.1 % atropine sulfate solution;
- introduction of 1 ml of 0.06 % corglycon solution per 20 ml of 40 % glucose solution i.v.;
- detoxification therapy.

If necessary, call an ambulance for hospitalization.

To prevent the development of collapse in a dental clinic, patients should monitor blood pressure. With low blood pressure (systolic – for men 110 mmHg, for women – 100 mmHg, diastolic – below 65 mmHg), it is advisable to correct it and be fully prepared to provide emergency care.

2.1.3. Shock

Shock is the most severe form of acute circulatory failure, which occurs due to the action of extreme factors on the body. It is characterized by a violation and extinction of all vital functions: hemodynamics, respiration, homeostasis, etc. In dental practice, the following types of shock can occur: traumatic, toxico-infectious, hemorrhagic, etc.

Hemorrhagic shock is the most serious complication of volume bleeding that can occur with lesions of the MFA and neck. Hemorrhagic shock is based on blood loss, which exceeds 25–30 % of CBV. The injuries to the great vessels – the facial artery and veins, branches of the external carotid artery and jugular vein are of particular danger. Damage to large vessels often leads to the development of shock, which is a crisis of microcirculation and the inability to ensure adequate oxygen consumption in tissues and the removal of toxic substances. Blood loss causes circulatory disorders, a marked decrease in blood pressure, an increase in hypoxia, acidosis, impaired water-electrolyte balance, impaired kidney function, etc.

The clinical picture of hemorrhagic shock is characterized by general inhibition, inadequate reactions, severe pallor of the skin, thirst, impaired consciousness, cold, sticky sweat, hypotension, tachycardia, hypothermia, hyporeflexia. Venous pressure decreases, and superficial veins decline.

Based on the pathogenetic prerequisites, providing emergency care for hemorrhagic shock provides for the following main measures:

- an immediate stop of bleeding (if necessary – surgical hemostasis as soon as possible);
- ensuring airway patency and eliminating hypoxia (mechanical ventilation, oxygen inhalation, etc.);
- infusion therapy (transfusion of plasma, whole blood or blood substitutes, albumin, glucose or physiological solution);
- elimination of pain (1–2 ml of 1 % morphine hydrochloride solution or 1–2 ml of 1–2 % promedol solution or 2–4 ml of 50 % dipyrone solution i.v. slowly or 3–6 ml of 2.5 % diclofenac sodium solution i.v. dropwise or i.m.), tranquilizers, antipsychotics, antihistamines are used to potentiate analgesia;
- introduction of 2 % novocaine or trimecaine solution (up to 20 ml) in the fracture or hematoma site;
- correction of hemodynamic disorders by the introduction of large doses of corticosteroids (prednisolone – up to 200–300 mg, dexamethasone – up to 30–40 mg);
- if inefficient, the use of mesatone, ephedrine, etc.;
- introduction of 2.0 ml of 12.5 % dicynone solution i.v. or i.m., 10.0 ml of 5 % amben solution or 100 ml of 5 % ε-aminocaproic acid solution i.v.

Emergency hospitalization in the Trendelenburg position in a specialized hospital or intensive care unit.

2.2
ALLERGIC REACTIONS

In dental practice, the doctor often encounters general allergic reactions of the body caused by side effects of drugs and composite materials. They can be manifested by angioedema of the tissues of the oral cavity, face and AS.

2.2.1. Angioedema

Angioedema (angioneurotic edema, Quincke's edema) develops when exposed to various allergens (food, household, medicinal, etc.), quickly and without precursors. In dentistry, quite often the cause of this allergic reaction may be the introduction of an anesthetic (novocaine, lidocaine), preserving agent (paraben), antioxidant (sodium disulfite). As a rule, angioedema has a mild clinical course. The first, and sometimes its only symptom, is limited swelling of the skin and subcutaneous fatty tissue of the lips, eyelids and the back surface of the hand. The process can also be localized on the mucous membranes of the respiratory tract and oral cavity, tongue, auricles, larynx and epiglottis, in muscles, subcutaneous fat, etc. Sometimes edema covers the entire face. Shortness of breath and hoarseness of the voice, signs of asphyxia appear. More often, the disease ends in recovery. However, if the process progresses, the disease can lead to the death of the patient as a result of the development of asphyxiation.

Medical care for Quincke's edema includes such measures:

- introduction of diphenhydramine – 1 % solution, 0.5–1 mg/kg i.m. or i.v.;
- prednisolone – 1–2 mg/kg i.m. or i.v.;
- furosemide – 2 % solution, 1–2 mg/kg i.m.;
- adrenaline – 0.1 % solution, 0.2–0.3 ml s.c.;
- if the allergen enters the body by the enteral route, it is advisable to use enterosorbents (activated carbon 0.5–1.0 g/kg, enterosgel).

In the absence of effect, an urgent tracheotomy should be performed.

2.2.2. Anaphylactic shock

Anaphylactic shock is one of the dangerous and severe manifestations of allergies. In dental practice, AS are caused by antibiotics (especially penicillin group preparations), LA (novocaine, lidocaine), sera, vaccines, vitamin preparations, iodine-containing substances, salicylic acid derivatives. An important role in the development mechanism of AS is played by an immediate reaction between an antigen and an antibody, which is accompanied by the release of a large number of biologically active substances (histamine, bradykinin, acetylcholine, etc.) into the patient's blood, causing arterial hypotension, bronchioles spasm, hypovolemia, edema, and increased blood coagulation. The severity of the clinical picture of AS depends on the severity of the described manifestations and can vary from mild to severe, as well as to instant death.

The first symptoms of the AS after exposure to a patient with a drug are a sharp deterioration in well-being, skin hyperemia, a feeling of fear, growing weakness, a throbbing headache, nausea, itching of the skin, pain behind the sternum, asphyxiation. In more severe cases, marked cyanosis, a frequent filiform pulse (sometimes the pulse is not heard at all), a sharp decrease in blood pressure (sometimes not detected), cold, sticky sweat, then – loss of consciousness, urinary incontinence, convulsions.

Emergency care involves the following steps:

1) immediate cessation of the introduction of drugs;

2) giving the patient a horizontal position, turn his head on his side, bring out the lower jaw, remove removable dentures;

3) if the drug is introduced into the limb, applying a tourniquet above the injection area for 25 minutes, and apply ice or a heating pad with cold water at the injection site for 10–15 minutes;

4) pricking the injection site with 0.5 ml of 0.1 % adrenaline solution with 5 ml of isotonic sodium chloride solution, introduction of 0.5 ml of 0.1 % adrenaline solution diluted in 10 ml of isotonic sodium solution chloride i.v. or i.m. slowly;

5) introduction of 4–20 mg of dexamethasone or 90–180 mg of prednisolone i.v.;

6) introduction of 2–4 ml of 2.5 % diprazine solution or 2–4 ml of 2 % suprastin solution, or 2 ml of 0.1 % tavegyl solution, or 5 ml of 1 % diphenhydramine solution;

7) introduction of 0.1 % atropine sulfate solution – 0.01 mg/kg i.v.;

8) in case of heavy breathing – introduction of 1–2 ml of 24 % euphyllin solution i.v.;

9) with severe acute heart failure – introduction of 0.05 % strophanthin solution at the rate of 0.25–0.5 mg per 1 time;

10) detoxification therapy using diuretics (furosemide, torasemide, mannitol);

11) replenishment of the volume of circulating blood by crystalloids and plasma substitutes.

In case of cardiac arrest, it is necessary to start an indirect heart massage, and, if possible, electropulse therapy and intracardiac administration of 0.1 % adrenaline solution – 0.4 ml, 10 %calcium chloride solution – 10 ml and 0.1 %atropine sulfate solution – 0.5 ml. If cardiac activity has not recovered, re-administration of the drugs in the above doses is carried out (calcium chloride is used once at primary cardiac arrest). With the restoration of cardiac activity – catheterization of a vein with the introduction of 200 ml of rheopolyglucin with the addition of 5 ml of 4 % dopamine solution.

AS can develop so quickly and unexpectedly that it is not always possible to take effective measures to eliminate it. Therefore, before using any medicine during dental procedures, it is necessary to take into account the patient's allergic history, including the hereditary one. It should be borne in mind that AS often occurs when using even small doses of a drug and does not depend on the method of its use.

2.3 STENOCARDIA

A dentist can observe one of the common forms of coronary heart disease – angina pectoris. The latter is based on a relatively short-term violation of coronary circulation, which is not accompanied by profound changes in the myocardium. The most characteristic feature of angina pectoris is acute pressing pain behind the sternum or in the area of the heart. It can radiate to the left shoulder, shoulder blade, on the inner surface of the left hand to the little finger. A temporary attack of pain (3–5 minutes) is associated with physical exertion or psycho-emotional stress. At the same time, the patient becomes pale, depressed, covered with cold sweat, and fear of death may appear.

Emergency care includes the following activities:

1) introduction of nitroglycerin (1–2 tablets. 0.0005 g under the tongue) or isoket aerosol (1–2 injections). In the absence of effect, the prescription is repeated with an interval of 5 minutes;

2) intake of acetylsalicylic acid 75–325 mg (to chew), an alternative is clopidogrel 150 mg per os;

3) use of nifedipine under the tongue (1–2 tablets 10 mg). In case of tachycardia – 40 mg of anaprilin under the tongue. Validol under the tongue or corvalol 25–40 drops enterally;

4) in case of severe attack – introduction of a mixture with 2 ml of 50 % dipyrone solution, 2 ml of 25 % papaverine solution and 2 ml of 1 % diphenhydramine solution s.c., i.m. or i.v.;

5) in case of severe psychomotor agitation – introduction of droperidol or sibazon (seduxen) i.v.;

6) prescription of 1 ml of 0.1 % atropine solution (in the absence of tachycardia) or 1–2 ml of 0.2 % platyphylline solution (with tachycardia) i.v.;

7) in case of a prolonged seizure (more than 20 minutes) and in the absence of an effect on preliminary measures – introduction of morphine hydrochloride i.v. slowly, i.v. or s.c.

Often a patient with severe episodes of angina pectoris must be transported to a hospital for stenting or bypassing of the coronary arteries, etc.

2.4 HYPERTENSIVE CRISIS

Patients with hypertension may be admitted to the outpatient appointment with the dentist. The development of complications of the latter – HC, can be caused by psycho-emotional or physical exertion, pain, fear and other adverse factors. HC is characterized by a sudden and significant increase in blood pressure, which leads to impaired cerebral, coronary and renal circulation with the development of neurovascular and humoral changes that occur against the background of a sharp excitation of the sympathoadrenal system. Three types of HC are distinguished: the first – with a predominance of the neurovegetative syndrome, the second – with the manifestations of water-salt syndrome, the third – with hypertensive encephalopathy. The choice of treatment for CH depends on its type, course, and expectable complications from the brain, heart, and kidneys.

Emergency care for type I HC:

- introduction of 6–10 ml of 0.5 % dibazol solution;
- enteral or parenteral 20–40 mg of furosemide;
- introduction of 5 ml of 0.1 % propranolol (anaprilin) solution per 10ml of isotonic solution of intravenous sodium chloride slowly at the rate of 1 ml in 1 min.;
- introduction of 1–2 ml of 2.5 % chlorpromazine solution or 1–1.5 ml of 10 % droperidol solution in oil (in case of severe fear and anxiety of the patient).

Emergency care for type II HC:

- introduction of 0.15–0.3 mg of clonidine in 10 ml of isotonic solution of sodium chloride i.v. or i.m.;
- introduction of 1.0 ml of 25 % benzohexonium solution i.v. slowly under the control of arterial pressure;
- prescription of verapamil 0.05–1.2 mg/min i.v. slowly, the total dose should not exceed 50 mg;

- prescription of 120–150 mg of furosemide or 50–100 mg of ethacrynic acid i.v.;
- introduction of 10.0 ml of 25 % magnesium sulfate i.v.

For the treatment of type III HC, which may be accompanied by convulsions and loss of consciousness, 10 ml of 25 % magnesium sulfate solution i.v. slowly and 2.0 ml of 0.5 % seduxen solution, as well as 5–10 mg of nifedipine (seduxen) under the tongue.

In the treatment of HC, it is important to remember the probability of a pronounced decrease in blood pressure and the development of hypotension. In this case, the patient is placed so that his lower limbs are above the head. The most effective vasopressor agent is dopamine.

2.5 ACUTE RESPIRATORY FAILURE

Primary respiratory arrest is extremely rare at the prehospital stage in dental practice. The cause of acute respiratory impairment may be an intracranial pathological process, airway obstruction, impaired systemic and pulmonary hemodynamics, and a toxic state of various origins. Impaired lung ventilation and gas exchange leads to a life-threatening condition – acute respiratory failure, which in turn is accompanied by a decrease in the diffusion of oxygen and carbon dioxide through the alveolar-capillary membrane, a decrease in oxygen in the blood, and an increase in carbon dioxide level.

There are three types of development of respiratory failure: central, peripheral and mixed. Respiratory disorders according to the central type occur in most cases in patients with traumatic brain injury and damage to the MFA with full airway patency. Such patients are prescribed mechanical ventilation. Peripheral breathing disorders can be caused by airway obstruction by mucus and saliva, blood, vomit mass, foreign bodies that enter the larynx or trachea. A clinical sign of this condition is the inclusion of additional muscles. First aid consists in sanitation of the oral cavity and pharynx from a foreign body, the introduction of an air vent tube, intubation of the trachea, tracheostomy or conicotomy.

The algorithm of action for acute respiratory distress includes:

1) ensuring airway patency (removal of a foreign body, mucus, blood, etc.);

2) carrying out artificial ventilation of the lungs, if there is no independent breathing or severe shortness of breath is observed;

3) carrying out oxygen therapy;

4) adequate painkillers in patients with severe trauma to the chest and abdomen;

5) the use of drugs that support the function of CVS, namely: cardiotonic (0.5 ml of 0.05 % strophanthin solution), antihypertensive (0.1–

0.2 mg/kg of arfonade i.v. or 150 mg of pentamine i.v. or i.m.) and those that increase resistance to hypoxia (sodium oxybutyrate, ascorbic acid, cytochrome C, etc.), reduce peripheral vascular spasm (chlorpromazine, dexamethasone).

In case of respiratory disorders of the mixed type, the main efforts should be aimed at eliminating the occlusion of the tracheobronchial tree and resuming its patency.

2.6
BRONCHIAL ASTHMA

An attack of bronchial asthma in a patient is possible in various situations, including dentist's appointment, which is caused by excessive agitation of the patient during dental interventions, and the use of medicines and materials with a pungent odor, which can lead to bronchospasm. In order to prevent possible complications, do not use local anesthetics containing bisulfite, avoid the use of acetylsalicylic acid (causes aspirin-induced asthma) and indomethacin (provokes bronchospasm). The main measures should be aimed at combating bronchospasm, swelling of the bronchial mucosa and hypoxia.

The emergency care algorithm includes the following steps:

1) giving the patient a half-sitting position;

2) introduction of 0.5 ml of 0.1 % adrenaline solution s.c.;

3) inhalational administration of orciprenaline (asthmopent, alupent) – two doses, or selective adrenergic agonists, in particular, berotec and salbutamol in the form of aerosol inhalations;

4) during an attack of moderate severity, prescription of 0.5 ml of 0.05 % alupent solution i.m.;

5) for the purpose of bronchodilating effect, the administration of 2.4 % intravenous solution of euphilinum is carried out, starting with an initial dose of 5–6 mg/kg, then – 0.9 mg/kg until the condition improves;

6) in case of severe condition – inclusion of dexamethasone (4–10 mg) or prednisolone (60–90 mg) i.v. into the complex therapy;

7) prescription of cardiac glycosides in the development of heart failure (0.5–1 ml of 0.06 % corglycon solution per 10–20 ml of 40 % dextrose solution or 0.9 % sodium chloride solution i.v., 0.5 ml of 0.05 % strophanthin solution per 10–20 ml of 40 % dextrose solution or 0.9 % sodium chloride solution i.v.).

8) oxygen therapy, if necessary, switch to mechanical ventilation;

9) carrying out tracheal intubation and transferring the patient to artificial lung ventilation with undecided growth of respiratory failure or with the occurrence of asthmatic status.

2.7
COMATOSE STATES

Coma – the most profound depression of the central nervous system, characterized by a complete loss of consciousness, lack of response to external stimuli and disorders of regulation of vital functions of the body. The development of a coma is based on a severe disorder of the central nervous system due to a trauma or a pathological process in the brain (hemorrhage, meningoencephalitis), the action of a toxic factor on the nervous system (diabetic, uremic, alcoholic coma, coma of an infectious origin) or the action of physical factors (temperature, electrical current, etc.).

Clinical signs of coma: loss of consciousness, increase or decrease in reflexes, muscle stiffness, cramps, deep breathing disorders (like the Cheyne – Stokes type), a sharp decrease in blood pressure, impaired swallowing. Coma can develop very quickly (with cerebral hemorrhage) or slowly (with endocrine disorders). It is easier to provide emergency care a patient who is in a precomatous state than with the development of a deep coma.

Emergency care measures to the patient in coma:

- ensuring airway (removal of mucus, mechanical ventilation, etc.);
- gastric lavage with a tube (coma caused by the action of a toxic agent);
- arterial hypertension – pacing with dopamine (1–2 μg/kg per 1 min);
- suspected cerebral edema – introduction of 100–150 ml of 10 % mannitol solution i.v. dropwise. Furosemide (2–4 ml of 1 % solution) is also administerd;
- for patients with convulsive syndrome – sodium oxybutyrate (10–20 ml of 20 % solution), sibazon (2 ml of 0.5 % solution), thiopental sodium (20–40 ml of 1 % solution).

Hypoglycemic coma is often the result of uncompensated diabetes mellitus or an overdose of insulin, insufficient intake of carbohydrates

with an adequate dose of insulin, intense muscle load or starvation. It is characterized by a sudden acute onset: hunger, tremors, headache, excessive sweating, severe weakness, palpitations, and chills. The patient's face is amimic, there is a trism of chewing muscles, uni- or bilateral Babinski's sign, the pupils are narrowed, there is no reaction to light, hypotension of the eyeballs, the skin is wet and pale, profuse cold sweat, breathing shallow, muffled heart sounds, arterial hypotension, bradycardia. There may be impaired consciousness, hallucinations, a sense of fear, tonic and clonic convulsions. Changes in the patient's condition develop very quickly, with no precursors.

With a hyperglycemic coma, muscle tone is sharply reduced, eyeballs are soft, profuse sweating is noted. In case of diagnostic difficulties, 30–40 ml of 40 % glucose solution should be administered intravenously and, if it is hypoglycemic coma, then the patient will quickly recover. When treatment is ineffective or there is no certainty that the diagnosis is correct, glucose administration can be repeated. The introduction of 1 ml of 0.1 % adrenaline solution contributes to an increase in blood glucose levels. If the patient became conscious, give him sweet tea, white bread, sugar.

The characteristic clinical manifestations (dead faint, dry skin, soft eyeballs, loud deep slow breathing, smell of acetone from the mouth, decreasing blood pressure, accelerated thready pulse) help to diagnose hyperglycemic coma. In this case, 50–100 IU of insulin s.c. or i.m. should be introduced immediately. Then, taking into account the patient's condition, insulin injections are repeated every 1–2 hours (400–500 IU s.c.). With hyperglycemic coma, cardiovascular agents (strophanthin, cordiamine, caffeine, camphor, etc.) are administered.

Hypothyroid coma is associated with a sharp decrease in the level of thyroid hormones in the blood, which leads to inhibition of all types of metabolism and enzymatic processes in the brain tissue. The toxic effect of carbon dioxide is noted, which accumulates in the body as a result of alveolar hypoventilation, hypothermia, adrenal and cardiovascular insufficiency are expressed. Coma develops gradually, drowsiness and progressive lethargy increase, which are replaced by a complete faint.

In the case of coma, the patient should be provided with access for air, while the temperature in the room should be above 25 °C. Introduce

prednisolone 90–120 mg i.v., thyroxine orally at the rate of 400–500 μg a day, then reduce the dose to 50–100 μg per day. To increase blood pressures, do not use adrenaline hydrochloride, the introduction of which can lead to myocardial infarction or atrial fibrillation. To improve metabolic processes, cocarboxylase, mildronate is introduced into the myocardium. To activate pulmonary ventilation, oxygen is inhaled through nasal catheters, 2–4 ml cordiamine is injected s.c.

2.8
CONVULSIVE DISORDERS

Severe psychoemotional stress in a patient during dental procedures can cause convulsive disorder. It occurs more often if there was epilepsy in past history. The clinical picture of convulsions does not depend on their etiology and is characterized by a sudden onset, expressed by the tension of individual muscle groups and motor excitement, accompanied by impaired consciousness. At the same time, the head throws back, arms are bent at the elbows, legs are extended, the pulse slows down until short-term cessation of breathing, marked tension of the masticatory muscles is noted, that can lead to biting of the tongue. This condition lasts no more than a minute and is replaced by a deep breath and recovery of consciousness. Diagnostic criteria for epilepsy are the presence of convulsive seizures earlier, and a history of malformations in childhoood, pregnancy toxicosis and infectious diseases of mother, Rh incompatibility, etc. An attack occurs suddenly: tonic-clonic seizures begin with twitching of the muscles of the face and reach the extremities, face becomes cyanotic, foam appears from the mouth, biting the tongue, frequent pulse, involuntary urination and defecation, the pupils dilate. At the end of a convulsive attack, lethargy or deep sleep occurs.

In the presence of frequent epileptic seizures, dental interventions should be avoided, and in case of their vital need to be treated in a hospital by resuscitation specialist and neurologist. To avoid the occurrence of seizures, preparations of the articaine group (ultracain, septanest) should be used for local anesthesia.

In case of seizures, such measures are provided:

- introduction of 25 % magnesium sulfatesolution – 10.0 ml i.v. slowly;
- if previous actions are insufficient in case of seizures – prescription of 2 ml of 0.5 % sibazon solution i.v.;
- to prevent cerebral edema – introduction of 0.4 % dexamethasone solution – 8–10 mg i.v., 20 % sodium oxybutyrate solution – 10–12 ml i.v., 1 % furosemide solution – 2 ml i.v.

In case of epileptic seizure, injury to the patient should be prevented, a bite of the tongue should be warned with caution, and airway should be ensured. After drug correction, provide oxygen inhalation, and in case of hyperthermia – physical cooling methods.

2.9 RENAL COLIC

Renal colic manifests itself as a pain syndrome against the background of an unexpected violation of the outflow of urine, intrarenal hemodynamics, and occurs with urolithiasis, pyelonephritis, kidney tumors, etc. Strong cutting pain is localized in the lumbar region, radiating to the genitals and thigh, accompanied by repeated vomiting, frequent urination, delayed discharge of gases and paresis of the intestine. Patients become restless, constantly changing body position, which is a consequence of intolerant pain. The attack is accompanied by hematuria (macro- or microhematuria), urinary excretion of salts and small stones.

Emergency care consists of the following activities:

- introduction of antispasmodics (2 % no-spa – 2 ml or 2 % no-spa forte 4 ml i.m., papaverine, galidor, etc.);
- the use of baralgetas 5 ml i.v.;
- introduction of 1 ml of 1 % morphine hydrochloride or 2 % solution of promedol or omnopon s.c.;
- prescription of 0.5–1 ml of 0.1 % atropine sulfate solution i.v.;
- in case of renal colic, heat should be provided to the lumbar region;
- for quickly removing stones, it is recommended to drink plenty of fluids (water, tea).

2.10
HEPATIC COLIC

Hepatic colic is the most typical symptom of a painful paroxysmal form of cholelithiasis. Its precursors are nausea, a feeling of heaviness in the right hypochondrium, epigastric region, which indicates the inflammatory nature of the disease. The patient develops a sharp intense pain of a cutting or tearing nature in the right hypochondrium. Irradiation of pain in the right scapula, collarbone, shoulder is noted, sometimes the pain spreads to the entire stomach, with nausea, vomiting of bile, which does not bring relief. During a pain attack: the abdomen swells, the muscles of the anterior abdominal wall are tense, breathing is weakened.

Emergency care for hepatic colic includes:

- introduction of peripheral m-anticholinergic drugs (0.1 % atropine sulfate 0.5–1 ml or 0.2 % platyphylline hydrotartrate – 1–2 ml s.c., 0.5 % gastrozepin – 2–4 ml i.m., prifinium bromide (riabal) – 2 ml (15 mg) i.v. or i.m.);
- the use of antispasmodics (2 % no-spa – 2 ml i.m.);
- prolonged pain – introduction of baralgetas – 5 ml i.v. or 2.5 % sodium diclofenac – 3 ml i.v.;
- the achievement of a positive effect is possible when taking nitro drugs (nitroglycerin, nitrosorbide, etc.).

2.11
INJURIES TO THE MAXILLOFACIAL AREA

In the practice of surgical dentistry, the doctor often encounters traumatic lesions of the MFA, which requires emergency care awareness. Injuries occur with sudden damage to tissues and organs, which lead to anatomical and physiological changes, accompanied by local and general reactions. The most common lesions include bruises, wounds, dislocations, bone fractures, etc. Depending on the volume and severity of the lesions, isolated or multiple injuries are distinguished.

2.11.1. Facial contusion

Contusion of the facial tissues develops as a result of closed mechanical damage to soft tissues without violating their integrity. It is caused by damage to tissue structures – subcutaneous fat, muscles, fascial layers and deep cellular spaces, blood vessels without tearing the skin. In case of the blood vessels rupture, there is a serous impregnation of the soft tissues and an accumulation of blood – a hematoma. A contusion is characterized by pain at the site of the injury, swelling, bruising, and impaired function.

Providing emergency care is based on the use of NNA. With recent bruises, ice must be applied to the injured areas.

2.11.2. Facial wounds

The clinical picture depends on the nature of the damaging agent and the morphological features of the wounds (cut, stab, chopped, lacerated, etc.). Wounds of the soft tissues can be combined with injuries of the teeth and jaws, that is combined. Depending on the depth of the wound, they can be superficial (within the skin and subcutaneous fat) or deep when muscles with vessels and nerves are damaged. Face wounds sometimes penetrate the oral cavity, nose, additional sinuses, accompanied by damage to the skull and other organs.

Providing emergency care is based on the following activities:

1) primary surgical treatment using antiseptics (3 % solution of hydrogen peroxide, 0.5 % solution of chlorhexidine, 1 % solution of iodinol, etc.);

2) elimination of wound defects using surgical methods;

3) use of analgesics (paracetamol 0.5 g, ketorolac 0.1 g, solpadeine 1 table 3 times a day enterally). If enteral administration is not possible, then parenteral administration of ketorolac, ketoprofen, etc.;

4) use of anti-inflammatory and regenerating drugs (ointments levomecol and levosin, aerosol livian, etc.);

5) carrying out rabies vaccination according to indications.

2.11.3. Dental dislocations and fractures

Dental dislocation is associated with a partial or complete rupture of periodontal fibers and damage to the neurovascular bundle of varying degrees. It can be isolated or combined with a fracture of the tooth root. The cause of the dislocation can be a blow, hard food, bad habits, as well as the use of elevators by a dentist to remove a tooth or roots. In case of incomplete dislocation, part of the periodontium ruptures or stretches, the tooth shifts to the dentition. With a complete dislocation, a periodontal gap of the entire root and a death of the neurovascular bundle, sometimes an alveolar fracture and tooth loss from the socket are observed. Patients complain of pain, a change in the position of the tooth or a defect in the dentition. Swelling of the tissues of the lips, hematoma of the mucous membrane are typical.

Dental fracture is always accompanied by a dislocation, which is explained by a simultaneous periodontal injury. A fracture of the crown and root of the tooth is isolated. Fractures of the crown can be partial, without damaging the pulp, or complete – with damage to the pulp. Patients complain of pain, mobility of the broken part of the tooth or its root, lack of part of the tooth.

Emergency care methods include:

- local anesthesia;
- fixing the tooth with a mouthguard or splint;
- if necessary – extirpation of the root pulp or tooth extraction;
- in case of violation of the integrity of the mucous membrane – treating with antiseptics;

- use of NNA (paracetamol, ketorolac);
- use of antimicrobial agents (lincomycin hydrochloride 0.5 g 2 times a day i.m., amoxicillin 0.5 g 2–3 times a day enterally, etc.).

2.11.4. Mandibular dislocation

The cause of the mandibular dislocation is the displacement of the articular head from the articular fossa as a result of excessive opening of the mouth, trauma, unsuccessful biting of solid food, etc. Acute and ordinary dislocations are distinguished. By localization, acute anterior dislocations are more common. In this case, the patient complains of severe pain and inability to close his teeth. There is a shift of the jaw forward, salivation, impaired swallowing, etc. The usual dislocation is associated with overextension of the ligaments of the joint. There is a slight asymmetry of the face, increased excursions and the maximum omission of the articular head of the lower jaw.

The following measures are used to provide emergency care:

- reduction of dislocation of the jaw and its immobilization;
- use of analgesics if necessary (more often with acute dislocation).

Further treatment is aimed at restoring the joint function. It is advisable to use physiotherapeutic methods.

2.11.5. Jaw fracture

Fractures of the bones of the facial region are accompanied by a partial or complete violation of the integrity of the bone, which occurs under the influence of mechanical factors. Fractures are distinguished by their nature and localization: open and closed, uni- and bilateral, of alveolar ridge, upper and lower jaw, etc. Most of them are characterized by the appearance of pathological mobility of fragments, malocclusion, and the presence of bruises or wounds at the lesion site, swelling, face symmetry disorder.

The clinical picture with fractures of different localization is characterized by peculiar manifestations: a) in the alveolar process – the mobility of the affected area, swelling, hematomas, ruptures of the mucous membrane; b) in the zygomatic complex – edema of the involved area, limited opening of the mouth, sometimes separation of the alveolar process or maxillary bones; c) in the mandibular bone – violation of the integrity of

the mucous membrane, soft tissue wounds, formation of fragments with their pathological mobility, malocclusion. The patient complains of pain when opening the mouth, pain in the jaw, aggravated by its movements. A positive "load syndrome" is typical – the occurrence of pain in the area of injury when pressing on the chin.

Important measures of emergency care:

- stopping bleeding;
- temporary immobilization of jaw fragments using means of fixation (four-tailed bandage, ligature fixation, etc.);
- conducting primary surgical treatment of the wound;
- elimination of pain in the injured area using NNA (ketanov, ketonal according to well-known schemes, etc.).

For the further treatment of fractures of the MFA, the patient is taken to a hospital where he is prescribed complex surgical, therapeutic and orthopedic therapy.

2.12 BLEEDING

A serious danger to the patient's life can be represented by bleeding as a result of injuries associated with damage to the soft tissues and bones of the upper limbs, surgical interventions, extraction of teeth, pathology of the blood coagulation system, etc. Blood loss can begin immediately after a violation of the integrity of the vessels or in a certain time after injuries. Bleeding in the soft tissues of the MFA can be hidden, that is, it occurs inside the latter, or the patient swallow's blood. The severity of clinical manifestations depends on the rate of blood loss, its volume, duration, as well as the severity of compensatory reactions of the body.

Common causes of bleeding include systemic diseases with blood coagulation or vascular wall diseases (hemophilia, hemorrhagic vasculitis, Werlhof's disease, vitamin C and K deficiency, etc.). Diseases with a hemorrhagic component (acute leukemia, Botkin's hepatitis, septic endocarditis, scarlet fever) lead to hemorrhage. Blood coagulation is reduced in individuals who receive indirect (phenylin, syncumar, etc.) and direct anticoagulants (heparin, fraksiparin), antiplatelet agents (acetylsalicylic acid, clopidogrel). Bleeding increases with arterial hypertension, cirrhosis, thrombocytopenia, and menopause.

With significant blood loss, hemodynamic disorders can occur (decreased cardiac output, decreased blood pressure, arrhythmias, impaired microcirculation in tissues), external and internal respiration, changes in the rate of blood coagulation, up to hemorrhagic shock. The clinical picture of the latter is characterized by pale skin, cold limbs, profuse sweat, agitation, tachycardia and a drop in blood pressure.

To stop external bleeding, hemostatic agents are widely used. The most effective is thrombin (125 IU), which is dissolved in a sterile isotonic solution of sodium chloride and moistened with gauze swabs for application to a bleeding surface. The effect comes quickly, because after 3–5 minutes the bandage can be removed. In case of resumption of

bleeding, the dressing is applied again. Do not administer thrombin i.v., i.m. or s.c.!

Hemostatic sponges from native plasma, thromboplastin are also applyed locally. The bleeding surface is dried with a cotton-gauze swab and a torn sponge is applied to it. The latter can be used for nasal packing, as well as for bleeding from the tooth hole after its removal. A special antiseptic sponge, which contains penicillin and furacilin, fibrin films, antiseptic suppositories, bioplastics are also used. Hemostatic and fibrin films, as well as bioplastics, are preferably soaked with a thrombin solution before use. If bleeding under the influence of local drugs does not stop, then general hemostatic agents are prescribed. The latter are the most effective and safe for bleeding caused by disorders in the physiological hemostasis system.

A specific therapeutic agent that is prescribed for conditions caused by a decrease in the content of prothrombin in the blood is vikasol. 0.5–1 ml of 1 % vicasol i.m. or 0.015 g orally solution is administerd 3 times a day for 3 days. Hemophilic type of bleeding – 10 % gelatin solution 1 tablespoon in 1–2 hours, 3 % hemophobin 1–2 tablespoons 3 times a day or 1.5 % hemophobin 1 ml 3 times a day i.m. It is effective to use 100 ml of 5 % aminocaproic acid solution or 2 ml of 12.5 % ethamsylate solution parenterally. In case of parenchymal and capillary bleeding caused by trauma, surgical intervention, as well as tooth extraction – 1 ml of 0.025 % adroxon solution i.m. or s.c. is prescribed. The latter is also prescribed locally, moistening gauze tissues and wads. A specific anti-hemorrhagic agent for bleeding caused by heparin is protamine sulfate. The drug is prescribed i.m. stream (slowly) or dropwise at the rate of 1 ml of 1 % solution during 2 minutes. The total dose is 5 ml.

During tooth extraction for various reasons, local and general, bleeding may occur. It is necessary to carefully examine the wound to find the source of bleeding. Bleeding can occur as a result of damage to the vessels of the bottom of the hole that feed the tissues of the tooth and periodontium, vessels of the injured mucous membrane, bone tissue of the alveolar process or inter-root septum. In rare cases, blood loss may be associated with damage to a vascular tumor or abnormally located vessels.

Emergency care for bleeding associated with tooth extraction involves:

1) removal of the blood clot;

2) washing the hole with 3 % solution of hydrogen peroxide and drying it with a gauze swab;

3) if bleeding continues from damaged soft tissues, catgut suturing is necessary;

4) in case of bleeding from the vessels of the bone tissue – squeezing with the forceps of the bleeding area of the bone;

5) to stop blood loss from the bottom of the hole after washing with antiseptic solutions, it is tightly plugged with iodoform turunda or turunda soaked in feracryl, aminocaproic acid, biological hemostatic drugs (hemostatic and gelatin sponges, fibrin film, placenta, etc.), etc.

6) to eliminate bleeding caused by common causes, measures aimed at increasing blood coagulation (preferably in a hospital) are applied. Antihemorrhagic therapy depends on the indicators of the coagulogram;

7) introduction of 10 ml of 10 % calcium chloride or calcium gluconate solution, 2–4 ml of 5 % ascorbic acid solution i.v.;

8) hypoprothrombinemia – prescription of 1 ml of 1 % solution of vicasol i.m., 100 ml of 5 % ε-aminocaproic acid solution i.v. dropwise.

Especially intensive antihemorrhagic measures should be carried out in patients with atherosclerosis, heart defects, and in children.

2.13
COMPLICATION OF LOCAL AND GENERAL ANESTHESIA

In dental practice, local and general complications may occur during anesthesia. They can be caused by LPO and hypersensitivity to it, type of anesthesia, traumatic injury, concomitant diseases, etc. Particularly severe disorders are manifested by respiratory disorders, heart rhythm, blood circulation, convulsions, and idiosyncrasy. Hematomas, post-injection pain, neuritis, myositis, etc. are also observed. With the development of certain complications, the doctor have to be skilled to provide emergency care.

2.13.1. Complications of local anesthesia

Complications of local anesthesia, firstly, can be of a general nature – faint, collapse (described in the relevant sections), and idiosyncrasy for the introduction of anesthetic.

The first type of general reaction is idiosyncrasy, which is due to increased sensitivity to a pharmacological agent. It is characterized by the appearance of general manifestations of intoxication (pallor of the face, feeling hot, red spots on the skin of the body, weakening of the pulse, tachycardia, etc.). Collapse may develop. More often idiosyncrasy occurs in children, women and senile people.

Providing emergency care consists of the following steps:

- cessation of the anesthetic administration;
- giving the patient a horizontal position;
- introduction of 1–2 ml of 1 % diphenhydramine solution i.v.;
- introduction of 30–60 mg of prednisolone i.v.

With a sharp drop in blood pressure, treatment is provided as with collapse. Secondly, complications of local anesthesia can occur during anesthesia as a result of some technical errors (eyeball injury, breaking off the syringe needle, etc.). These manifestations are infrequent if the dentist

correctly performs the anesthesia technique. In addition, due to the use of carpule anesthetics, needle breaking is rare.

Another group of complications occurs after anesthesia and is observed more often than the previous one (hematomas, post-injection pain, neuritis, myositis, etc.). With increased sensitivity to anesthetic or overdose, side effects of drugs can also be observed – anxiety, tremors, quinidine-like effects on the heart, convulsions, etc.

A hematoma occurs as a result of loss of blood from an affected vessel and its impregnation of tissues, which more often occurs when conducting posterior superior alveolar nerve block. Bleeding can also result from coagulopathy or hemophilia. Visually, the doctor notes the tissue deformation, which is growing.

Emergency care:

- pressing soft tissues to the bone for 3–5 minutes;
- bleeding of the vessel – pressing the injection site with a swab moistened with 3 % hydrogen peroxide solution;
- if necessary, introduction of coagulants (100 ml of 5 % ε-aminocaproic acid solution i.v. dropwise, etc.);
- if necessary, use of anticonvulsants, sedatives (diazepam, thiopental sodium) and anti-allergic drugs (diphenhydramine, suprastin, etc.) i.m. or enterally.

If further suppuration of the hematoma occurs, it is necessary to conduct its dissection and drainage.

Post-injection pain can be observed with the rapid administration of an anesthetic and indicate the detachment of the periosteum. If necessary, NNA should be prescribed enterally.

When a complication such as neuritis occurs, which is associated with a nerve trunk injury, the patient complains of a decrease in tissue sensitivity. More often this condition is observed when conducting mandibular and infraorbital nerve block. Analgesics i.m. or enterally are prescribed. Then treatment is carried out according to well-known principles (see "Pharmacotherapy of pain in neurodentistry").

Myositis can be the result of muscle damage during mandibular anesthesia. Assistance includes the use of NNA and antihistamines i.m. or enterally.

When using local anesthetics that contain adrenaline or norepinephrine as a result of their resorption, a palpitation may occur, and in rare cases, arrhythmias and ventricular fibrillation. It is advisable to use sedatives and corvalol (30–70 drops). In the absence of effect, it is necessary to call a specialist.

2.13.2. Complications of general anesthesia

Complications that arise during general anesthesia can be caused by the type of anesthesia, the drug itself, the main and concomitant disease, etc. Quite often they can develop from the side: CVS – heart rhythm disturbance, hyper- or hypotension, respiratory system – hypoxia, hypercapnia, bronchospasm, nervous system – brain hypoxia, mental disorders, convulsions, violation of thermoregulation.

To prevent possible complications, the anesthetist should adhere to the basic rules for general anesthesia:

- careful choice of anesthetic;
- implementation of anesthesia on an empty stomach;
- in children before anesthesia – use of oxygenation, etc.

The surgeon of the dental clinic have to be skilled in emergency care techniques, if necessary, carry out artificial respiration, indirect heart massage, perform a tracheotomy, etc. Drug treatment is based on the use of symptomatic drugs: antiarrhythmic, antihypertensive, anticonvulsant, painkillers, etc.

2.14
CLINICAL DEATH

Clinical death is a state of the body that occurs when blood circulation and breathing stop, and lasts until irreversible changes occur in the cerebral cortex (4–5 minutes). It manifests itself as a sudden or prolonged violation of the vital functions of a person, caused by an increase in the severity of the condition. Diagnostic criteria are the absence of pulsation in the main arteries (although cardiac activity may persist), spontaneous breathing (there may be agonal breathing), loss of consciousness, dilated pupils (corneal reflex preserved), tonic-clonic convulsions, acrocyanosis.

Clinical death must be ascertained no more than 5–10 seconds and resuscitation should be started immediately:

1) ensuring free airway: the patient's position on the back on a hard surface, occipital extension of the neck (put a tight roller under the shoulder girdle), removal of the lower jaw, tongue extension, oropharynx sanitation, elimination of obstruction of the tracheo-bronchial tract, introduction of an S-shaped air duct;

2) conducting an impact into the precardial region with the edge of the palm in an oblique direction under the xiphoid process in the direction of the head and shoulder blades;

3) starting "mouth-to-mouth" or "mouth-to-nose" artificial ventilation with a frequency of age norms;

4) checking the patency of the airways and the possible presence of a foreign body in them, conducting another 5 inhalations if spontaneous breathing does not appear. Monitoring the effectiveness of artificial ventilation is the uniform raising or expansion of the chest during air injection;

5) starting closed heart massage simultaneously with artificial ventilation. The ratio of mechanical ventilation and compression is 2 inhalations and 15 pressures on the sternum (about 2 times per second). A more effective ratio is 2 : 30.

The effectiveness of cardiopulmonary resuscitation is the disappearance of objective signs of clinical death. With insufficient effectiveness of the measures taken – electrical or drug-induced defibrillation.

Drug Defibrillation:

1) introduction of 0.1 mg/kg of adrenaline (1:10000) with isotonic solution of sodium chloride 1:1 i.v., if venous access is impossible – endotracheally (1:1000), in the absence of effect, repeat after 3–5 minutes in the same dose, quickly, as much as possible – 0.2 mg/kg;

2) asystole or severe brady dysystole – 0.02 mg/kg atropine intravenously or endotracheally, after 3–5 minutes, repeat to a maximum dose of 2 mg;

3) deep respiratory depression – naloxone 0.1 mg/kg i.v. or endotracheally, quickly, can be repeated;

4) to prevent the occurrence of fibrillation – lidocaine 1 mg/kg i.v.

If resuscitation is successful – catheterization of the main veins and infusion of refortan, stabisol 4–6 ml/kg at the rate that supports effective blood circulation or 4 % sodium bicarbonate solution 1 mg/kg for every 10 min of resuscitation. Immediate hospitalization to the intensive care unit.

2.15

THE LIST OF EQUIPMENT AND DRUGS FOR EMERGENCY CARE AT DENTAL OFFICE

Equipment list:

- tonometer and phonendoscope;
- sterile bandage and cotton wool, adhesive plaster;
- tourniquet;
- oxygen bag;
- oxygen tube;
- a blood transfusion set needle with a high gauge;
- cheek retractor;
- tracheotomy cannula;
- tongue forceps;
- i.v. stand;
- i.v. infusion set;
- syringes.

List of drugs:

Adrenaline hydrochloride – solution for injection, 0.1 %, 1 ml ampoules No.10.

Aminazine – solution for injection, 2.5 %, 1 ml ampoules No.10.

Aminocaproic acid – solution for injection, 5 %, 100 ml in bottles.

Amiodarone – solution for injection, 5 %, 3 ml ampoules No.10.

Analgin:

- solution for injection, 25 %, 2 ml ampoules No.10;
- solution for injection, 50 %, 2 ml ampoules No.10.

Anaprilin – solution for injection, 0.1 %, 5 ml ampoules No.10.

Atropine sulfate – solution for injection, 0.1 %, 1 ml ampoules No.10.

Baralgetas – solution for injection, 5 ml ampoules No.5.

Berotec – aerosol, 100 μg/dose, 10 ml (200 doses) metal tubes.

Caffeine and sodium benzoate – solution for injection, 10 %, 1 ml ampoules No.10.

Calcium chloride – solution for injection, 10 %, 5 ml or 10 ml ampoules No.10.

Clonidine – solution for injection, 0.01 %, 1 ml ampoules No.10.

Concentrated hydrogen peroxide – solution for external use, 50 ml bottles.

Corglycon – solution for injection, 0.06 %, 1 ml ampoules No.10.

Cordiamine – solution for injection, 25 %, 1 ml ampoules No.10.

Corvalol – drops for oral administration, 25 ml bottles.

Dexamethasone – solution for injection, 0.4 %, 1 ml ampoules No.25.

Dibazol:

- solution for injection, 1 %, 1 ml ampoules No.10;
- solution for injection, 1 %, 5 ml ampoules No.10.

Dicinon – solution for injection, 12.5 %, 2 ml ampoules No.10.

Diphenhydramine – solution for injection, 1 %, 1 ml ampoules No.10.

Dopamine – solution for injection, 0.5 %, 5 ml ampoules No.10.

Droperidol – solution for injection, 0.25 %, 5 ml and 10 ml ampoules No.10.

Ethyl alcohol – solution for external use, 70 %, 100 ml bottles.

Euphyllin – solution for injection, 24 % 1 ml, or 2.4 % in 5 ml ampoules No.10.

Furosemide – solution for injection, 1 %, 2 ml ampoules No.10.

Glucose:

- solution for injection, 5 %, 200 ml or 400 ml bottles;
- solution for injection, 10 %, 200 ml bottles;
- solution for injection, 40 %, 20 ml ampoules No.10.

Hemostatic sponge with amben – 0.8 g dry substance in hermetically sealed bottles.

Heparin – solution for injection, 5 ml 25.000 IU (5000 IU/ml) bottles.

Insulin – solution for injection, 40 IU/ml, 10 ml bottles No.1.

Iodine – alcohol injection for external use, 2–5 %, 5 ml bottles.

Ketanov – solution for injection, 3 %, 1 ml ampoules No.10.

Lidocaine – solution for injection, 2 %, 2 ml ampoules No.10.

Magnesium sulfate – solution for injection, 25 %, 5 ml or 10 ml ampoules No.5.

Mannitol – solution for infusion, 30 ml bottles.

Mesatone – solution for injection, 1 %, 1 ml ampoules No.10.

Naloxone – solution for injection, 0.04 %, 1 ml ampoules No.10.

Nifedipine – tablets, 0.005, 0.01, 0.02 g blisters No.10.

Nitroglycerin – sublingual tablets, 0.0005 g No.40.

Norepinephrine hydrotartrate – solution for injection, 0.2 %, 1 ml ampoules No.10.

No-spa:

- solution for injection, 2 %, 2 ml ampoules No.5;
- tablets, 40 mg blisters No.10.

Papaverine hydrochloride – solution for injection, 2 %, 2 ml ampoules No.10.

Platyphylline – solution for injection, 0.2 %, 1 ml ampoules No.10.

Prednisolone – solution for infusion, 3 %, 1 ml ampoules No.3.

Rheopolyglucin – solution for infusion, 200 ml or 400 ml bottles.

Sibazon – solution for injection, 0.5 %, 2 ml ampoules No.10.

Sodium chloride:

- isotonic solution for infusion, 0.9 %, 200 ml or 400 ml bottles;
- solution for injection, 0.9 %, 5 ml or 10 ml ampoules No.10.

Sodium thiosulfate – solution for injection, 30 %, 5 ml ampoules No.10.

Strophanthin – solution for injection, 0.05 %, 1 ml ampoules No.10.

Sulfocamphocaine – solution for injection, 10 %, 2 ml ampoules No.10.

Suprastin – solution for injection, 2 %, 1 ml ampoules No.5.

Thrombin – solution for injection, 125 IU or 250 IU bottles.

Validol – tablets, 0.06 g, strip cell packs No.10.

Verapamil – solution for injection, 0.25 %, 2 ml ampoules No.10.

Section 3

DRUG CHARACTERISTICS

3.1
PSYCHOTROPIC DRUGS

Psychotropic drugs include drugs used in case of violations of human mental activity. The neurochemical basis of the action of psychotropic drugs is associated with the effect on the enzymatic synthesis and cleavage of neurotransmitters, their deposition in the vesicles of presynaptic endings, exit into the synaptic cleft, or interaction with postsynaptic receptors.

Classification of psychotropic drugs:

- psychodysleptics (hallucinogens) – mescaline, Indian hemp preparations (marijuana, hashish); lysergic acid diethylamide derivatives;
- antipsychotics (chlorpromazine, levomepromazine, meterazine, frenolone, triftazin, chlorprothixene, haloperidol, droperidol);
- tranquilizers (diazepam, chlordiazepoxide, phenazepam, nozepam, lorazepam, mezepam, meprotan, mebicar, trioxazine, afobazole);
- sedatives (sodium and potassium bromide, tincture of valerian, motherwort, valocormide, corvalol, peony infusion, magnesium sulfate);
- antidepressants (imizine, amitriptyline, azaphen, pyrazidol, lithium carbonate);
- psychostimulants: psychomotor stimulants (caffeine and sodium benzoate, phenamine, meridil, sydnocarb, sydnophen); nootropic and GABAergic agents (piracetam, aminalon, phenibut);
- adaptogens (lemongrass fruits tincture, ginseng root tincture, leuzea liquid extract, eleutherococcus liquid extract, pantocrine).

Psychotropic drugs in dental practice find their application in all its areas: surgical, therapeutic, orthopedic and orthodontic. Any dental intervention, as a rule, leads to the emergence of a stressful reaction of the body caused by excessive psycho-emotional stress (excitement, fear), which causes the development of vegetative-vascular dystonia, impaired heart function, and others. Children are especially susceptible to stress reactions.

Dental procedures often require premedication, the purpose of which is to prevent psycho-emotional disorders. The most widely used for this purpose are tranquilizers, antipsychotics and drugs, which have a significant impact on the psychoemotional sphere, inhibit vegetative reactions.

3.1.1. Antipsychotics

Neuroleptics (antipsychotic drugs) by chemical structure are divided into the following groups:

- phenothiazine derivatives (chlorpromazine, levomepromazine, triftazin, thioridazine, neuleptil);
- thioxanthene derivative (chlorprotixen);
- butyrophenone derivatives (haloperidol, droperidol);
- dibenzodiazepine derivatives (clozapine);
- substituted benzamides (sulpiride).

Antipsychotics are able to influence certain mediator structures of the central nervous system. Carrying out dopamine-, adreno- and seroton-blocking actions, they impede the transmission of nerve impulses from the frontal lobes to the underlying structures of the brain, balance the mediator background. The drugs block the central and autonomic nervous systems and have a peculiar calming effect, reduce psychomotor agitation, irritation, cause emotional inertness, reduce conditioned reflex activity, and eliminate delusions and hallucinations.

Aminazine (chlorpromazine) is the classic, best-studied broad-spectrum antipsychotic. The psychotropic effect of which, with parenteral administration, develops rapidly, causing a slowed down course of mental processes, a decrease in anxiety, tension, fear, psychomotor agitation, speech retardation, and the occurrence of general sedation. The main site of action of chlorpromazine is the network formation of the brain stem, where it interacts with the corresponding receptors, providing a stabilizing effect on the membrane and reducing the functional activity of neurons. The antiemetic effect of chlorpromazine is based on a decrease in the excitation of adrenoreceptors of the trigger zone of the vomiting center. Adrenergic blocking effect is accompanied by vasodilatation of the capillary bed and a decrease in blood pressure. The drug is very slowly excreted from the body. Traces of chlorpromazine metabolites can be detected 12 months after treatment.

In dental practice, chlorpromazine as a part of antipsychotic mixtures (simultaneously with antihistamines and analgesics) is used to potentiate analgesia for pain or to relieve acute psychomotor agitation. In general practice, chlorpromazine is prescribed for psychoses, especially schizophrenia.

This drug should not be used for coma, damage to the brain and spinal cord, hypotension, heart failure, etc. With prolonged use of chlorpromazine, depression may develop, antipsychotic syndrome with the phenomena of parkinsonism, tachycardia, agranulocytosis, increased blood coagulation, liver damage, weight gain, nephrotic syndrome, optic atrophy, intestinal paresis, menstrual irregularities, decreased potency, etc.

A strong antipsychotic effect is exerted by trifthazin, for which stiffness and stupor are completely atypical. Thioridazine has a milder effect, so it has found its application in both psychiatric and therapeutic practice. Neuleptil reduces proneness to conflict, malignance; it is considered a corrector of behavior. Chlorprotixen combines a calming and antipsychotic effect, has a moderate antidepressant effect. Sulpiride is characterized by antipsychotic, stimulating, timoleptic and antiemetic effects.

Butyrophenone derivatives have the most pronounced effect in relation to the elimination of delirium, hallucinations. Haloperidol is an effective drug in this group, which can cause extrapyramidal disorders (muscle tension, tremor). Droperidol acts strongly, but not for long, it has a pronounced analgesic, anti-shock, anti-arrhythmic and antiemetic effects. In combination with fentanyl, droperidol is used in anesthetic practice for NLA.

Droperidol and haloperidol are widely used in dentistry. Taking into account the ability of antipsychotics to reduce the state of mental stress, fear, physical activity, they are prescribed for sedation before dental interventions, which are accompanied by severe pain, as well as in combination with painkillers. The combined drug thalamonal containing 2.5 mg of droperidol and 0.05 mg of fentanyl 1 ml is used for NLA patients with myocardial infarction. Chlorpromazine, levomepromazine, frenolone have an analgesic effect, so they are used in the treatment of trigeminal neuralgia.

Many antipsychotics are used in the treatment of withdrawal symptoms in patients with alcoholism, elimination of vomiting, potentiation of the action of drugs for anesthesia. A significant part of patients can show resistance to drugs, therefore, less toxic atypical antipsychotics (clozapine,

olanzapine) are widely used, which are well established in clinical practice and do not have extrapyramidal side effects.

3.1.2. Tranquilizers

Tranquilizers (anxiolytics, ataractics, minor tranquilizers) – means that eliminate or prevent a feeling of fear, anxiety, relieve emotional stress without causing marked inhibition and drowsiness in healthy patients and patients with neurosis. A wide range of pharmacological activity and a relatively small number of side effects have led to their widespread use in many fields of medicine. Compared to antipsychotics, tranquilizers do not show an antipsychotic effect (they do not eliminate delusions, hallucinations), and their administration is not accompanied by extrapyramidal disorders.

By origin, tranquilizers are divided into:

1) benzodiazepine derivatives – diazepam (sibazon, seduxen), chlordiazepoxide (elenium), phenazepam, lorazepam (ativan), oxazepam (tazepam);

2) propanediol derivatives – meprotan (meprobamate);

3) ddiphenylmethane derivatives – amisyl;

4) GABA derivatives – phenibut;

5) others – mebicar, afobazole, oxylidine, hydroxyzine, tenoten.

The most studied is the mechanism of action of benzodiazepine derivatives, which activate specific receptors and increase their affinity for an inhibitory mediator – GABA. As a result, the opening of chlorine canals is facilitated and GABAergic synaptic inhibition is increased.

According to the mechanism of action on the receptor, benzodiazepines are divided into two groups: receptor agonists (all drugs of this group); receptor antagonists (flumazenil).

The following pharmacological effects are inherent in tranquilizers:

1) tranquilizing (anxiolytic, antiphobic) – lies in the ability of drugs to cause emotional calmness, that is, to remove psycho-emotional stress, fear and anxiety associated with the presence of a specific conflict situation. The most powerful tranquilizing effect is in diazepam, phenazepam, lorazepam, chlordiazepoxide;

2) sedative – expressed in the elimination of superexcitation and motor activity. This type of action is inherent in all drugs, but is poorly ex-

pressed in medazepam, oxazepam and mebicar – "daytime" tranquilizers. There are also isolated tranquilizers, which have a stimulating effect (for example, gidazepam);

3) neurotropic (muscle relaxant and anticonvulsant). Benzodiazepine tranquilizers are referred to as central muscle relaxants, because they have an effect on the receptors of the inserted neurons of the spinal cord and the parts of the brain responsible for the skeletal muscle tone. The muscle relaxant effect is the most pronounced in seduxen (diazepam), phenazepam, weaker – in nosepam and medazepam. The anticonvulsant effect of the drugs is associated with an effect on the hippocampal receptors. The leading agents in anticonvulsant therapy are seduxen and clonazepam;

4) vegetotropic (vegetostabilizing) – drugs reduce the activity of the sympathetic-adrenal system, i.e. weaken the autonomic components of emotional reactions. This effect is used in the treatment of hypertension, arrhythmias, diencephalic crises, etc.

For clinical practice, it is important to distribute tranquilizers, taking into account their pharmacological and side effects on "typical" and "atypical". "Typical" tranquilizers have anxiolytic, hypnotic, muscle relaxant effects. This group includes derivatives of benzodiazepines: diazepam, clonazepam, phenazepam, lorazepam, oxazepam, medazepam, gidazepam. The group of "atypical" tranquilizers (they often have a little-known mechanism of action) includes amisil, oxylidine, mebicar, trioxazine, afobazole, which also exhibit an anti-anxiety effect, but do not cause muscle relaxation, mnemonic disorders, and dependence syndrome characteristic of the previous group.

In dentistry, tranquilizers are prescribed in combination with analgesics for the treatment of pain, and are used for sedation during surgical interventions in the MFA. They are also used to eliminate mental and muscle tension, fear, anxiety, to prevent stress in the treatment of dental pathology. To enhance the effect, they are prescribed the day before and 30–40 minutes before the intervention, and for sedation – 2–4 hours before the operation. For "balanced anesthesia" (ataralgesia) in combination with atrong analgesics, antipsychotics and nitrous oxide, sibazon (diazepam) is widely used, which has a pronounced sedative, hypnotic, muscle relaxant, anticonvulsant effect, and does not affect the cardiovascular and respiratory systems. Chlozepide, mezapam, nozepam are used in dentistry

to establish contact with the patient and adapt to emotional situations of dental care. Amisyl, which in addition to the anxiolytic effect has an antispasmodic, antihistamine, anti-serotonin and local anesthetic effect can be used for sedation and elimination of cough, as well as to eliminate hypersalivation after dental surgery. In general practice, indications for the use of tranquilizers should be considered: neurosis, sedation, ataralgesia, insomnia, epilepsy, spastic conditions of skeletal muscles and withdrawal symptoms in alcoholism and drug addiction.

Anxiolytic drugs should not be prescribed to drivers, dispatchers and other people whose professional activities require a quick reaction. When taking drugs alcohol is forbidden to drink. Undesirable effects of tranquilizers can occur in the form of attention and memory disorders (especially short-term ones), drowsiness, dizziness, muscle weakness, gait disturbance (ataxia), tolerance and dependence, teratogenic effect, tachycardia and decreased blood pressure, nausea and dry mouth. In case of prolonged use, there is a "withdrawal syndrome" (sleep disturbance, irritability, sometimes convulsions). In acute poisoning with tranquilizers, as an antidote, a benzodiazepine receptor blocker, flumazenil (anexate) is used. If necessary, artificial lung ventilation is performed.

3.1.3. Sedatives

Sedatives are considered substances of plant and mineral origin, which have a general calming effect on the body. They enhance the inhibition processes in the central nervous system, reduce its reflex excitability, eliminate irritability, psycho-emotional instability, expressed in general anxiety. Sedatives are classified by origin:

1) substances of plant origin:
- rhizomes of valerian roots and their combination with other plant substances;
- motherwort, passiflora, peony, Greek valerian (rhizomes with roots), ordinary hop (cones), etc.

2) bromides: sodium bromide, potassium bromide, bromocamphor.

The group drugs are characterized by good tolerance, absence of serious side effects and age restrictions. In usual doses, they do not cause muscle relaxation, ataxia, mental and physical dependence phenomena, in connection with which they are often used on an outpatient basis. In den-

tistry, sedatives are used for sedation and complex treatment in therapeutic and surgical pathologies against the background of neurotic disorders.

Valerian has an effect on the functions of the central nervous system, reducing its excitability, and has an antispasmodic effect. Valerian preparations are used as sedatives for nervous disorders, insomnia, in the complex of preparations for surgical intervention, menopause, etc. Side effects are manifested in the form of drowsiness, weakness, and slight dizziness. With a decrease in dose or discontinuation of the drug, these phenomena disappear. The motherwort herb is similar to valerian in pharmacological properties. It is prescribed in the form of tincture or extract, as a sedative for increased nervous excitability, cardiovascular neurosis, in the early stages of hypertension. It is widely used for excessive excitability in children. Passiflora extract, in addition to its calming effect, also has some anticonvulsant activity. It is used as a sleeping pill and as an additional tool in the treatment of epilepsy.

Bromides (sodium bromide and potassium bromide) replace an equivalent amount of chlorine in the tissues of the body. Small doses of bromine enhance the inhibition process, without reducing the processes of excitation. Large doses of bromine significantly increase the strength of the inhibition process in the cerebral cortex, which in some cases can lead to the disappearance of conditioned reflexes. Bromine preparations are prescribed for neurasthenia, hysteria and neurosis-like conditions, accompanied by increased irritability, insomnia, occur against any somatic pathology, including dental. Bromides can accumulate, causing "bromism", which is manifested by runny nose, conjunctivitis, skin rashes, bronchitis, drowsiness, memory and vision impairment, bradycardia, etc. When using very large doses, acute poisoning can occur – bromine intoxication and kidney irritation symptoms (hematuria, etc.). There are combined therapeutic forms (often in the form of potions) that contain tinctures of valerian, lily of the valley, belladonna, hawthorn, peppermint oil, bromides, barbiturates and others (corvalol, valocormide, valocordin).

3.1.4. Antidepressants

Antidepressants are a group of drugs that are designed to treat depressive conditions. The classification of antidepressants is based mainly on the mechanism of action:

I. Medicines that inhibit capturing monoamines by neurons:

1. Non-selective agents that block neuronal uptake of serotonin and norepinephrine (imizine, amitriptyline, azaphen, maprotiline, etc.).

2. Selective agents that block predominant uptake of serotonin by neurons (fluvoxamine, fluoxetine, sertraline, paroxetine, etc.).

II. Monoamine oxidase inhibitors:

1. Non-selective agents – MAO-A and MAO-B inhibitors (nialamide).

2. Means of selective and reversible action – MAO-A inhibitors (pyrazidol, moclobemide).

Pharmacological effects of antidepressants are primarily associated with a timoleptic effect: improving mood and eliminating lethargy, longing, oppression of thought processes, and restoration of interest in life. Antidepressants have sedative, anxiolytic, or psycho-energizing effects. They have an atropine-like effect. The clinical result appears only after 5–10 days and later from the start of treatment. To consolidate the effect, prolonged use of drugs is necessary (6–12 months).

In dental practice, antidepressants are used for premedication along with analgesics, as well as for potentiation of postoperative analgesia – antideprenalgesia (for example, promedol with amitriptyline). Drugs are also prescribed to reduce salivation during surgical interventions, to treat depression caused by the damage to the MFA or an upcoming surgical intervention.

Imizin (imipramine) – the first antidepressant from the group of non-selective drugs, increases the effect of monoamines by inhibiting the reuptake of norepinephrine by neurons. It increases the content of serotonin, suppressing its reuptake, increasing its inhibitory effect of serotonin on the limbic system. Imipramine reduces motor inhibition, regulates mood. It has a peripheral M-anticholinergic effect, and antispasmodic and antihistame action. Side effects: dry mouth, accommodation disturbance, tachycardia, constipation, urinary retention (effects associated with the M-anticholinergic effect), excessive central nervous system excitement, hallucinations, insomnia, headache, tremor, allergic reactions, jaundice, rarely – hematoxicity, agranulocytosis, orthostatic collapse, arrhythmia, weight gain.

Amitriptyline (tryptizol). Unlike imizine, amitriptyline is better tolerated, exhibits a sedative, pronounced M-anticholinergic and antihistamine

effect. Azaphen, unlike other tricyclic antidepressants, does not have M-anticholinergic activity. Clomipramine is effective. Drugs of this group are not prescribed simultaneously with MAO inhibitors, since severe complications (convulsions, coma) can occur. Fluvoxamine (fevarin), fluoxetine (portal), sertraline (zoloft), paroxetine (paxil), citalopram (cipramil) are the drugs of selective action blocking the capturing serotonin by neurons. These drugs have a long antidepressant effect, practically do not have an M-anticholinergic effect, and have a sedative effect.

MAO inhibitors, reducing the destruction of monoamines, contribute to their accumulation in the brain. MAO inhibitors can be reversible and irreversible. There are also drugs that selectively act on one type of enzyme (MAO-A), affecting the balance of norepinephrine and serotonin, as well as drugs of a "mixed", non-selective effect (MAO-A and MAO-B) – additionally responsible for the release of dopamine, phenylethylamine and tyramine. With simultaneous administration of drugs and food products containing tyramine or its tyrosine precursor (cheese, milk, smoked meats, chocolate), complications in the form of HC ("cheese" or tyramine syndrome) may appear. The latter is due to the fact that tyramine is metabolized in the liver by MAO. MAO inhibitors suppress microsomal liver enzymes and prolong the action of non-inhalation anesthetics, NA, alcohol, antipsychotics, etc.

Nialamide (nuredal) is an antidepressant with a stimulating effect on the central nervous system. It has a timoanaleptic effect, less than that of tricyclic drugs. It can be used in the treatment of depressive conditions and complex therapy of pain syndromes in dental practice. Pyrazidol (pirlindole) is a reversible MAO inhibitor. It blocks the deamination of serotonin and NA, exerting an insignificant effect on tyramine, as a result of which the "cheese" syndrome usually does not occur.

3.1.5. Psychostimulants

Psychomotor stimulants are drugs that increase physical and mental performance, mood, reduce fatigue, the need for food. They are classified by chemical structure:

- purine derivatives (caffeine and sodium benzoate);
- phenylalkylamine derivatives (phenamine, sydnocarb);
- piperidine derivatives (meridil).

These drugs improve the conditioned reflex activity of the body, accelerate the excitation in neurons, increase the processes of summation, irradiation of impulses in the central nervous system, etc. Their stimulating effect on the central nervous system, in particular on the centers of the medulla oblongata, develops rapidly, and resistance to physical activity increases. Drugs in this group reduce inhibitory processes. A typical representative of psychomotor stimulants is caffeine, which is an alkaloid found in tea leaves, coffee beans, nuts and other plants.

Caffeine has psychostimulating and analeptic effects. The mechanism of psychostimulating action is the blockade of brain tissue phosphodiesterase, the accumulation of cyclic 3,5-adenosine monophosphate (c-AMP) and the stimulation of glycogenolysis. Antagonism with adenosine, which inhibits the function of the central nervous system, is of particular importance. Under the influence of caffeine, mental activity is stimulated, mental and physical performance, physical activity increase, and the duration of the response to external irritations is reduced. The stimulating effect depends on the type of nervous activity (for the weak type, lower doses of caffeine are needed than for the strong one). It is also known that caffeine in small doses causes a predominantly stimulating effect; in excessively large doses it suppresses (depletion of the function of nerve cells).

Analeptic effect is associated with the effect on the centers of the medulla oblongata – respiratory, vasomotor. In addition, caffeine excites the vagus nerve centers. Often there is an increase in the frequency and depth of breathing, when using large doses, tachycardia can be observed. Caffeine stimulates the vasomotor center, which increases vascular tone. Its antispasmodic effect on the smooth muscles of the vessels of some organs causes a short-term decrease in their tone, which reduces the load on the myocardium. Caffeine and other xanthines (theobromine, theophylline) reduce pressure in the pulmonary artery. The effect of caffeine on blood pressure is associated with its cardiotropic and vascular effects. With arterial hypotension, caffeine increases or normalizes blood pressure. The drug helps to increase the secretion of the glands of the stomach, increase the total metabolism, blood glucose and increase urine output.

In dental practice, caffeine can be used to potentiate analgesia, provide emergency care and to stimulate mental activity in the complex treatment of pathology of the MFA. Caffeine is also used in the treatment of

arterial hypotension, headache at the background of migraine attack and hypotension. In combination with NNA, it is a part of combined preparations (citramone, farmadol, etc.). Side effects: nausea, vomiting, anxiety, agitation, insomnia, tachycardia, arrhythmia. In case of prolonged use, addiction and mental dependence develop.

Phenylalkylamine derivatives include phenamine (amphetamine). In clinical practice, the drug is not used in connection with the development of mental dependence. Its admission to improve athletic performance is prohibited. The effect of sydnocarb is similar to the action of phenamine, but the effect develops gradually, lasts longer, no dependence is observed. Meridil, in comparison with phenamine, is less active, but does not cause peripheral adrenomimetic effects and mental dependence.

3.1.6. Nootropic drugs

Nootropic drugs due to beneficial effects on the metabolic processes of the brain improve psychical and mental activity. Nootropic drugs are divided into the following groups:

1) pyrrolidone derivatives – racetam (piracetam, pramiracetam);

2) GABA derivatives (aminalon, gammalon, sodium hydroxybutyrate, phenibut);

3) neuropeptides and their analogues (semax, tyroliberin);

4) cerebrovascular agents (sermion, vinpocetine, cinnarizine, pentoxifylline, xanthinol nicotinate, nimodipine (nimotop);

5) pyridoxine derivatives (pyritinol);

6) antioxidants (mexidol, melatonin, berlithion, tocopherol acetate, etc.);

7) ethimizol, potassium orotate, cerebrolysin, actovegin; anticholinesterase (galantamine, rivastigmine); M-cholinomimetics; amino acid preparations (glutamic acid, glycine, etc.), preparations of other groups.

Nootropic drugs have the following properties:

- improve memory, learning;
- increase the resistance of the brain to extreme influences;
- have antiasthenic action;
- can carry out psychostimulating (glutamic acid) or sedative and tranquilizing (glycine) action.

Most drugs of the nootropic group have the ability to potentiate analgesia, which is used in the treatment of acute pain, especially of neu-

ropathic origin in dental practice. Piracetam is the main representative of nootropic drugs. By its chemical structure, it is a cyclic compound of GABA. The improvement in mental activity, memory, and learning ability caused by piracetam is associated with its effect on glutamate receptors. The antioxidant effect is associated with a predominant effect on energy metabolism. Piracetam has low toxicity, has antidepressant, anticonvulsant, cardioprotective effects.

In preparation for dental procedures, piracetam can be used to correct side effects of tranquilizers in people with asthenic syndrome, reduced mental activity (senility, alcoholism, stroke, skull injuries, etc.). The drug combines well with cardiovascular and psychotropic drugs, potentiates the effect of antidepressants, cinnarizine. Side effects: dyspepsia, irritability, sleep disturbance.

Aminalon (gammalon) is GABA. It improves blood circulation in the brain; due to the normalization of the level of GABA has anticonvulsant and antihypoxic properties. Blood pressure decreases, especially in conditions of arterial hypertension, contributes to the development of bradycardia. The drug exhibits a mild psychostimulating effect; in cases of high blood glucose it has a hypoglycemic effect. Aminalon is indicated for memory loss after injuries, stroke, infectious diseases. Used in the complex treatment of arterial hypertension, paralysis, complications of cerebral arteriosclerosis. Side effects: dyspepsia, sleep disorders, sensation of heat, hypotension, bradycardia.

Vinpocetine (cavinton) is a semisynthetic derivative of the white vinca alkaloid. Stimulates cerebral circulation, increases oxygenation of brain tissue and absorption of glucose. Reduces platelet aggregation, inhibits phosphodiesterase, increases the level of c-AMP, modulates ion canals, affects the metabolism of HA. It is indicated for neurological diseases associated with cerebrovascular insufficiency, memory impairment, aphasia, and menopause. Side effect is insignificant (arterial hypotension, extrasystole).

Pentoxifylline (trental) blocks phosphodiesterase and promotes the accumulation of c-AMP, provides brain tissue with oxygen, and improves the rheological properties of blood. It is indicated for cerebral arteriosclerosis, coronary heart disease, peripheral circulation disorders. Side effects: nausea, vomiting, gastralgia, dizziness, hyperemia of the facial skin, decreased blood pressure with parenteral administration, urticaria.

Tanakan (Ginkgo Biloba liquid extract) is a vasodilator, neuroprotector, antihypoxant, and antiplatelet agent. It is indicated for encephalopathy, traumatic brain injuries, decreased intelligence. Side effects: dyspepsia, headache, allergic reactions.

3.2

LOCAL ANESTHETICS AND ANESTHETIC DRUGS

Knowledge of the pharmacokinetics and pharmacodynamics of local and general anesthetics, their adequate use allow the dentist to more confidently and efficiently perform the necessary surgical interventions.

3.2.1. Local anesthetics

Local anesthetics are agents that cause a limited blockade of pain sensitivity, preventing the emergence and entry of nerve impulses into the central nervous system. In medical practice, the following classifications of local anesthetics are used.

1. By chemical structure:
- esters – anaesthesin, dicain, cocaine, benzofurocain, novocaine;
- replaced amides – lidocaine, articaine, mepivacaine, pyromecaine, bupivacaine, levobupivacaine, prilocaine, trimecaine, ethidocaine, ropivacaine.

2. By the type of anesthesia:
- surface anesthesia – anesthesin, dicain, pyromecain;
- infiltration and conduction anesthesia – novocaine, trimecaine, lidocaine, articaine, mepivacaine;
- spinal anesthesia – lidocaine, bupivacaine, sovcain;
- all types of anesthesia – lidocaine;
- intraligamentary anesthesia – lidocaine, mepivacaine, articaine.

3. By duration of action:
- short action: novocaine (30–50 min);
- medium action – lidocaine, trimecaine, mepivacaine, pyromecaine, articaine, prilocaine (60–90 min);
- long-term action – bupivacaine, tetracaine, ethidocaine, ropivacaine (> 90 min).

For effective and safe use in medical practice, the following requirements are imposed on anesthetics: drugs must have high analgesic properties and selectivity of action, a sufficient duration of effect and range of therapeutic effect, not to irritate tissues and not to narrow vessels.

Local anesthetics are weak bases. In the clinic, they are usually used in the form of salts (hydrochlorides), that improves their solubility and increases the stability of solutions. In the environment of the body, these substances exist either in the form of a non-ionized base, or in the form of a cation. The cationic form of LA binds to receptors located on the inner side of the surface of the cell membrane and causes blocking of canals for Na ions, which leads to the termination of nerve conduction. If the movement of Na ions is blocked on a separate segment of a nerve, conducting a pulse is impossible. These processes occur not only on the membranes of nerve fibers, but also in the neurons of the autonomic ganglia and in the central nervous system, myocardium, and cardiac pacemakers.

An increase in the level of extracellular calcium partially blocks the action of LA due to an increase in the surface potential of the membrane and puts it into a resting state. And an increase in the concentration of extracellular potassium depolarizes the membrane potential, enhances the effect of drugs.

LA have a wide range of pharmacological activity, this justifies the variety of indications for their use in clinical practice.

Pharmacological effects of local anesthetics:

- local anesthetic (analgesic);
- anti-shock;
- sedative;
- antispasmodic (except cocaine and mepivacaine);
- decrease in myocardial excitability;
- anticholinergic;
- antipruritic;
- anti-inflammatory;
- improving of microcirculation.

In dental practice, for anesthesia of the mucous membranes of the oral cavity, 5–20 % solutions of anaesthesin, 3–5 % solutions of pyromecain and 2–10 % solutions of lidocaine, etc. are used. Surface anesthesia of the cornea of the eye, nasal passages, and skin integument is carried out

as a rule with 0.25–0.5 % solutions. In orthopedic dentistry, LA are used before imprinting. Infiltration anesthesia is carried out by layer-by-layer saturation of tissues with anesthetics, for which 0.25–0.5 % (rarely – 1 %) solutions are used. For conduction anesthesia during operations and in the postoperative period, 1–2 % solutions are used. For spinal anesthesia, as a rule, 2–5 % solutions are used.

In general medical practice, LA are used to relieve pain in pancreatitis, peritonitis, renal or hepatic colic, acute pleurisy, injuries and diseases of the peripheral nervous system. Preparations in 0.25–0.5 % concentration solutions may be used for perinephric, vagosympathetic, circulatory blockade. Lidocaine and trimecaine are used as antiarrhythmic drugs. LA are used in the complex treatment of skin itching, neurodermatitis, eczema. Some diagnostic procedures (gastrofibroscopy, bronchography, etc.) require the use of anesthetics. The choice of LA and the method of its application in each specific situation are, first of all, due to the alleged soreness of the surgical intervention and its duration. Table 8 shows the comparative characteristics of the anesthetic activity and toxicity of individual drugs.

Table 8

Anesthetic activity and LA toxicity (in arbitrary units)

Anesthetic	Anesthetic activity	Toxicity
Articaine	5	1,5
Bupivacaine	8–16	7–8
Dicain	High	10
Lidocaine	3–4	1,5–2
Mepivacaine	4	2
Novocaine	1	1
Prilocaine	4	1–1,5
Trimecaine	3	1,5
Sovcain	High	25

Tables 9 and 10 show the maximum permissible doses of individual drugs and the duration of anesthesia.

Table 9

Duration of anesthesia

Anesthetic	Without vasoconstrictor (min)	With vasoconstrictor (min)
Articaine	55–65	170–185
Bupivacaine	120–140	180–240
Lidocaine	30–60	120–130
Mepivacaine	45–90	120–360
Novocaine	15–30	30–40
Prilocaine	30–90	120–360

Table 10

Maximum permissible doses of LA (mg/kg)

Anesthetic	Without vasoconstrictor	With vasoconstrictor
Articaine	– 4	7 5 (children)
Bupivacaine	2	1
Lidocaine	4,5	7
Mepivacaine	4,5	6,5
Novocaine	7	14
Prilocaine	6	8

The occurrence of side effects of LA is primarily associated with an increase in the recommended therapeutic doses. The resorptive effect of drugs on the central nervous system is characterized by drowsiness, dizziness, headache, weakness, auditory (noise or ringing in the ears) and visual impairment, depression of consciousness or anxiety. Paresthesia and paresis, nausea, vomiting, diarrhea, nystagmus, tremor, spastic muscle contraction, cramps followed by CNS depression and death may occur. In-

crease the risk of severe complications, acidosis and hypercapnia. Cocaine causes euphoria, which is associated with the probability of addiction development.

The effect of LA on CVS is manifested by a decrease in heart rate and hypotension (with the exception of cocaine and mepivacaine). Bradyarrhythmias or cardiac arrests are also probable. Bupivacaine is more cardiotoxic than other LA. levobupivacaine is deprived of such a side effect. It should be emphasized that a part of side effects (tachycardia, increased blood pressure, coronary spasm) in combined anesthetics may be associated with the action of adrenaline. Intramuscular administration of LA (usually benzofurocain) can cause local irritating effects in the form of burning. Sovcain, when applied topically, can cause an inflammatory reaction of the skin. Allergic reactions (bronchospasm, angioedema) is caused, as a rule, by esters, which are metabolized to PABA derivatives in significant quantities. Amide anesthetics rarely cause such side effects.

In case of an overdose of LA, disturbances such as dizziness, motor agitation, disorientation, nystagmus, tremor, impaired consciousness, collapse, cardiac arrest, respiratory depression, convulsions, death can occur.

Contraindications to the use of local anesthetics:

- hypersensitivity to group drugs;
- emotional and mental instability of the patient, requiring the use of anesthesia;
- operations in the oral cavity with a high probability of severe bleeding, which threatens blood aspiration and asphyxia;
- global circulatory disorders;
- diseases of the central nervous system (meningitis, tumors, poliomyelitis, etc.);
- severe diseases of CVS (hypertension, heart failure, cardiogenic shock, especially with rhythm disturbances);
- serious disturbances in the rhythm and conduction of the heart: sick sinus syndrome, bradycardia, AV block;
- decompensated diabetes;
- septicemia;
- pustular skin conditions;
- kidney and liver failure;
- angle-closure glaucoma;

- severe myasthenia gravis;
- children's age up to 1 year;
- seizures in past history;
- fluoride, cyclopropane, chloroform anesthesia;
- pernicious anemia with cerebrospinal symptoms;
- use of anesthetics with vasoconstrictors for anesthesia of the fingers, toes, nose, genitals and other organs with insufficient blood supply (threat of gangrene!);
- irrational use of PABA derivatives (novocaine) in the treatment by sulfonamides;
- local anesthetics in combination with a vasoconstrictor are contraindicated in the risk group: patients with hypertension, pregnant women, children under 5 years, patients with thyrotoxicosis or other endocrine diseases, athletes who should undergo doping control in the near future. The use of LA with a minimum content of a vasoconstrictor (or without it) is required for patients of senile age.

Features of the use of LA in dental practice:

- the choice of LA is primarily based on the predictable morbidity of the manipulations and the necessary duration of anesthesia;
- to prevent toxic effects, the use of minimal doses of LA is necessary. In the case of inevitability of the use of large doses, it is advisable to carry out sedation with benzodiazepines with sibazon (diazepam) at a rate 0.1–0.2 mg/kg, parenterally;
- the choice of LA, taking into account an alleged pain during manipulation and the upcoming duration of anesthesia;
- it is advisable to use more effective and convenient for use carpule anesthetics (ubistesin, ultracain, etc.). The carpule contains an anesthetic solution ready for use with other ingredients: a vasoconstrictor, stabilizer, etc.;
- if necessary, the anesthetic effect of drugs should be prolonged using vasoconstrictors (at the rate of 1 drop of 0.1 % adrenaline solution per 5–10 ml of LA, D_{max} – 5 drops). It should be remembered that with repeated injections of LA with epidural anesthesia, tachyphylaxis may occur (loss of effectiveness);
- it should be borne in mind that convulsive syndrome can be a serious complication of the use of LA. Its stopping is carried out by

thiopental (1–2 mg/kg), diazepam (0.1 mg/kg i.v.). The motor component is also eliminated by succinylcholine (0.1–0.2 mg/kg);

- it must be remembered that in combination treatment, some drugs (for example, SA) can reduce the effect of anesthetics or increase their toxicity (antiarrhythmic drugs).

Table 11 provides recommendations for the use of LA at dental clinic.

Table 11

Recommendations for the use of LA at dental clinic

Medicine	Application ways	Synonyms
Anaesthesin	For superficial anesthesia of the skin, mucous membranes, wound, ulcer, burn surface – 5–20 % oil solutions, 5–20 % ointments, powders, aerosols (amprovizol)	Benzocaine, norcain, paresthesin, topanalgin
Articaine	With uncomplicated tooth extraction, filling, tooth turning; ultracain DS-Forte is used if a longer anesthesia is necessary (pulp amputation, root apex resection, osteotomy, etc.). The maximum dose is 12.5 ml (6 carpules)	Ultracain DS ultracain DS Forte, alfacaine, septanest, ubistesin
Benzofurocain	For infiltration anesthesia in dentistry – 2–5 ml of 1 % solution	
Bupivacaine	For infiltration anesthesia – 0.25 % solution; conduction, epidural anesthesia – 0.75 % solution, caudal – 0.25–0.5 % solution. For blockade of peripheral nerves – 0.25–0.5 % solutions	Marcain, narcaine, carbostezin, anecaine
Dicain	When removing foreign bodies, surgeries – 2–3 drops. An increased dental sensitivity – 0.25–0.5–1 % solution, in the form of paste	Tetracaine, lantocaine, rexocaine
Lidocaine	For infiltration anesthesia – 0.25–0.5 % solution. For terminal anesthesia of the oral mucosa – 2 % solution 10 ml (5–10 % solution). In the form of aerosol (lidestin) – in dentistry. For conduction anesthesia – 1–2 % solution (resp. 40, 20 ml – maximum). For blockade of the nerve plexuses – 1–2 % solution (resp. 20, 10 ml – maximum)	Xycain, xylocaine, anestecaine, lignocaine, marcain, xylodont, lignospan, xynolor

Medicine	Application ways	Synonyms
Novocaine	For infiltration anesthesia – 0.25–0.5 % solution; conduction anesthesia – 1–2 % solution; epidural anesthesia – 2 % solution (20–25 ml); spinal anesthesia – 5 % solution (2–3 ml)	Aminocaine, procaine, protocaine, syntocaine, pancain, paracain,
Pyromecain	For superficial anesthesia – 1–5 ml of 0.5–1 % solution and 5 % ointment	Bumecaine
Ropivacaine	For surgical interventions, relief of acute pain. Used for lumbar, thoracic, epidural anesthesia, peripheral nerve blockade and infiltration anesthesia (0.75 % solution). The amount of the drug depends on the nature of the disease.	Naropin
Trimecaine	For infiltration anesthesia – 0.125 %, 0.25 % and 0.5 % solutions (resp. 1500, 800, 400 ml – maximum). For anesthesia – 1–2 % solution (resp. 40, 20 ml). For peridural anesthesia – 1 %, 1.5 %, 2 % solutions. For blockades – 2 % solution (up to 10 ml). For local anesthesia in dentistry – in the form of pastes (also containing dicain, lydase, sodium carbonate)	Mesocaine, mesdicaine
Cyanest octapresin (combination drug)	It contains prilocaine hydrochloride and filepresin. It is used for infiltration anesthesia in dentistry, when deep ischemization of the injection zone is not needed; 1–2 ml of 3 % solution is administered.	

3.2.2. Anesthetic drugs

Anesthetic drugs (general anesthetics) affect the central nervous system, cause temporary loss of consciousness, inhibition of all types of sensitivity, decreased muscle tone and reflex activity, moderate inhibition of the vital centers of the medulla oblongata. According to the method of administration into the body, they can be divided into agents for inhalation anesthesia, which are introduced into the body through the respiratory tract and for non-inhalation anesthesia, which are usually administered intravenously.

General anesthetics cause blockade of transneuronal (synaptic) transmission in the central nervous system. The importance of the effect of

drugs is associated with physicochemical properties (ability to dissolve in lipids, effect on oxidative processes, adsorption on the membrane of nerve cells, the formation of unstable bonds with proteins of the central nervous system neurons, the formation of crystalline hydrates, etc.). Despite the difference in the biological and physicochemical mechanisms of action, all anesthetics act on the membrane of neurons, change its permeability to sodium and potassium ions and disrupt the depolarization process, which prevents the emergence of an action potential, as a result of which transneuronal transmission of excitation is blocked.

Immediately after the introduction of anesthetic into the body, the first stage of analgesia or stunning develops. It is characterized by a decrease in pain sensitivity, confusion, but maintaining contact with the patient. Tactile sensitivity persists. Although the duration of the analgesia stage is short (5–10 minutes), it can be used for short-term operations as an independent method of pain relief. In outpatient dental practice, anesthesia at the stage of analgesia is very convenient, because reflexes are not eliminated, and contact with the patient remains. Removing reflexes can lead to aspiration of blood, pus and the development of asphyxiation. The stage of analgesia can be prolonged using premedication and maintaining a certain concentration of anesthetic substances in the inhaled air.

At the second stage, complete loss of consciousness, motor and speech excitement, significant fluctuations in blood pressure, heart rhythm and respiration are observed, which is explained by the complete inhibition of the effect of the cerebral cortex on the lower sections and is accompanied by a secondary violation of the subcortical structures and increased reflex activity. During this period, you can not carry out any surgical intervention, because respiratory arrest, fibrillation and cardiac arrest can occur.

At the stage of surgical anesthesia (third stage), oppression of the cortex, subcortical formations and spinal cord leads to a complete loss of consciousness, sensitivity, reflexes, relaxation of skeletal muscles, normalization of blood pressure, while pulse is reduced, breathing becomes rhythmic, because the function of the vital centers of the medulla oblongata remains. At this stage, 4 levels of anesthesia depth are distinguished, which are regulated depending on the severity of the upcoming operation. Most surgical procedures are performed at this stage.

After stopping the inhalation of the anesthetic, the stage of awakening begins, while the functions of the central nervous system are restored in the reverse order. In the case of an overdose of drugs, deep depression of the vital structures of the medulla oblongata is observed, breathing and blood circulation are disturbed, the pupils expand sharply, death occurs from paralysis of the respiratory center and respiratory arrest.

At present, mononarcosis is rarely used in its pure form. Combined and mixed anesthesia is used to enter quickly into anesthesia and reduce complications from the use of general anesthetics. When preparing for operation, premedication is performed – sedatives and painkillers are prescribed to the patient. Ditilin, tubocurarine and other drugs are used to relax bone muscles. Atropine is used to eliminate negative vagal reflexes. If necessary, antihistamines, cardiovascular and other drugs are introduced into preoperative regimens.

Certain requirements are imposed on general anesthetics. They should be highly active, ensure good controllability of anesthesia (preferably without an arousal stage) and excretion from it, good regulation of its depth, low toxicity, and a wide range of anesthetic action. The latter represents the difference between the concentration of the drug in the blood that causes the stage of anesthesia and the concentration that inhibits vital centers). Drugs should not irritate the mucous membranes and damage the vascular endothelium, cause severe capillary bleeding, etc. There is a classification of drugs for anesthesia:

1. Drugs for inhalation anesthesia:
   - volatile liquids: chloroethyl, chloroform, ether, fluorotane, methoxyflurane, enflurane, isoflurane, trichloroethylene;
   - gaseous substances: nitrous oxide, cyclopropane, xenon.
2. Drugs for non-inhalation anesthesia: propanidid, thiopental sodium, hexenal, ketamine hydrochloride, midazolam, propofol, predion, alktezin, etomidate.

3.2.3. Drugs for inhalation anesthesia

For inhalation anesthesia, the following requirements are met: the ideal anesthetic should be inert, well absorbed and rapidly excreted through the respiratory tract. Isoflurane, which the title of the "gold standard" of inhalation anesthesia in the 90s received, meets these requirements the

most. The following is a general description of a number of drugs used in anesthesiology.

Ether for anesthesia is a volatile liquid that was first widely used. When inhaled ether vapors develop anesthesia. The drug is characterized by pronounced anesthetic activity, a wide range of effects and low toxicity. However, the introduction of anesthesia develops slowly (after 12–20 minutes). There is a long stage of excitement, which complicates the introduction of anesthesia. Awakening after ether anesthesia occurs in 20–40 minutes. And for several hours, post-anesthesia sleep, prolonged analgesia is observed. Ether is a cellular poison and, when applied topically, has a weak antimicrobial and local anesthetic effect, causing hyperemia of the mucous membranes. After the excitation stage, a decrease in tissue sensitivity is observed. At body temperature, the ether quickly evaporates, cooling and drying the tissues, that allows to use it to treat carious cavities and root canals before filling them in dental practice. The disadvantages of the drug are irritating effects on the respiratory tract (laryngospasm, bronchopneumonia) and a pronounced stage of excitement. To reduce the complications of ether, ether-oxygen anesthesia is used, as well as a combination of ether with nitrous oxide, fluorotane.

Fluorotane (halothane) is a volatile non-flammable liquid. Introduction to anesthesia occurs quickly (after 3–5 minutes); the stage of excitation is short. This type of anesthesia is easily manageable. Awakening occurs after 5–10 minutes, after an anesthetic sleep is short. Fluorotane has a great breadth of action. It has practically no analgesic effect; this requires the early prescription of a painkiller after surgery. Fluorotane moderately inhibits the respiratory center, reduces myocardial contractility and blood pressure, and causes bradycardia, arrhythmias, and hypotension. Among the side effects of the drug, it is worth highlighting the possibility of liver damage (hepatitis). Against the background of fluorotane anesthesia, epinephrine should not be used (it is advisable to use mesatone) and NA. Fluorotane is used for anesthesia often in combination with nitrous oxide and ether. Sometimes it is used in outpatient anesthesiology practice.

Enflurane is a volatile liquid. The drug is similar to fluorotane, but less active and safer when used with adrenaline. Almost no undesirable hepatotoxic effect. Sometimes it provokes convulsions. Isoflurane – an isomer

of enflurane, is weaker than halothane and enflurane, it dissolves in lipids, provides a quick entering anesthesia. It is poorly metabolized (100 times less than halothane) and therefore its hepatotoxicity, both for the patient and for the staff, is low. Isoflurane, less than other drugs, sensitizes the heart to catecholamines and suppresses CVS, but it can dilate peripheral vessels. Today, the drug is widely used in anesthesiology.

Methoxyflurane is a volatile liquid with high narcotic and analgesic activity, it is characterized by a slow introduction into anesthesia (10–15 minutes) and a gradual recovery, prolonged preservation of analgesia, good muscle relaxation, and the absence of irritating effects on the mucous membranes. The drug is characterized by nephrotoxicity and increased sensitivity of the myocardium to catecholamines. Due to toxicity, self-anesthesia is not used.

Trichloroethylene is a volatile liquid. It is a powerful anesthetic. Characteristics of the drug: quick introduction to anesthesia, good analgesia (both when injected into anesthesia, and after recovery), rapid awakening. It is used for short-term anesthesia and for analgesia for minor surgical interventions or pain manipulations, for autoanalgesia for severe pain that cannot be eliminated by narcotic analgesics (myocardial infarction, trauma, childbirth, trigeminal neuralgia). In dental practice, trichloroethylene is used in outpatient anesthesiology (sometimes in combination with LA) for pain relief during operations and dental treatment in patients with increased psychoemotional irritability. It increases the sensitivity of the heart to catecholamines.

Chloroform and chloroethyl are strong anesthetics, have a narrow range of narcotic effects and high toxicity, in connection with this, they are currently practically not used in anesthesiology. At dental clinic, they are used topically as a part of mixtures for the anesthesia of hard tooth tissues (Platonov's composition), pulp (with phenol), the mucous membrane (together with LA, menthol and ether).

Chloroethyl is a volatile liquid. When applied to the skin, it evaporates quickly, causing severe cooling, tissue ischemia, decreased sensitivity. This property of chloroethyl can be used for short-term local anesthesia during small surface surgeries (opening abscesses, removing mobile teeth, etc.). Chloroethyl is not suitable for the anesthesia of hard tooth tissues, since their cooling causes sharp pain.

Nitrous oxide – a colorless gas, does not ignite, but supports combustion. It meets most general anesthetic requirements. Inhalation of nitrous oxide provides a quick entring anesthesia and a quick wake up. The drug is characterized by weak anesthetic activity, its action does not cause sufficient muscle relaxation, therefore, a mixture of 80 % nitrous oxide and 20 % oxygen is used. Side effects are manifested by nausea, vomiting, bradycardia, muscle twitching, blood pressure fluctuations, etc. Before anesthesia, medical preparation is carried out of the patient. Nitrous oxide is often combined with other general anesthetics (ether, fluorotane). The drug causes intoxication and severe analgesia and therefore can be prescribed for the relief of severe pain attacks. Nitrous oxide is used for pain relief during childbirth, dressings of surgical patients, transportation of injured victims in the postoperative period.

Cyclopropane is a colorless gas, does not irritate the mucous membranes, and has a high analgesic and anesthetic activity. Its force of narcotic action exceeds nitrous oxide. Anesthesia is well controlled. They are used relatively rarely due to extreme explosiveness. Introduced in a mixture with oxygen using special equipment.

Xenon is an inert gas, odorless, without color and taste, is in the air, does not burn, is chemically indifferent, does not undergo biotransformation in the body, does not irritate the respiratory tract, is released through the lungs unchanged and easily controlled. Its discovery occurred 100 years ago, and its first clinical use was recorded 50 years ago. Xenon is stronger than nitrous oxide 1.5–2 times. A concentration of 70–80 % causes the surgical stage of anesthesia in 5–6 minutes. Awakening is easy, occurs after 2–3 minutes with a complete recovery of consciousness and pleasant subjective sensations. It has no toxic effects, mutagenic, teratogenic and embryotoxic properties, does not inhibit immunity. Xenon can be used in planned and emergency surgery, urology, orthopedics, traumatology, gynecology, ophthalmology, especially in patients with cardiovascular pathology.

3.2.4. Non-inhalation anesthesia

Unlike inhalation, non-inhalation anesthesia is less manageable. In dental practice, its implementation is complicated due to insufficient access of the anesthesiologist to the oral cavity. Therefore, it is more con-

venient to intervene in the MFA under introductory intravenous anesthesia with intubation of the trachea through the nose. The advantages of non-inhalation anesthesia can be considered: absence of arousal stage, the ability to start anesthesia right in the ward. Drugs for non-inhalation anesthesia according to the duration of action are divided into 3 groups:

1) short-acting drugs (up to 10–15 minutes) – propanidid (sombrevin) and ketamine (ketalar), propofol, etomidate;

2) medium duration (up to 20–40 minutes) – hexobarbital (hexenal), sodium thiopental and sodium hydroxide (predion), alktezin;

3) long-acting drugs (> 60 minutes) – sodium oxybutyrate.

Propanidid (sombrevin) with i.v. introduction creates an ultra-short effect, which is explained by its rapid hydrolysis by blood esterases. Anesthesia occurs after 30–40 seconds without an excitation stage and lasts 3–5 minutes. Convenient in outpatient practice for short-term operations, since after 20–30 minutes its action completely stops (without post-anesthetic depression). In dentistry, propanidid can be used for complicated tooth extraction, reposition of fragments, with fractures and dislocations of the jaw, when removing sutures, etc.

Ketamine is a non-competitive antagonist of excitatory amino acids (NMDA receptors). In medical practice, it is used for quick and short anesthesia (5–20 min). Ketamine causes "uncoupling anesthesia", i.e. deep anesthesia and light sleep (the patient's eyes can remain open), pharyngeal reflexes are preserved (not so much as to exclude the throwing of the contents of the oral cavity into the respiratory tract), muscle tone is enhanced, respiratory function can be suppressed and blood pressure may increase. High analgesic activity of the drug lasts up to 6–8 hours. These drugs are applied for short-term operations that do not require muscle relaxation or in combination with other drugs for anesthesia. I.v. introduction can cause pain and redness along the vein, an increase in blood pressure and heart rate; when awakening – psychomotor agitation, hallucinations and disorientation, which can last up to 24 hours. I.v. introduction of sibazon before ketamine anesthesia reduces psychomotor agitation upon awakening and helps to relax skeletal muscles during anesthesia. Ketamine sub-drug doses (approximately 0.4 mg/kg i.v.) have a pronounced analgesic property. In case of acute pain, the analgesic effect of ketamine injected into a vein usually develops over 10 minutes and lasts 2–3 hours. Recently, with some

success, the drug is used for chronic neurogenic pain (postherpetic neuralgia, glossopharyngeal neuralgia, etc.), pain in oncological practice, etc. Due to the pronounced side effects of ketamine, memantine and dextromethorphan are considered more promising antagonistic agents.

Thiopental sodium is a dry porous mass of yellow-green color, readily soluble in water. Solutions are prepared ex tempore in sterile water for injection. The drug is administered intravenously slowly, sometimes rectally. Anesthesia occurs immediately after completion of the injection ("at the end of the needle"). This is due to the rapid penetration into the brain. After a single dose, anesthesia lasts on an average of 20 minutes. Thiopental sodium is used mainly for administration in anesthesia with the subsequent use of other anesthetics. The drug does not sufficiently relieve pain, suppresses autonomic reflexes, because painful manipulations can cause fluctuations in blood pressure, heart rhythm disturbances, and even shock. It should be remembered that thiopental sodium is slowly biotransformed in the liver, has a long half-elimination period from the blood (about 10 hours). Therefore, with repeated administration, there is a risk of overdose. In case of respiratory depression and impaired cardiac activity, bemegrid is prescribed intravenously.

Sodium hydroxybutyrate (gamma-hydroxybuthyrate, GHB) is a white crystalline powder. It has a specific smell; it is easily soluble in water. Sodium oxybutyrate is a precursor of GABA, but unlike the latter, it easily penetrates the blood-brain barrier. The drug mainly stimulates GABA receptors located at the presynaptic ends, thus reducing the release of acetylcholine and NA. In small doses, the drug causes hypnotic and sedative effects; in large doses it produces anticonvulsant and narcotic effects. It should be noted that the drug has a pronounced antihypoxic effect. Introduction is i.v. slowly, less often – i.m. or enterally. I.v. introduction causes a stage of analgesia after 7–10 minutes, which is moderately expressed. The surgical stage of anesthesia occurs after approximately 30 minutes and lasts 2–4 hours. Sodium oxybutyrate is used mainly as basic anesthesia, often with drugs that suppress breathing. Propofol (diprivan) is a widely used agent for intravenous anesthesia, which has a short-term effect and quickly causes a medical sleep for 30 seconds. The resumption of consciousness is fast. Diprivan has all the necessary unique qualities (a clear dose-effect relations, ultra-short action, lack of cumulation, easy

handling). Studies show the benefits of supplementing analgesia with diprivan, fentanyl, or calypsol.

Midazolam is a derivative of benzodiazepine, depresses the central nervous system, has a sedative, anticonvulsant, muscle relaxant effect, and potentiates the effect of sleeping pills, narcotic and analgesic drugs. As a means of anesthesia, they are administerd i.m. and i.v. Midazolam may combined with ketamine, analgesics. Side effects: with intravenous administration, breathing can be depressed; therefore, when using the drug, equipment for artificial ventilation of the lungs is needed, allergic reactions, short-term amnesia, weakness can occur. Do not prescribe the drug enterally for patients whose profession requires a quick physical and mental reaction. Etomidate (hypnomidate, radenarkon) – causes anesthesia after 20–30 seconds and lasts for 8–10 minutes. It is used for initial anesthesia, with short-term surgical interventions, in obstetric practice, neurosurgery, ophthalmology. Side effects: slight respiratory depression, a slight decrease in blood pressure. Alktezin is used for induction of anesthesia in combination with other anesthetic drugs or for "mononarcosis". It has a large breadth of therapeutic effect (4.2 times greater than that of thiopental). Anesthesia occurs in 20–30 seconds and lasts 15–30 minutes. Undesirable side reactions can be reduced if tranquilizers, anticholinergics, analgesics, antihistamines are used before the introduction of drugs for anesthesia. Muscle relaxants are often prescribed to relax skeletal muscles, and short-acting ganglioblockers – for controlled hypotension.

3.3
ANALGESIC DRUGS

Analgesics (Greek an – without, algos – pain,) – drugs that weaken or relieve pain. Unlike anesthetic drugs, they do not turn off consciousness, do not inhibit other types of sensitivity. According to the chemical structure, nature and mechanisms of pharmacological activity, modern analgesic drugs are divided into two main groups: narcotic and non-narcotic. Recently, the terms "opioid analgesics" and "non-opioid analgesics" have been used accordingly. The separation is based on the following criteria:

- strength and nature of the analgesic action. NA relieve any pain, NNA mainly suppress pain caused by inflammation;
- ability to cause euphoria, sleep, drug dependence. NA cause euphoria, drowsiness, drug dependence, NNA do not cause these phenomena respectively;
- effect on the center of respiration. NA suppress respiration, NNA do not suppress respiration.

3.3.1. Narcotic analgesics

Over 20 alkaloids contain opium. By chemical structure, these are derivatives of piperidine phenanthrene, having the properties of NA (morphine, codeine) and papaverine, which has a myotropic antispasmodic effect on the unstripped muscle tissue of internal organs and blood vessels. Narcotic analgesics by origin are divided into: a) natural compounds that are obtained from opium – morphine, codeine, omnopon; b) compounds obtained by synthesis – promedol, fentanyl, pentazocine (lexir, fortral), piritramide (dipidolor), tramadol (tramal). Anesthetics isolated from opium are commonly called opiates, and their synthetic substituents are called opioids or opiate-like agents. According to the selectivity and nature of the action of drugs on opiate receptors, NA are classified as follows:

1) opiate receptor agonists:

- 2) a group of morphine and structurally similar synthetic compounds (ethylmorphine, codeine, methadone, morphilong, morphine, omnopon, oxycodone, propoxyphene);
- 3) derivatives of phenylpiperidine and other opioid synthetic analgesics (fentanyl, piritramide, trimeperidine (promedol), prosidol, loperamide).

2) opiate receptor agonist-antagonist (butorphanol, nalorphine, nalbuphine, pentazocine);

3) partial opiate receptor agonists (buprenorphine);

4) opiate receptor agonists with a mixed mechanism of action (tramadol);

5) opiate receptor antagonists (naloxone, naltrexone);

6) drugs of other groups (nefopam);

7) combination agents (prodein, sedalgin, spasmoveralgin, thalamonal, valorone, etc.).

Classification of NA according to their duration of action:

1) long-acting: lofentanil (up to 10 hours), morphilong (up to 24 hours), duragesic (up to 72 hours);

2) medium duration: morphine, promedol, tramadol, buprenorphine, butorphanol (3–8 hours);

3) short-acting: fentanyl (20–30 min);

4) ultra-short action: alfentanil (15–20 min).

The basis for elucidating the mechanisms of the analgesic effect of NA was the discovery of endogenous opioid peptides (enkephalins, endorphins) in the 70s. Endogenous opioids act as neurotransmitters of complex systems that inhibit pain. They are able to interact with specific opioid receptors.

Morphine and its analogues interacting with opioid receptors (mainly μ, κ, σ) that are located on the presynaptic membrane of the thin primary afferents of the spinal cord, reduce the release of mediators of nociceptive signals. The presynaptic effect of morphine is due to the opening of potassium (μ- and σ-receptors) or blocking of calcium (μ-, σ-receptors) canals. Both processes lead to a decrease in the movement of calcium ions at the end of C-fibers, thus causing a decrease in the release of pain mediators. The presynaptic effect of morphine, which leads to a decrease in the release of mediators, is regarded today as the most effective component

in the mechanism of development of analgesia. The effect of morphine on the postsynaptic membrane is manifested in hyperpolarization and inhibition of the activity of neurons of the posterior horns involved in the conduction of pain impulses.

NA reinforce the inhibitory effect of individual structures of the midbrain and medulla oblongata on the activity of neurons in the spinal cord. Morphine causes changes in the emotional sphere, that can cause a decrease in the negative sensation of pain. Under the influence of morphine-like substances, the flow of pain impulses in the area of the thalamus, the reticular formation, is suppressed, inhibiting their passage into the cerebral cortex.

One of the main reasons for the development of drug dependence regarding morphine and its analogues is euphoria. The desire to feel this condition once again determines the repeated use of the drug and causes mental and physical dependence on the drug. It is assumed that NA, by activating the described receptors, inhibit the release and synthesis of endogenous peptides by the feedback principle. After their cancellation, there arises a deficiency of both the endogenous peptide and, of course, the drug that is administered. Withdrawal syndrome (lat. abstinence – containment) develops, which manifests itself in the form of mental, autonomic, cardiovascular and other disorders. The danger of addiction limits the use of NA. In addition, in the case of their repeated use, tolerance develops, that is, their effect is weakened. Therefore, to obtain an analgesic effect, increasing doses of the drug are needed.

In dental practice, NA is used in the pre- and postoperative periods, with injuries and operations of the MFA, for pain relief in cancer patients. NA can not be used for fractures of the upper jaw, which are often accompanied by traumatic brain injury, since they, expanding the vessels of the brain, increase intracranial pressure. Dental interventions are often performed on the background of NNA or ataralgesia in combination with local anesthesia. To reduce severe toothache in pulpitis, periodontitis, and for sedation in dentistry, codeine and NNA combinations are used. Codeine is a part of pentalgin (at the same time as amidopyrine, analgin, caffeine and phenobarbital), sedalgin (with caffeine, phenacetin and acetylsalicylic acid), solpadeine (with paracetamol and caffeine), etc.

Morphine is a typical representative of the NA group of opiate receptor agonists, which is taken as the "gold standard" in most studies and in the literature. Its main effect is painkilling (develops while maintaining consciousness). Under the influence of morphine, the subjective assessment of pain and attitude to it changes. At the same time, a change in the parameters characterizing the pain reaction is observed: the threshold for pain perception increases, the period of pain tolerance lengthens, and emotional and behavioral reactions to pain are weakened. Analgesia is accompanied by changes in the mental sphere: self-control decreases, imagination is excited; in some cases there is euphoria or drowsiness.

Central effects of morphine:

- analgesia – more pronounced than that of NNA;
- respiratory depression (associated with inhibition of the stem mechanisms of its regulation);
- suppression of cough reflex (associated with inhibition of the expiratory center);
- sedative effect – depression of consciousness, impaired mental activity;
- sleeping pill – superficial sleep (occurs more often in young people);
- euphoria, disappearance or dulling of unpleasant emotions;
- nausea, vomiting (due to activation of the trigger zone at the bottom of the IV ventricle);
- rigidity of the muscles of the body (realized at the spinal level);
- increased spinal reflexes (due to the elimination of downward inhibition of a simple two-neural reflex);
- myosis, associated with an increase in the tone of the core of the oculomotor nerve;hypothermia, decreased basal metabolic rate;
- bradycardia and arterial hypotension are associated with increased tone of the vagus nerve core;
- effect on the production of hormones – decreased secretion of ACTH, increased secretion of prolactin and antidiuretic hormone.

Peripheral effects:

- restriction of peristalsis, constipation effect;
- increased tone of smooth muscles of the ureters, bladder and sphincter of the urethra, decreased urination;

- increased tone of smooth muscles of the biliary tract and sphincter of Oddi;
- increased tone of the muscles of the bronchi and smooth muscles of the uterus.

Inhibition of the center of respiration is typical of morphine. In small doses, it reduces the frequency and deepens respiratory movements, and in large doses it reduces not only the frequency, but also the depth of the respiratory movements. At the same time, ventilation decreases, signs of hypoxia develop. In case of an overdose of morphine, death occurs from paralysis of the respiratory center. Penetrating the placenta, it can cause respiratory depression. Morphine is especially dangerous for patients with respiratory failure (emphysema, bronchial asthma). All NA reduce cough, suppressing the cough center of the medulla oblongata, but increase the accumulation of secretions in the airways. Vomiting is associated with the initiation of chemoreceptor trigger zones of the medulla oblongata. However, most often, especially in large doses, morphine exerts an antiemetic effect due to blockade of the emetic center, therefore, in case of morphine poisoning, emetics are ineffective. Morphine causes constriction of the pupils, and "pinpoint" pupils are feature of chronic poisoning.

Morphine, stimulating the nucleus of vagus nerve, causes bradycardia, can help to lower blood pressure. The drug enhances the spasm of the sphincter of the digestive canal, thus leading to a slowdown, and sometimes cessation of the transition of intestinal contents from one section to another – there is a "fixing effect". This is also facilitated by a decrease in the secretion of bile, a decrease in the secretion of the digestive glands, pancreas (constipation). Spasm of sphincter of Oddi inhibits the release of bile and increases pressure in the gallbladder. Morphine reduces diuresis by cramping the sphincters of the bladder.

For practical use, the following drugs are of importance. Promedol is a synthetic drug that acts 3–4 times weaker than morphine, has a moderate antispasmodic effect, less depresses the respiratory center, and to a lesser extent excites the vagus nerve center and vomiting center. Tramadol is a synthetic drug, a less powerful opioid analgesic. In the mechanism of its action, two components are distinguished: interaction with opioid receptors, and also the effect on the activity of monoaminergic systems. In particular, at the level of the spinal cord, tramadol enhances

inhibitory serotonergic and adrenergic mechanisms. Unlike other opioids, it depresses breathing slightly, does not significantly affect the digestive tract, and has significantly less narcogenic potential. After the introduction into the vein, the analgesic effect occurs after 5–10 minutes, when taken orally – after 30–40 minutes, the effect lasts 3–5 hours. Fentanyl is a synthetic drug, stronger than morphine in analgesic properties, with intravenous administration, the effect occurs in 1–3 minutes and lasts 15–30 minutes. It is usually used with droperidol for NLA. Naloxone is a "pure" competitive NA antagonist. It removes the effect of morphine-like agents on opiate receptors. The effect lasts about 1–3 hours and can be re-entered, since the effect of a longer period. In case of an overdose, i.v. administration of naloxone normalizes respiration after 1–2 minutes. In addition, the drug is used for alcoholic coma, shock states, and some mental illnesses.

Almost all side effects of NA are associated with their pharmacodynamics. The main side effects of μ-receptor agonists are respiratory depression. Nausea, vomiting, and urinary retention may occur. Fentanyl is characterized by the development of severe rigidity of muscles of central origin. With the systematic administration of morphine, tolerance develops. A big disadvantage of NA is the development of a painful addiction due to its ability to cause euphoria. Dependence is supported by withdrawal symptoms, which develops 6–12 hours after drug administration, has a severe course and can end fatally. Anxiety, fear, aggressiveness, heart palpitations, fluctuations in blood pressure, pain in the abdomen, muscles and joints, diarrhea, cramps, etc develops.

Acute morphine poisoning is characterized by respiratory depression, a sharp narrowing of the pupils (with severe hypoxia, they can be dilated), cyanosis, hypothermia, coma. Death occurs from paralysis of the respiratory center. Therefore, the main treatment is aimed at restoring breathing. The most effective method is mechanical ventilation with tracheal intubation. The antidotes of morphine-like agents are nalorphine, naloxone and naltrexone. In case of NA poisoning, naloxone, a specific antagonist that is administered intravenously (0.4–0.8 mg), is often used. In case of morphine poisoning, the stomach is repeatedly washed with 0.05–1 % solution of potassium permanganate, which oxidizes morphine and a suspension of activated carbon; salt laxative is also prescribed.

3.3.2. Non-narcotic analgesics

Non-narcotic (non-opioid) analgesics differ from opioids significantly in pharmacological properties. By the strength of the analgesic effect, these drugs are significantly inferior to NA, their effect is mainly manifested in inflammatory pain (arthritis, myositis, neuralgia), and in case of traumatic or postoperative pain they are less effective. NNA do not suppress respiration, do not cause euphoria and drug dependence, do not have soporific effect, and do not suppress the cough center. The drugs of this group have pronounced anti-inflammatory and antipyretic effects.

Classification by chemical structure:

- derivatives of salicylic acid: acetylsalicylic acid, diflunisal, sodium salicylate;
- derivatives of acetic acid: indomethacin (methindole), sulindac, aceclofenac, diclofenac (orthophen), ketorolac (ketorol), tolmetin;
- derivatives of propionic acid: ibuprofen (brufen), naproxen (naprosyn), ketoprofen;
- derivatives of anthranilic acid: mefenamic acid, flufenamic acid;
- pyrazolones: phenylbutazone, oxyphenylbutazone, azapropazone;
- oxicams: piroxicam, meloxicam, tenoxicam;
- sulfonanilide derivatives: nimesulide (mesulid);
- para-aminophenol derivatives: paracetamol;
- coxibs: celecoxib, etoricoxib, parecoxib, rofecoxib;
- derivatives of other chemical compounds: nabumetone, etodolac, amizon.

All of these drugs have a number of common properties:

- are widely used to treat pain of moderate intensity, mainly associated with inflammatory processes;
- less effective in case of intense pain, inferior in strength to opioid analgesics;
- are available for outpatient treatment and do not require participation of medical personnel;
- when used, additional analgesia can be obtained in combination with adjuvant drugs and opioids;
- have dose restrictions: with a further increase in it, the analgesic effect does not increase;

- non-opioid analgesics do not cause the development of tolerance or physical dependence;
- most drugs are relatively inexpensive.

It is important to understand that intensity of pain syndrome that accompanies inflammation is more dependent on the genesis of the inflammation, previous treatment, the sensitivity of the body to drugs, etc. In the development of pain, an important role belongs to release of PG that interact with biogenic amines (bradykinin, histamine, etc.) and increase the sensitivity of pain receptors. This happens this way: under the influence of damaging factors, arachidonic acid is released from the phospholipids of the cell membrane. As a result of the cyclooxygenase and lipoxygenase pathways of its transformation, eicosanoids – PG, thromboxane, leukotrienes appear, which cause typical biochemical effects.

The pharmacological effects of NNA are associated with the fact that they suppress the activity of the COX enzyme, under the influence of which PG are formed in the tissues of the body from unsaturated fatty acids, which are involved in inflammation, fever and pain. So, acting on nerve endings, PG increase their sensitivity to bradykinin – a peptide that is formed in tissues and is a stimulator of pain receptors. The existence of several isoforms of COX has been established. In particular, COX-1 provides the synthesis of PG that regulate the normal physiological functions of cells. The activity of COX-2 is enhanced by the influence of pro-inflammatory stimuli; this enzyme stimulates the synthesis of PG involved in the development of inflammatory reactions. Suppressing PG synthesis by inhibiting the synthesis of COX-2, NNA reduce the sensitivity of nerve endings to bradykinin, histamine, serotonin, and reduce tissue edema in the focus of inflammation, thereby weakening the mechanical compression of nociceptors in it.

Pain in case of pulpitis, in particular, is associated with the accumulation of prostacyclins in the vascular tissue of the tooth, which contributes to the expansion of blood vessels, the appearance of edema and congestion, and the compression of exudate nerve endings. The central analgesic effect of NNA is associated with the penetration of drugs through the BBB and the blockade of PG synthesis in the centers of the hypothalamus. In addition to this mechanism, due to blocking of COX-1 and COX-2, transmission of pain impulses at the level of dorsal roots of ganglia of the spi-

nal cord is reduced. Therefore, the peripheral analgesic effect of NNA is considered as a consequence of eliminating inflammation and preventing sensitization of pain receptors of PG. Inhibition of COX-1 is the cause of the main side effects of NSAID – peptic ulcer of the stomach and intestines, impaired renal function.

Non-narcotic analgesics lower body temperature, only if it rises. They reduce the content of PG in the cerebrospinal fluid and reduce the activating effect of pyrogens on hypothalamic cells. This leads to an increase in heat transfer and increased sweating. The desensitizing effect of NNA develops slowly, within 3–6 months and to a greater extent it is expressed in indomethacin, diclofenac sodium, piroxicam, mefenamic acid. The desensitizing effect is associated with a decrease in the synthesis of E_2 PG in the focus of inflammation, which reduces the chemotaxis of monocytes and T lymphocytes. It is also known that E_2 PG take part in preparing for the division of lymphocytes and their blast transformation, therefore, NNA, blocking the synthesis of E_2 PG, inhibit this process.

Currently, in the treatment of severe pain (especially long-term), the advantage belongs to selective or specific drugs that have fewer side effects and are better tolerated by patients. For clinical practice, the following drugs are important. Meloxicam (movalis, rheumaticam) is the most used derivative of oxycam. It has a triad of NNA effects. It belongs to the category of drugs with pronounced pharmacological properties. The drug has a long-lasting effect, which makes it possible to be limited to a single dose per day. Nimesulide (mesulid) is a sulfonanilide derivative, a selective COX-2 inhibitor. It has a pronounced analgesic, anti-inflammatory, antipyretic effect. It has the ability to suppress the formation of free radicals (without affecting hemostasis and phagocytosis). In dentistry, it can be used for intense pain, but is not recommended for prolonged use. Celecoxib (celebrex) is a drug of a new class of coxibs, a specific COX-2 inhibitor. It has a significant analgesic, chondroprotective and anti-inflammatory effect, does not affect platelet aggregation. The drug is for dystrophic and inflammatory diseases of the musculoskeletal system, rheumatism, etc. Parecoxib sodium (dynastat) is the first parenteral selective inhibitor of COX-2. It has a powerful analgesic effect, which occurs quickly and continuously. It is administered parenterally – 20 or 40 mg once. The drug does not affect platelet aggregation and bleeding time, has fewer

gastroduodenal side effects than traditional NSAID. Aceclofenac (airtal) is a derivative of acetic acid of selective action. Refers to the new generation of the NSAID gold standard. It has high efficiency due to the multifactorial mechanism of action on inflammatory mediators. It has excellent gastrointestinal tolerance.

In clinical practice, non-selective analgesics are often used, which in the absence of contraindications have good tolerability. Ketolorac (ketanov, ketorol) is a derivative of heteroaryl acetic acid. The analgesic effect of this drug is one of the strongest and exceeds the effect of aspirin, indomethacin or naproxen. In dentistry, it is used for intense pain (traumatic, postoperative). It is highly effective in eliminating pain associated with large abdominal, orthopedic and gynecological operations. Ketoprofen (ketonal) is a derivative of propionic acid. One of the most powerful analgesics, well tolerated. It is successfully used in the treatment of postoperative pain. Dexketoprofen (dexalgin) – inhibits the synthesis of PG in the structures of the spinal cord. The precursor of dexalgin – ketoprofen is a racemic mixture of two stereoisomers, but only S-(dex)ketoprofen has an analgesic effect, L-enantiomer only increases toxicity and metabolic load. Dexalgin interacts with COX 5 times more active than racemic ketoprofen and 100 times more powerful than L-enantiomer. Diclofenac sodium (orthophen, voltaren) has a high analgesic and anti-inflammatory activity. It is well tolerated by patients. Lornoxicam (xefocam) is a modern analgesic and anti-inflammatory drug. In dentistry, it can be used for severe postoperative pain and toothache, inflammatory processes. Ibuprofen (brufen) is characterized by a triad of effects of NNA, but anti-inflammatory activity is less pronounced. Naproxen has a longer action compared to ibuprofen and a significantly pronounced anti-inflammatory effect.

Paracetamol (panadol, efferalgan) has a moderate analgesic and antipyretic effect. The drug does not damage the gastric mucosa and is able to prevent the ulcerogenic effect of other drugs (especially aspirin). Paracetamol practically does not disturb the electrolyte balance, does not affect blood clotting, and does not irritate the digestive canal. It forms metabolites that can damage bakers (in TA), and enhances the hemolysis of red blood cells – sometimes it contributes to the development of anemia. To potentiate analgesia, it is recommended to combine other NNA with paracetamol (ibuprofen, aspirin, meloxicam, diclofenac, etc.). Acetylsalicylic

acid (aspirin) – is a classic drug with moderate analgesic and anti-inflammatory effects. Aspirin is also known as an antiplatelet agent to prevent the formation of postoperative blood clots, the prevention of cavernous sinus thrombosis in surgical dentistry, as well as in general medical practice for coronary heart disease, cerebrovascular accident, etc. Pyrazolone derivative – analgin is an analgesic, antipyretic and anti-inflammatory drug. In Ukraine, the drug is mainly used in emergency care. With intravenous administration, it is well absorbed, acts quickly, strongly and for a short time. With the course administration of analgin, negative effects on hematopoiesis (agranulocytosis) were found, in connection with which, most countries refused to use it. Mefenamic acid is inferior in activity to indomethacin and orthophen. In case of local application in low concentrations, it improves the regeneration processes, has a moderate analgesic and anti-inflammatory effect, and stimulates the formation of endogenous IFN.

NNA are widely used in dental practice, as effective remedies for pain of inflammatory and neurological nature, which often occur in the MFA. Drugs are prescribed for toothaches, pain after tooth extraction, pericoronitis, periostitis, osteomyelitis, pulpitis, periodontitis, neuralgia, neuritis, stomatitis, arthritis, arthrosis, etc. NNA are the most used over-the-counter drugs in general medical practice. They are used for rheumatism and inflammatory diseases of connective tissue, myalgia, radiculitis, arthritis, etc. They are widely used for relief of postoperative and traumatic pain. Analgesics of selective action (nimesulide, celecoxib, parecoxib, etodolac, aceclofenac, etc.) are of great importance for medical practice, since they cause fewer complications.

Local use of NNA for inflammation and tissue injuries helps to increase blood circulation, excretion of biologically active substances with an irritating effect, reduce spastic muscle tension and increase range of motion. Salicylic acid in small concentrations (1–2 %) has a keratoplastic effect, promotes the healing of ulcers and wounds. In high concentrations (5–10 %), its keratolytic effect is manifested, thus leading to painless exfoliation of the epithelium during hyperkeratosis. Salicylic acid also has antimicrobial and antifungal effects, and has antienzyme activity.

Side effects of drugs in this group are:

- ulcerogenic effect (gastric bleeding – 0.5–3 % of identified side effects);

- nausea, lack of appetite, stomatitis, vomiting, gastralgia, diarrhea (10–30 %);
- skin complications – urticaria, photosensitivity, itching of the skin (12–15 %);
- toxic effect on the kidneys – interstitial nephritis, lowering of glomerular filtration, increased chronic renal failure (butadione, analgin, aspirin, ketorolac);
- hepatotoxic effect (more often – paracetamol, indomethacin, diclofenac, nimesulide);
- violation of neurosensory sphere – dizziness, headache, feeling of tiredness, sleep disorder (1–10 %);
- mental disorders – hallucinations, confusion, depression, drowsiness (indomethacin, aspirin);
- decrease in hearing acuity (aspirin, diflunisal);
- hematological complications – hypochromic, hemolytic anemia, thrombocytopenia (pyrazolone derivatives);
- neutropenia, agranulocytosis (analgin, sodium metamizole). The use of analgin, as well as butadione is prohibited or limited in many countries!
- clouding of the cornea, change in visual fields (more often – ibuprofen, indomethacin);
- severe encephalopathy in combination with liver damage – Reye's syndrome (aspirin, especially in children under 12 years when using the drug against a viral infection!);
- teratogenic effect;
- inhibition of labor;
- asthmatic triad, rhinitis, conjunctivitis (aspirin, pyrazolone).

Less common are acute pulmonary edema (salicylates in toxic doses), hypersensitive pneumonitis (naproxen, ibuprofen, sulindac, phenylbutazone), fever (ibuprofen), carditis (phenylbutazone), pancreatitis (sulindac), acute proctitis (mefenamic acid), vasculitis (phenylbutazone, indomethacin, naproxen). Due to the probability of side effects that are especially life-threatening (agranulocytosis, aplastic anemia, inhibition of platelet function), use of pyrazolone derivatives (analgin, butadione), as well as phenacetin is sharply limited in many countries. More often adverse reactions occur from the gastrointestinal tract (gastropathy, duodenop-

athy, esophagopathy). Methods for improving the tolerance of NSAID are shown in the section "Non-steroidal and steroidal anti-inflammatory drugs". In practical dentistry, one should adhere to the basic principles of rational use of NNA.

I. When choosing an analgesic, it is necessary to take into account the correspondence of the severity of pain to the strength of the analgesic effect of the drug:

- in case of severe pain, powerful NNA are used – ketorolac (ketanov), parecoxib (dynastat), dexketoprofen (dexalgin), lornoxicam (xefocam), diclofenac potassium (rapten-rapid), meloxicam (movalis), nimesulide (nise, nimesil);
- for moderate pain, ibuprofen, paracetamol, mefenamic acid, etc are prescribed.

II. For the treatment of acute and chronic pain, pharmacokinetic properties of analgesics must be taken into account:

- for acute pain syndromes, analgesics should be used that, according to the pharmacokinetics (absorption, elimination), correspond to this type of pain (ketorolac, ketoprofen, diclofenac potassium, ibuprofen, mefenamic acid, paracetamol, etc.);
- for chronic pain, it is advisable to use analgesics with a long action (meloxicam, celecoxib, ibuprofen long, mesulid, diclofenac retard, etc.).

III. In the treatment of pain, the dose and the route of administration should be carefully determined: in acute cases or exacerbations of chronic pain, it is advisable to use the maximum therapeutic doses of the drugs and choose the parenteral route for their administration.

IV. The duration of therapy is determined depending on the diagnosis, the characteristics of the clinical course of the disease, the individual tolerance of the drug and the severity of side effects.

V. To prevent side effects, do not prescribe toxic drugs (analgin, butadione, indomethacin, phenacetin, ketorolac, nimesulide).

VI. To potentiate the analgesic effect, auxiliary preparations should be used (caffeine, diphenhydramine, drotaverine, sibazon, amitriptyline, mydocalm, etc.).

VII. It is necessary to limit the prescription of NNA as much as possible during pregnancy and lactation.

3.4

NON-STEROIDAL AND STEROIDAL ANTI-INFLAMMATORY DRUGS

In dental practice, treatment of inflammation is a complex task which is based on the consistent use of modern NSAID and GCS. For pharmacotherapy of a moderate inflammatory process (stomatitis, periodontitis, periostitis, arthritis, etc.), NSAID are often prescribed – topically or enterally. Local glucorticosteroid preparations are also suitable for this purpose. Severe inflammatory processes with pronounced destructive and exudative components (erythema multiforme, lichen planus, arthritis and arthrosis, osteomyelitis, etc.) are advisable to be stopped by the use of NSAID parenterally and GCS enterally or parenterally.

3.4.1. Non-steroidal anti-inflammatory drugs

All NSAID are characterized by anti-inflammatory, antipyretic and analgesic effects. NSAID are nonspecific in action, i.e. their effect is expressed with inflammation of any genesis and localization of the process, but drugs of different groups differ from each other in the strength of the indicated action. In general, NSAID are noted for good tolerance, do not accumulate, are rapidly excreted from the body, and cause fewer side effects compared with GCS. The dose of these drugs and the regimen are determined individually. Non-steroidal anti-inflammatory drugs include:

I. Derivatives of arylcarboxylic acid:
- derivatives of salicylic acid (acetylsalicylic acid, diflunisal);
- derivatives of anthranilic acid (mefenamic acid).

II. Derivatives of arylalkanoic acid:
- arylacetic acid (diclofenac, aceclofenac, ketorolac);
- derivatives of indoleacetic acid (indomethacin, sulindac, etodolac);
- derivatives of arylpropionic acid (ibuprofen, naproxen, ketoprofen).

III. Derivatives of enolic acid:

- pyrazolone derivatives (phenylbutazone, oxyphenylbutazone, metamizole);
- oksikams (piroxicam, meloxicam).

IV. Derivatives of various groups:

- sulfonamides (see TA) (nimesulide);
- benzylsulfonamides (celecoxib);
- naphthols (nabumeton);
- choline salicylate;
- benzydamine.

V. Combined drugs:

- arthrotec (diclofenac + misoprostol);
- dolaren (diclofenac + paracetamol).

Inflammation is a universal reaction of the body in response to the action of exo- and endogenous damaging factors. Visual manifestations of the inflammatory reaction appear in the form of redness, fever, soreness and impaired function of the affected organs. It should be noted that due to the peculiarities of the anatomical structure of the MFA, inflammation in dental practice can become pronounced, spread rapidly and be accompanied by severe pain, fever and other general reactions of the body. Under the influence of various etiological factors (microorganisms, toxins, etc.), phospholipase A_2 is activated in the focus of inflammation, under the influence of which arachidonic acid is released from the phospholipids of cell membranes. There are two ways of its metabolism: the first – COX enzyme oxidizes arachidonic acid and includes it in the cycle of formation of inflammatory and pain mediators – PG, the second – lipoxygenase enzyme participates in the cycle of creating leukotrienes, which are mediators of allergies. In platelets, endoperoxides turn into active substances thromboxanes, which have a pronounced aggregation effect and contribute to vasoconstriction. During the synthesis of PG and leukotrienes, free oxygen radicals are also formed. During inflammation, all types of metabolism intensify, pH decreases, the osmotic pressure rises, thus contributing to swelling of colloids. Inflammatory mediators (PG, histamine, kinin, etc.) cause an increase in vascular permeability, an increase in the amount of exudate, etc.

The mechanism of action of NSAID is associated with inhibition of COX, resulting in reduced synthesis of endoperoxides, PG and inflamma-

tory mediators. NSAID do not significantly affect the processes of alteration. The drugs normalize microcirculation, reduce the activity of hyaluronidase and inhibit the synthesis of thromboxane, and prevent the formation of microthrombi. They affect the energy metabolism of the cell; reduce the level of ATP in the tissues of the inflammatory cell, which leads to the separation of the processes of oxidative phosphorylation and inhibition of anaerobic glycolysis. NSAID inhibit free radical reactions that enhance inflammation and contribute to its spread. See also section 3.3. "Analgesic drugs".

Different NSAID are characterized by unequal inhibitory activity on COX-1 and COX-2. For example, indomethacin, acetylsalicylic acid and piroxicam are more active in relation to COX-1 than in COX-2, therefore they are most dangerous due to side effects, especially gastrointestinal ones. NSAID are selective COX-2 inhibitors (nimesulide, meloxicam, celecoxib), have a pronounced anti-inflammatory effect and cause fewer adverse reactions.

In dentistry, NSAID are used for the complex treatment of inflammatory processes that are localized in the MFA (abscesses, phlegmons, osteomyelitis, pulpitis, periodontitis, periodontitis, necrotizing ulcerative gingivitis and stomatitis, glossitis, arthritis of the TMJ, neuritis, facial and trigeminal neuralgia, etc.). Methyl salicylate is applied locally in the form of balm with arthritis of the TMJ, as well as with myositis. In the treatment of necrotizing ulcerative lesions and for anesthesia, 0.25–1 % solution of mefenamine sodium salt is also used. Indications for use are inflammatory and dystrophic periodontal processes, hyperesthesia of the exposed neck of the teeth, wedge-shaped defects in periodontal disease. For diseases of the mucous membrane or periodontium, a salicylate choline gel (Mundisal) is prescribed, which is respectively applied to the affected area (3–4 times a day) or inserted into the gingival pockets (1–2 times a day). Diclofenac sodium (2 % ointment) is used for applications on the mucous membrane or as a therapeutic basis for periodontal dressings. Indomethacin in the form of a 1–10 % gel or 5–10 % ointment is used for gum applications (sp. TA) and instillations in periodontal pockets. NSAIDs are also prescribed in the treatment of inflammatory processes in airborne diseases and neuropathic diseases, nerve tissue, musculoskeletal system, muscles, connective tissue, hyperthermia, inflammatory pain syndrome, hypercoagulable syndrome.

For practical use, the following drugs are important. Derivatives of salicylic acid: salicylic acid, acetylsalicylic acid, sodium salicylate, salicylamide, methyl salicylate. The drugs have anti-inflammatory, analgesic, antipyretic effects. Acetylsalicylic acid (aspirin) has more powerful effects. In connection with the emergence of new powerful NSAID and the undesirable effects of the latter, its use is limited.

Derivatives of phenylacetic acid. A representative of this group, diclofenac sodium (orthophen) compares favorably with other NSAID in that it has fewer side effects, has a pronounced anti-inflammatory activity (not inferior to indomethacin). In this regard, if there is a need for long-term treatment, diclofenac sodium may be the drug of choice. Diclofenac sodium is prescribed orally or parenterally – 75–150 mg per day. The drug is a part of therapeutic pastes, which are used in the treatment of periodontitis, inflammation of the oral mucosa and other inflammatory processes.

Derivatives of propionic acid. A typical representative of this group is ibuprofen (brufen). This drug is advisable to prescribe for chronic and torpid inflammatory processes with severe pain (non-rheumatic lesion of the TMJ). Ibuprofen is favorably distinguished by its good tolerability. The daily dose of ibuprofen is 1.2–2.4 g. A naphthylpropionic acid derivative naproxen (naprosyn) has a similar property to ibuprofen. It has a pronounced anti-inflammatory, analgesic and antipyretic activity, is slowly excreted.

Derivatives of anthranilic acid. Mefenamic and flufenamic acids belong to this group. The drugs have a moderate analgesic and antipyretic activity. The anti-inflammatory effect is low. Their advantage is good tolerance, low risk of ulcerogenic effect. They have the ability to stimulate the synthesis of interferon. Mefenamic acid has antiviral, immunomodulatory effects. In low concentrations, it enhances the regeneration processes in the oral mucosa, which is very important for dental practice. Derivatives of pyrazolone are phenylbutazone (butadione), oxyphenylbutazone. Butadione has 1.5–2 times more anti-inflammatory properties than acetylsalicylic acid. Indications for the use of butadione are the same as for salicylates. High effectiveness of topical use of butadione in inflammatory diseases of the venous system (phlebitis, thrombophlebitis) should be noted. In connection with a pronounced side effect, it is rarely used.

Derivatives of indoleacetic acid. A representative of the subgroup indomethacin (methindole) has a pronounced anti-inflammatory, analgesic and antipyretic effect. The daily dose of the drug is selected individually, it should not exceed 0.05–0.075 g. It has a significant side effect, is not widely used.

Meloxicam (movalis, melbek) is a selective COX-2 inhibitor of the oxycam group, most often used in dental practice. This is a powerful anti-inflammatory drug that has analgesic, antipyretic, chondroprotective effects. 7.5 mg 2 times a day or 15 mg orally after meals once a day is prescribed. It is also available for parenteral (i.m.) administration – 15 mg. Celecoxib is a highly selective inhibitor of COX-2, has high efficacy with good tolerance from the gastrointestinal tract – 100–200 mg per day. Nimesulide is a selective COX-2 inhibitor, has an antipyretic, analgesic, anti-inflammatory effect – 0.1 g 2 times a day. It should not be prescribed in long courses. Aceclofenac (airtal, infenac) – has anti-inflammatory and analgesic effects, similar to diclofenac and indomethacin, due to the blockade mainly of COX-2. The drug is safer than traditional NSAID, especially in relation to the gastrointestinal tract and CVS. 100 mg is prescribed 2 times a day.

The anti-inflammatory effect of nabumetone is close to naproxen and is distinguished by its duration. It is used in the treatment of inflammatory diseases of the TMJ. Choline salicylate possesses the properties typical for NSAID, and also performs antimicrobial (relative to gram-positive and gram-negative flora) and antiviral (antiherpetic) effects. It is used for local therapy of infectious-inflammatory, ulcerative-necrotic, radiation, fungal infections of the oral mucosa, periodontal diseases and myalgia, arthralgia, neuralgia, etc. Amizon has a moderate analgesic, anti-inflammatory, antipyretic and immunomodulating effect. The drug is used orally for pain syndromes associated with osteochondrosis, arthritis, neuralgia, and herpetic meningoencephalitis.

Side effects of most NSAID: allergic manifestations, damage to the mucous membrane of the digestive canal (ulcerogenic effect), which are predetermined by the antiprostaglandin effect of the drugs. Inhibition of white blood shoot, bronchospasm may occur. Side effects of NSAID are described in the section 3.3. "Analgesic drugs".

Methods of prevention of the side effects of NSAID and improvement of their tolerance:

1) selective COX-2 inhibitors, drugs and drug combinations with paracetamol, which have a low ulcerogenic effect:

- nimesulide, meloxicam, nabumeton, celebrex;
- preparations enclosed in a shell of polyvinyl acetate (micristine);
- benorylate (fat-soluble ester of acetylsalicylic acid and paracetamol);
- dolaren (diclofenac + paracetamol);
- brustan (ibuprofen + paracetamol);

2) prodrugs such as nabumeton, sulindac (form active metabolites that lose their ability to accumulate in the stomach);

3) combined NSAID simultaneously with synthetic analogues of prostaglandins: arthrotec (diclofenac and misoprostol);

4) simultaneously with NSAID, drugs that improve microcirculation (trental), which reduce their toxic effect on the gastric mucosa (anticholinergics, sucralfate, omeprazole, ranitidine).

3.4.2. Steroidal anti-inflammatory drugs

A wide range of physiological and pharmacological effects of GCS makes these drugs almost universal. The adrenal cortex produces about 40 steroid hormones – GCS, MCS, and compounds with estrogenic and androgenic properties. Most of them are of vital importance.

GCS classification by origin:

1) natural (hydrocortisone, cortisone);

2) synthetic (prednisolone, triamcinolone, dexamethasone).

The following pharmacological effects are typical for GCS: anti-inflammatory, anti-shock, immunosuppressive, metabolic, detoxification, desensitizing, permissive. The mechanism of the anti-inflammatory action of GCS begins with their penetration through the cell membrane, which is associated with the cytoplasmic complex, which is transported to the nucleus and interacts with glucocorticoid effector elements, stimulating or inhibiting their expression. The anti-inflammatory effect of GCS is associated with preventing activation of phospholipase A_2 in the membranes of vascular endothelial cells, limiting the release of arachidonic acid from phospholipids and inhibiting the synthesis of PG (E_2, F_2). There is a decrease in COX expression, inhibition of hyaluronidase and synthesis of biologically active substances, a decrease in the formation of free radicals, the release of fluid, macrophages and leukocytes from the vascular bed,

and inhibition of the formation of edema and granulocyte shaft. GCS stabilize cell and lysosomal membranes, which prevents the release of lysosomal enzymes with proteolytic activity, as a result of which the first phase of inflammation, alteration, is inhibited. The inhibition of the exudation stage is associated with the active prevention of GCS formation of edema. The migration and mobility of leukocytes, phagocytosis, and the formation of antibodies are reduced by a decrease in the blood of T helpers and B lymphocytes. Slowing the reparative phase of inflammation associated with a decrease in the reproduction of fibroblasts, the synthesis of precolagen and its maturation, etc.

The mechanism of desensitizing and anti-allergic action of GCS is associated with inhibition of histamine release in inflammatory tissues and desensitization of histamine H_1 receptors to the allergy mediator. The mechanism of immunosuppressive action of GCS is associated with inhibition of the activity of T and B lymphocytes, a decrease in the production of interleukins and other cytokines, and a decrease in the level of circulating lymphocytes, macrophages and antibodies.

The anti-shock effect of GCS is to increase the concentration of catecholamines in the tissues, reduce the release of biogenic amines, increase heart contractions, increase the volume of circulating blood. An important component of the anti-stress effect of drugs is the antitoxic effect of GCS. The drugs affect almost all types of metabolism: they contribute to the synthesis and deposition of glycogen in the liver and muscles, increase the level of glucose in the blood due to the activation of gluconeogenesis. The utilization of amino acids for the latter leads to inhibition of protein biosynthesis and enhances its catabolism, which ultimately helps to reduce the regenerative processes of lymphoid tissue and immune bodies. By enhancing the process of lipolysis, GCS increase the level of free fatty acids. They have mineralocorticoid activity, contribute to the retention of sodium and water and increase the excretion of calcium and potassium. The permissive action of GCS is associated with an increase in the sensitivity of tissue receptors to the action of catecholamines.

Indications for the use of GCS in dentistry are: arthritis and arthrosis of the TMJ, osteomyelitis, lichen planus, erythema multiforme, pemphigus, dermatitis herpetiformis (Duhring's disease), chronic eczematous cheilitis, diseases of periodontium, pulp and oral mucosa. The high biological ef-

fectiveness of GCS allows them to be widely used in dental practice locally, relying on the anti-inflammatory, anti-allergic effect of these drugs. GCS for topical use have a powerful pharmacological spectrum of action: anti-inflammatory, epidermostatic, anti-allergic, local analgesic. The latter is associated with a decrease in edema, itching, heartburn. Depending on the strength of the local anti-inflammatory effect, GCS differ in the level of activity. Ointments, gels, liniment, lotions, aerosols, solutions are applied topically.

The anti-inflammatory activity of local GCS depends on the active substance, as well as its percentage concentration. Local GCS different in activity are shown below.

The lowest activity:

- 0.25–2.5 % hydrocortisone;
- 0.25 % methylprednisolone acetate (medrol);
- 0.04 % dexamethasone (hexadrol);
- 0.5 % prednisolone (metiderm);
- 0.2 % betamethasone (celestone).

Low activity:

- 0.01 % fluocinolone acetonide (fluonide, synalar);
- 0.025 % triamcinolone acetonide (aristocort, kenalog);
- 0.03 % flumethasone pivalate (locorten).

Medium activity:

- 0.1 % triamcinolone acetonide;
- 0.025 % fluocinolone acetonide.

High activity:

- 0.05 % betamethasone dipropionate (diprosone);
- 0.5 % triamcinolone acetonide;
- 0.2 % fluocinolone acetonide (synalar).

The highest activity:

- 0.05 % betamethasone dipropionate on an optimized basis (diprosone);
- 0.05 % clobetasol propionate (dermovate).

Fluorinated GCS have the most powerful anti-inflammatory effect. But when they are used, local side effects often arise: atrophy of the skin, striae, telangiectasia, hirsutism, hypo- and hyperpigmentation. In addition, all GCS can locally provoke a viral, bacterial or fungal infection. Therefore,

it is advisable to combine them with antibiotics (synalar H, locacorten H, kenalog, triderm).

The drugs are applied to the mucous membrane in the form of applications or inserted into the gingival pockets, where they are held with a medical dressing or paraffin. It should be remembered that these agents inhibit the regeneration processes and it is advisable to use them at the healing stages. In cases of local application, they are practically not absorbed and do not have side effects on the macroorganism. Prolonged use of GCS in excessive amounts may be accompanied by side effects due to the resorptive effect and, in particular, helps to suppress local immunity and delay osteosynthesis.

Indications for the use of corticosteroids at clinic: shock conditions (including anaphylactic shock), rheumatism with a pronounced exudative component, bronchial asthma, acute and chronic allergic diseases; hypoglycemic conditions, diffuse connective tissue diseases; skin diseases, rejection reactions during homotransplantation of organs and tissues.

The following types of glucocorticoid therapy are distinguished: replacement, suppressor, pharmacodynamic. In intensity, the latter can be intense with i.v. use of GCS in large doses, which is canceled simultaneously after 1–2 days, limiting – doses of corticosteroids are more than physiological, which is gradually canceled, long-term – doses that exceed physiological, GCS withdrawal – very slow rate. Dosage of GCS is carried out depending on the severity of the disease, body weight, blood pressure, etc. If it is necessary to replace one drug with another, the equivalence of their doses in arbitrary units (mg) should be taken into account: cortisone – 25, hydrocortisone – 20, methylprednisolone – 4, prednisolone – 5, triamcinolone – 4, dexamethasone – 0.75, betamethasone – 0.75. To prevent withdrawal symptoms, dose reduction should be carried out gradually. When used in dentistry, relatively small doses (15–30 mg per day) and courses (up to 1 month), dose reduction is carried out according to the scheme: 2.5–5 mg 1 time per week. In the treatment it is necessary to use high-grade protein nutrition with salt restriction. In case of side effects and the need to use GCS, "cover" preparations are used (sedatives, antihypertensives, diuretics, which improve metabolism).

Side effect of GCS on metabolism: negative nitrogen balance, hyperglycemia, hyperlipidemia; on the central nervous system: mood chang-

es, agitation, depression, psychosis; on the endocrine system: inhibition of the function of HPAS; on the gastrointestinal tract: peptic ulcer, gastrointestinal bleeding, pancreatitis, fatty liver; on the blood: coagulation disorders, thromboembolism, hemorrhage; On the skeletal system: osteoporosis, destruction of the vertebrae, spontaneous fractures: on the CVS: arterial hypertension, edema, arrhythmias; On the immune system: exacerbation of latent infections, slowing down the healing processes in the tissues after surgery. Local effects may appear: erythema, vascular telangiectasias, pustules, papules, acne. Drugs can cause defects in the physical development of the fetus (especially an increased risk of a split palate in newborn), so they can not be prescribed to pregnant women. A complication of treatment is withdrawal syndrome, which manifests itself as headache, increased fatigue, insomnia, anorexia, nausea, vomiting, euphoria, fever, as well as arthralgia, myalgia, orthostatic reactions, weight loss, a relapse of the disease is possible. GCS are contraindicated in the presence of gastric ulcer and duodenal ulcer, diabetes mellitus, tuberculosis, acute viral infections, systemic mycosis, parasitic diseases, a tendency to exacerbate chronic infections, osteoporosis, hypertension, kidney failure, chronic circulatory failure, pregnancy, and mental disorders.

For clinical practice, the following drugs are important. Hydrocortisone has an anti-inflammatory, anti-allergic and immunosuppressive effect. It is able to suppress HPAS (on the basis of the feedback principle), which determines the insufficiency of the cortical substance of the adrenal glands, especially in the case of a sharp withdrawal of the drug. Prednisolone is a dehydrogenated analogue of hydrocortisone. In terms of anti-inflammatory activity, it exceeds hydrocortisone by 3–4 times, to a lesser extent affects water-electrolyte metabolism, gives fewer side effects. Methylprednisolone acts similarly to prednisolone. It has a longer effect. It does not exert a psychotropic effect, to a lesser extent affects the processes of exchange. Triamcinolone is also more active than hydrocortisone (5 times). Moreover, it practically does not affect water-electrolyte metabolism. Dexamethasone is one of the most active glucocorticosteroids (30 times more active than hydrocortisone) with a weak effect on water-electrolyte metabolism, but it quickly causes depression of HPAS with prolonged use.

3.4.3. Mineralocorticoids

Mineralocorticoids are represented by a group of steroid hormones that primarily affect water-electrolyte metabolism. Their excretion by the cortical substance of the adrenal glands depends on the concentration of electrolytes in the blood and tissue fluid. MCS are able to retain sodium ions and water in the body, contributing to the elimination of potassium. With adrenal hypofunction, dehydration, decreased muscle tone, cardiac abnormalities, skin discolouration ("bronze disease") is observed. In clinical practice, deoxycorticosterone acetate is used, which is effective in case of insufficiency of the adrenal gland, muscle weakness. Side effects: increased blood pressure, swelling.

3.5
VITAMIN PREPARATIONS

Vitamins are specific biologically active substances (activity is manifested in very small doses), which are absolutely necessary for vital functions. Some vitamins (e.g. vitamin D) are hormone-like substances. Vitamins can be considered as universal components of cellular metabolism, which, together with hormones and enzymes, play a huge role in metabolic processes in the body, in particular in cellular respiration, ensuring the functions of the nervous system and endocrine glands, regulating immunobiological, detoxification processes, inflammation, etc.

Basically, vitamins enter the body with food (mainly plant origin), a small part of them is synthesized by intestinal microflora. A person's daily need for vitamins depends on gender, age, physiological state, labor intensity, nature of food (consumption of carbohydrates or proteins, quantity and quality of fats), climatic conditions, and is subject to significant changes. In case of insufficient content of these substances in the diet, hypovitaminosis can develop, and in their complete absence – vitamin deficiency with symptoms characteristic of each vitamin. A deficiency of vitamins in the body can be associated with a violation of their absorption in diseases of the gastrointestinal tract, violation of shallow substances, as well as pathology of liver function, or increased need of vitamins, as is the case with certain physiological and pathological conditions (pregnancy, hard physical work, infections, intoxication, taking some drugs). With a pronounced deficiency of a certain vitamin, serious conditions and diseases can develop – scurvy, rickets (in children), anemia, beriberi disease, damage to the nervous or cardiovascular system, vision organs, endocrine glands, gastrointestinal tract, etc.

In dental practice, a deficiency of vitamins, first of all, is manifested by damage to the oral cavity – a violation of the trophism of the oral mucosa, regeneration of the teeth. The dentist must present the physiological and drug effects of vitamins, signs of their deficiency in the body, indica-

tions and contraindications for their use. The deficiency of vitamins can be replenished by prescribing a diet with the appropriate content of vitamins. This method has little effect; therefore, it is necessary to prescribe vitamins as medicines (pharmacodynamic therapy). Most often, vitamins are used to treat hypovitaminosis and vitamin deficiency (vitamin replacement therapy). In addition, vitamins can increase the body's resistance to pathogenic environmental factors. They are used to stimulate the functions of an aging organism (adaptive vitamin therapy). In case of excessive consumption of vitamins, hypervitaminosis can develop, side effects in the form of allergies and dyspepsia rarely develop.

Vitamin classification is based on their physicochemical properties. There are groups of water- and fat-soluble vitamins:

1) water-soluble vitamins: thiamine (vitamin B_1), riboflavin (vitamin B_2), pyridoxine (vitamin B_6), nicotinic acid (vitamin PP), folic acid (vitamin B_9), cyanocobalamin (vitamin B_{12}), calcium pantothenate (vitamin B_5), pangamic acid (vitamin B_{15}), ascorbic acid (vitamin C), rutin (vitamin P), biotin (vitamin H);

2) fat-soluble vitamins: retinol (vitamin A), tocopherol (vitamin E), ergocalciferol (vitamin D_2), cholecalciferol (vitamin D_3), phylloquinone (vitamin K_1).

3.5.1. Water-soluble vitamins

Thiamine (vitamin B_1) is a product of plant and microbial origin. It participates in the oxidative decarboxylation of keto acids. Its phosphorylated derivatives (especially cocarboxylase) play an important role in the regulation of carbohydrate and fat metabolism.

In case of insufficient intake of vitamin, beriberi develops, the characteristic manifestations of which are muscle weakness, polyneuritis, paresis, paralysis. Pseudoneurasthenia may occur, which is manifested by increased mental fatigue, depression, headache, and dyspepsia. In the acute case, cardiovascular collapse may develop. Vitamin B_1 deficiency in dental practice is manifested by heartburn, a violation of the taste and trophism of the mucous membrane, and hyperesthesia. The daily need for thiamine is provided by taking 0.5–1.5 mg of this substance.

At clinics synthetic drugs are mainly used – thiamine bromide, thiamine chloride, benfothiamine, decarboxylase, etc. In dentistry, in the com-

plex treatment of glossalgia, trigeminal and facial neuralgia, stomatitis, periodontitis, symptomatic lesions of the mucous membrane and lichen planus, vitamin B_1 is used at the rate of 5–50 mg per day. Thiamine is often included into the complex of medications for multiple caries. In case of periodontal disease, vitamin B_1 is used as electrophoresis on the gums (from the anode) in a mixture with novocaine. In chronic aphthous recurrent stomatitis and erosive form of lichen planus, it is administered in a mixture with 0.5 % novocaine solution under papules, aphthae or erosions. In individually selected doses, the vitamin is prescribed for beriberi disease, polyneuritis, neurosis, CVS deseases, peptic ulcer disease, intoxication, etc. Vitamin B_1 is the most toxic drug from water-soluble vitamins. Its side effects are characterized by a drop in blood pressure, the occurrence of cardiac arrhythmias, and depression of the central nervous system. Thiamine preparations cause a violation of the activity of liver enzymes. Allergic reactions, up to AS may occur. Thiamine should not be used with vitamins B_2 (urinary excretion of the latter increases), B_{12} (increased allergenic properties of thiamine), nicotinic acid (increased rate of destruction).

Riboflavin (vitamin B_2) is found in large quantities in dairy products, meat, cereals, and yeast. It participates in many redox processes. Taking part in tissue respiration, it ensures the normal functioning of avascular (epithelial) tissues, the lens, and the brain. It is also necessary for the formation and destruction of monoamines both in the central nervous system and in peripheral tissues, the synthesis of erythropoietin, the regulation of liver function, and others. Characteristic signs of vitamin B_2 deficiency are dermatitis (especially on the wings of the nose, in the nasolabial folds), cracks in the corners of the mouth, stomatitis, glossitis, visual impairment, normochromic anemia. The daily requirement in riboflavin for an adult is about 3 mg (for children, depending on age – 0.6–2.3 mg). For therapeutic purposes, in dental practice, riboflavin is prescribed for cracked lips that do not be cured well, eczematous cheilitis, generalizable form of periodontitis, glossitis, ulcerative lesions of the gums, lupus erythematosus, etc. Vitamin B_2 preparations are widely used for disorders of the central nervous system, acute and chronic hepatitis, acute heart failure, pneumonia, dysbiosis, aging, etc.

Pyridoxine (vitamin B_6) is found in herbal products, as well as in the liver, heart and kidneys. Vitamin B_6 is involved in the processes of decar-

boxylation, transamination and deamination of amino acids, as well as in the exchange of glutamic acid and GHB. Pyridoxine is involved in the exchange of serotonin and catecholamines, helps to improve myocardial contractility, stimulates hematopoiesis, central nervous system function, bile secretion, and improves metabolic processes in the mucous membrane. In dentistry, pyridoxine is indicated for neuralgia and trigeminal neuritis, glossalgia, gingivitis, lichen planus, periodontal disease (especially stomach ulcers, chronic hepatitis, and also when prescribing antibiotics). The daily need for it for an adult is 1.5–2.5 mg (for children, depending on their age – 0.5–2 mg). Pyridoxine cannot be mixed in the same syringe with solutions of thiamine or cyanocobalamin, in powder with ascorbic and nicotinic acids (physicochemical interaction). Pyridoxine is also used in case of minor chorea, poliomyelitis, parkinsonism, neuritis, myocardial dystrophy, insufficient blood circulation, gastric ulcer, tuberculosis, dermatitis, anemia, diabetes mellitus, etc.

Nicotinic acid (vitamin PP, vitamin B_3) is synthesized by plants and microorganisms. The largest amount is found in the liver, kidneys of animals, in legumes and crops, in yeast. It participates in the formation of two important coenzymes: NAD and NADP, which are necessary in redox processes. Nicotinic acid is involved in the regulation of carbohydrate and protein metabolism, functions of the central nervous system, CVS, gastrointestinal tract and hematopoietic systems, etc. In case of hypovitaminosis, fatigue, headache, forgetfulness, irritability, muscle weakness, glossitis, marginal gingivitis, stomatitis, diarrhea and dermatitis are observed. Severe deficiency of vitamin PP in humans leads to the development of pellagra (rough skin), the main signs of which are dermatitis, diarrhea, dementia. The average daily requirement for vitamin PP is 20 mg. For the purpose of treatment, nicotinic acid is prescribed at a dose of 50–500 mg per day. In dentistry, nicotinic acid is used to treat stomatitis, glossitis, glossalgia, periodontitis, lichen planus, erythema multiforme, systemic lupus erythematosus, facial neuritis, ulcerative lesions of the mucous membrane with torpid course, fungal diseases, etc. When using pellagra, the drug is used orally in complex with ascorbic acid and retinol. In case of seizures, stomatitis, glossalgia, nicotinic acid is prescribed together with thiamine bromide, riboflavin, ascorbic acid. Nicotinic acid is widely used in the treatment of atherosclerosis, heart failure, hepatitis, diseases of the

kidneys, brain, alcoholism and wounds that do not be cured well. In case of an overdose of the vitamin, liver dystrophy, inhibition of the functions of the immune system, and a violation of the sensitivity of the skin can develop. With a quick intravenous administration, a sharp drop in blood pressure can occur, and when taken orally, redness of the skin of the face, neck and upper body, itching and sensation of tingling of the skin appear.

Ascorbic acid (vitamin C) is found in large quantities in rose hips, lemons, oranges, spruce needles, as well as in the liver and kidneys of cattle. It is not synthesized in the human body. Ascorbic acid is actively involved in redox processes. Its presence is necessary for normal tissue respiration. Vitamin C activates proteolytic enzymes, takes part in the synthesis of steroid hormones and precolagen. Ascorbic acid tones the sympathetic nervous system, activates cellular and humoral processes, stimulates growth, regulates vascular wall permeability, promotes regeneration processes, and affects the process of creating supporting tissues (including bone and dentin). It activates the immune system and the disinfecting function of the liver, increases the body's resistance to infection, prevents the oxidation of hemoglobin, and has antioxidant and desensitizing properties. Vitamin C cannot be synthesized and accumulate in the body, which explains the rapid development of its hypovitaminosis. Vitamin deficiency leads to the development of scurvy (scorbutus), which manifests itself as follicular, muscle hemorrhages, gum bleeding, loosening and loss of teeth, fatigue, hemorrhagic rashes on the skin, anemia, and increased susceptibility to infections.

In dentistry, vitamin C is indicated in the treatment of manifested scurvy in the oral cavity, periodontal disease, stomatitis, gingivitis (especially with increased bleeding), erosions, ulcers, wounds that do not be cured well, glossalgia, multiple caries, purulent-inflammatory processes of the coronary artery disease, chronic intoxication, bleeding, etc. Ascorbic acid is also used in the treatment of infectious diseases, intoxications, allergic processes, radiation injuries. It is advisable to use it for prolonged wound healing, in the postoperative period, atherosclerosis, diabetes mellitus, mental and physical stress, during pregnancy and lactation. For treatment, synthetic vitamin C is used. It is administered orally in the form of tablets, dragee, and also parenterally. The daily requirement in vitamin C for adults is 50–100 mg (children – from 20 to 80 mg). In case of scurvy, vitamin C is

prescribed orally 0.2–0.3 g 4 times a day during the first week, 0.1 g 3 times a day during the second week, 0.05 g 3 times during the third weeks. The therapeutic effect is increased in case of administration with vitamin P (rutin). Hypervitaminosis can cause suppression of the function of the insular apparatus, hypertension, kidney damage, increased blood clotting.

Rutin (Vitamin P). This group includes flavonoids, catechins and other substances of a polyphenolic nature contained in many plants (rose hips, lemons, walnuts, black currant berries, mountain ash, tea leaves, etc.). Vitamins of group P are involved in redox processes, tissue respiration, inhibit the activity of hyaluronidase and possess antioxidant activity. The effects of vitamin P are in reducing the exudation of the liquid part of the plasma and the diapedesis of blood cells through the vascular wall, choleretic and mild antihypertensive effect. The daily requirement for vitamin P has not been established. In dental practice, rutin is used to treat gingivitis, stomatitis, generalized periodontitis, hemorrhagic diathesis, allergic and radiation injuries of the oral mucosa. The drug is prescribed in tablets at a dose 0.02–0.05 g 2–3 times a day. No adverse effects were noticed. Rutin can be used in allergic processes, rheumatism, hypertension, chronic liver disease.

Cyanocobalamin (vitamin B_{12}) in the human body is synthesized by intestinal microflora, accumulates in large quantities in the liver, kidneys. Coenzyme forms of cyanocobalamin are involved in the transfer of mobile methyl groups and hydrogen. The vitamin takes part in redox processes, synthesis of protein and nucleic acids; therefore it is considered a stimulant of hematopoiesis, plastic processes, growth. It affects the metabolism of carbohydrates and lipids, improves liver antitoxin function, participates in the synthesis of myelin and acetylcholine. In dental practice, vitamin B_{12} is used in the complex therapy of periodontitis, stomatitis, lichen planus, glossalgia, and trigeminal neuralgia. The drug is administered i.m. or s.c. Cyanocobalamin is prescribed at a dose 50–100 μg after 1–2 days. Among the side effects are allergies, development of hypercoagulation, etc. Vitamin B_{12} cannot be administered in the same syringe with vitamins B_1 and B_6. Cyancobalamin is also used for hypovitaminosis and vitamin deficiency, anemia of various origins, diseases of the liver, stomach, as well as for neuritis, neuralgia.

Folic acid (vitamin B_9) promotes hematopoiesis; therefore it is involved in the synthesis of purine and pyrimidine bases, in the conversion of ami-

no acids. The transition of folic acid to its active form occurs with the participation of cyanocobalamin and ascorbic acid, so the drug is prescribed together with these vitamins. The main biological effect is the stimulation of the maturation of red blood cells in the bone marrow. In dental practice, folic acid is prescribed for diseases of the mucous membrane (gingivitis, stomatitis, glossitis), because it helps to normalize the reparative processes of the mucous membrane. Vitamin B_9 is indicated for pernicious and macrocytic anemia, chronic gastroenteritis and intestinal tuberculosis.

Pangamic acid (vitamin B_{15}) is found in brewer's yeast, seeds of various plants, in the liver, etc. It activates oxidative processes, improves lipid metabolism, reduces hypoxia, increases the content of glycogen and creatine phosphate in the muscles, and is a donor of methyl groups. In dental practice, vitamin B_{15} is used for the complex treatment of periodontitis and diseases of the mucous membrane. 100–300 mg are prescribed per day. Sometimes there is an allergy to the drug. Pangamic acid is prescribed for chronic hepatitis, cirrhosis, atherosclerosis, alcohol intoxication.

Pantothenic acid (vitamin B_5) is found in the liver, kidneys, egg yolk, caviar, peas, dash, brewer's yeast. Being a part of coenzyme A and other coenzymes, the vitamin plays an important role in the processes of oxidation, acetylation and synthesis of GCS, acetylcholine, hemoglobin, etc. It normalizes the functions of the nervous system, has a detoxifying effect in the case of SA and AG, etc. In dental practice, this vitamin is prescribed for neuritis and neuralgia of the trigeminal and facial nerves, glossitis, stomatitis, cheilitis, generalized periodontitis, trophic lesions, burns, tooth decay, etc. Pantothenic acid is also used in the form of calcium pantothenate enterally and parenterally 1–2 times a day. It is also used for hepatitis, cirrhosis, bronchitis, circulatory failure, neuritis and neuralgia, trophic ulcers and burns.

3.5.2. Fat-soluble vitamins

Retinol (vitamin A) comes with food (animal liver, egg yolk, butter, etc.) and is synthesized from the plant pigment carotene, which is found in carrots, apricots, wheat grains, etc. Retinol is necessary for the normal function of cell and subcellular membranes, it enhances protective immune responses. This vitamin in its action is called anti-infectious. Retinol is involved in oxidation reactions, tissue respiration, and protein synthesis. At the same time, it contributes to the healing of ulcers, epithelialization and

regeneration of the mucous membranes of the gastrointestinal tract, biliary and UT. Retinol promotes the growth and development of the body, is involved in the synthesis of visual retinal pigment. In case of insufficient intake of vitamin in the body, gloomy vision (hemeralopia) and the ability of the eye to dark adaptation ("night blindness") are impaired. The mucous membrane of the eye becomes dry (keratitis), the cornea becomes soft (keratomalacia). In case of hypovitaminosis, pneumonia, pyelitis, colitis, etc. can develop as a result of tissue epithelial damage. The daily requirement for vitamin A is 1.5 mg or 5000 IU (for an adult). In dentistry, vitamin A is prescribed for tissue hyperkeratosis – leukoplakia, lichen planus, erosive-ulcerative processes in the epithelialization stage, burns, frostbite, inflammatory-dystrophic forms of periodontitis. The drug is often used to treat ocular, skin lesions, as well as in the complex treatment of patients with spasmophilia, hepatitis, cirrhosis, gastric and duodenal ulcers, chronic bronchopulmonary diseases, chronic infections, anemia. In case of prolonged use, the symptoms of hypervitaminosis can be observed: lethargy, drowsiness, headache, bone pain, vomiting, itching, hair loss, increased intracranial pressure, dizziness, visual impairment, meningism. In case of an overdose, vitamin D is prescribed.

Calciferol (vitamin D). In clinical practice, ergocalciferol (vitamin D_2) and cholecalciferol (vitamin D_3) are most often used. Provitamin D_2 is found in large quantities in brewer's yeast, mushrooms and ergot, while provitamin D_3 is a part of animal tissues and human skin. Vitamin D_2 (ergocalciferol) is formed by ultraviolet radiation from provitamin – ergosterol. Vitamin D_3 is found naturally in the fat of the liver of tuna, halibut, and whales. Vitamins of group D are needed for the regulation of phosphorus-calcium metabolism in the body. One of the important effects of vitamin D is that it increases the permeability of the intestinal epithelium to calcium and phosphorus, and also regulates their absorption in the tissues. Vitamin D is controlled by the process of mobilizing calcium from bone tissue, which is necessary for bone growth.

In case of vitamin D deficiency in the child's body, the mineralization of bone and cartilage tissue is disrupted and rickets develop. With the latter, the appearance of the child is characterized by an enlarged stomach, a large head, a violation of the skeletal system, timing and order of teething. In adults, a significant deficiency of vitamin D is manifested by osteomala-

cia. The need for vitamin depends on the age and physiological state of the body. For infants, the daily dose of vitamin D is 400 IU, for an adult, 100–200 IU is enough. This amount of vitamin is provided through proper nutrition. In dentistry, vitamin D is used to prevent and treat tooth decay, stimulate the healing processes of the MFA fractures, treat periodontitis, and mucosal lesions. Ergocalciferol is also used for the prevention and treatment of rickets, osteomalacia in children, as well as for disorders of the parathyroid gland with hypocalcemia, psoriasis, lupus of the skin and mucous membranes, active pulmonary tuberculosis, chronic liver and kidney diseases, etc. Excessive vitamin D content can cause acute and chronic poisoning. These conditions are manifested by pathological demineralization of bones and calcium deposition in the kidneys, blood vessels, heart, central nervous system damage (lethargy, drowsiness, anxiety and convulsions), an increase in body temperature and blood pressure. Possible lethal result.

Tocopherol (vitamin E) – reproduction vitamin. The source of the vitamin are vegetable oils, rose hips, eggs, etc. The daily requirement of the child for vitamin E is 5–10 mg, for adults – 20–30 mg. Tocopherol is a structural component of cell membranes. He participates in important biochemical processes of the body – activates the processes of tissue respiration, affects the metabolism of proteins, carbohydrates and cholesterol. This vitamin is essential for normal human reproduction. Tocopherol increases the synthesis of collagen in the subcutaneous basis and bones, contractile proteins in the striated and non-stripped muscles, myocardium, and has antioxidant properties. At the same time, it reduces the process of platelet aggregation, and in the lungs it protects against damage to the alveoli, contributing to the synthesis of surfactant. Vitamin E deficiency causes a violation of embryogenesis and reproductive organs (sterility, muscular dystrophy, fatty liver infiltration, degeneration of the spinal cord). In dentistry, vitamin E is used to reduce the permeability and fragility of capillaries in inflammation and erosive-ulcerative lesions of the mucous membrane, in the treatment of periodontal disease, diskeratosis, and in the stage of epithelization. Sea buckthorn oil (oleum hippopheae) and wild rose oil (oleum rosae), which contain vitamins E, A and F., are widely used. These drugs improve wound epithelization, prevent tissue sclerosis, therefore they are used for erosive-ulcerative processes and radiation injuries in the oral cavity, cracks of lips, etc. Tocopherol is used for muscular dystrophy, ischemic

heart disease, violation of the functions of the sex glands, dermatitis. Vitamin E is widely used in obstetric, gynecological, cardiological, geriatric, pediatric practice. Vitamin E is prescribed orally and i.m. at a dose 15–300 mg per day (in the form of 5 %, 10 % and 30 % oil solutions), as well as topically for application or for insertion into the gingival pockets. To increase its effectiveness, it is advisable to combine it with vitamin A.

Vikasol (vitamin K). The main source of vitamin are plants (alfalfa, spinach, pine needles, cauliflower, rose hips, etc.). There are several compounds of vitamin K (K_1–K_7). The mechanism of action of vitamin K is associated with its effect on the biosynthesis of blood coagulation factors (prothrombin, proconvertin, fibrinogen). In addition, it contributes to the synthesis of ATP, creatine phosphate, a number of enzymes. The biochemical role of vitamin K is to influence the final stage of prothrombin molecule formation at the post-translational level. With a lack of vitamin K, there is a decrease in the content of coagulation factors, a manifestation of which is bleeding of tissues, the development of hemorrhagic diathesis. In dental practice, vikasol is used for bleeding of the mucous membrane, generalized periodontitis. The drug is prescribed orally in the form of a powder and tablets or injected i.m. for3–4 days, and then – a break, after which treatment is continued. In case of an overdose, hyperprothrombinemia and hyperthrombinemia may develop. Sometimes toxicosis and convulsions may develop. Vitamin K is used for increased bleeding, predefined deficiency of coagulation factors, an overdose of anticoagulants, during preparation for surgery, septic processes, radiation sickness, etc. A widely used form of vitamin K is its synthetic analogue, vikasol, which is used in the form of tablets and ampoules. Its action is detected after 12–18 hours. The highest doses: single – 0.03 g, daily – 0.06 g.

Multivitamin preparations. In some cases, vitamins mutually reinforce the effects of each other; in some cases, the toxicity of vitamins decreases with combined use. These and other features of the action determine their combined use, both for prophylactic and therapeutic purposes. The combination of vitamins can be carried out both by individual selection of vitamins and the use of ready-made preparations. Ther are domestic and foreign multivitamin preparations: aevit, undevit, hendevit, essentiale (vitamins and phospholipids). Unicap, oligovit, multi-tabs, alfavit, duovit, materna contain vitamins and minerals.

3.6
ANTIOXIDANTS

Antioxidants are drugs that can inhibit free radical oxidation in the body or eliminate active oxygen species and peroxide compounds. During and at the end of it, non-toxic products (H_2O and CO_2) are formed. Along with biological oxidation, the body can undergo reactions of direct addition of oxygen to subtribution – auto-oxidation. Typically, these reactions begin with the formation of particles with an unpaired electron – free radicals, and the intermediate compounds are peroxides, respectively, these processes are called free radical or peroxidation. The latter develops as a chain avalanche-like process, which draws in new molecules of the substrate.

The increase in free radical oxidation in the body is observed in many diseases. Common characteristic features for them are an increase in the hydrophilicity of membranes and, as a consequence, an increase in their permeability, differentiation of respiration and phosphorylation, disruption of the connection of phospholipids with structural and receptor proteins of cell membranes, damage to nucleic acids and inactivation of enzymes, lysis of lysosome membranes, which is accompanied by exit from lysosomes, which is accompanied by exit from phospholipases and other hydrolytic enzymes that can cause autolysis of the cell. The participation of free radical mechanisms in the pathogenesis of atherosclerosis and its thrombonecrotic effects (heart attack, stroke), diabetes mellitus, chronic non-specific lung diseases, diseases of the reproductive system, as well as radiation damage, hepatitis, decreased cellular and humoral immunity, intoxication with membrane poisons has been proved. In dental practice, an increase in the processes of free radical oxidation is observed with periodontitis, gingivitis, ulcerative stomatitis, inflammatory processes of soft tissues and bones, etc.

The development of free radical lipid peroxidation can be stopped using inhibitors that restore free radicals to a stable molecular form, unable to continue the chain of autooxidation. Substances that inhibit the free radical oxidation of organic compounds by oxygen are called antiox-

idants. The inhibition of lipid peroxidation in the body is carried out by an antioxidant system, which includes a chain of antioxidants that can inhibit the free radicals that are formed, and a group of enzymes (catalase, glutathione peroxidase, superoxide dismutase) that eliminate active oxygen species and peroxide compounds. According to their actions, antioxidants are divided into direct and indirect. The former consist of compounds that directly eliminate free radicals. They are effective in both in vivo and in vitro conditions. Indirect antioxidants are effective only in the body, so they include substances that are involved in the synthesis of directly acting antioxidants or antioxidant enzymes. By chemical nature, antioxidant preparations are classified as follows:

I. Direct antioxidants:

- phenolic compounds (tocopherols, polypherols, vitamin P, dibunol, probucol);
- carboxylic acids (ascorbic, citric);
- thiol compounds (cysteine, glutathione);
- glucosides (eleutherococcus extract, ginseng tincture);
- 3-hydroxypyridines (emoxypine, mexidol);
- 1,4-dihydropyridines (diludine);
- 1,2,4-triazolines (thiotriazolin).

II. Indirect antioxidants:

- amino acids (methionine, glutamic acid, lipoic acid, lipamide);
- derivatives of nicotinic acid (nicotinamide, nicotinic acid, complamin);
- inducers of antioxidant enzymes (riboflavin);
- aminothiols (cystamine);
- trace elements (selenium).

III. Enzyme preparations (ceruloplasmin, superoxide dismutase).

Antioxidant preparations in therapeutic doses do not exhibit physiological or biochemical effects in a healthy body. The protective effect of antioxidants is nonspecific and manifests itself under various influences (radiation exposure, the action of toxins, inflammation, etc.).

3.6.1. Direct antioxidants

The classic antioxidant of cell membranes is tocopherol, which in clinical practice is used in the form of acetate. Tocopherol is involved in the transfer

of hydrogen, and therefore, in the redox transformations that occur in the muscle, connective and other tissues of the body. In the case of vitamin E deficiency, increased autooxidation of fats leads to the accumulation of lipid peroxidation products, especially in rapidly proliferating tissues. Vitamin E is used to treat diseases in the pathogenesis of which the participation of autooxidation has been established: atherosclerosis, diabetes mellitus, bronchopulmonary pathology, reproductive system dysfunction, etc.

In clinical practice, antioxidant dibunol is used which has a wide spectrum of biological activity and, depending on the dose, is able to suppress protein biosynthesis by inhibiting the inclusion of amino acids and inhibiting RNA synthesis, increase liver oxygenase activity, promoting the biotransformation of many compounds. Dibunol improves tissue regeneration by accelerating the transition of cells to the phase of DNA synthesis. The direction of action of dibunol depends on the level of antioxidant activity of lipids, so different doses of the drug can predetermine a multidirectional effect. In dental practice, dibunol (pastes and ointments) is used to treat periodontitis. Allergic reactions may occur. Dibunol is used in the complex treatment of heart attack and stroke; it is used in the treatment of tumors (especially bladder), etc. Probucol is close in the structure to dibunol, has a hypocholesterolemic and direct antioxidant effect. It has similar indications for use, except for cancer. The active component of ginseng and eleutherococcus preparations are glucoside substances (panaxazides, eleutherosides), which have antioxidant, hypocholesterolemic properties, affect both mental and physical activity of people. They increase the body's resistance to cooling, overheating, immobilization, trauma, intoxication, etc. In dentistry, the latest drugs are used for periodontitis, mucosal lesions, and multiple caries.

In clinical practice, ascorbic acid is widely used (see. "Vitamin preparations"). Many bioflavonoids (rutin, quercetin, flacumin) exhibit pronounced antioxidant properties due to the direct antiradical effect. Their ability to detect a preserving effect with respect to ascorbic acid, with which they are prescribed for diseases of the oral mucosa is of particular interest. Bioflavonoids are included in the composition of pastes for the treatment of periodontitis.

Emoxipin is effective for rapid excessive growth of free radical processes. It is used for local treatment of periodontitis, gingivitis, stomatitis.

Sometimes pain, itching, redness may appear at the injection site of the drug. Emoxipin is prescribed for acute radiation sickness; during the influence of high-intensity light (it has a retinoprotective effect). Mexidol exhibits antioxidant, antihypoxic, membrane stabilizing, nootropic, anticonvulsant and anxiolytic effects. It increases the body's resistance to shock, hypoxia, ischemia, intoxication, etc. The drug improves and stabilizes brain metabolism, improves microcirculation and rheological properties of blood, improves memory, and performance. In dentistry, mexidol is used to treat periodontitis and diseases of the oral mucosa. The drug is prescribed for the pathology of the CVS, liver, intoxication, etc. Thiotriazoline is a synthetic hepato- and cardioprotector. The drug activates the antioxidant system and inhibits the oxidation of lipid peroxide in ischemic areas of the myocardium, stabilizes and reduces the size of the necrosis zone, improves the rheological properties of the blood. It exhibits immunomodulating, anti-ischemic, membrane-stabilizing, anti-inflammatory and anabolic activities. In dentistry, thiotriazoline is used to treat periodontitis and diseases of the oral mucosa. Thiotriazolin is prescribed in the treatment of coronary heart disease, myocarditis, cardiomyopathy, liver diseases, etc.

3.6.2. Indirect antioxidants

Indirect antioxidant – lipoic acid, exhibits an antioxidant effect due to coenzyme properties, helps to restore glutathione and stimulates the antiradical chain of the antioxidant system. Glutathione precursors are methionine, glutamic acid, and complamin. These compounds exhibit antioxidant effects and normalize lipid metabolism. In dental practice, drugs are used in the treatment of periodontitis and mucosal pathology. Antioxidant complexes tri-V-plus, triovit contain direct and indirect antioxidants, trace elements (selenium).

The wide spectrum of action of antioxidants, the absence of a pharmacological effect in physiological conditions, the substitution nature of their administration and heteroprotective properties – all this determines the importance of using antioxidants in extreme conditions, in the complex therapy of dental pathology, atherosclerosis, cancer, etc. Taking into account the characteristics of antioxidants, the basic principles of their use as a means of prevention and treatment of chronic pathology should be highlighted: a) priority use of natural bioantioxidants; b) taking into

account the nutritional factor (prescription of direct antioxidants in the winter-spring period, and indirect antioxidants in summer and autumn); c) simultaneous administration of lipid-soluble and hydrophilic antioxidants; d) inclusion of the components of the antioxidant defense system in the complex preparations and an adequate choice of the dose of drugs (taking into account not only body weight, but also the person's age, the nature of its nutrition).

3.7

MEANS STIMULATING REGENERATION PROCESSES AND INFLUENCING THE EXCHANGE OF SUBSTANCES IN HARD TOOTH TISSUES

This group of drugs is used in dental practice to accelerate recovery processes in the body. Taking into account their pharmacological properties, drugs are widely used to stimulate the healing of wound surfaces, trophic and radiation ulcers, burns, complex therapy of inflammatory processes of the oral mucosa, soft tissues, for the prevention and treatment of caries, osteoporosis, and fractures of the upper limbs.

3.7.1. Means that affect the regeneration processes

The term "reparative regeneration" refers to the process of resuming the structure and functions of an organ after illness, injury, overload, etc. To stimulate it, first of all, it is necessary to detect a traumatic agent, damaged non-viable tissues and other factors (stress, inflammation, infection, uncomfortable dentures, etc.) that inhibit updating processes. The pharmacological regulation of the regeneration process is based on the stimulation of protein synthesis and the activation of protective mechanisms that ensure the functioning of the body as a whole. To stimulate the regeneration processes, different groups of drugs can be used:

- vitamin preparations (especially vitamins of plastic metabolism – folic acid, vitamins B_{12}, B_6, B_1, C, A, E, etc.);
- steroidal anabolic agents (retabolil, methandrostenolone, phenobolil, etc.);
- non-steroidal anabolic agents (sodium nucleinate, methyluracil, riboxin, potassium glycerophosphate, etc.);

- biogenic stimulants (solcoseryl, chonsurid, aloe, fibs, humisol, peloidin, placenta extract for injection, combuten, etc.);
- immunomodulators (levamisole, thymalin, tactivin, prodigiosin, pyrogenal, polyoxidonium, proteflazide, licopid, imudon, echinacea preparations, etc.);
- nonspecific stimulators of regeneration of plant and animal origin (sea buckthorn, rosehip, fir oil, as well as carotolin, apilac, propolis, rumalon, cerebrolysin, bee-bread, etc.).

The effect of vitamin preparations and immunomodulators on the regeneration processes is considered in the sections: "Vitamin preparations" and "Immunotropic agents".

In clinical practice, a positive effect was noted in the vast majority of drugs in this group. A significant effect on the regeneration processes is possessed by preparations of anabolic steroids, which contribute to the synthesis of proteins, muscle, bone and second tissues, stimulate synthetic processes in the body. They enhance oxidative phosphorylation and the formation of macroergic compounds. The effectiveness of drugs of this group is manifested under the predominance of anabolic processes in the body, for example, during convalescence after debilitating diseases. For the manifestation of effects, high-calorie protein nutrition and vitamins are necessary. Anabolic steroids are used for osteoporosis, bone fractures, aplastic anemia, diabetic angiopathies, various processes of dystrophic origin. Retabolil, which has a pronounced and long-lasting anabolic effect, increases appetite, improves well-being, performance. The drug enhances protein synthesis, promotes nitrogen metabolism in the body, calcium, potassium, phosphorus retention, reduces the content of cholesterol, β-lipoproteins, and blood phospholipids. It is used for chronic diseases that are accompanied by a negative nitrogen balance, infectious diseases, trophic lesions, in patients after treatment with cytostatics and the use of radiation therapy, to enhance the healing of fractures of bone marrow fractures. 5 % oil solution of retabolil is prescribed intramuscularly – 0.025–0.05 g once every 2–3 weeks. The course is 8–10 injections. Phenobolil has properties similar to the previous drug. It is indicated for generalized periodontitis in patients with asthenic syndrome, fractures, trophic ulcers of the oral mucosa. The drug is prescribed in oil 1–2 ml i.m. 1 time per week. The course of treatment is 3–5 injections.

Methandrostenolone is prescribed according to indications similar to phenobolil for 1–2 months.

Non-steroidal anabolic agents include drugs that stimulate the biosynthesis of nucleic acids (substrate activation). These are either precursors of purine and pyrimidine bases, or products of partial hydrolysis of nucleic acids. Unlike steroidal anabolic drugs, they do not possess hormonal activity and have low toxicity. Increasing the synthesis of nucleic acids and proteins, stimulating the separation of cells, they not only speed up the regeneration processes, but also improve their quality, contributing to the healing of wounds and ulcer surfaces, resume tissue function, make the scar more plastic. In addition, they stimulate an increase in white blood cells in the blood, activate specific and nonspecific immunity. Their action develops gradually, over 3–4 weeks. Sodium nucleinate and methyluracil have a stimulating effect on metabolic processes – nucleic acid synthesis and protein metabolism. They speed up the reproduction and growth of cells, wound healing, renewal of the mass and function of damaged organs, activate leukopoiesis and leukocyte activity, contribute to the creation of antibodies, lysozyme, complement, properdin, IFN, and have anti-inflammatory effects. They are prescribed in the complex therapy of acute ulcerative-necrotic processes, trophic ulcers, burns, fistulas, jaw fractures, osteomyelitis, chronic processes in the salivary glands, etc.

Effective influence on metabolic, bioenergetic, enzymatic processes, as well as generally stimulation of regeneration is carried out by preparations of biogenic stimulants. Solcoseryl (actovegin) is a protein-free preparation obtained from the blood of cattle, which is an active stimulator of regeneration processes. The drug activates cellular metabolism by facilitating the transport of glucose and oxygen, increasing their intracellular utilization, stimulating ATP synthesis, regeneration and revascularization. Solcoseryl has a membrane-stabilizing and cytoprotective effects. In dental practice, it is prescribed for stomatitis, gingivitis, periodontitis, for burns, trophic and pressure sores ulcers of the oral mucosa, necrotizing ulcerative processes, alveolitis, and injuries. It is introduced i.m. and i.v. 2–4 ml once a day or applied topically in the form of ointment, jelly, dental adhesive paste or gel. Humisol accelerates tissue regeneration; therefore, the drug is used for trophic ulcers and chronic erosive-ulcerative lesions of the oral mucosa – 1–2 ml i.m. once a day.

Suspension and placenta extract increase the protective properties of the body, accelerates the epithelization of wounds. It is used to increase the immunological reactivity of the body and in chronic erosive-ulcerative lesions of the oral mucosa. Plasmol is a drug that has a nonspecific analgesic effect. It is used for symptomatic stomatitis, which developed on the background of bronchial asthma or duodenal ulcers, arthritis, trigeminal neuralgia, pain syndromes. Chonsurid is obtained from the hyaline cartilage of cattle trachea. It is applied in torpid regeneration process, trophic ulcers, bedsores. Collagen film accelerates the regeneration process and has antiseptic properties. The film is applied topically to an ulcer or erosion. Aloe liniment improves tissue regeneration and epithelization. A thin layer of it is applied to erosive-ulcerative or radiation injuries of the mucous membrane of the oral cavity or lips. Combuten is a drug that is obtained from cattle skin or Achilles tendons. It stimulates reparative processes in the wound, accelerates the growth of granulations and epithelization.

In dental practice, apilac (royal jelly), propolis (bee glue), honey and bee-bread (honey with a high content of plant pollen) can help to stimulate regeneration, improve trophic processes, increase immunity, etc. The drugs are used to treat wounds, ulcers, aphthae, erosion that can not be cured well. Propolis is used as an anti-inflammatory, analgesic. Its 4–20 % alcohol solutions are used to anesthetize hard tissues of the tooth. Glucosamine is involved in the biosynthesis of proteoglycans of hyaluronic acid. The drug has a chondroprotective effect, contributes to the deposition of calcium in bone tissue. It is used for TMJ osteoarthritis, osteochondrosis, spondylosis, periarthritis. Rumalon, which contains an extract from the cartilage of young animals and bone marrow, is used for joint diseases that are accompanied by degenerative changes in the cartilage tissue of the joints.

Mumijo is an ancient "miracule balm" that has been used in folk medicine for millennia. The drug contains a large amount of micro- and macroelements, metal oxides, a number of vitamins, essential oils, bee venom, tar-like substances. It stimulates the regeneration processes, activates the healing processes of wounds and fractures, and has anti-inflammatory, antitoxic, and general strengthening effect. Sea buckthorn oil, rosehip oil and carotolin (oil extract of carotenoids from the flesh of rose hips) stim-

ulate regeneration processes. The preparations contain unsaturated and saturated fatty acids, carotenoids, tocopherols, vitamins B, C, P and other organic substances. They are used to accelerate the healing of wounds, burns, trophic and radiation ulcers, cracks. 1 teaspoon of sea buckthorn oil is used enterally 2–3 times a day for 1 month. Locally, drugs are used for applications, inhalations or administered on turundas (in periodontal pockets). Juices, decoctions, infusions, and tinctures of medicinal substances (St. John's wort, kalanchoe pinnata, greater plantain, calendula officinalis, comfrey, marsh dried flower, sophora japonica, etc.) stimulate regeneration processes and produce antibacterial and anti-inflammatory effects. They are applied for the treatment of infectious and inflammatory processes of the mucous membrane of the mouth and throat, periodontal tissues, to improve the healing of wounds and burn lesions in the form of applications, baths, rinses.

3.7.2. Means that affect the metabolism in hard tissues of the tooth

In dentistry, drugs containing micro- and macroelements – calcium, phosphorus, fluoride are most often used to regulate the metabolism in the hard tissues of the tooth and bone. They are necessary for the normal growth, development and formation of hard tooth tissues (enamel and dentin), bones, as well as for their restoration and strengthening.

The inorganic matrix of the bone and hard tissues of the tooth is a spatial lattice of hydroxyapatite, which consists of hydroxyl ions of calcium and phosphorus. The composition of apatite crystals also includes ions of fluoride, zinc, strontium, iron, silicon, manganese, copper and other trace elements. Enamel resistance to pathogenic effects depends on the balance of two dynamic processes – de- and remineralization. A decrease in the activity of remineralization processes or an increase in demineralization causes the loss of mineral components by solid tissues, which is manifested by a kind of dissolution of hydroxyapatite. The introduction of calcium, phosphorus and other trace elements into the hard tissues of the tooth and bone helps to restore their mineral component, as it creates the conditions for the recrystallization of hydroxyapatite. Calcium, phosphorus, fluoride preparations are widely used for the prevention and treatment of lesions of hard tissues of the tooth, the prevention of caries, they are the basis for the treatment of multiple caries and its initial stages, as

well as non-carious lesions of the teeth. Together with other drugs, they are prescribed for the treatment of inflammatory and dystrophic periodontal lesions.

One of the local effects on the hard tissues of the tooth is remineralizing therapy. Remineralization (secondary artificial mineralization) of tooth hard tissues is possible because enamel and dentin are permeable to ions and molecules of chemicals. The remineralizing solutions are based on calcium, phosphorus and fluoride salts. The main indications for remineralization is the presence of single or multiple spots on the teeth (focal demineralization) – the initial multiple caries, enamel hypoplasia. In the complex of local effects on dentinogenesis, odontotropic agents occupy a special place, the action of which is based on stimulation of the protective properties of the pulp, which is manifested by the formation of secondary dentin (reparative). Most often they use preparations made on the basis of calcium hydroxide (calcemin, calcin-paste) and calcium salts (calcium gluconate, calcium glycerophosphate), less often zinc (zinc and zinc-salicylic paste) or oxide (zinc-eugenol paste). The main indications for the use of odontotropic drugs are: acute deep carious process, devital amputation of pulp, biological treatment of pulpitis, filling the root canal to stimulate the formation and mineralization of the apex of the root of the tooth in permanent teeth in children.

Classification of agents that affect metabolism in the hard tissues of the tooth and bone:

- calcium preparations (calcium gluconate, calcium glycerophosphate, calcium chloride, calcium lactate, calcium phytate, calcium);
- phosphorus preparations (calcium glycerophosphate, phytin, hefephytin, phosphate flit, neutra-phos, infos, lipocerebrin, cerebrolecithin);
- fluorides (sodium fluoride = ossin = coreberon = fluosin, disodium monofluorophosphate, fluoride, vitaflor, gels, solutions, cements that contain sodium fluoride);
- bisphosphonates (alendronate = fosamax, clodronate, etidronate);
- ipriflavone (osteoquine);
- calcitonin (sibacalcin, hydroxide, elcatonin);
- combined preparations (vitrum-calcium, calcemin, cal-C-vita, calcium-D_3 nycomed, osteogenon).

Calcium preparations. The body contains more than 1400 g of calcium (more than 99 % in bones in the form of phosphates). Calcium deficiency in the body can be associated with a lack of phosphorus and vitamin D in the intestine and impaired acid-forming functions of the stomach. Calcium ions are involved in the transmission of nerve impulses that provide skeletal and smooth muscle contraction, reduce vascular permeability due to the vasodilating, membrane-stabilizing effect on the smooth muscles of blood vessels, providing normal myocardial contractility. They are necessary for blood coagulation processes, participate in the processes of blood formation, metabolism, prevent the penetration of microorganisms into the blood, so they increase the body's resistance to infections and toxins. A decrease in the content of calcium ions in blood plasma and tissues can cause various pathological processes. Acute hypocalcemia causes the development of tetany. Chronic calcium deficiency can be accompanied by skeletal and smooth muscle dysfunction of the CVS, coagulation disorders and the development of osteoporosis.

In dental practice, various preparations of calcium, phosphorus and fluoride are used. Calcium preparations are used for the prevention of caries and the treatment of diseases of tooth hard tissues (multiple caries, non-carious defects in tooth hard tissues) to ensure the strength of bone tissue and tooth enamel (plastic role). Sometimes calcium preparations are prescribed for the treatment of inflammatory processes in periodontium. Calcium preparations, together with other agents that stimulate osteogenesis (calcitonin, vitamins of group D), contribute to the reduction of osteoporosis cells, and bone densification of the tips of the interdental membranes. In addition, calcium preparations have an anti-inflammatory and anti-edematous effect, which is explained by a decrease in the permeability of the walls of blood vessels, and also have an anti-allergic effect. The need for it increases in pregnant women and during lactation, in infants, younger children and the elderly.

For remineralization therapy for caries and non-carious lesions of the tooth, calcium gluconate is used. For applications – 10 % solution of calcium gluconate, which is applied to previously cleaned teeth. To increase the effect of remineralizing therapy, the application of 2 % sodium fluoride solution is repeated. Calcium gluconate is also used for oral administration (0.25 tablets; 0.5 g) for the treatment of caries and periodontal

diseases. Other preparations which contain calcium are also used to improve metabolic processes in tooth hard tissues: calcium chloride, calcium lactate, calcium phytate, calcium nitrate, etc. Calcium chloride is used in case of multiple caries and inflammatory periodontal diseases in the form of 10 % solution by electrophoresis or applications and less often than calcium gluconate, can be used enterally as 5 % solution (there are indications of its local irritating effect). It is also known that calcium chloride can contribute to a shift in the pH of the medium towards acidosis, since chlorine ions released during the deposition of calcium in the bones replace bicarbonates from extracellular fluid. Calcium lactate has an effect similar to calcium gluconate, but it is more effective effect when administered orally (0.5 g tablets). The highest calcium content in mg per 1 g of salt is calcium carbonate (400 mg), calcium glycerophosphate (191 mg), calcium gluconate (90 mg), calcium chloride (270 mg), calcium lactate (130 mg). It should be remembered that calcium preparations are contraindicated at the same time as cardiac glycosides. They should be used with caution for urolithiasis, a tendency to thrombosis, as well as for atherosclerosis, an increased content of calcium in the blood (normal blood calcium levels range 2.5–2.75 mmol/l).

Phosphorus preparations. Phosphorus is one of the most important elements of a living cell, especially there is a lot of it (mainly in the form of calcium phosphate) in bones and teeth. Calcium metabolism is closely related to phosphorus metabolism. Inorganic phosphates can reduce serum calcium and increase bone reactivity to parathyroid hormone. The absorption of calcium and phosphorus in the wall of the small intestine primarily depends on their ratio; it is regulated by vitamin D and parathyroid hormone. Products which contain both calcium and phosphorus ions are more effective on the impact on the hard tissues of the tooth and bone. Calcium glycerophosphate, calcium phosphate, calcium monophosphate, etc. are most often used in dental practice. Calcium and phosphorus ions must be introduced in such a concentration that saliva is a supersaturated solution in comparison with them. The ratio of calcium to phosphorus should be 1:1.5 (pH 7.2–7.4). Calcium glycerophosphate is used as a restorative, tonic for overwork, exhaustion, rickets. Its main effect is associated with increased anabolic processes. The drug is used to prevent caries, in the complex therapy of diseases of hard tissues of the tooth.

Phytin is a complex organic phosphorus preparation containing a mixture of calcium and magnesium salts. It contains 36 % organically bound phosphoric acid, has anabolic activity, including enhancing bone growth and development. The drug is used for the prevention and treatment of multiple caries, inflammatory processes in the periodontium. In addition to dental practice, they are also used for rickets, osteomalacia, anemia, and tuberculosis. Among the agents that increase the mineralization of tooth tissues, one can name phosphate cement, which contains glycerophosphate (5 %) and sodium fluoride (5 % and 2 % of 2 % of the total mass of cement powder, respectively), and cement Fluosit, which contains 11 % sodium monophosphate. Tooth resistance to pathogens is also enhanced by toothpastes, which include soluble calcium salts (gluconate, glycerophosphate, chloride), phosphoric acid salts (potassium and sodium hydro- and dihydrogen phosphates), trace elements (fluoride, molybdenum, vanadium, and copper in free form). It must be remembered that insoluble compounds of calcium, phosphorus, trace elements do not affect the processes of remineralization (chalk, dicalcium, tricalcium phosphates, etc.). Toothpastes Pearl, Arbat containing calcium glycerophosphate, etc. have a mineralizing effect. Lipocerebrin, cerebrolecithin also contain phosphorus. Indications for their prescription can be: dental diseases (multiple caries, generalized periodontitis), as well as hypotension, neurasthenia, rickets, etc. The drugs are taken orally. Contraindications are not established. The choice of the optimal ratio of active components in mineralizing agents is a difficult task. The problem is greatly facilitated by the use of natural products, in particular, bone hydrolyzate – remodent. It is obtained from animal bones. The composition of the remodent includes: calcium – 4.35 %, phosphorus – 1.35 %, magnesium – 0.15 %, potassium – 0.2 %, sodium – 16 %, chlorine – 30 %, organic matter – 44 %, trace elements (manganese, iron, zinc, copper) – the rest is up to 100 %. Remodent is used for carious and non-carious lesions of hard tissues (applications and rinses).

Fluoride preparations belong to pathogenetically substantiated means of caries prophylaxis and increase enamel resistance to cariogenic factors. Fluoride is a vital element that is necessary not only for the full maturation of tooth enamel, formation, preservation of bone tissue in childhood, etc. Fluoride ions, enhancing the formation of hydroxyapatite from calcium ions and phosphates, help to prevent the occurrence of osteoporo-

sis, and also reduce the probability of occurrence of mineral deposits in the walls of blood vessels. Fluorides interact with one of the main mineral components of enamel – hydroxyapatite, contributing to the formation of hydroxyfluoroapatite, which is characterized by higher thermodynamic resistance and greater resistance to acids. When replacing hydroxyl ions with fluoride ions, the binding energy doubles, which helps to reduce the permeability of enamel. It has been shown that fluoride in optimal doses positively affects enamel protein metabolism.

In order to prevent caries, sodium fluoride, potassium fluoride, tin fluoride, aminofluoride, titanium fluoride is more often used. These agents are characterized by anti-carious activity. When prescribing fluoride preparations (both local and resorptive), the following principles must be observed:

- fluorides are prescribed taking into account their content in drinking water (not more than 0.3–0.5 mg/l);
- when choosing fluoride-containing agents, the possibility of their binding, for example, with calcium compounds, which reduces their activity should be taken into account;
- the optimal fluoride concentration for local caries prophylaxis is 1–2 % (based on fluoride ion).

For the prevention of caries, fluorides are used in several forms. So, with fluoride content in water of less than 0.5 mg/l, it is advisable to carry out its fluorination. General prevention of caries can also be carried out by taking fluorides enterally in the form of tablets of sodium fluoride, vita-fluoride, fluorinated salt and fluorinated milk. Sodium fluoride is the main of fluoride preparations, which is used to prevent caries and treat diseases of hard tissues of the tooth. Sodium fluoride tablets contain 0.5 mg, 1 mg, 2 mg of the drug. The dose is set depending on the age and fluoride content in drinking water. When the concentration of ionized fluoride in water is 0.1–0.3 g, children under 5 years of age are prescribed 1.1 mg/day, from 6 years – 2 mg/day. The tablets are taken after meals, chased down with water. The course of treatment lasts 6–8 months annually. The protective effect of fluoride is manifested in relation to both those teeth that have erupted and those that have not erupted. Vitaflor is an anticariotic agent for oral administration. This is a liquid combination fluoride drug. One teaspoon (5 ml) of vitaflor contains 3300 IU of retinol palmitate,

400 IU of ergocalciferol, 0.06 g of ascorbic acid, 0.0011 g of sodium fluoride (respectively, fluoride ions – 0.0005 g). The pharmacological properties of the drug are due to the presence in its composition of vitamins A, D, C and fluoride, which in combination have a beneficial effect on tooth tissue. Vitamin A promotes the development of teeth and the formation of the skeleton, vitamin D regulates the exchange of phosphate and calcium ions in the body, promotes their absorption in the intestine and the timely accumulation in the newly formed bone tissue. Fluoride, accumulating in the teeth, intestines, and to a lesser extent in cartilage, strengthens these tissues. Vitamin C, on the contrary, limits the deposition of fluoride salts in tissues, preventing the development of its side effects. The drug is not prescribed if the fluoride content in water exceeds 1.5 mg/l, as well as with the appearance of symptoms of D- and A-hypervitaminosis.

One of the methods of local caries prevention is the use of fluoride varnishes based on natural tars (fir, cedar). A single application of fluoride varnish on the tooth surface is equivalent in effectiveness to repeated use of fluoride solutions. Fluoride varnish – a composition of natural tars of a dark yellow color, viscous consistency, containing 2.9 % fluoride. The varnish has high adhesion to teeth, can stay on them for a long time, which contributes to the interaction of fluorides with enamel. Fluoride is applied to the surface of the teeth, starting with the lower jaw, in a thin layer. The teeth are coated with fluoride three times with an interval of 1–2 days. The procedure is repeated after 6 months. An effective method for the prevention and treatment of caries is the method of deep fluoridation, which is carried out by special preparations "Enamel-sealing liquid". Inorganic and organic fluoride compounds are used for local prevention and treatment of diseases of hard tooth tissues. The most commonly used fluorides are sodium, potassium, tin, iron, titanium and aminofluoride. To rinse the oral cavity, 0.1–0.2 % sodium fluoride solution is usually used. Rinsing with fluoride solution is contraindicated for children under 5 years. In case of accidental ingestion of a sodium fluoride solution, 1–2 tbsp. of 10 % solution of calcium chloride should be taken, which is able to bind fluoride. Among other more active fluoride compounds, tin fluoride (8 % solution), which is used in mineralizing solutions, is of particular interest. It not only affect the structure of enamel, but also has an antibacterial effect on the microflora of the oral cavity.

For applications, 1–2 % solution or sodium fluoride gel is used. It is recommended to carry out 2 times a year. For application, 1–2 % gel of sodium fluoride on 3 % agar can be used, which forms a thin film in the contact with teeth. Gels are effective in the case of their introduction by electrophoresis. Fluodent and Fluocaril, Helios, etc. belong to gels. If there are wedge-shaped defects and hyperesthesia of the hard tissues of the tooth, 5 % phosphate fluoride cement can be used. Its applicates are kept on the teeth for 5–10 days, which contributes to the saturation of the tooth hard tissues with fluoride ions. One of the popular methods of local caries prevention is fluoridation of teeth with the help of fluoride-containing toothpastes. Fluorides give pastes pronounced anti-carious activity. The content of free fluoride ion in the paste should not exceed 1–2 %. Fluoride-containing pastes should not include calcium-containing abrasives, because fluoride easily combines with calcium and becomes biologically inactive. Fluoride pastes can be recommended in areas where the fluoride content in drinking water does not exceed 0.5 mg/l. They should be applied 2–4 times a year, along with other preventive and therapeutic measures. In the intervals between their use, toothpastes with a different mechanism of action (antimicrobial, remineralizing, etc.) are prescribed.

In dentistry, the use of exogenous fluoride is also important for the treatment of periodontitis, and in implantology, in patients with manifestations of osteoporosis in the bones of the upper limbs. It should be remembered that excessive intake of fluoride in the body is dangerous, leading to inhibition of various metabolic links in the cells (primarily glycolysis). In the early period of fluoride intoxication, typical dark spots on the enamel may appear, and later, disorders of the musculoskeletal system and second body systems may occur. The damage of the skeleton begins with an increase in bone density and the appearance of exostoses on the spine, pelvic bones, skull bases and ribs. In addition, muscle and nervous system lesions are noted. Calcium chloride solution is an antidote for poisoning with soluble salts of fluoric acid.

Bisphosphonates are synthetic derivatives of phosphonic acids with the replacement of an oxygen atom in a molecule by a carbon atom. Representatives of this group – alendronate, clodronate, zoledronate are antiresorbents, they are tightly bound to the mineral components of bone tissue and inhibit its resorption. They are used for osteoporosis of vari-

ous origins and ectopic calcifications. An indication for the use of antiresorbents is generalized periodontal disease, accompanied by progressive destruction of the alveolar ridge, periodontal disease in women in the postmenopausal period. Also indications are bone damage during metastasis. Bisphosphonates are usually used in combination with calcitonin. Bisphosphonate therapy should be long-term. The duration of remission after stopping the administration of bisphosphonates is usually longer than with calcitonin therapy and can exceed 2 years.

Ipriflavon. It suppresses directly bone resorption, inhibiting osteoclastogenesis. It is used for primary osteoporosis (postmenopausal and senile) and secondary osteoporosis (post-traumatic, caused by prolonged therapy with GCS). Ipriflavone is prescribed orally 200 mg three times a day.

Calcitonin. The main biological effect is inhibition of bone resorption due to inhibition of the number of osteoclasts. Calcitonin affects the organic composition of bones, inhibiting the breakdown of collagen. At clinic, natural pig calcitonin (calcitrin, calcitar), synthetic human calcitonin (sibacalcin) and synthetic salmon calcitonin (myacalcin, calcinar) or eel calcitonin (elcatonin) are used. There are various modes of use – parenteral (50–100 IU) and intranasal (salmon calcitonin at a dose of 50–100 IU). In the complex treatment, osteogenon is used – the ossein-hydroxyapatite complex, which affects the activation of bone tissue synthesis. It is applied at a dose 2–4 tablets 2 times a day. No side effects have been identified. Contraindications are hypercalcemia, hypercalciuria. Compounds of calcium with vitamin D have an osteochondroprotective effect. For example, calcemin (calcium citrate + calcium carbonate + vitamin D_2 + copper + zinc + manganese + boron) and calcium-D_3-nycomed (calcium + vitamin D_3). Features of the differentiated use of calcium, phosphorus and fluoride preparations are presented in more detail in the section "Pharmacotherapy in dentistry".

3.8

ENZYME AND ANTIENZYME DRUGS

The dynamic balance of metabolic processes in the body is regulated by biological catalysts – enzymes and their inhibitors – antienzymes. The activity of enzymes and antienzymes depends on the influence of low molecular weight compounds – coenzymes, most of which are derivatives of vitamins and are an integral part of the active centers of enzymes. In case of impaired synthesis or activity of enzymatic systems, a pathological condition develops – fermentopathy, which can lead to serious consequences for the body. Yes, due to a deficiency of phenylalanine hydroxylase, there is a mental inferiority in children. Deficiency of glucose-6-phosphate dehydrogenase contributes to the development of hemolytic anemia, especially when using SA and nitrofurans. Violation of metabolic processes can lead to impaired functioning of coenzyme systems. One of the ways to treat fermentopathy is to replenish an enzyme or coenzyme deficiency. In case of insufficiency of the secretory function of the gastrointestinal tract, enzyme preparations pepsin, pancreatin, natural gastric juice, and others are used. Coenzyme preparations cocarboxylase and lipoic acid positively affect the processes of tissue respiration in heart failure, anemia, and hypovitaminosis. In clinical practice, cases of excessive activation of enzyme systems sometimes occur. These disorders are typical for acute pancreatitis, when increased activation of proteolytic enzymes leads to increased bleeding. In such cases, enzyme inhibitors – aprotinin (trasylol, contrykal) are prescribed. The systematization of drugs of this pharmacological group may have the following form:

I. Enzymes:

1) proteolytic enzymes (trypsin, chymotrypsin);

2) fibrinolytic enzymes (streptoliase, fibrinolysin, streptokinase, streptodekase, urokinase, alteplase);

3) DNA depolymerizing enzymes (ribonuclease, deoxyribonuclease);

4) enzymes that reduce the viscosity of hyaluronic acid (lydase, ronidase);

5) enzymes that improve digestion (pepsin, natural gastric juice, solizym, pancreatin, festal, mezym-forte).

II. Coenzymes (cocarboxylase, lipoic acid, pyridoxalphosphate, flavinate, riboflavin mononucleotide).

III. Antienzymes (enzyme inhibitors):

1) inhibitors of proteolytic enzymes (aprotinin);

2) fibrinolysis inhibitors (aminocaproic acid, tranexamic acid).

3.8.1. Enzymes

This group of drugs has recently been widely used in dental practice. Known enzyme preparations from animals (pepsin, trypsin, chymotrypsin, ribonuclease, deoxyribonuclease, lydase, collagenase), microbial (terrilytin, hygrolitin, streptokinase) and plant (papain, bromelain) origin. The spectrum of therapeutic action of enzymes is diverse. They exhibit proteolytic, anti-inflammatory, decongestant, anticoagulation effects. The mechanism of the proteolytic action of enzymes is multifaceted; first of all, it is associated with their ability to cleave peptide bonds in the protein molecule of necrotic tissues into small fragments that are better removed. Therefore, they help to cleanse wounds from necrotic tissue. Enzymes actively influence the exudative phase of inflammation (reduce it), have a stimulating effect on the phagocytic activity of leukocytes; thin out thick secretion and exudate. It is important that they improve microcirculation, as well as stimulate reparative processes and do not affect healthy tissues. The anticoagulant effect of the drugs is due to the activation of the anticoagulation system.

In therapeutic dentistry, proteolytic enzymes are prescribed for necrotizing ulcerative gingivitis or stomatitis, oral candidiasis, abscessed periodontitis, generalized periodontitis, erosive form of lichen planus, purulent periodontitis, herpetic stomatitis, exudative erythema multiforme, trigeminal neuralgia, etc. In surgical dentistry, enzymes are used in the treatment of purulent and necrotic processes of soft tissues and bones of the upper limbs, trophic ulcers, burns, and thrombophlebitis. Enzyme preparations are also prescribed before autodermoplasty and for the prevention of postoperative complications. These drugs are widely used for suppurative incendiary processes in the lungs and pleura.

Enzyme preparations are applied topically in the form of applications, instillations, irrigation and electrophoresis, systemically i.m. and i.v. Locally 1–5 % solutions of enzymes on novocaine, and 0.2–1 % injections are ase. Uncleaned preparations of chymopsin, ronidase, and terrilytin are used only locally on purulent wound surfaces and for inhalation. Enzymes can be included in pastes and emulsions for insertion into the gingival pockets along with ABD. They are also included in toothpastes and powders to increase the effectiveness of toothbrushing. Colagenase is a part of the Iruxol ointment for the treatment of necrotizing ulcerative lesions of the oral mucosa and generalized periodontitis. Highly purified crystalline enzyme preparations trypsin and chymotrypsin are well tolerated by patients, have minor side effects, especially in case of their local application. Among the side effects are allergic reactions, intoxication as a result of absorption of necrolysis products and local irritant effect. To reduce side effects, the drug is not recommended to be left for a long time in the area of pronounced pathological purulent-necrotic changes. The use of enzyme preparations is contraindicated in the presence of allergization of the body, with malignant tumor processes, increased bleeding, decompensation of cardiac activity, liver and kidney pathology.

The following enzyme preparations are of clinical importance for dental practice. Trypsin is locally prescribed for purulent wounds of soft tissues and oral mucosa in the form of baths, applications and inhalations (1–5 % concentration in isotonic solution). The drug is often used in combination with antibiotics in the form of therapeutic pastes, hardening dressings, emulsions. Trypsin is administered intramuscularly at a dose 0.005–0.01 g (5–15 injections per course) or in the transition fold (5–6 injections per course). Chymotrypsin accelerates the resorption of hematomas, enhances the effect of antibiotics. For i.m. injections, 0.005–0.01 g of the drug is used (10–15 injections per course). With this method of administration, pain and swelling at the injection site can be observed. In case of necrotizing ulcerative processes of the mucous membrane, topical solution of terrilytin is used (1 ml has an activity of 40–50 UI). To prepare it, the contents of the bottle (200 IU) are dissolved in 4–5 ml of distilled water for injection or an isotonic solution of sodium chloride, or 0.25 % solution of novocaine. Gauze or cotton strips moistened with a solution are applied to the wound surface for 15–20 minutes. With exacerbation

of generalized periodontitis, which is accompanied by the appearance of purulent discharge from the periodontal pockets, terrilytin is additionally administered by electrophoresis. To do this, 0.05 g (200 IU) of terylitin is dissolved in 5 ml of tris-glycine buffer (pH 8.3). Electrophoresis is carried out from the cathode for 10 minutes; the current strength is 1–3 mA. The drug maust not be applied into the cells of inflammation and bleeding cavities, as well as to the ulcer surfaces of malignant tumors!

Deoxyribonuclease causes the rapid depolymerization of deoxyribonucleic acids with the formation of deoxyribonucleotides, reduces the viscosity of purulent exudate and inhibits the reproduction of DNA containing viruses (herpes, adenoviruses, etc.). It is applied with purulent wounds and diseases of viral origin locally (0.2 % solution) and in the form of injections. Lydase (hyaluronidase) depolymerizes hyaluronic acid, which glues connective tissue and thereby increases tissue permeability for various factors and improves fluid drainage in the interstitial space. Duration of action is about 48 g. The contents of the bottle – 0.1 g (64 IU) are dissolved in sterile 0.5 % novocaine solution and injected into the scar tissue or hypertrophied interdental nipples, hematoma, nerve exit points. The course of treatment is 10–12 injections daily or every other day. It is applied to eliminate contractility of the TMJ, scars after burns on the face and oral mucosa, hematomas, hypertrophic manifestations, as well as traumatic lesions of the trigeminal nerve branches.

Recently, lysobact (lysozyme), which is an enzyme of protein nature, is widely used. It has antiseptic and antiviral activity. The tablets are slowly absorbed (2 tablets 3–4 times a day, the course of treatment is 8 days). The dissolved mass must be retained in the oral cavity as long as possible. Do not swallow the pill! Phlogenzym is a combination drug that contains bromelain, trypsin and rutin. The drug has anti-inflammatory, fibrinolytic, thrombolytic, antiplatelet and decongestant action. Enzymatic components contribute to the rapid breakdown of metabolic products of the inflammatory process. Rutin resumes vascular wall permeability, which leads to a decrease in edema and hematomas. Phlogenzym reduces blood viscosity, prevents the formation and promotes the lysis of blood clots that have already formed. The drug has anti-inflammatory, fibrinolytic, thrombolytic, antiaggregant and decongestant forms of action. Phlogenzym is recommended for early postoperative acute inflammation, repeated

and chronic infections, and immune disorders. Phlogenzym is prescribed at a dose 2 tablets 3 times a day before surgery and 3 tablets 3 times a day after surgery. There may be long courses in the treatment of indications. Serratiopeptidase (serrata) is a proteolytic enzyme isolated from the non-pathogenic intestinal bacterium Serrata E 15. Clinical studies have shown that serratiopeptidase has fibrinolytic, anti-inflammatory and decongestant activity. By hydrolysis of bradykinin, histamine and serotonin, it directly reduces the dilatation of capillaries and controls their permeability. In case of periodontitis, serratiopeptidase is proposed for the main treatment regimen as an additional method (in case of chronic course – 5 mg 3 times a day, with exacerbations – 10 mg 3 times). The enzyme is also used for sports injuries, the risk of transplant rejection, fractures and dislocations, as well as for edema caused by surgery in the MFA. Polysim-4 is a preparation of the original structure, which consists of medicinal plants of the Crimea (immortelle, hawthorn, etc.) and thin homogenates of animal origin. The drug renews the body's immune defense, normalizes metabolism, activates the drainage functions of the urinary system, improves hematopoiesis, carries out regenerative and wound healing effects. In surgical dentistry, it is included in the pre- and postoperative treatment complex to optimize wound healing.

3.8.2. Antienzymes

This group of drugs is used in clinical practice to reduce the activity of certain enzyme systems. Drugs that inhibit protease activity are most common in medicine. Natural (contrykal, pantrypin) and synthetic (aminocaproic and aminomethylbenzoic acids) drugs – proteolysis inhibitors. Most often they are used to treat acute and chronic pancreatitis, in the pathogenesis of which the leading role is played by the process of activation of proteolytic enzymes that cause destruction and autolysis of the pancreatic tissue. Aprotinin (contrykal) inhibits the kinin and thrombin systems, inactivates kallikrein, thromboplastin, trypsin, chymotrypsin, fibrinolysin and plasminogen activating enzymes. It prevents the development of destructive processes in the pancreas.

In dental practice, they are used for generalized periodontitis, necrotizing ulcerative lesions of the oral mucosa. The drugs slow down the destructive processes in the tissues, affect the microvasculature of the prob-

lem area, reduce swelling, have a positive effect on periodontal disease and stimulate regenerative processes. It is prescribed locally (applications) or by electrophoresis. Contrykal (gordox, trasylol) is not absorbed from the gastrointestinal tract and is administered intravenously. Side effects are manifested in the form of local and general allergic reactions, phlebitis, fever and intoxication with necrolysis products. Among the side effects of enzyme inhibitors, allergic reactions of varying degrees may develop.

3.9
AGENTS INFLUENCING HEMOSTASIS

The problems of hemostasiology in modern clinical medicine are caused by the widespread occurrence of thromboembolic complications and their significant growth in pathological processes caused by the disease itself and, sometimes, by treatment complications. In this case, an important role belongs to the timely prescription of thrombolytics and anticoagulants. Situations when it is necessary to stop bleeding (during trauma, operations, etc.) require in-depth awareness of the pharmacology of the procoagulant and drugs that inhibit fibrinolysis. In dental practice, it is necessary to correct the hemostasis system during bleeding, which is predetermined by an injury to the nose or tooth extraction. Bleeding may occur due to the destruction of a blood clot in case of violations of the postoperative regimen or in the pathology of the blood coagulation system (hemophilia, thrombocytopenia). Hemostatic agents are also used during preparation for operations, which are accompanied by increased bleeding.

The process of blood coagulation is a complex reaction that occurs in several phases. In the first, longest phase, prothrombinase is formed due to a cascade of enzymatic processes. In the second phase of blood coagulation, prothrombinase adsorbs prothrombin on its surface and turns it into thrombin. After the second, the third phase of blood coagulation quickly begins, when, under the influence of thrombin, plasma fibrinogen turns into fibrin, which provides coagulation hemostasis. Next comes the refraction of the clot.

The pharmacological effect on the processes of increased thrombosis or decreased blood coagulation is carried out by various groups of drugs.

3.9.1. Directly acting anticoagulants

Directly acting anticoagulants include heparin, an acidic mucopolysaccharide consisting of glucuronic acid and glucosamine residues esterified

with sulfuric acid. In the body, heparin produces basophils. It belongs to natural anticoagulant factors. Heparin activity is determined using the biological method – by the ability to change blood coagulation time and is expressed in units of action (1 mg of international standard heparin contains 130 IU). In the body, heparin binds to antithrombin and second serine proteases, which are involved in the folding process. Heparin inhibits all phases of blood coagulation. In large doses, it reduces the aggregate and adhesive properties of platelets, forms complexes with proteins that possess fibrinolytic activity. By enhancing the activity of lipoprotein lipase, heparin lowers blood lipids. The drug has anti-inflammatory, anti-allergic, immunosuppressive, antitoxin properties, improves microcirculation.

Heparin is used to prevent and treat thrombosis and a thromboembolic process (stroke, myocardial infarction), to prevent blood coagulation during operations on the heart and blood vessels, for blood transfusion, to connect an artificial kidney, and to prevent postoperative thromboembolism. Single and daily doses depend on the state of the coagulation system, heparin tolerance and individual patient sensitivity. In acute thrombosis, heparin begins to be injected intravenously stream every 4 hours. The dose of heparin is 30.000–80.000 IU per day. In case of an overdose of the drug and the occurrence of dangerous bleeding, it is necessary to introduce 1 % solution of protamine sulfate at a rate of 1 ml of the drug per 1000 IU of heparin. In addition, when using heparin, allergic reactions, thrombocytopenia, cyanosis, shortness of breath, hematomas, hair loss, etc. can be observed. The modern drug atenativ (antithrombin III) inactivates thrombin due to the formation of covalent bonds and the suppression of the activity of blood coagulation factors (IXa, Xa, plasmin, etc.). The drug has an anticoagulant effect.

Widely used in clinical practice are low-molecular directly acting anticoagulants – nadroparin (fraksiparin), enoxaparin (clexane), bemiparin (cibor), etc. These agents differ from standard heparin in a more pronounced anticoagulant effect; have greater bioavailability, a longer half-day after s.c. injection, ease of dosing and prediction of the corresponding reaction, the possibility of outpatient use, the absence of the need for routine laboratory control, as well as a lower risk of thrombocytopenia and osteoporosis. Drugs are used to prevent thromboembolism. In practice, clexane has a high clinical effect. However, the new oral anticoagulant rivaroxaban has

Table 12

Classification of drugs that affect hemostasis

Group	Drug	
	Direct action	Indirect action
Anticoagulants	Heparin, nadroparin, (fraxiparin), enoxaparin (clexane)	Neodicumarin, warfarin, fepromaron, phenylin, omefin
Fibrinolytics	Fibrinolysin, profibrinolysin	Streptokinase, alteplase (actilyse), urokinase, tenecteplase (metalyse), reptilase
Antiplatelet agents		Acetylsalicylic acid, pentoxifylline (trental), vinpocetine (cavinton), piracetam, parmidin, dipyridamole (chimes), ticlopidine (ticlid), clopidogrel (plavix, trombone)
Fibrinolysis inhibitors	Aprotinin (contrykal)	ε-aminocaproic acid, tranexamic acid
Procoagulants (hemostatics)	Thrombin, fibrinogen, isogenic fibrin sponge, antiseptic sponge with kanamycin	Vitamin K, vikasol

several advantages over the latter. It is much more effective, reduces the risk of venous thromboembolism. Moreover, with small courses of therapy, rivaroxaban did not show hepatotoxic effects.

3.9.2. Indirect anticoagulants

Indirect anticoagulants are synthetic substances, antagonists of vitamin K, inhibit the blood coagulation process by affecting the synthesis of coagulation factors in the body. The action of these drugs is associated with a violation of the biosynthesis of prothrombin (II), proconvertin (VII) and other coagulation factors (IX, X). Indirect anticoagulants are prescribed for the prevention and treatment of thromboembolic complications. They are classified according to speed and duration of action into three groups: 1) febromaron, warfarin, syncumar (the effect of these drugs manifests itself gradually and reaches a maximum after 24–48 hours and

even 72 hours, they have the most pronounced cumulative properties.); 2) neodicumarin (its effect is faster and often reaches a maximum after 16–18 hours, the cumulative effect is less pronounced than with the drugs of the previous group); 3) phenylin and omefin (the effect of these drugs, especially phenylin, appears after 8–10 hours.). The most active drug in this group is warfarin, which has found wide clinical application. It is almost completely absorbed in the intestine, does not penetrate into milk, and is better tolerated. 5–10 mg enterally per day is administered for a long course. In case of an overdose of anticoagulants, hemorrhagic complications can appear due to an excessive decrease in blood coagulability. To eliminate these phenomena, vitamins K, P, and ascorbic acid preparations are prescribed. Hepatotoxicity, nephrotoxicity, etc. may also be observed.

3.9.3. Blood clot lysis medications

Along with the coagulation system, the body has an enzymatic fibrinolytic system, which plays an important role in regulating the formation of blood clots and their dissolution. Plasma-derived drugs that have a direct proteolytic effect on fibrin (fibrinolysin) and compounds that are primarily plasminogen activators (streptoliase, urokinase, alteplase) are thrombolytics. This group is widely used in the treatment of thromboembolic complications. It is obtained from donated blood by activation of plasminogen with trypsin. In clinical practice, fibrinolysin is used simultaneously with heparin in the form of a fibrinolysin-heparin mixture (10.000 IU of heparin per 20.000 IU of fibrinolysin), usually administered intravenously. The daily dose is 40.000–60.000 IU. In case of an overdose, bleeding may occur, to stop it 100 ml of 5 % solution of aminocaproic acid is administered. Streptolyase is a drug containing the streptokinase enzyme isolated from a culture of β-hemolytic streptococcus. It is an indirect activator of fibrinolysis, acts on a blood clot not only externally, but also penetrates, accelerating lysis. Administered intravenously, the dose is determined individually. Alteplase (actilyse), a recombinant preparation of tissue plasminogen activator, belongs to new fibrinolytic agents. It causes fibrinospecific thrombolysis without affecting the reduction of plasma fibrinogen. It is effective in the first 6–12 hours for thromboembolic complications. The drug does not have antigenic properties, it can cause hemorrhagic complications. The recombinant drug tenecteplase (metalyse) has great activity.

3.9.4. Antiplatelet agents

Inhibitors that exert an antiplatelet effect include COX-1 inhibitors (acetylsalicylic acid) and phosphodiesterase (pentoxifylline, cavinton). Most often in clinical practice, acetylsalicylic acid is used. The antiplatelet effect of the latter is stored on average 3–4 days. It is considered advisable to prescribe the drug 1 g per day after 3 days. Currently, in chronic cases of increased thrombosis or for the purpose of its prevention, aspirin preparations are used, which contain 70–100 mg of acetylsalicylic acid (aspecard, cardioaspirin) or with the addition of magnesium oxide (cardiomagnyl, fodder Magnesium) to prevent negative effects on the gastrointestinal tract. Pentoxifylline blocks adenosine receptors, which contributes to the accumulation of c-AMP, an endogenous antiplatelet agent. Ticlopidine and clopidogrel are antiplatelet agents that disrupt the interaction of ATP with receptors in the platelet membrane. Ticlopidine (ticlid) in its activity exceeds aspirin, but its effect develops more slowly. The anti-aggregation effect of the drug reaches a maximum after 4–7 days and is stored for 4–10 days. The use of clopidogrel in comparison with ticlopidine is associated with a lower risk of toxic effects on the bone marrow. Cavinton predetermines the expansion of blood vessels in the brain, improves the supply of oxygen to the brain, increases the level of c-AMP and has an antiplatelet effect. It is advisable to use antiplatelet agents for the complex treatment of periodontal lesions, oral mucosa, which develop against the background of vascular pathology.

3.9.5. Direct procoagulants

Directly acting procoagulants are substances that enhance blood coagulation in vivo and in vitro. They include thrombin, fibrinogen, hemostatic sponge, etc. Thrombin is a dry enzyme obtained from the blood plasma of donors in the form of prothrombin. The drug converts fibrinogen into the fibrin monomer in the body and activates the fibrin stabilizing factor, then a fibrin thrombus is formed. The activity of the drug is expressed in units of activity. Intravenous administration of thrombin is unacceptable, because it can lead to widespread intravascular coagulation with a lethal effect! S.c. and i.m. administration can cause thrombosis of adjacent vessels! In inflammatory processes of periodontal disease, bleeding from the oral cavity during Werlhof's disease, gauze swabs, tissues,

fibrin sponges are moistened with a solution of thrombin and applied to the bleeding surface. It is used in the form of a special film, cotton wool, sometimes aerosol. To stop bleeding, a human blood plasma protein is used – fibrinogen, which is especially effective for bleeding against the background of hypo- and afibrinogenemia. It is also used prophylactically during preparation for surgery at dental clinics. A freshly prepared fibrinogen solution is administered intravenously according to individual indications. The modern drug is octaplex, which is a concentrate of the prothrombin complex (a combination of II, VII, IX, X coagulation factors). It is used in the treatment of bleeding and preoperative prophylaxis of bleeding, which is associated with an acquired deficiency of the prothrombin complex, especially caused by treatment with indirect anticoagulants. Ethoxylate (dicynone) and calcium dobesilate (doxyum), which have an activating infusion on the formation of thromboplastin, are noted as a hemostatic effect in parenchymal bleeding.

Medical gelatin is used to enhance hemostasis. This is a product of partial hydrolysis of collagen in bones and cartilages of animals. 5–10 % solution enterally or 10 % solution i.v. is prescribed. Wilate is a drug that contains von Willebrand factor (factor VIII), which resumes the adhesion of platelets to the vascular subendothelium at the site of injury. This ensures primary hemostasis and decreases coagulation hours in patients with hemophilia.

Among local drugs, various types of hemostatic sponges, films, etc. are used to stop bleeding. Isogenic fibrin sponge is applied topically, in a dry form, to a surface that bleeds, plugging cavities (including bone tissue). Aseptic sponge with kanamycin has hemostatic and bactericidal effect. In case of large (purulent) wounds, a long-term treatment is carried out (2 weeks). A hemostatic collagen sponge is prepared from a collagen solution. This is a dry porous mass in the form of plates. It is used for bleeding caused by injuries and lesions of the face and mucous membrane of the oral cavity, MFA. A gelatin sponge made from specially treated gelatin (also contains furacilin) can be used to stop bleeding from a hole after the removing of a tooth. It is absorbed independently.

Gelfoam – a preparation of purified gelatin of pig skin. It is used to stop bleeding during any surgical interventions in the oral cavity and tooth area. It resolves itself. Caproferr is used to stop bleeding from the

root canal of the tooth or periodontal tissues during surgery. The drug is impregnated with a cotton swab and injected into a bleeding wound. In case of prolonged bleeding, it can be left in the wound for a day. it exfoliates itself. Hemophobin – 3 % solution of pectins in isotonic sodium chloride, which is used for bleeding from root canals, surgical interventions in the MFA. A swab soaked in the preparation is applied to the bleeding area. Feracryl in the form of 1 % solution is advisable to apply during curettage and gingivotomy on periodontal tissues. Wads impregnated with the drugare applied to the site of bleeding for 10–15 minutes. Adroxon (0,025 % solution) is used to stop capillary bleeding with injuries to the face, oral mucosa. Oxycelodex is a hemostatic filling material. It is used topically after tooth extraction.

3.9.6. Indirect procoagulants

This group includes preparations of vitamin K, which is found in plants (spinach, cauliflower, wild rose), animal tissues (pork liver), and can also be obtained by synthesis (vikasol). Deficiency of vitamin K in the body is accompanied by a decrease in the content of prothrombin in the blood, which can cause dangerous bleeding. Vitamin K and its water-soluble analog vikasol in the human body are involved in the biosynthesis of prothrombin (factor II), proconvertin (factor VII), Christmas factor (factor IX), Stuart – Prower factor (factor X). Also, the drug increases platelet adhesion, inhibits biosynthesis of PG and has an activating effect on the formation of thromboplastin (coagulation factor III). The action develops 12–18 hours after administration. Vitamin K is used to prevent bleeding during pregnancy, surgical interventions, including dental, with liver diseases and prolonged chemotherapy (accompanied by oppression of microflora, which synthesizes vitamin K). The dose of vikasol for adults is 0.015–0.03 g, for i.m. administration – 0.01–0.015 g. Vikasol is prescribed for 3–4 days, then, after a break, the drug is continued.

As agents that activate the blood coagulation system, calcium preparations are used (calcium chloride, calcium gluconate and calcium lactate). Ionized calcium has hysiological activity. Due to the increased amount of calcium ions, the course of all three phases of blood coagulation is accelerated, platelet adhesion is increased. Calcium preparations are used for gastric, intestinal, pulmonary and uterine bleeding, hemorrhagic diathesis.

Calcium chloride is administered 5–10 ml i.v. slowly 1–3 times a day. If the latter gets under the skin or muscle, necrosis may occur!

3.9.7. Fibrinolysis inhibitors

These drugs are used in conditions caused by a sharp increase in the activity of the fibrinolytic system (massive damage to internal organs, vein walls, septicemia, etc.). Synthetic preparations (aminocaproic, para-aminobenzoic, tranexamic acids) and animal-derived inhibitors (pantrypin, gordox, contrykal) are isolated. Aminocaproic acid is used for bleeding caused by liver diseases, acute pancreatitis, anemia – intravenously, orally and topically. Intravenous dropwise intruduction is administered in the form of 5 % or 10 % solution on isotonic sodium chloride solution – 100–500 ml. Locally (on turundas), it is used to stop bleeding from root canals or gingival pockets. Amben (para-aminobenzoic acid) is close to aminocaproic acid in pharmacological properties. It is administered enterally, intramuscularly and intravenously. Tranexamic acid is highly effective for bleeding (especially pulmonary, postoperative, meno- and metrorrhagia). It is administered enterally, intramuscularly and intravenously. In medical practice, fibrinolysis inhibitors of animal origin are known having a wide spectrum of action. They are used as emergency care in conditions caused by activation of autolysis processes (traumatic shock, acute pancreatitis). They inhibit the activity of trypsin, chymotrypsin, kallikrein, plasmin, and other enzymes. Aprotinin (contrykal) obtained from cattle lung tissue is indicated for hyperfibrinolytic bleeding, acute pancreatitis, postoperative bleeding. 10.000–40.000 IU is administered i.v. slowly in 300–500 ml of isotonic sodium chloride solution.

3.10
ANTI-ALLERGIC AGENTS

Allergy is the body's immune response to exogenous and endogenous antigens. The consequences of this reaction are diseases such as urticaria, seasonal and perennial allergic rhinitis, bronchial asthma, food allergies. Histamine, which is secreted in large quantities from its depots, leads to the development of such clinical symptoms as edema and hyperemia of the skin or mucous membranes, itching, runny nose, etc. In the body, histamine is synthesized from the amino acid histidine and is deposited in basophilic granulocytes, as well as in platelets, eosinophilic granulocytes, lymphocytes and various biological fluids. In these cells, histamine is in an inactive form in complex with proteins, sulfate polysaccharides, heparin sulfate, and chondroitin. Histamine is distributed unevenly. Higher concentrations are found in the skin, gastrointestinal mucosa, blood vessels, heart, lungs, in the zone IV of the ventricle of the brain, as well as in the tissues of the basophilic granulocytes of the pituitary gland, hypothalamus. Standing out from the depot, histamine interacts with special receptors (H_1, H_2 and H_3). To oppress allergic processes, antihistamines, detoxification, sorbing drugs, GCS, mast cell stabilizers, calcium preparations are widely used. A description of the anti-allergic effect of GCS is presented in the section "Non-steroidal and steroidal anti-inflammatory drugs". The role of GCS in the pharmacotherapy of allergic processes of the oral mucosa and periodontium is discussed in sections that reflect the pharmacotherapy of the corresponding diseases.

3.10.1. Antihistamines

These symptomatic agents find their application in the complex treatment of allergic processes, their action is aimed at reducing the unwanted effects of histamine (spasm of the smooth muscles of the bronchi, itching, swelling, etc.).

One of the most well-known classifications that have clinical significance is the generational classification of antihistamines. The drugs of the first and second generations and their metabolites are distinguished; in the literature they are often called third-generation drugs. It should be noted that the classification of antihistamines is based on their degree of selectivity for histamine H_1 receptors, as well as the presence or absence of side effects.

Generation I:

- diphenhydramine (dimedrol);
- clemastine (tavegyl);
- chloropyramine (suprastin);
- chlorofenamine (claritin);
- mebhydrolin (diazolin);
- quifenadine (phencarol);
- promethazine (pipolfen, diprazine);
- cyproheptadine (peritol).

Generation II:

- astemizole (gismanol);
- dimetindene (fenistil);
- loratadine (claritin);
- terfenadine (histadine);
- azelastine (allergodil);
- cetirizine (cetrine, zyrtec).

Generation III:

- desloratadine (febris, aeriusl);
- fexofenadine (telfast);
- norastemizole.

Antihistamines based on the principle of competitive antagonism prevent or reduce the following effects of histamine: spasm of the smooth muscles of the bronchi, intestines, myometrium, reduce hyperemia, itching, penetration of the capillary wall with the development of edema and sweating of the liquid. A decrease in blood pressure, allergic reactions, and local effects of histamine (skin hyperemia, local edema in the form of a bladder, soreness) are partially warned. Antihistamines also induce effects not caused by receptor blockade. First of all, it is a depressing (sedative) effect, as well as a deterioration in the psychomotor function of the

central nervous system. This is most typical for diphenhydramine, diprazine, suprastin and tavegyl, therefore, these drugs are not recommended for drivers, pilots and machine operators. Antihistamines have anti-nausea, anti-emetic, anti-Parkinson, atropine-like, anti-arrhythmic, α-adrenergic blocking and local anesthetic effects. Indications for the use of antihistamines are allergic conditions (urticaria, allergic rhinitis, hay fever, drug allergy), atopic and contact dermatitis, serum sickness, eczema, instings. Diphenhydramine and diprazine are used as sleeping pills or local anesthetics. The effect of antihistamines with a pronounced effect on the central nervous system function is used to treat patients with parkinsonism, in cases of vestibular disorders, vomiting, and for the prevention of marine and airborne diseases.

The first generation antihistamines – diphenhydramine, tavegyl, diprazine, suprastin, phencarol, have been widely used in medical practice since the early 40s of the XX century. These drugs are characterized by moderate antihistamine activity, non-selective blockade of receptors, and the presence of a pronounced inhibitory effect on the function of the central nervous system, etc. Side effects include pain in the epigastric region, dyspepsia, constipation, dry mucous membranes of the mouth and nose, exacerbation of glaucoma, tremor of the extremities. Second generation antihistamines – terfenadine and loratadine began to be used from the beginning of the 80s. When using terfenadine, a pronounced antihistamine effect is noted.

The drug is well tolerated, does not cause an inhibitory effect on the central nervous system function and cholinergic reactions. The antihistamine effect of loratadine (clarithin, loratadine-KMP) develops after 30–40 minutes, reaches its maximum effect after 8–12 hours and lasts about 24 hours. Desloratadine also refers to a long-acting antihistamine that does not have a sedative effect. Drugs should be used with caution in patients with renal and hepatic insufficiency. Fexofenadine (alfast, telfast), which is a metabolite of the second-generation drug terfenadine, is referred to the third generation antihistamines. This is an antihistamine that does not show sedation, so it was the first drug that was approved in many countries for use by aviation pilots and air traffic controllers. It prevents the occurrence of hyperemia and vesicles in patients with seasonal allergic rhinitis and chronic idiopathic urticaria.

3.10.2. Other drugs

For the treatment of allergic diseases, agents are used that inhibit the mast cells from releasing allergic reaction mediators. Drugs of this group block calcium canals in mast cell membranes, stabilize them and thereby prevent mast cell degranulation and endogenous release of histamine, serotonin, bradykinin and other anaphylaxis mediators. Cromolyn sodium (intal) inhibits cellular infiltration of the bronchial mucosa and the formation of delayed-type hypersensitivity. Nedocromil sodium has the ability to inhibit all stages of the inflammatory response in bronchial asthma and asthmatic bronchitis at the cellular level. Ketotifen (zaditen) refers to the membrane stabilizers of mast cells, has a prophylactic effect, it is used mainly to prevent allergic lesions (bronchial asthma, asthmatic bronchitis, etc.). It has anti-anaphylactic and moderate sedative effects. Histaglobulin is a complex compound of histamine with gamma globulin. The anti-allergic effect of the drug is based on the stimulation of antibody production and the ability to inactivate histamine. In the treatment of allergic processes, it is often used together with antihistamines. The drug is administered s.c. first 1 ml, then 2 ml with an interval of 2–4 days (4–10 injections). Sodium thiosulfate is used as a desensitizing agent in the complex treatment of diseases of the mucous membranes, lupus erythematosus, generalized periodontitis, etc. It also produces anti-toxic and anti-inflammatory effects. 5–10 ml of 30 % solution are administered intravenously, 2–3 ml of 10 % aqueous solution are administered orally. Euphyllin and adrenaline affect the peripheral reactions of organs with allergies; therefore, they are often used for symptomatic treatment of emergency conditions.

3.11
ANTISEPTIC DRUGS

Antiseptics are drugs that are prescribed to disinfect the skin, mucous membranes, burns and wound surfaces. These drugs are used in the practice of a dentist for prophylactic or therapeutic purposes, they are included in the treatment regimen of almost all dental diseases. The antimicrobial mechanisms of most antiseptics are caused by denaturation of the cytoplasmic protein of microorganisms, impaired permeability of plasma membranes or inhibition of enzyme activity, which ultimately leads to disruption of the basic metabolic processes of the microorganism. Antiseptics must meet the following requirements:

a) have a wide spectrum of antimicrobial activity and a sufficiently high activity, including in the presence of biological substrates;

b) do not have a local irritant, allergenic and toxic effect on the macroorganism;

c) must be chemically resistant, available for widespread use;

d) have the corresponding organoleptic properties.

According to the chemical structure, the following groups of antiseptics used in dental practice are distinguished:

- halogens and halogen-containing compounds;
- oxidizing agents;
- acids and alkalis;
- compounds of heavy metals;
- phenol group;
- formaldehyde group;
- dyes;
- alcohol group;
- nitrofuran derivatives;
- cationic detergents;
- natural antiseptics;
- preparations of different chemical groups.

In dental practice, this group of drugs is used for disinfecting the skin, antiseptic treatment and treatment of diseases of the mucous membranes, tooth tissues, wound surfaces, postoperative cavities, as well as for disinfecting instruments, rooms, etc. The daily use of antiseptics requires the treatment of many dental diseases, in the genesis of which an important role is played by the association of oral microorganisms. There are a large number of therapeutic forms of antiseptic agents (solutions, lozenges, ointments, pastes, films, aerosols, gels, soaps, etc.). Antiseptics are used in dentistry by irrigation, lubrication, rinsing, application, mouth wash, bathing, dressing, drainage, electrophoresis, etc. More modern methods of introducing antiseptics are vacuum antiseptic wounds, foam or film antiseptic coatings, hydrogels, pulsating jets, perforated drainage. The choice of antiseptic depends on the causative agent of the disease, the characteristics of the clinical course of the disease and the somatic condition of the patient.

3.11.1. Halogens

This group consists of chlorine and iodine preparations. Iodine preparations used as antiseptics can be divided into groups: preparations containing elemental iodine (alcohol iodine solution, Lugol's solution) and organic iodine preparations which slowly release iodine (ioddicerin, povidone-iodine, iodoform, iodinol, iodonate, iodopyrone). Iodine preparations have a destructive effect; they replace hydrogen atoms in the amino group of protein molecules, which leads to protein denaturation and the death of microorganisms. They exhibit antibacterial, antifungal, deodorizing, astringent, irritating and cauterizing effects. A solution of alcohol iodine is prescribed to treat the surgical field, wound surface for furunculosis, fungal skin diseases, as an irritating, distracting agent for myositis, neuralgia. Lugol's solution is a solution of iodine in an aqueous solution of potassium iodide. It is used to lubricate the mucous membranes of the throat and larynx in inflammatory and infectious diseases. Iodinol – a drug based on iodine, potassium iodide, polyvinyl alcohol. It is prescribed for periodontal diseases, for the treatment of stomatitis, chronic periodontitis, purulent wounds, odontogenic sinusitis, and burns. Ioddicerin (contains iodine, dimethyl sulfoxide, glycerin, potassium iodide), unlike other drugs, iodine does not accumulate, prevents painful, irritating, necrotic effect. It

has a significant antimicrobial effect. Povidone-iodine is not irritating and is prescribed by similar indicators. For external use, solution concentrations of 7.5 % and 10 % are used. Iodoform is prescribed in the form of ointments and pastes for the treatment of infected wounds and ulcers, for the treatment of root canals, and as a mummifying agent.

Iodine preparations are widely prescribed in dentistry for stomatitis, gingivitis, periodontitis, and pulpitis. They are used in inflammatory processes of the oral mucosa, for the treatment of root canals with periodontitis, for the treatment of infected wounds, with purulent osteomyelitis of the jaw bones, and candidiasis of the mucous membranes. Other indications for the use: a) in dermatology, venereology – with pyoderma, herpes skin, trichomoniasis, gonorrhea; b) in surgery – for the treatment of purulent wounds, burns, frostbite, purulent processes in t+he soft tissues, gangrene, pleurisy, peritonitis; c) in obstetrics and gynecology – for the prevention of complications after abortion, for the treatment of erosion, mastitis; d) in otolaryngology – for the treatment of otitis media, maxillary sinusitis, sinusitis, with bacteriocarrier in the URT. With prolonged use of iodine preparations and with increased sensitivity to them, iodism phenomena may occur (runny nose, urticaria, Quincke's edema, lacrimation, cough, fever, etc.).

Chlorine preparations are widely used. Their bactericidal effect is associated with the action of free chlorine and hypochlorous acid, which are released from its aqueous solutions. Atomic chlorine replaces hydrogen in the amino group of protein molecules, causes denaturation of proteins in the cytoplasm of microorganisms. Atomic oxygen, which is formed during the decomposition of hypochlorous acid, oxidizes the proteins of the microbial cell, enhances the bactericidal effect. Free chlorine actively interacts with microorganisms, organic and inorganic compounds. Organic chlorine compounds are chloramine and pantocid. In dentistry, 2–4 % solution of chloramine is used to treat a tooth cavity during caries and for antiseptic treatment of root canals. Chloramine B in the form of 0.25–0.5 % solution is used to treat infected wounds of the mucous membranes, washing periodontal pockets. Chloramine and pantocid are used to disinfect hands, patient care items and excrement, pantocid – for chlorination of drinking water. The activity of chloramine is higher in an acidic environment. With prolonged use, chloramine solutions can cause irritation.

3.11.2. Oxidizing agents

The composition of this group includes hydrogen peroxide and potassium permanganate. Oxidizing agents are capable of disrupting the course of redox processes in microorganisms, which ultimately leads to their death. In tissues, when the catalase enzyme interacts with hydrogen peroxide, molecular oxygen is formed, which is a weak antimicrobial agent. Molecular oxygen in the form of foam promotes leaching of pus, blood clots, and tissue detritus from wounds. In wounds not contaminated with protein residues, hydrogen peroxide forms atomic oxygen, which has an antimicrobial effect. The drug enhances blood coagulability, facilitating the transition of fibrinogen to fibrin, has a deodorizing and whitening effect. In dental practice, concentrated hydrogen peroxide is used to whiten a tooth crown. Root canals are washed with 3 % solution of hydrogen peroxide. To rinse and lubricate the mucous membrane of the oral cavity, solutions of hydrogen peroxide of low concentration (0.25 %) are used. For the treatment of hypertrophic gingivitis, 5 % solution of hydrogen peroxide (injection into the base of the papilla) is used. Concentrated hydrogen peroxide can cause mucosal burns. The drug is not used for deep wounds, nor is it injected into the cavity due to the risk of embolism. Potassium permanganate has a more pronounced antiseptic effect than hydrogen peroxide, but short-term. When interacting with tissues, it releases atomic oxygen and manganese dioxide, so gas formation is not observed. Atomic oxygen has an antiseptic effect, and manganese dioxide combines with tissue proteins, forming albuminates, and has an astringent and cauterizing effect. The effect of potassium permanganate is attenuated in the presence of protein. Potassium permanganate is widely used for rinsing the mouth (0.01–0.1 %), washing the wounds and mucous membranes with stomatitis, gingivitis (0.05–0.1 % solution). In the form of 2–5 % solutions, it is used to treat burns, which contributes to the rapid healing without suppuration, 0.02–0.1 % potassium permanganate solutions are used for the complex treatment of poisoning with alkaloids, phosphorus preparations.

3.11.3. Acids and alkalis

In dentistry, weak inorganic and organic acids are used. Their antimicrobial activity substantially depends on the degree of dissociation. Inor-

ganic acids exhibit a more pronounced effect compared to organic acids, since they easily dissociate. Antimicrobial activity also depends on the anion and the ability of acids to dissolve in lipids. Boric, lactic, and acetic acids, which have high lipidotropy, easily penetrate into the cell. A shift in pH to the acid side adversely affects the microorganism. Interacting with the proteins of the skin and mucous membranes, acids form dense, insoluble albuminates, exerting antimicrobial, anti-inflammatory, fungicidal effects. In high concentrations, tissue is cauterized (coagulation necrosis).

In dental practice, boric, carbonic and benzoic acids are widely used. 2–4 % solution of boric acid is used to rinse the mouth with bacterial and fungal stomatitis, to neutralize an unpleasant odor from the oral cavity. Boric acid is added to dental powders. Benzoic acid is used to rinse the mouth with gingivitis, and in the form of 5–10 % ointment – for mycotic cheilitis, seizures, etc. A weak solution of carbonic acid is used for cryodestruction in pulpitis. Strong inorganic acids are rarely used in dental practice, as they contribute to malignancy of the tissue. It must be remembered that the resorptive effect of acids can cause acidosis (decompensated), which is manifested by a violation of the vital functions of the body (decreased blood pressure, respiratory depression).

The bases (alkalis), interacting with the proteins of the mucous membrane, form albuminates, which penetrate deep into the tissues. Strong bases (sodium and potassium hydroxide) can cause tissue necrosis. Weak bases (sodium bicarbonate, sodium tetraborate) have a cleansing and softening effect. The shift of the reaction of inflammatory exudate to the alkaline side of the base contributes to its dissolution, reduction of edema and acceleration of the course of the inflammatory reaction. Solutions (0.5–2 %) of sodium bicarbonate, sodium tetraborate (borax) are used to rinse and lubricate the oral mucosa in case of inflammation, including fungal etiology. These solutions are used in the form of baths for periodontitis, periostitis, and abscesses to reduce swelling and improve trophic tissue. Sodium bicarbonate, calcium carbonate and magnesium carbonate reduce the sensitivity of tooth hard tissues during periodontal disease. Among the weak alkalis in medical practice, a solution of ammonia a (25 ml per 5 l of warm water) is widely used to treat the surgeon's hands. As an odontotropic agent, calcium hydroxide is used, which activates the processes of regeneration and mineralization in tooth tissues, inhibits the

development of inflammation, and has a desensitizing effect. Calcium hydroxide preparations (calcin and calmecin) are used to prepare linings on the bottom of the carious cavity with deep caries and pulpitis (while maintaining the viability of the pulp). Sodium hydroxide is used in dental practice as a catalyst for resorcinol-formalin liquid. In the treatment with the above drugs, complications may occur in the form of a burn of the mucous membrane and periodontal tissues.

3.11.4. Heavy metal compounds

The bactericidal action of heavy metal salts is associated with the formation of albuminates when interacting with proteins. The pharmacological effect of the action of salts of heavy metals on the tissue depends on how pronounced protein denaturation is. Salts of heavy metals can cause gelation (compaction) of proteins on the surface of the cell, that is, produce an astringent effect; deeply cauterize tissue (up to necrosis). The bactericidal effect of salts of heavy metals depends on the degree of their dissociation and the concentration of metal ions in the solution. The strength of the antimicrobial and traumatic effects of the drug depends on the density of the formed albuminates. During the formation of lush albuminates, the metal can freely penetrate into the depth of the tissue, damaging it. Dense albuminates limit the penetration of metals into the cell. By this property, the formed heavy metal albuminates are arranged in the following sequence: aluminum, lead, bismuth, iron, copper, zinc, silver, gold, and mercury. Salts of the first three metals (aluminum acetate, lead acetate, and bismuth nitrate basic, etc.) have a predominantly astringent and weak antimicrobial effect. The local effect is largely dependent on salt concentration. Yes, copper and zinc preparations (copper sulfate, zinc sulfate) in small concentrations (0.25–0.5 %) have an astringent effect and are used in ophthalmology, urology, and in high concentrations (10–20 %) they are cauterizing agents. Zinc oxide is used in the form of ointments, powders for the treatment and prevention of dermatitis and other skin lesions. Silver nitrate (lapis) has astringent (up to 2 %) and cauterizing (up to 5 %) actions.

Silver nitrate is used in dentistry for the treatment of hypersensitivity of tooth hard tissues, disinfection of foldable root canals, cauterization of aphthae, ulcerative lesions, etc. The clinic also uses colloidal and protein

silver preparations (respectively, colargol and protargol), which treat purulent wounds and inflammations of the mucous membrane. Silver nitrate is also prescribed for the treatment of erosion and skin ulcers, lesions of the mucous membranes of the eyes (trachoma, conjunctivitis). Its concentrated solutions are used for cauterization of granulation.

The strongest antiseptics of this group are mercury preparations (mercury dichloride, mercury amidochloride, mercury oxide yellow). Mercury dichloride (mercuric chloride) was previously used to disinfect clothes and other patient care items, except metal ones (mercuric chloride causes corrosion of metals). They cannot be used to disinfect vomit and excrement, since proteins bind mercury ions. In dentistry, 1–2 % mercury yellow ointment is used to treat chronic inflammatory processes (neuritis, abscess, arthritis of the TMJ). In ophthalmology, weakly dissociated mercury compounds are used – mercury amidochloride in solution and mercury oxide yellow in the form of an ointment. Heavy metal salts are also used for the preparation of filling materials. So, zinc oxide is a filler for filling materials. Copper, silver and mercury are part of the corresponding amalgam. With prolonged use of salts of heavy metals, a cytotoxic effect may occur due to the blockade of thiol enzymes in the tissues. With the resorption of heavy metals, especially mercury salts, which are easily absorbed, acute poisoning can develop, which is manifested by a chemical burn of the mucous membrane of the digestive tract, central nervous system depression, weakening of cardiac activity, collapse, and severe damage to the kidneys and liver. Bismuth and lead preparations also have a toxic effect on these organs. In case of poisoning, the stomach is carefully washed with water, tea infusion with activated charcoal. Milk, raw eggs are administered. At the same time, unithiol is administered intravenously. Symptomatic agents are also prescribed (sympathomimetics, plasma substitutes, vasoconstrictors, cardiac glycosides, NA). Heavy metal compounds are partially secreted by the oral mucosa, resulting in a dark border on the gingival margin, especially in the area of decayed teeth.

3.11.5. Phenol group

High concentrations of phenol (carbolic acid) have a bactericidal effect, causing the denaturation of microorganism proteins. In the presence of protein, its activity does not decrease. The mechanism of pronounced anti-

bacterial activity of phenol is also associated with an inhibitory effect on enzymes, especially dehydrogenases. Phenol is able to exert a local anesthetic effect after the phase of irritation, in high doses it is a cauterizing agent. The use of phenol as an antiseptic is limited, due to its ability to easily penetrate into tissues and cause a toxic effect. In case of severe poisoning, paralysis of the respiratory center may occur. Phenol in the form of mixtures (camphor-phenol, phenol-formaldehyde) is rarely used to treat hard tooth tissues and the root canal of the tooth, and anesthesia after pulp amputation. Phenol is also a part of devitalizing pastes for the treatment of pulp stump and coagulation of granulation tissue ingrown into the root canal. Phenol solution (3 %) is used to disinfect rooms, linen, and tools.

Tricresol is used for antiseptic treatment of the pulp stump after amputation and disinfection of the root canal. Resorcinol is noted for its high antimicrobial activity and low toxicity. A saturated solution of resorcinol is used in the form of resorcinol-formaldehyde liquid and paste, respectively, for root canal impregnation and filling. In a small concentration (2 %), resorcinol exerts a keratoplastic effect, and in a high concentration (20 % or more) – keratolytic. Resorcinol with phenol, basic fuchsin, boric acid, acetone, ethyl alcohol is a part of fucorcin. Thymol differs from phenol in less toxicity. The drug has antibacterial, deodorizing and fungicidal effects. Its 5 % solution is used for tooth decay for washing carious cavities, anesthesia, is added to therapeutic pastes, and is recommended for rinsing. Thymol is a part of Septolete. The composition of tar includes phenol, cresol, resins, etc. It is used in the form of 20–30 % ointment externally for skin diseases and trophic ulcers. Tar is a component of the Vishnevsky's balsamic liniment. In dental practice, vagothyl is also used. It has a bactericidal, trichomonacid, regenerating (epithelizing) effect. It is used for instillation in periodontal pockets and for cauterizing granulation tissue.

3.11.6. Formaldehyde group

Formaldehyde in medical practice is used in the form of a 40 % solution called formalin. Formaldehyde and formalin have a pronounced antimicrobial activity, due to the easy penetration of drugs into cells, the ability to cause dehydration and coagulation of proteins and the death of microorganisms. Formaldehyde has astringent, tanning, disinfecting effect. The ability of the drug to take water from the surface layers of cells

leads to the densification and drying of the skin. 3–5 % formalin solution (formidron) is used to treat excessive sweating. Previously, formaldehyde was used to disinfect rooms, hands, tools (0.5–1 % solution). A soap solution of formaldehyde, lysoform, is also used to disinfect hands and rooms. In dental practice, 10 % formalin solution is applied for disinfection of the root canals, necrotization and mummification of the pulp after its devitalization. Formaldehyde is a part of mummifying pastes (resorcinol-formalin, paracin, Ribler's paste, resoform, foredent). Pastes usually consist of a powder (zinc oxide, barium sulfate) and a liquid (a mixture of resorcinol and formaldehyde solution). The paste is polymerized in the presence of a catalyst – 10 % sodium hydroxide solution. Resorcinol-formalin paste is used for root canal filling.

3.11.7. Dyes

This group includes drugs with different chemical structures, including brilliant green and methylene blue; they are active mainly against gram-positive microflora. Ethacridine lactate has a sufficient antimicrobial effect on both gram-positive and gram-negative microbial flora. Mechanism of action: the dye cation displaces hydrogen from the compounds necessary for the life of microorganisms. Moreover, they also form sparingly soluble complexes with acidic groups of mediators and amino acids, disrupt the metabolism of microorganisms. The drugs exhibit mainly bacteriostatic action. Brilliant green has a detrimental effect on the culture of Staphylococcus aureus in water in a concentration of 1:10 000 000. In the form of 1–2 % aqueous or alcoholic solution, it is used to treat pyoderma, blepharitis, purulent ulcer, and cheilitis in dentistry. The antibacterial activity of the drug increases in an alkaline environment, but significantly decreases in the presence of organic substances. Ethacridine lactate (0.1–0.2 % solution) is used to treat inflammatory processes of the mucous membrane (rinsing, lubrication), used in surgical, gynecological, urological, ophthalmic, dermatological practice. The drug has low toxicity; its activity also increases in an alkaline environment. Protein and other organic substances do not affect the antimicrobial activity of ethacridine lactate. Methylene blue is somewhat inferior in antimicrobial activity. Its 0.5–2 % solution is used in the treatment of candidal, aphthous stomatitis (to lubricate aphthae), burns, and other inflammatory processes of the

skin and mucous membranes. It is used to treat certain poisonings as an antidote. So, in case of cyanide poisoning, 1 % aqueous solution of methylene blue or 1 % of its solution in 25 % glucose solution is administered intravenously. Methylene blue is also prescribed for nitrate poisoning.

3.11.8. Alcohol group

In medical practice, ethyl alcohol is mainly used as an antiseptic, irritating and cauterizing agent. The antimicrobial mechanism is associated with both the dehydrating property of alcohol and the ability to denature the protein. The antimicrobial effect is most pronounced in 70 % alcohol. In high concentration due to the formation of dense gelified films, its activity may be lower. In the absence of 80–90 % proteins in the medium, alcohol acquires powerful antibacterial activity. 70 % solution of ethyl alcohol is used for the preparation of antiseptic and anesthetics, tinctures, extracts, and 96 % solution is used for antiseptic treatment of hard tooth tissues. Ethyl alcohol is widely used for disinfection of hands (70 %), surgical field (40–70 %), instruments (96 %).

3.11.9. Nitrofuran derivatives

Antiseptics from the group of nitrofuran derivatives are characterized by high antimicrobial activity and relatively low toxicity; they are used as antiseptics and chemotherapeutic agents. The most used as an antiseptic furacilin (nitrofural), has antimicrobial, antifungal, antiprotozoal properties. The mechanism of action is associated with the restoration of the nitro group into an amino group, impaired protein synthesis, enzyme systems, redox processes, cellular respiration of pathogens. The drug has a bacteriostatic or bactericidal effect depending on the concentration; it is prescribed for rinsing, irrigation in the form of 0.01 % solutions for gingivitis, stomatitis, and other diseases of the oral mucosa. It is recommended drug for washing wounds, mucous membranes, cavities. Furazolidone can be prescribed topically in solutions (1:25000) for the treatment of burns, wound infections.

3.11.10. Cationic detergents

The composition of this group includes synthetic substances that have high surface activity, antibacterial, detergent and emulsifying prop-

erties. By chemical properties, most of them are quaternary ammonium bases. The mechanism of action of surface detergents is associated with their ability to accumulate on the interface, as a result of which the surface tension of the cell membrane changes, its permeability and osmotic equilibrium, biologically active substances of the cell enter the environment – osmotic shock. This causes the death of the microbial cell. Surface detergents are widely used to treat the hands of medical personnel before surgery and to prepare the surgical field (zerigel, rocal). In dental practice, surface detergents are used for antiseptic treatment of the oral mucosa in inflammatory processes, as well as for washing carious cavities and root canals, disinfection of materials and tools.

One of the most widely used drugs is chlorhexidine bigluconate. It has the properties of chlorine preparations and detergents, exhibits rapid pronounced antibacterial and fungicidal effects. It is used to treat the surgical field, instrumentation, with purulent-septic processes (washing surgical wounds, bladder). When processing the surgeon's hands, dryness, itching of the skin, dermatitis may appear. In dentistry, it is prescribed in the form of solutions for irrigation, rinsing. The drug is a part of the Corsodyl and Metrogyl Denta. An effective modern chlorhexidine-based agent for local antibacterial and anti-inflammatory therapy in the oral cavity is the self-adhesive dental film Diplen-Denta X and Diplen-Denta HD (together with dexamethasone). The film – soft, thin, transparent – adheres without softeners to soft, hard, wound, burned surfaces of the oral cavity (with stomatitis, gingivitis, periodontitis, red flattened lichen, postoperative wounds, injuries, burns, etc.). The therapeutic effect is achieved quickly, the release of the therapeutic component occurs within 6–8 hours. The undesirable effect of chlorhexidine is manifested in a change in the color of the teeth (tan), and in case of violations of the modes of use, its systemic effect (vestibulotoxicity) may occur.

Etonium, which is a bis-quaternary ammonium compound, is widely used. The drug has a bacteriostatic and bactericidal effect, has a local anesthetic activity, and stimulates wound healing. In dental practice, it is used for trophic ulcers, dermatosis, stomatitis (0.5 % solution) and gingivitis; 7 % paste is used to fill the teeth canals. Dimethyl sulfoxide has anti-inflammatory, antioxidant, surface-active properties. In case of skin lesions, 10–30 % solution is applied in the form of applications and irriga-

tion. It is a part of ioddicerin and other drugs. Decamethoxin (decasan) is used in purulent and fungal processes (gingivitis, periodontitis, etc.), and also as an antiseptic for the treatment of hands, the surgical field and the disinfection of suture and surgical material. 0.025–0.01 % solution of the drug is used for application and irrigation.

Miramistin has a high antibacterial activity against bacteria, fungi and viruses, and stimulates local immunity. A wide range of antimicrobial activity (gram-positive and gram-negative, aerobic and anaerobic, spore-forming and asporogenic bacteria, among which are hospital-resistant antibiotic-resistant strains). Its versatility, safety of use allow for effective prevention and empirical therapy of infectious and inflammatory processes. It is prescribed for the treatment of periodontitis and periodontal disease, for the medical treatment of carious cavities, tooth canals after extirpation of the pulp, and the hygienic treatment of removable prostheses. In surgical practice, they are used to treat purulent wounds, with superficial and deep burns. In dermatology – with strepto- and staphyloderma, candidiasis of the skin and mucous membranes. Depending on the indications, 0.01–1 % solution of the drug or ointment are used.

In dental practice, for rinsing and irrigation with gingivitis, periodontitis, stomatitis, stomatidine is administerd, which contains hexetidine, which has a wide range of effects on bacteria and fungi. Hexetidine – is adsorbed on the oral mucosa, where its concentration persists for 65–72 hours. The effect of the drug is associated with inhibition of the formation of thiamine, which negatively affects the growth of microorganisms and fungi. It is produced in the form of 0.1 % aqueous solution and has broad indicators in the treatment of purulent wounds, burns, toxic and infectious lesions of the oral cavity. Hexetidine is a part of hexoral, which has antibacterial, antifungal, hemostatic, analgesic effects. Givalex incorporates hexetidine, choline salicylate and chlorobutanol. Choline chloride and chlorobutanol have analgesic and anti-inflammatory activity. The drug is prescribed for stomatitis, gingivitis, periodontitis, aphthae and teething pain, to ensure hygiene and postoperative monitoring of the oral cavity. It has antibacterial, anti-inflammatory, analgesic effects. Cationic detergents (dequalinium chloride, benzalkonium chloride, chlorhexidine bigluconate) are part of the combined preparations – hexalysis, sibedin, septolete, sibicort, etc. These drugs have antimicrobial, anti-inflammatory, analgesic ef-

fects. They are used for infectious and inflammatory processes of the oral cavity. Anionic detergents (green soap, etc.) are inferior to cationic ones in surface-active and detergent properties.

3.11.11. Natural antiseptics

Chlorophyllipt is a drug from eucalyptus that acts on staphylococcus, streptococcus, pneumococcus, pathogenic Escherichia coli, Klebsiella, Proteus, etc. The drug has the highest bacteriostatic and bactericidal activity against antibiotic-resistant staphylococci, while stimulating humoral and phagocytic defense. It is used for applications and instillations (in a ratio of 1:50 0.25 % solution of novocaine), for rinsing the oral cavity with stomatitis, periodontitis, for the treatment of purulent-inflammatory processes. Maraslavin is a herbal preparation of wormwood, thyme, which has anti-inflammatory, deodorizing, astringent, sclerotic, regenerative effects. It is used for instillations in the periodontal pockets for periodontitis. Maraslavin can cause a burning in the tongue. Novoimanin – a drug made of St. John's wort. It acts mainly on gram-positive flora. It has anti-inflammatory effect, stimulates regeneration. 0.01 % solution of the drug is used for periodontal tissue diseases, gingivitis, stomatitis, necrotizing ulcerative lesions in the oral cavity.

Salvia is a drug from sage, effective against gram-positive microflora. Its 1 % water-alcohol solution, diluted 4–10 times, is used to treat chronic inflammatory processes of the mucous membrane, necrotizing ulcerative, aphthous and herpetic stomatitis. Sanguiritrinum is a macklea drug that acts on gram-positive and gram-negative flora, yeast-like fungi, Trichomonas. It is used in the form of 0.2 % alcohol and 1 % aqueous solution to treat periodontitis, burns, etc. Sodium usninat has an antimicrobial effect against gram-positive flora. It is used in the form of oil (0.5 %) and water-alcohol (1 %) solutions for diseases of the mucous membrane.

Polyminerol is a colloidal, saline solution containing Mg, Ca, Cl, F, Br, Fe. The drug has anti-inflammatory, regenerative, slightly analgesic, sclerosing effects. It is used in periodontics for rinsing, instillation, dressings. Etericide – a drug that is made from fish oil. It has an antibacterial effect on staphylococcus, proteus, Pseudomonas aeruginosa and Escherichia coli. it stimulates the processes of epithelization, is used for applications, instillations, and in case of inflammatory processes in the oral cavity.

Balis-2 is a product of the fermentation of microorganisms. It has an antibacterial effect against staphylococcus, protea, Pseudomonas aeruginosa. Microcide is an antibiotic of the penicillin group, which disrupts the synthesis of the membrane of microorganisms, is active against a number of gram-positive, gram-negative microorganisms. In dentistry, it is used for rinsing the mouth, in case of stomatitis, the treatment of infected wounds, phlegmon, erosion. Lysozyme inhibits the growth of gram-positive bacteria (less – gram-negative). It has anti-inflammatory, mucolytic effect, stimulates non-specific immunity. 0.05 % solution is applied. Gramicidin is an antimicrobial drug that increases the permeability of the microbial membrane for inorganic cations and causes its osmotic instability. It is prescribed for the treatment of periodontitis, gingivitis, stomatitis.

3.11.12. Antiseptics of other groups

Stomatophyt containing extracts from oak bark, chamomile flowers, sage leaves, arnica grass, thyme, peppermint grass, calamus rhizomes has various pharmacological properties (antibacterial, anti-inflammatory, analgesic). Stomatophyt, in addition to the above ingredients, also contains benzocaine. Tralbex contains dry purified rhubarb extract, salicylic acid and ethyl alcohol (61 %). it is recommended for lubrication of aphthae and other injuries of the oral mucosa. Vinylin (Shostakovsky's balm) has anti-inflammatory, bactericidal, enveloping effect, improves tissue regeneration. 20 % solution and ointmen are used. It is a part of the preparations vinisol and levovinisol. Cygerol has a necrolytic, antibacterial effect and stimulates reparative processes. Oil (10–20 %) solutions and ointments are used. Citral has analgesic, anti-inflammatory effect, a pleasant smell, low toxicity. It is used for irrigation of the oral mucosa.

For topical use, depending on what is shown here, there are a large number of combined antiseptic agents: algipor, fitosept, dioxol, lifusol, Fastin-1, stopangin, septogal, parodium, pansoral, givalex, septolete, jox, ioddicerin, etc. Many of them are for due to additional components, they possess a wider spectrum of action relative to microorganisms. They are also characterized by analgesic, anti-inflammatory, regenerating, deodorizing properties, which determine their advantages when choosing pharmacotherapy in dental practice.

3.12

ASTRINGENT, ENVELOPING, ABSORBENT AND DETOXIFICATION DRUGS

These agents have a wide range of pharmacological effects (local anesthetizing, antiseptic, analgesic, anti-inflammatory, astringent, enveloping, adsorbing, detoxifying, hemostatic, keratoplastic, deodorizing, reparative, etc.), therefore they are widely used in the treatment of mucosal diseases, surgical treatment of wounds, etc. Detoxifying agents are widely used in emergency conditions or severe surgical pathology.

3.12.1. Astringent agents

Astringent drugs react with tissue proteins and determine the compaction of the surface layer of tissues, reduce its permeability, film the surface of the skin, mucous membrane, protect nerve endings and relieve pain. Astringent drugs by their nature are divided into two groups: inorganic (salts of heavy metals) and organic (plant origin). Salts of heavy metals (bismuth basic nitrate, lead acetate, copper sulfate, zinc sulfate, silver nitrate) in small concentrations have a tanning property. Their solutions are prescribed for rinsing in case of gingivitis and stomatitis.

Astringent organic products do not show a pronounced tanning effect and to a lesser extent they dry the tissues. They are used in chronic inflammatory processes, and in the period of dehydration, with necrotizing ulcerative lesions of the mucous membrane, burns, radiation stomatitis, cracks, for treating facial skin before surgery, for poisoning with heavy metal salts, and bad breath. Oak bark in the form of a decoction is prescribed for rinsing and mouth baths 3–4 times a day. St. John's wort is used in the form of infusion, decoction and tincture. The latter is used for 30–40 drops to 0.5 cups of water for rinsing, irrigation and mouth baths.

Salvia – a complex drug from sage leaves, affecting gram-positive microflora, stimulates the regeneration of the mucous membrane. 0.1–0.25 % water-alcohol solution is administerd for rinsing. Rhizomes of the bistort, cinquefoil, rhizome and root of great burnet, blueberries, bird cherry, calamus root are used in the form of sap, a decoction for rinsing, mouth baths, applications.

Romazulan (chamomile extract) has an antiseptic, anti-inflammatory and deodorizing effect, improves the reparative properties of the epithelium. 1 teaspoon to 1 glass of water is applied for irrigation, rinsing, and mouth baths. Rotocan is a complex preparation that contains chamomile, yarrow, and calendula. It has anti-inflammatory, analgesic, bactericidal, hemostatic, antioxidant effects, improves metabolic processes in tissues. It is applied for rinsing (1 teaspoon in 1 glass of water). Arnica tincture has a hemostatic, anti-inflammatory, analgesic and regenerative property. it is used for rinsing (1 teaspoon in 1 cup of warm water).

Tannin powder is used in the form of 1–2 % aqueous solution for rinsing and irrigation, 5–10 % glycerin solution for lubricating the mucous membrane. With a solution of tannin, the stomach is washed in cases of poisoning with salts of alkaloids and heavy metals with which it forms insoluble compounds. Halascorbin is a complex compound of the sodium salts of ascorbic and gallic acids. it is applied in the form of 1 % aqueous solution for irrigation, applications, mouth baths.

3.12.2. Enveloping drugs

These are high molecular weight compounds that form colloidal solutions in water. Covering the surface of the skin of the mucous membrane with a thin layer, these drugs protect the nerve endings from irritating substances. Most enveloping drugs have adsorbing properties, as a result of which they prevent contact of the harmful agent with nerve endings. Most often, polysaccharides of plant origin are used (mucus from rice, corn and potato starch, mallow leaves and flowers, decoctions from the roots and leaves of marshmallow, comfrey, flax seeds, oats). White clay is used as an enveloping drug for cheilitis, ulcerative gingivitis, arthritic and ulcerative stomatitis. Colloidal solutions that have enveloping properties can also form some inorganic substances (magnesium trisilicate, aluminum oxide hydrate, etc.). They are often prescribed orally for catarrhal and

ulcerative lesions of the mucous membrane of the digestive canal. In case of acute poisoning by substances that determine local irritation, enveloping agents are prescribed enterally and in enemas to reduce absorption and protect the mucous membrane.

In dental practice, enveloping agents are used in the treatment of lesions of the oral mucosa, the course of which is characterized by the formation of erosion or ulcers, a sensation of pain. A decoction of the marshmallow root, infusion of common mallow is used in acute inflammatory processes of the oral mucosa. Decoction of the root of the comfrey is used in acute inflammatory processes as a means of enveloping and stimulating regeneration. A decoction or mucus of flax seeds is prepared ex tempore, recommended for rinsing, mouth baths in acute inflammatory processes of the mucous membrane. Starch in solutions is used to protect the mucous membrane from the influence of irritants and to slow the absorption of drugs.

3.12.3. Adsorbent and detoxification drugs

Adsorbents, sorbents are small insoluble indifferent substances with high adsorption ability, which bind different substances on their surface, thereby reducing the absorption of the latter, mechanically protecting the mucous membrane and the sensitive nerve endings located in it. The essence of sorption-application therapy is sorption of pathogenic microorganisms, toxins and wound fluid from pathological foci. In this case, continuous and prolonged administration of drugs to a specific place occurs. Sorption promotes effective detoxification and nonspecific hypersensitivity of the lesion, normalization of local immunity.

Sorbent preparations differ in some properties, indications and method of application. White clay (kaolin) is used for lesions of the oral mucosa and periodontal diseases in the form of dusting powder, as well as medical pastes and toothpastes. The application dressing Wave is created on the basis of carbon non-woven material, which contributes to the intensive cleaning of wounds from purulent-necrotic tissues and exudate. This is an effective treatment for purulent wounds that are poorly healed, trophic ulcers, burns of chemical and thermal origin. The dressing is used alone or in combination with antiseptic drugs or proteolytic enzymes. Fibrous carbon sorbent is used for sorption dressings during the entire period of

wound cleaning to the appearance of granulations. Activated carbon fiber material (AVVM "Dnepr" MN) is a carbon adsorbent for local application and sorption therapy. It is applied in the form of tissues and bandages. Polymethylsiloxane (PMS, silard) has pronounced sorption properties, provides detoxification and reduced microbial contamination in the lesion of the oral mucosa, accelerates the cleaning of the wound surface from necrotic plaque. Sorbents SKN, SKN-2M are used for application sorption in case of purulent infected wounds, ulcers of the oral mucosa in a pure form or in combination with antibiotics, antiseptic agents, enzyme preparations as a dusting powder on wounds. Spherical and fibrous carbon sorbents, organosilicon sorbents, magnetosorbents and preparations based on low molecular weight polyvinylpyrrolidone have sorption and detoxification properties. Spherical carbon sorbents: carbovit, enterosgel, enteroxicam, ultraoxicam belong to hemo- and enterosorbents. There are selective sorbents (SKM-22, enterorad, carborad, ultrasorb) that are used for demetallization and excretion of radionuclides. For sorption detoxification and correction of the immune status, biospecific sorbents of the type SKN-ADP, SKNoloz, etc. are used. Fibrous carbon sorbents contain hydrophobic fibers, which, unlike granular carbon, have a much larger contact surface, high adsorption rate and adhesiveness to the wound surface.

Organosilicon sorbents (polyorganosiloxanes) have a high adsorption capacity relative to organic substances (amines, alcohols, carbohydrates, etc.) and pronounced hydrophobic properties. These are high molecular weight polymers in the form of white porous solids that do not dissolve and do not swell in organic solvents and water. The representative of magnetic sorbent UMS is a composition based on carbon hemosorbent SKN and magnetite. The drug can be kept in a constant magnetic field in a certain place, and therefore it can be used to occlude bleeding vessels, "seal" the fistula, cleanse infected wounds and supply drugs to the pathological focus.

As a method of detoxification, enterosorption has recently spread, which helps to eliminate toxic substrates of histogenic and bacterial origin from the body by diffusing them into the intestinal lumen from the blood. Enterosorbents based on synthetic active carbonates of spherical granulation (SKN, SCS), fibrous carbon sorbents, organosilicon sorbents (polymethylsiloxane) and some preparations based on low molecular weight

polyvinylpyrrolidone (enterodes) are used. In dentistry, these drugs are used for Vincent's stomatitis, gangrenous and herpetic stomatitis, exudative erythema multiforme, pemphigus, poisoning, intoxication, autoimmune diseases and allergic lesions of various origins. Polymethylsiloxane (PMS) is an organosilicon hemosorbent with high hydrophobicity, which has properties for immobilization of large molecules and possibility for the formation of various bonds in combination with microporosity. When creating drugs of prolonged action, it is used as a carrier.

Enterodes (low molecular weight polyvinylpyrrolidone) is an oral detoxification drug. It sorbs toxins and removes them through the intestines. Inorganic polymer silicon dioxide (silex) has a unique complex of sorption activity. It is used for detoxification in botulism, foodborne diseases, toxic hepatitis, allergies, purulent-septic processes, alcohol and drug intoxication, mushroom poisoning. In dentistry, it can be used for stomatitis, periodontitis, complications after tooth extraction, etc. It is prescribed enterally and applied topically by enemas and applications. Multisorb, a universal energy sorbent of the 4th generation, is a natural detoxifier based on activated biopolymers (cellulose, pectin, legnine, etc.). It is introduced into the diet for various intoxications, purulent-inflammatory processes, used in the complex treatment of viral hepatitis A and B and external – in the treatment of purulent wounds, atrophic ulcers and burns. It is prescribed orally in dosed packets.

The use of drugs with detoxification properties in dentistry is indicated for exudative erythema multiforme, necrotizing ulcerative, herpetic and gangrenous stomatitis, Stevens – Johnson syndrome, pemphigus, phlegmon, osteomyelitis, etc.), because the course of these diseases is accompanied by significant intoxication of the body. Such drugs are gluconeodez, haemodez, neohaemodez, neocompensan, which are based on low molecular weight polyvinylpyrrolidone and have the ability to form complexes with substances toxic to the body. Neohaemodez is a parenteral drug that binds toxins circulating in the blood and quickly eliminates them mainly with urine. It enhances glomerular filtration and diuresis, differs from the molecular weight of haemodez (12600 ± 2700) in a lower mass (8000 ± 2000), which accelerates its excretion by the kidneys. Non toxic.

Drugs that are based on sorbitol – sorbilact, reosorbilact are prescribed for shock conditions, acute liver and kidney failure, blood loss,

prolonged purulent processes, etc. Polyglukin is a sterile 6 % solution of partially hydrolyzed dextran. It is used for prophylactic and therapeutic purposes in case of traumatic, surgical, burn shock and acute blood loss. Rheopolyglukin is a 10 % solution of dextran in isotonic sodium chloride solution. Its ability to bind and neutralize toxins is somewhat less than that of neohaemodez. Polyamine is an aqueous solution of amino acids and D-sorbitol. It is used for intoxications and diseases associated with protein-amino acid disorders. Hydrolysin is a product of hydrochloric acid hydrolysis of cattle blood proteins. It improves the metabolism of proteins and amino acids, contributing to the normalization of proteinemia and aminoacidemia.

3.13
ANTIBIOTICS

Antibacterial agents are the most common group in medical practice. More than 7000 antibacterial drugs are known, but about 200 have been used in world medical practice. Antibiotics (lat. anti – against and bios – life) are substances of microbial, plant and animal origin that have high antimicrobial activity, which is based on the principle of antagonism. The terms "antibacterial agents", "antibiotics", "chemotherapeutic agents" combine all drugs that suppress the vital activity of infectious disease pathogens (bacteria, fungi, viruses, protozoa). These drugs include substances: a) natural – produced by microorganisms; b) semi-synthetic – obtained as a result of modification of the structure of natural preparations; c) synthetic. The nature of the action of the drugs can be bactericidal, which means the complete destruction of the cells of the infectious agent and bacteriostatic, i.e. based on the cessation of division of its cells. The ABD activity spectra are characterized as "wide" ("ultra-wide") and "narrow" ("anti-staphylococcal", "anti-anaerobic", etc.).

With odontogenic infection, systemic antibiotics amoxiclav, amoxicillin, their compounds with β-lactamase inhibitors, CS, lincomycin hydrochloride and clindamycin are more often used. For periodontal diseases, macrolides, local and systemic tetracyclines, and FQ are used. With an infectious process of moderate severity, macrolides, penicillins, linkozamids, CS should be prescribed, using the appointment enterally or locally. In severe cases of the disease in a hospital, parenterally, it is necessary to use CS, carbapenems, FQ, AG, clindamycin, and combinations thereof. Antibiotics are widely used in the treatment of diseases that are caused by infectious agents. In dentistry, they are often used to treat acute infectious and inflammatory diseases, as an application to surgical methods.

The classification of antibacterial drugs is as follows.

1. Penicillins:

1) natural – benzylpenicillin (potassium and sodium salt, esters, novocaine salt), phenoxymethylpenicillin, bicillin-3, bicillin-5;

2) semi-synthetic:

a) resistant to penicillinase (methicillin, oxacillin, cloxacillin, dicloxacillin, nafcillin, fluloxacillin);

b) wide spectrum of action (ampicillin, amoxicillin, carbenicillin, ticarcillin, azlocillin, piperacillin);

c) combined:

- contain β-lactamase inhibitors (clavulanic acid, sulbactam, tazobactam) – amoxiclav, augmentin (amoxicillin + clavulanic acid), unasyn (ampicillin + sulbactam);
- other combinations – ampiox (ampicillin + oxacillin), ampiclox (ampicillin + cloxacillin), vampilox (amoxicillin + cloxacillin + lactobacterin).

2. Cephalosporins:

- 1st generation: cefadroxil, cefazolin, cephalexin, cephaloridine;
- 2nd generation: cefaclor, cefamandole, cefoxitin, cefotetan, cefuroxime;
- 3rd generation: cefoperazone, cefotaxime, ceftazidime, ceftriaxone, cefodizime, moxalactam, cefixime;
- 4th generation: cefepime, cefpirome;
- combined (inhibitor-protected) CS: sulperazone (cefoperazone + sulbactam), sulbactomax (ceftriaxone + sulbactam).

3. Monobactams: aztreonam, karumonam.

4. Carbapenems: imipenem/cilastatin, meropenem, biapenem.

5. Macrolides: erythromycin, oleandomycin, spiramycin, midecamycin, roxithromycin, clarithromycin.

6. Azalides: azithromycin.

7. Lincosamides: lincomycin, clindamycin.

8. Tetracyclines: tetracycline, metacycline, doxycycline.

9. Aminoglycosides: streptomycin, neomycin, kanamycin, gentamicin, tobramycin, sisomicin, amikacin, netilmicin.

10. Glycopeptides: vancomycin, teicoplanin, ristomycin.

11. Ansamycins: rifampicin.

12. The group of chloramphenicol: chloramphenicol, synthomycin.

13. Preparations of the steroid structure: fusidic acid, fusidin-sodium.

14. Polypeptides: polymyxin, gramicidin S, bacitracin.

15. Various drugs: phosphomycin, spectinomycin, mupirocin.

Classification by antimicrobial spectrum:

1) drugs that act mainly on gram-positive bacteria (penicillins, macrolides, lincosamides, glycopeptides, I–II generation CS);

2) drugs that act mainly on gram-negative bacteria (monobactams, aminoglycosides, I–II generation FQ, generation III CS, polymyxin);

3) drugs with a wide spectrum of activity (inhibitor-protected, penicillins, IV generation CS, carbapenems, III generation AG, III–IV generation FQ, tetracyclines, chloramphenicol).

General principles of rational antibacterial therapy:

- the use of ABD should be carried out at the earliest period of the disease after diagnosis;
- before starting treatment, an allergological history should be collected and diagnostic allergological tests performed;
- it is important to prescribe ABD, to which the pathogenic cell is highly sensitive, that is, its growth and reproduction ceases when medium therapeutic doses are prescribed;
- in the absence of the ability to conduct quickly bacteriological studies, empirical treatment should be started with broad-spectrum drugs, focusing on predictable pathogens;
- it is necessary to create quickly a therapeutic concentration of ABD in the tissues, which would prevent the separation and growth of microorganisms;
- it is necessary to use correctly the methods of ABD applying (parenteral, enteral, topical), its single, daily and course dose;
- it is worth using such ABD that exclude or limit their harmful effect as much as possible;
- to increase the effectiveness of treatment using synergistic combinations of ABD, but do not prescribe drugs with unidirectional undesirable effects;
- to improve the effect of antibiotic therapy, it is rational to use simultaneously drugs of other groups (antiseptic, enzymatic, anti-inflammatory, antihistamines, immunostimulating agents, etc.);
- prophylactic use of ABD is permissible only for certain indications (planned and emergency interventions in surgical practice, perfor-

ming surgical procedures in a group of immunocompromised patients, penetrating wounds of the skull, prevention of sepsis in debilitated patients, contact with patients with especially dangerous infections, etc.).

3.13.1. Penicillins

This group of ABD is one of the most used in clinical practice. Penicillins disrupt the formation of the bacterial wall during mitosis, are competitive inhibitors of transpeptidases that catalyze the formation of interpeptide compounds in the structure of peptidoglycan at the final stage of cell synthesis. This leads to cell death. Among the natural penicillins, benzylpenicillin is the most widespread in infections caused by gram-positive microflora (streptococcus, pneumococcus, staphylococcus non-β-lactamase producing, pathogens of gas gangrene, botulism, tetanus, diphtheria, anthrax, some strains). Among gram-negative bacteria, meningococcus, gonococcus, actinomycetes and spirochetes are sensitive to it. Staphylococcus resistance to natural penicillins is associated with beta-actamase production. It is important to consider the comparative activity of drugs relative to staphylococci, which do not form penicillinase: benzylpenicillin – 1 (active); methicillin – 0.01–0.025; oxacillin – 0.1–0.2; dicloxacillin – 1.0–0.5 and in relation to penicillinase-forming staphylococci: benzylpenicillin – 1 (not active); methicillin – more than 50; oxacillin – more than 250; dicloxacillin – more than 250. Now methicillin and oxacillin are practically not effective.

Broad-spectrum drugs:

- aminopenicillins: ampicillin, amoxicillin, carboxypenicillin, carbenicillin, ticarcillin (do not affect Pseudomonas aeruginosa);
- ureidopenicillins: piperacillin, meslocillin, azlocillin (affect Pseudomonas aeruginosa).

The action of these drugs extends to pathogenic Escherichia coli, pathogens of typhoid fever, Shigella, Proteus mirabelle, hemophilic bacillus influenzae. Preparations are inactivated by β-lactamases. The characteristic property of carbenicillin (in large doses) and ticarcillin is activity against Pseudomonas aeruginosa. Penicillins of the fifth generation (acylureidopenicillins) with increased activity and an extended range include piperacillin, meslocillin and azlocillin. The main advantage of ureidopenicillins is the high anti-pseudomonas effect, most pronounced in piperacil-

lin. To combat the destructive effect of β-lactamase, ampicillin, amoxicillin, ticarcillin are combined with inhibitors of these enzymes (clavulanic acid, sulbactam, tazobactam). The latter do not have significant antibacterial activity, but have the properties of irreversibly binding β-lactamases of microorganisms, increasing the sensitivity of microorganisms to penicillins. So, amoxiclav contains amoxicillin and clavulanic acid. Penicillins are widely used in dental practice in acute purulent inflammatory processes (periostitis, osteomyelitis, abscess, phlegmon, odontogenic sinusitis and sepsis, TMJ arthritis, generalized periodontitis and purulent diseases of the oral mucosa, contaminated wounds, and burns).

For empirical therapy, a wide range of penicillins should be selected (amoxicillin, ampiclox, amoxiclav, etc.). Taking into account the presence of microbial associations in the inflammation cell, a combination of penicillins with AG, FQ, CS, metronidazole, lincosamides, macrolides, rifampicin, chloramphenicol is used.

Adverse reactions of penicillins are usually minor and do not require treatment. Particular attention should be paid to the allergological history of the patient. It should also be remembered that all penicillins are characterized by cross sensitization. An undesirable effect on the central nervous system (increased neuronal excitability) is typical. When taken orally, large doses can lead to gastrointestinal upset and manifest as nausea, vomiting, and diarrhea. Methicillin has a higher nephrotoxicity, and therefore is practically not used. In children, when prescribing methicillin and nafcilin, granulocytopenia sometimes develops. Carbenicillin can cause hypokalemic alkalosis, bleeding, as well as a decrease in hemoglobin, thrombocytopenia, reversible leukopenia (with prolonged use). When using inhibitor-protected penicillins (unasyn), a transient increase in liver transaminases may develop. Prolonged use of penicillins can cause oral candidiasis. The local manifestation of the toxic effect of penicillin is expressed in pain reactions, thrombophlebitis, or the degeneration of a nerve accidentally infiltrated by injection. In pregnancy, penicillins, including those that are protected, are used without restriction. When breastfeeding newborns, it is not advisable to use penicillins, since this can lead to sensitization, development of candidiasis and diarrhea. In newborns and young children, cumulation of penicillins and an increase in the risk of their neurotoxic effect (the occurrence of seizures!) may occur. It is not

advisable to use penicillins with SA in connection with a decrease in the antibacterial effect. It should be remembered that at high doses of the potassium salt of benzylpenicillin with potassium preparations, potassium-sparing diuretics (spironolactone), captopril, there is a risk of hyperkalemia. And the simultaneous use of antiseptic penicillins (azlocillin, piperacillin) and anticoagulants can cause bleeding.

3.13.2. Cephalosporins

This is the most numerous and important group for the medicine, represented by semi-synthetic drugs with a wide spectrum of action, suitable for the treatment of almost all nosological forms, since they exhibit a bactericidal effect. The structure and mechanism of action of CS are similar to penicillin, but are capable of incomplete cross-allergy with them. They are resistant to the destructive action of β-lactamases of gram-negative bacteria compared to penicillins. They exhibit bactericidal action. Streptococci, methicillin-sensitive Staphylococcus aureus, epidermal staphylococcus, gonococcus, hemophilic bacillus, E. coli, Klebsiella, Proteus are susceptible to all CS. Serration, indole-positive, cytrobacter are resistant even to generation III CS. MRSA, C. Jekeium, X. Maltophilia, Listeria monocytogenesis, Legionella are not sensitive to single CS. Most CS are administered parenterally, and others – orally. They are well distributed, penetrate into bone tissue. With inflammation of the meninges, the contents of cefotaxime, ceftazidime, ceftriaxone in the cerebrospinal fluid approaches 30–50 %. They penetrate through the placenta and capsule of abscesses. The breakdown products of tissues do not affect their bactericidal activity. The classification of CS by generations, which is based on the chemical structure of drugs, taking into account their chemotherapeutic spectrum and clinical criteria, is more widely used in practice.

Generation I CS (cefazolin, cephalexin, cefradine, cefadroxil) are highly active against gram-positive cocci, including pneumo-, strepto- and staphylococci. They are more resistant to staphylococcal β-lactamases than other generations. Among gram-negative bacteria, Escherichia coli, Klebsiella and Proteus mirabelle, anaerobic cocci (pepto- and peptostreptococci) are sensitive to CS.

Generation II CS (cefaclor, cefamandole, cefoxitin, cefotetan, cefuroxime, cefuroxime axetil). In general, they are active against the same organ-

isms of generation II CS, but they act better against some gram-negative bacteria (enterobacteria, Klebsiella, including cephalotin-resistant species and indole-positive protein).

Generation III CS (cefoperazone, cefotaxime, ceftriaxone, cefixime, cefodizime, cefpodoxime axetil). Their main distinguishing features are an expanded spectrum of action in relation to gram-negative flora and the ability to penetrate into the central nervous system. They are active against Enterobacter, Citrobacter, S. marcescens, Providencia, as well as β-lactamase-producing species Haemophilus and Neisseria. Ceftazidime and cefoperazone show sufficient activity against P. aeruginosa. Only ceftizoxime and moxalactam are active to B. fragilis. Cefodysim (modivid) stimulates immune system reliably (increases te activity of T killers, stimulates chemotaxis, phagocytosis, etc.).

Generation IV CS (cefpirome, cefepime). They have an extended spectrum of activity against numerous microorganisms. They act powerfully against PRSA and some MRSA and coagulative negative staphylococci. The disadvantage of cefepime is the lack of effect against MRSA. They act effectively against the main gram-negative bacteria found in hospital conditions: Enterobacter, Pseudomonas, Acinetobacter.

Generation V CS – ceftobiprole (zeftera). A new antibiotic that has unique β-lactam activity relative to MRSA. The expansion of the activity spectrum with respect to the generation I and IV CS is achieved due to a significant increase in the affinity of the ceftobiprole molecule for PSB-2a. It is effective against most gram-negative pathogens resistant to traditional drugs.

The classification of CS groups is necessary and convenient for clinical practice, taking into account the features of the spectra of antibacterial action:

- group 1 – the most active to gram-positive microorganisms (cephalotin, cephaloridine, cefradine, cefazolin, cephalexin);
- group 2 – highly active to gram-negative bacteria of the enterobacteria group (cefuroxime, cefotaxime, ceftriaxone, cefotiam, cefamandole);
- group 3 – active to gram-negative bacteria, including Pseudomonas aeruginosa and akinetobacteria (cefoperazone, ceftazidime, cefsulodine);

• group 4 – active to anaerobes (cefoxitin, lactamocef, cefotetan).

In outpatient dental practice, drugs of the CS group (cefadroxil, cefuroxime axetil) can be prescribed for necrotizing ulcerative lesions of the oral mucosa, generalized periodontitis, gonococcal stomatitis, joint infections caused by staphylococci resistant to penicillin, as well as other strains of microorganisms and their microorganisms. In surgical dentistry, it is advisable to use preparations of CS group for severe and complicated infections of soft tissues and the skeletal system, as well as for pre- and postoperative prevention. In general medical practice, CS are prescribed for severe infections of the URT and LRT, intra-abdominal infections, sepsis, purulent meningitis, and infections of the skin, soft tissues, bones and joints, acute gonorrhea, before and after surgery.

Side effects of the drugs are negligible, but given the wider use in the clinic, the total number of adverse reactions is higher than that of penicillins or AG. Allergic reactions occur in 2 % of patients. Active accumulation of cephaloridine in the renal tubule epithelium may contribute to the development of nephritis and cystitis. Nephrotoxicity is manifested by cefaclor and cephalotin. With prolonged courses, CS show a direct toxic effect on the liver. Large doses of cephalexin, cephaloridine are able to inhibit GABA, which contributes to encephalopathic disorders. Ceftriaxone causes stagnation of bile, acute cholecystitis. Parenteral CS can cause hematomas, bleeding (coumarin-like action), and phlebitis. Biological complications may occur – dysbiosis, candidiasis and pseudomembranous colitis. In connection with the ability to inhibit alcohol dehydrogenase of the central nervous system, a disulfiram-like effect (cefoperazone) is typical. During pregnancy, CS should be prescribed very carefully. In severe infections, cefepime, ceftazidime, ceftriaxone can be empirically prescribed for monotherapy. The effectiveness of CS increases with the use of drugs that are combined with β-lactamase inhibitors – sulbactam and clavulanic acid. Sulperazone (cefoperazone + sulbactam) and sulbactomax (ceftriaxone + sulbactam), which are resistant to extended β-lactamases are used at clinic. In the treatment of life-threatening infections or against the background of immunosuppression, CS are combined with AG, carbenicillin, vancomycin, metronidazole, and macrolides. In case of simultaneous use with tienam, antagonism may occur. Some combinations with tetracycline, chloramphenicol, erythromycin, clindamycin help to weaken the action of both components.

3.13.3. Monobactams

The representative of this group, aztreonam, has a selective spectrum of activity against aerobic gram-negative bacteria. It provides high resistance to β-lactamases formed by most gram-negative bacteria. Multiresistant strains resistant to ampicillin, AG, cefotaxime, cefoperazone (salmonella, shigella, protea, E. coli, Klebsiella, gonococcus, meningococcus, etc.) are sensitive to the drug. In surgical and therapeutic dentistry, aztreons are mainly prescribed for severe infections caused by gram-negative bacteria. The drug is intended for parenteral use. Indications for use are infections caused by gram-negative microorganisms that are sensitive to the drug, meningitis, peritonitis, respiratory tract infections, intra-abdominal and pelvic infections, infections of the skin and soft tissues, bones and joints, etc. It is prescribed parenterally. Side effects are manifested in the form of nausea, vomiting, taste disturbances, diarrhea, skin lesions, pancytopenia, increased hepatic transaminases, decreased prothrombin time, dysbiosis, stomatitis. If necessary, it can be used in combination with penicillins, CS, macrolides, clindamycin and AG. It is known that aztreonam increases the effectiveness of aminopenicillins more than AG.

3.13.4. Carbapenems

Carbapenems are a new class of drugs structurally resembling β-lactams. These antibiotics include imipenem/cilastatin (tienam, lastinem), meropenem, biapenem. Imipenem/cilastatin consists of 2 parts: antibiotic imipenem and a specific enzyme, an inhibitor of cilastatin, which inhibits its destruction in the kidneys. It has the widest spectrum of activity among known ABD in relation to gram-positive aerobes and anaerobes. It is able to cover microorganisms, for the influence of which four antibiotics were previously used (generation III CS, AG, metronidazole and ampicillin). Tienam possesses unique antibacterial properties; it is not damaged by ordinary β-lactamases of plasmid and chromosomal origin. The drug penetrates well through the cell wall and contributes to the rapid death of the microorganism. Natural resistance to carbapenems is typical for chlamydia, mycoplasma, corynebacteria, mycobacterium tuberculosis and leprosy, flavobacteria, fungi. Secondary resistance of microorganisms to carbapenems develops rarely and slowly, cross-resistance within the group does not occur. They are highly effective in microflora resistance to penicillins, CS, AG.

In dentistry, tienam can be used in the treatment of severe acute purulent inflammatory processes (osteomyelitis, phlegmon, TMJ arthritis, sepsis, extensive contaminated wound and burn ulcers of the MFA) caused by microorganisms resistant to other drugs. It is indicated for the treatment of mixed severe infections, especially against the background of concomitant pathology: pneumonia, sepsis, endocarditis, infection of bones and joints. This drug is not prescribed for the treatment of meningitis. It is known that under the influence of thienam, fewer endotoxins are released than with ceftazidime.

Meropenem acts 2–4 times weaker than tienam relative to staphylococci, but exhibits 2–8 times greater activity against gram-negative enterobacteria and pseudomonas. Meropenem causes a low release of endotoxin, which is important in the treatment of severe sepsis caused by gram-negative bacteria. To increase activity against methicillin-resistant S. aureus, it is recommended to combine meropenem with teicoplanin, vancomycin, or piperacillin. Doripenem (doribax) is a new representative of the carbapenem series of antibiotics. It is highly effective in relation to nosocomial infections caused by gram-negative pathogens, the most important of which is Pseudomonas aeruginosa.

Side effects of tienam are infrequent, moderate and transient. These include local allergic and inflammatory reactions, dyspepsia, leukopenia, thrombocytopenia, encephalopathy, arterial hypotension, impaired liver and kidney function, pseudomembranous colitis, dysbiosis. When i.v. infusions are prescribed, myoclonus, mental disorders, paresthesias, hallucinations, confusion, epileptic seizures can be noted. In 1 % of patients, urine staining in red is observed. In comparison with tienam, meropenem lacks nephrotoxicity and neurotoxicity. Carbapenems are sometimes used in combination treatment. It must be emphasized that carbapenems should not be combined with penicillins, CS, and monobactam due to the fact that, with respect to these antibiotics, the drug induces the production of chromosomal β-lactamases. Antagonism is observed when combining tienam with chloramphenicol. β-lactams should not be prescribed after carbapenems. Combination with ganciclovir is not recommended (risk of generalized seizures). During pregnancy and lactation, carbapenems can be used when the potential benefit of them exceeds the risk.

3.13.5. Macrolides

Antibiotics of the macrolide group attract specialists with their high therapeutic activity, wide antimicrobial spectrum of action and low toxicity. The spectrum of their action is similar to penicillins, and the characteristic features are: bacteriostatic effect, suppressing activity against gram-positive cocci (streptococcus, staphylococcus), activity against non-bacterial pathogens (mycoplasmas, chlamydia, spirochetes), very low toxicity, the absence of cross-allergy with β-lactams. They are considered "reserve" drugs, since microorganisms resistant to penicillin, tetracycline, chloramphenicol, and streptomycin are sensitive to them. Macrolides are distinguished by the spectrum of action. So, oleandomycin is inferior to erythromycin in terms of its effect against gram-positive microorganisms. A wider spectrum of action is possessed by "new" macrolides (generation II) clarithromycin, roxithromycin. New macrolides are effective against gram-negative bacteria: campylobacter, listeria, gardnerella and some mycobacteria. Moreover, azithromycin and roxithromycin are superior to erythromycin and other macrolides in terms of their effect against gram-negative bacteria, as well as doxycycline, amoxicillin, cefaclor.

According to the effect on the microflora, 2 generations of macrolides are distinguished:

- generation I – erythromycin, oleandomycin.
- generation II – spiramycin, roxithromycin, josamycin, clarithromycin, midecamycin.

Indications for their use in dentistry are acute purulent-inflammatory processes caused by drug-sensitive microflora (periostitis, osteomyelitis, phlegmon, abscessed periodontitis, odontogenic sepsis, pyoderma, infected wounds). The drugs are prescribed in case of intolerance to penicillins and cephalosporins or allergies to them. In infections that are typical for dental practice, midecamycin (macropen) has proven itself well. This drug penetrates well into the tissues of the oral cavity, and its concentration in the parotid, submandibular lymph glands, in the tissues of the tongue, gums and tooth pulp exceeds that in serum. Midecamycin is effective in the treatment of periodontitis, purulent gingivitis and other infections caused by gram-positive microorganisms, while it has better tolerance to patients. In the treatment of periodontitis (including juvenile), erythromycin, rovamycin, clarithromycin are used. Indications for the prescription of

macrolides are tonsilopharyngitis, otitis media, sinusitis, pneumonia, infections of the skin and soft tissues, gonococcal, gastric ulcer and toxoplasmosis. It is important that macrolides are used for chlamydial infections (urethritis, cervicitis, pneumonia). Rovamycin is effectively used for toxoplasmosis (including pregnant women). Drugs are acid-resistant, thus they can be administered orally. They can also be used topically in the form of ointments for the treatment of purulent skin lesions and infected wounds.

Macrolides with systemic application sometimes cause unwanted reactions from the upper gastrointestinal tract (nausea, vomiting, pain). Pain, taste change, rash, transient increase in transaminase activity can also appear. With prolonged use of erythromycin, cholestatic hepatitis may develop, which is accompanied by jaundice. Sometimes drugs cause reverse ototoxic reactions, and with i.v. administration – thrombophlebitis. During pregnancy, undesirable effects of erythromycin, josamycin, spiramycin were not found. The prescription of macrolides to women who breastfeed (except for erythromycin) and children under 6 months should be prevented. To increase efficiency and expand the spectrum of action, macrolides are prescribed in the form of combinations with tetracyclines, AG, CS, SA, chloramphenicol. They should not be combined with lincosamides (antagonism!).

3.13.6. Azalides

Azithromycin (sumamed, azimed) is active against pyogenic streptococci, S. pneumoniae, S. viridans, staphylococci, enterococci. Among gram-negative microorganisms, the drug is active against H. influenzae, H. parainfluenzae, B. catarrhalis, B. pertussis, B. parapertussis, L. pneumophila, Shigellae, Salmonellae, Yersiniae, E. coli. In addition, the drug is highly active against many pathogens of sexually transmitted diseases (N. gonorrhoeae, C. trachomatis), most anaerobes, spirochetes (T. pallidun, B. burgdorferi), mycoplasmas, C. pneumoniae, L. monocytogenes. Azithromycin is superior to other macrolides in its effect on gram-negative bacteria. Compared with erythromycin, it has greater oral bioavailability. Azithromycin is absorbed by phagocytes more than penicillins, erythromycin, tetracycline, which leads to its accumulation in foci of inflammation in concentrations exceeding the minimum inhibitory concentration hundreds of times! High concentrations of azithromycin in tissues persist for

5–7 days after taking the last dose. Indications for the prescription of azithromycin in dentistry are moderate infections caused by microflora sensitive to the drug. Other indications for prescribing azithromycin are: infections of the airborne erythrocyte sedimentation syndrome and neuralgia, skin, acute nonspecific (chlamydial) and gonococcal urethritis, gastric ulcer associated with Helicobacter pylori, soft tissue infections. Azithromycin is better tolerated by macrolides and has a short course of use (3–5 days). Sometimes nausea, diarrhea, abdominal pain, vomiting, flatulence, a transient increase in the activity of liver enzymes, allergic reactions can be observed. Azithromycin is not prescribed for pregnant women.

3.13.7. Lincosamides

The discovery of lincosamide antibiotics in the 70s was a significant step forward in the treatment of polymicrobial infections caused by gram-positive aerobic and gram-negative anaerobic organisms. Lincomycin is a highly effective drug against staphylococci (including PRSA, active against MRSA), streptococci (except enterococci), non-spore-forming anaerobes. Some strains of Actinomyces, Veillonella and Bifidobacterium exhibit high sensitivity to lincomycin. Most strains of Bacteroides, Fusobacterium, and anaerobic cocci are sensitive to lincomycin. The drug has no cross-resistance with penicillin, tetracycline, erythromycin, chloramphenicol, and neomycin. In high concentrations, lincomycin accumulates in bone tissue. Clinical data indicate high efficacy and low toxicity of the drug in the treatment of lesions of the skin and soft tissues, bones and joints, including odontogenic origin. In dentistry, in addition to infections of hard tissues (periostitis, acute and chronic osteomyelitis, periodontitis), volumetric operations associated with prosthetics are also considered. Local use of lincomycin (in the form of 2 % ointment) is indicated in cases of sensitive microflora in case of necrotizing ulcerative lesions of the oral mucosa, periodontal tissue diseases, skin diseases, infected wounds.

An important indication for the prescription of lincomycin is acute and chronic osteomyelitis, the development of which is most often associated with Staphylococcus aureus or streptococcus, spreading by the hematogenous route. Treatment with acute hematogenous osteomyelitis, especially its septic form with simultaneous damage to several bones, demonstrat-

ed its rather high efficiency. The duration of treatment with lincomycin in acute osteomyelitis is 10–14 days, and in chronic – 1 to 3 months after healing. Indications for the prescription of the drug in general practice: infections of the airway and sepsis, skin, soft tissues, intra-abdominal and pelvic infections, sepsis, major traumatic operations, especially associated with prosthetics.

Combination of lincomycin with CA or AG are often used. Lincomycin is a low-toxic drug. Its most serious complication with long-term treatment is severe pseudomembranous colitis, for which metronidazole is used. Relatively rarely observed leukopenia, thrombocytopenia, allergic reactions, etc. In order to increase the effectiveness of therapy, combinations of lincomycin with penicillins, AG, rifampicin, and metronidazole are used. Combinations of lincomycin with erythromycin or chloramphenicol, which is explained by the effect of LPO on one target in ribosomes, are considered to be antagonistic. Combinations of lincomycin with CS or AG is often used.

Clindamycin is a semi-synthetic derivative of lincomycin, 8 times more active than lincomycin in terms of its effect on Staphylococcus aureus and Streptococcus aureus. In relation to Staphylococcus aureus, the drug is more active than erythromycin, including affecting MRSA. It is highly active against gram-positive and gram-negative anaerobes, actively affects plasmodia and toxoplasma, the causative agent of trachoma. It is well distributed in most tissues and body environments, with the exception of the brain. The half-day is shorter compared to lincomycin. In bone tissue, the concentration of clindamycin is about 50 % of the concentration in serum. The drug is concentrated in polymorphonuclear leukocytes, stimulates phagocytosis, easily penetrates saliva, periodontal tissues, and abscesses.

Indications for the use of clindamycin in dentistsry are similar to lincomycin. Clindamycin is considered the drug of choice in the treatment of osteomyelitis, including anaerobic origin and septic arthritis. With an infection of the oral cavity (periodontal abscess, periodontitis), the drug may also be prescribed. Obligatory anaerobes are known to be released in most patients with odontogenic infections.

Clindamycin can also be considered the drug of choice for empirical antibiotic therapy for generalized periodontitis. Side effects are not often observed, but the probability of pseudomembranous colitis during its use

is greater than in other ABD (0.3–21 % of cases). To increase the effectiveness of therapy, clindamycin is prescribed in the form of a combination with AG, which is more effective than traditional use (penicillin + gentamicin). The drug is used with penicillins, rifampicin, metronidazole. Clindamycin is not recommended to pregnant women who breastfeed and newborns. It should be remembered that it is not advisable to combine lincosamides with drugs for anesthesia, NA, non-depolarizable muscle relaxants, due to increased neuromuscular blockade and the risk of respiratory arrest.

3.13.8. Tetracyclines

Broad-spectrum antibiotics have a bacteriostatic nature of action, inhibit protein synthesis. They are active against many types of gram-positive and gram-negative microorganisms, spirochetes, rickettsia, clostridia, chlamydia, some protozoa and viruses. Activity against gram-positive cocci is comparable to penicillins. They affect intracellularly located microorganisms. Due to the widespread use of tetracyclines in outpatient practice, the spread of microorganism strains resistant to these drugs is typical (especially S. aureus and gram-negative bacilli). Tetracyclines are well absorbed and distributed in most body fluids, have a high ability to pass through the placenta and into breast milk.

In dentistry, in the presence of sensitive microflora, it is possible to use tetracyclines enterally with generalized periodontitis, periostitis, osteomyelitis, necrotizing ulcerative and burn lesions of the oral mucosa, gonococcal stomatitis. In practical medicine, metacycline and doxycycline are most often used in various dosage forms for infections of soft tissues, periostatitis and osteomyelitis. Indications for the appointment may also be infections of the LRT (caused by mycoplasmas, chlamydia), intestinal infections, helicobacteriosis, syphilis, plague, cholera leptospirosis, etc. With various purulent infections in surgery, it is not advisable to use tetracyclines. The latter is associated with drug resistance of many strains of staphylococci and enterobacteria. It is also not prescribed for the treatment of severe postoperative complications, sepsis.

In medical practice, the representative of this group – doxycycline is more often used; the resistance of microorganisms to it is less developed. The drug also has convenient pharmacokinetics, which determines its

Table 13

Rules for the use of lincomycin

Dose	Solvent volume	Time (hour)	Features of the introduction
600 mg	100 ml	1	Lincomycin should not be administered intravenously bolus fast. I.v. infusion of the drug is carried out after dilution of 1.0 g of lincomycin in 100 ml of the corresponding solution (at least 1 g). When infusing solutions that exceed the concentration or administered at a faster rate, severe cardiopulmonary complications may occur. In the presence of even more severe infections, the dose can be increased. For healthy testers, for 7 days, 2100 mg was administered in 250 ml of physiological solution for 2 hours 4 times a day. The total daily dose of the drug was 8.4 g.
1.0 g	100 ml	1	
2.0 g	200 ml	2	
3.0 g	300 ml	3	
4.0 g	400 ml	4	
These doses, if necessary, are repeated to the maximum recommended dose (8 g)			

Table 14

Doses of lincomycin recommended at clinic

Infections	Enteral	Intramuscular	Intravascular
Severe infections (adults)	500 mg every 8h	600 mg each 24h	600 mg every 8–12 hours. Intravenous administration of the drug is carried out with 5 % glucose solution or saline
More severe infections (adults)	500 mg every 6h	600 mg each 12h	
Severe infections (children)	30 mg/kg of body weight per day, divided into 3–4 equal doses	10 mg/kg body weight every 24h	10–20 mg/kg of body weight per day, divided into 2–3 doses, the infusion interval is the same as in adults
More severe infections (children)	60 mg/kg of body weight per day, divided into 3–4 equal doses	10 mg/kg body weight every 24h	

single administration during the day. Doxycycline is considered less toxic than other tetracyclines; it is used both as monotherapy and in combination with AG. In severe infections, the new generation III tetracycline – tigecycline showed an equivalent activity to carbapenems. The drug is indicated for complicated intra-abdominal infections of the skin and soft tissues. Tetracyclines are often used topically in the form of suspensions or officinal ointments: tetracycline hydrochloride (1 % and 3 %), hyoxysone, geocorton, oxyzone (containing oxytetracycline hydrochloride and hydrocortisone acetate), aerosols: oxycyclosol (contains oxytetracycline and prednisolone), oxycort (the main components are oxytetracycline and hydrocortisone).

Long-term use of tetracyclines for general treatment may be associated with a high risk of side effects. In particular, lesions of the dentofacial and skeletal systems (osteomalacia), a change in staining of teeth with dark colors are typical. The catabolic effect of tetracyclines leads to hypotrophy, a decrease in resistance to infections, and a violation of neuromuscular transmission. From the gastrointestinal tract, nausea, vomiting, diarrhea, dysphagia, anorexia can be observed. On the part of the skin, a maculopapular or erythematous rash, photosensitivity are sometimes noted. The development of anemia, thrombocytopenia, neutropenia, eosinophilia, jaundice, hyperbilirubinemia, azotemia, increased activity of transaminases and urea in the blood is not ruled out. Tetracyclines are not recommended for children under 14 years of age, pregnant and women who breastfeed.

When tetracyclines are used by a pregnant woman (especially in the first trimester), a newborn child may experience disturbances in the formation of both a milk and a permanent bite, a toxic effect on the child's bone system (inhibition of children's growth, shortening of the fibula, enamel hypoplasia, etc.) is expressed. If it is necessary to increase the antibacterial effect, clinics widely use combinations of tetracyclines with macrolides, SA, AG, nitrofurans, fusidic acid, etc. Tetracyclines increase the effect of indirect anticoagulants and weaken the effects of contraceptives. It should be remembered that drugs of this group should not be used simultaneously with drugs of antacids, calcium, magnesium, iron, since this leads to a decrease in their absorption. Carbamazepine, phenytoin, barbiturates increase the hepatic metabolism of tetracyclines.

3.13.9. Aminoglycosides

Antibiotics of this group occupy one of the most important places in the treatment of infectious diseases. The activity of AG in relation to a wide range of gram-negative aerobic microorganisms is of particular importance for practical medicine. They act weaker on staphylococci, streptococci, enterococci, do not affect anaerobic microorganisms. They are characterized by a more pronounced effect against gram-negative aerobic microorganisms, including Pseudomonas aeruginosa. The mechanism of action is to block protein synthesis by ribosomes. The nature of the action of AG is bacteriostatic and bactericidal (depending on the concentration in the blood). Drugs are rapidly absorbed and well distributed. The main routes of administration are i.v. and i.m.; AG can be administered in serous cavities, endobronchially, endolumbarly. In a non-metabolized form, they are excreted by the kidneys, so this must be taken into account if their function is impaired.

Generation I AG include streptomycin, kanamycin, monomycin and neomycin; generation II AG – gentamicin; generation III AG – tobramycin, sisomicin, amikacin, netilmicin. The antimicrobial effect in different drugs is not uniformly expressed. According to the degree of decrease in antibacterial activity, AG are positioned as follows: amikacin – netilmicin – sisomicin – gentamicin – tobramycin – neomycin – kanamycin – monomycin. Indications for the prescription of AG in dental practice are diseases caused by mixed microflora: acute odontogenic septic diseases, infected wounds, generalized periodontitis, and necrotizing ulcerative lesions.

An important feature of the action of AG (streptomycin, kanamycin) is their effectiveness in specific processes caused by tuberculosis, including dental practice. These drugs are used to prevent purulent processes after surgical procedures. Indications for AG are also life-threatening infections of soft tissues, bones, kidneys, respiratory tract, gastrointestinal tract, septicemia, peritonitis, tuberculosis infection, etc.

AG are used for osteomyelitis by the method of intraosseous injection. In severe purulent processes, they can be used simultaneously locally on gauze tissues soaked with an antibiotic solution (40–80 mg of gentamicin sulfate per 20–30 ml of boiled water). 0.1 % aqueous solution is administered into the periodontal pocket for 10–15 minutes. To lubricate the oral mucosa, 0.1 % ointment of gentamicin sulfate or 2 % ointment of

neomycin sulfate is used. AG are often included in official combined ointments (Diprogenta, Kenacomb, Locacorten-H, Triderm, etc.), as well as in the main prescriptions of emulsions and pastes.

AG are toxic antibiotics (they exhibit nephro-, oto-, vestibulo-, neuro-, hepatotoxic effects, carry out neuromuscular blockade). Allergic reactions are rare. In decreasing toxic effect, AG can be arranged as follows: neomycin – monomycin – kanamycin – dihydrostreptomycin – gentamicin – streptomycin – tobramycin – amikacin – netilmicin. An exceptionally safe drug is netilmicin. Allergic reactions are rare. It should be remembered that pregnant women are prescribed AG, only by life-saving indication.

AG exhibit a synergistic effect on microorganisms in combination with β-lactam antibiotics. A highly effective combination in severe processes is considered to be "aminoglycoside + clindamycin." The appointment of two AG at the same time can lead to increased oto- and nephrotoxicity. Due to the increase in side effects, it is not advisable to use them with vancomycin, amphotericin, drugs for anesthesia, opioid analgesics, etc.

3.13.10. Glycopeptides

This group of drugs includes vancomycin, teicoplanin, ristomycin. Vancomycin is highly active against gram-positive bacteria, including those resistant to second ABD (staphylococci, streptococci, enterococci, corynebacil, including penicillin-forming and MRSA). It affects clostridia, actinomycetes. The mechanism of action is based on impaired cell wall synthesis.

In dental practice, vancomycin is prescribed prophylactically during tooth extraction for patients who suffer from severe flaws/heart defects, rheumatism and cannot tolerate, at the same time, penicillins. The drug is prescribed for severe infectious inflammation, which can not be treated with penicillins, central nervous system and other ABD, as well as their intolerance. Indications for use are also severe systemic infections, purulent processes of soft tissues, staphylococcal endocarditis and enterocolitis, pseudomembranous colitis, prevention of postoperative complications. Vancomycin has high toxicity (anaphylactoid reactions, nephro-, oto-, hematotoxicity, dizziness, headache, thrombophlebitis at the injection site, reverse neutropenia, Stevens – Johnson syndrome, vasculitis), so its purpose in clinical practice requires special attention. Teicoplanin in

comparison with vancomycin is more active in relation to Staphylococcus aureus and Enterococcus aureus. It has indications similar to vancomycin, but slightly fewer side effects. Ristomycin is active against staphylococcus resistant to other ABD. Gram-negative bacteria acts when used in large doses. It has a predominantly bactericidal effect. The resistance of microorganisms develops slowly. it is hematotoxic. Side effects develop in 25 % of cases. Pregnant women who breastfeed are prescribed glycopeptides carefully due to the risk of neuro- and ototoxic effects. Children and newborns are prescribed only for very severe infections.

3.13.11. Ansamycins

A representative of the rifampicin group can be prescribed for infections caused by staphylococcus (including resistant strains), streptococcus, gonococcus, many strains of enterococcus, anaerobes, tuberculosis mycobacterium, Pseudomonas aeruginosa, Escherichia, protea, chlamydia and other main conditions for the use of rifampicin in dentistry is the presence of pathogens sensitive to the drug. Rifampicin is prescribed for osteomyelitis and other purulent processes. Other indications: tuberculosis, infections caused by MRSA, osteomyelitis, pneumonia, leprosy, a carrier of meningococcal infection. Side effects of rifampicin can be manifested by allergies, headaches, disorientation, nausea, vomiting, diarrhea, anorexia, erosive gastritis, urticaria, fever, leukopenia, interstitial nephritis, etc. Urine, skin, and sputum become orange-red when treated with the drug. If necessary, rifampicin can be combined with AG, carbenicillin, biseptol, and tetracycline. In case of staphylococcal endocarditis, a combination of the drug with FQ is advisable. It should be remembered that rifampicin is a powerful inducer of microsomal oxygenase; it can reduce the concentration of indirect anticoagulants, digoxin, contraceptives, etc. in the blood.

3.13.12. Chloramphenicol

Chloramphenicol (levomycetin) is a bacteriostatic ABD with a wide spectrum of action against gram-positive and gram-negative microflora. It is active against gram-negative anaerobes and intracellular microorganisms. Secondary resistance develops slowly and is not cross-sectional. Indications for the use in dentistry are necrotizing ulcerative lesions of

the mucous membrane, burns, gonococcall stomatitis. Chloramphenicol can be used in the form of 1–10 % liniment for the treatment of the mucous membrane, and combination pastes that contain the drug – for the treatment of pulpitis by biological method. Levomycetin is also a part of officinal aerosol preparations: legrazol, levovinisol, ointments iruxol, levosin, levomecol and corticomycetin. Synthomycin has a less pronounced antibacterial effect and greater toxicity. It is used locally in the form of 1 %, 5 %, 10 % emulsion or liniment. Indications for the administration of chloramphenicol are also fulminant forms of meningitis, brain abscesses, intraabdominal and pelvic infections, generalized forms of salmonellosis, typhoid fever, etc. With general treatment, it can cause haemopoiesis, dyspeptic symptoms, bleeding, visual disturbances, peripheral neuritis, dysbacteriosis, slowing wound healing. Severe intoxication occurs in infants ("gray", cardiovascular syndrome). The hematotoxicity of chloramphenicol increases in conjunction with SA, nitrofurans, ristomycin, griseofulvin. Chloramphenicol is combined with macrolides and polyene antibiotics. Antagonism is observed when combining chloramphenicol with lincomycin. It is worth remembering the ability of chloramphenicol to inhibit metabolic processes.

3.13.13. Steroids

Fusidic acid and fusidin sodium are natural protistaphylococcal antibiotics (including PRSA and MRSA). They affect the causative agents of diphtheria, clostridia, mycobacteria, and listeria. They can suppress microorganisms resistant to erythromycin, chloramphenicol, etc. Resistance of sensitive microorganisms occurs quickly. The mechanism of action is bacteriostatic, when using large doses – bactericidal. In dentistry, drugs can be prescribed for generalized periodontitis, necrotizing ulcerative lesions, burns of the oral cavity, infected wounds, gonococcal stomatitis. They are also indicated for staphylococcal infections: pneumonia, surgical infections, mastitis, otitis media, and carbuncle. They relate to low-toxic drugs and are mainly used enterally. Side effects: abdominal pain, nausea, diarrhea, allergic rashes, eosinophilia, increased activity of transaminases in the blood, and thrombophlebitis (intravenous administration) are sometimes observed. It is well combined with other ABD (tetracyclines, penicillins).

3.13.14. Polypeptides

Representatives of the polymyxin group mainly affect gram-negative microorganisms (enterobacteria, salmonella, Escherichia coli and Pseudomonas aeruginosa, etc.). In dentistry, they can be used in the treatment of purulent inflammatory processes. With necrotizing ulcerative lesions and burns of the mucous membrane, they can be used topically in the form of a 2 % ointment of polymyxin M sulfate or a solution for applications and irrigation. Gramicidin is more active relative to gram-positive bacteria. It has a pronounced hemolytic effect. It is applied only locally. Purulent exudate does not change its activity. Gramicidin in the form of oil (2 ml of 2 % alcoholic solution of gramicidin diluted with 50–60 ml of fish oil) or water (2 ml of 2 % alcoholic solution of gramicidin – 200 ml of distilled water) solution is prescribed in the form of irrigation and applications with necrotizing ulcerative and aphthous lesions of the mucous membrane, phlegmons, boils, burns, etc.

3.14
SYNTHETIC ANTIBACTERIAL DRUGS

This group includes various chemical compounds synthesized later than sulfanilamide preparations, which differ from them and antibiotics in the structure, mechanism and spectrum of antibacterial action. All of them have high antibacterial activity, but derivatives of quinolone and imidazole are more important for dental practice in the treatment of acute infectious and inflammatory diseases.

Synthetic antibacterial agents are classified as follows:

1) quinolones/fluoroquinolones – ciprofloxacin, ofloxacin, norfloxacin, pefloxacin, levofloxacin, moxifloxacin, gatifloxacin;

2) oxazolidinones – linezolid;

3) nitroimidazoles – metronidazole, tinidazole, ornidazole, secnidazole;

4) sulfanilamides – etazole, sulfadimezin, sulfonomethoxin, sulfadimethoxine, biseptol, phthalazole;

5) nitrofurans – furacilin, furadonin, furazolidone, nifuroxazide;

6) 4-, 8-hydroxyquinoline – nitroxoline, quinosole;

7) quinoxalines – dioxidine.

3.14.1. Quinolones/fluoroquinolones

This class of drugs includes two main groups of drugs: non-fluorinated quinolones and fluoroquinolones, which differ significantly in structure, activity, pharmacokinetics and breadth of indications for use. By the mechanism of action, FQ are fundamentally different from other ABD, which ensures their high activity and bactericidal action in relation to resistant, including multiresistant strains of microorganisms. They block DNA gyrase (topoisomerase), which prevents the coagulation of RNA strands and inhibits the growth of bacteria in this way. Their ability to penetrate the bacterial membrane is also important. Drugs are determined by convenient pharmacokinetics, which allows to treat infections of different localiza-

tion. Important advantages of this group of drugs: rapid and pronounced antibacterial (bactericidal) effect, relatively liquid and slow development of microorganism resistance, the ability to penetrate tissues (including bone), a stimulating effect on the immune system, extremely low toxicity, convenient mode of use (1–2 times a day).

Generational classification:

- generation I (nalidixic acid, oxolinic acid, pipemidic acid);
- generation II (lomefloxacin, norfloxacin, ofloxacin, pefloxacin, ciprofloxacin);
- generation III (levofloxacin, sparfloxacin);
- generation IV (moxifloxacin, gatifloxacin).

Non-fluorinated quinolines (generation I) are characterized by moderate activity against certain gram-negative microorganisms; they do not create high concentrations in the blood and tissues. The ultra-wide spectrum of antimicrobial action of the second generation drugs covers staphylococci (including MRSA), streptococci, enterobacteria, legionel, and pseudomonas aeruginosa, acinetobacter, chlamydia, other generation III and especially generation IV FQ ("respiratory") are highly active relative to pneumococci. In terms of effectiveness and relevance to practice, the preparations are not inferior to generation III and generation IV CS. The disadvantages of most known FQ (except for generation III and IV) are low activity against gram-positive microflora in comparison with gram-negative, low efficiency or lack of it against anaerobes of the bacteroid genus. In clinical practice, ciprofloxacin (ciprobay, ciprinol) is often used, which is one of the most effective drugs against gram-negative flora (gonococci, Branhamella catarrhalis, Haemophilus influenzae, Pseudomonas aeruginosa). It is active against staphylococci and streptococci, including Streptococcus faecalis. All FQ are administered enterally, and some of them (ciprofloxacin, pefloxacin, ofloxacin, levofloxacin) are also parenteral. The rationally selected combination of ciprofloxacin and tinidazole in the preparation "Cifran CT" allows to recommend it for the treatment of purulent-inflammatory diseases and open fractures of the upper limbs, to prevent the development of inflammatory complications that occur in patients after removal of jaw tumors during dental implantation. FQ are highly effective drugs in the treatment of various pathologies of infections of the genitourinary system (including prostatitis, gonorrhea), gastrointes-

tinal tract, airborne diseases and malignant neoplasms, skin, bones, joints and soft tissues, intestinal, intra-abdominal infections, meningitis, sepsis, postoperative and postpartum complications.

Recently, new FQ appeared on the Ukrainian market – levofloxacin, moxifloxacin, gatifloxacin. Their fundamental novelty is associated with the expansion of the spectrum of action against gram-positive microorganisms. It is also important that the concentration of levofloxacin in tissues is 30 times higher than that in blood serum. Gatifloxacin has a uniquely broad spectrum of antimicrobial activity. The presence of FQ medical forms for intravenous and enteral administration in combination with high bioavailability allows for step therapy. The high bactericidal activity of FQ allowed for the development of a number of drugs (ciprofloxacin, norfloxacin, moxifloxacin) for topical application in the form of eye and ear drops.

The frequency of side effects when prescribing FQ is relatively low (1–4 %). Symptoms include headache, sleep disturbances, anxiety, insomnia, drowsiness, and dizziness. Ototoxicity, visual impairment, paresthesia, tremors, convulsions, arthralgia, skin reactions, gastrointestinal discomfort, diarrhea, photosensitivity may occur. The risk of developing seizures is increased in patients with cerebrovascular accident, traumatic brain injury. Musculoskeletal disorders, arthropathy, arthralgia, myalgia, and leukopenia rarely occur. In older people, the risk of tendon rupture increases when using FQ in combination with GCS. The neurotoxic effect of drugs can be enhanced with the simultaneous use of NSAID, derivatives of nitroimidosole and xanthines. It is advisable to combine FQ with erythromycin, penicillins, CS, AG, vancomycin, clindamycin, metronidazole, etc. Antagonism is observed in case of their simultaneous use with nitrofurans. It should be remembered that the use of FQ is inappropriate during pregnancy, breastfeeding and in children under 15 years of age.

3.14.2. Oxazolidinones

The main representative of this new group of synthetic drugs that have found application in clinical practice is linezolid. It is active against most, both aerobic and anaerobic gram-positive microorganisms. Linezolid exhibits moderate activity (in vitro) against M. catarrhalis, H. influenzae, Legionella spp., N. gonorrhoeae, B. pertussis, F. meningosepticum, P. mul-

tocida, as well as Vasteroides spp., Prevotella spp., F. nucleatum. Linezolid has a predominantly bacteriostatic effect due to impaired protein synthesis. There is no cross-resistance with other classes of antimicrobial agents. Indications for use (including dentistry) are infections caused by multiresistant gram-positive cocci (MRSA and MRSE).

The drug is often used for community-acquired and nosocomial pneumonia. Adverse reactions manifest as headache, nausea, vomiting, abdominal pain, diarrhea, taste change, reverse anemia, and thrombocytopenia. An increase in the activity of transaminases and alkaline phosphatase, an increase in the level of bilirubin in the blood is noted. If necessary, linezolid is used in a combination with FQ. It should be remembered that the use of linezolid during pregnancy, breastfeeding is inappropriate.

3.14.3. Nitroimidazoles

The drugs of this group – metronidazole, tinidazole, ornidazole, secnidazole, ternidazole attract the attention of clinicians in connection with the ability to actively influence anaerobic microorganisms (bacteroides, clostridia, peptostreptococci, etc.) the role of which in the etiology of infectious processes has increased significantly. Ornidazole is more effective than metronidazole in anaerobic pathogens of infection (its effect is compared with clindamycin, inhibitor-protected penicillins, chloramphenicol or carbapenems). Trichomonads, amoeba, balantidia, and lamblia are also sensitive to this group of drugs. They have a bactericidal effect.

In dentistry, drugs can be successfully used for the treatment of osteomyelitis, phlegmon, infections of the oral cavity and peridental tissues. Metronidozole is resistant to the action of purulent exudate enzymes, in connection with which they are applied topically in the form of applications and instillations of 1–2 % solution for the treatment of acute ulcerative gingivitis and infections affecting the lips. Metrogyl Denta gel is widely used topically for the treatment of periodontitis. Indications: CNS infections, intra-abdominal, gynecological infections of LRT, soft tissues, bones, joints, peritonitis, lung abscess, gas gangrene, purulent appendicitis, pseudomembranous colitis, amoebic dysentery, liver abscess, etc. Side effects of nitroimidazoles are not often observed. Dyspeptic symptoms, dizziness, tremors, irritability or depression, temporary loss of consciousness, impaired coordination, convulsions, cytopenia, periph-

eral neuropathy, and dysuria, dark staining of urine, candidiasis, and allergic reactions may occur. A dentist can note the patient's complaints about the coated tongue and metallic taste, dry mouth. During treatment with metronidazole, you can not drink alcohol (the development of a disulfiram-like reaction). Ornidazole, in contrast to metronidazole, is better tolerated, a less pronounced sensation of metallic taste is compatible with alcohol (it does not inhibit aldehyde dehydrogenase and does not cause a disulfiram-like reaction). Not prescribed for children under 5! Preparations of this group are well combined with many antibacterial agents (β-lactams, AG, FQ, macrolides, vancomycin, SA). The activity of nitroimidazoles can decrease with the simultaneous use with metabolic inducers (phenobarbital, rifampicin) and increase with the use of inhibitors (cimetidine). Drugs may enhance the effect of indirect anticoagulants.

3.14.4. Sulfonamides

Sulfanilamides are synthetic broad-spectrum antibacterial agents. Due to the long time of use, they have lost their effectiveness. SA inhibit the growth of many gram-positive (weakly affect staphylococcus) and gram-negative (except Pseudomonas aeruginosa) bacteria, chlamydia and protozoa. The activity of SA is significantly inferior to antibiotics. Combined drugs such as sulfamethoxazole/trimethoprim (bactrim, biseptol), sulfapyridazine, sulfamonomethoxin, sulfalene are characterized by a wider spectrum of antibacterial action. The mechanism of action of SA is bacteriostatic, associated with the principle of competitive inhibition (based on their similarities to PABA, used by many bacteria for the synthesis of folic acid). SA significantly differ in pharmacokinetic parameters, in particular, the features of absorption, half-life and metabolism. In dentistry, the classification of sulfonamides is based on their pharmacokinetics.

I. Well absorbed from the digestive tract:

1) short action (streptocide, norsulfazol, sulfadimezin, urosulfan, ethazole, sodium sulfacyl);

2) medium action (sulfasalazine);

3) long-term action (sulfapyridazine, sulfamonomethoxin, sulfadimethoxine);

4) increased action (sulfalene).

II. Insufficiently absorbed from the gastrointestinal tract (sulgin, phthalazole, phthazine, salazopyridazine).

III. Combined (co-trimoxazole – bactrim, biseptol).

SA in the presence of sensitive microflora can be intended in dental practice for combined chemotherapy of purulent-inflammatory processes and infected wounds. As a monotherapy, SA is rarely used in the treatment of necrotizing ulcerative processes of the mucous membrane, generalized periodontitis, erysipelas, gonococcal stomatitis. Indications for use: infections of the URT and UT, toxoplasmosis, malaria, nocardiosis, and sanitization of carriers of meningococcus. It is necessary to strictly observe the daily and course doses of the drugs. SA and combined preparations, which are prescribed for local treatment (bactrim suspension, inhalypt aerosol, sodium sulfacyl solution), are applied topically in the form of applications and instillations for gingivitis, stomatitis, alveolitis, pericoronitis, periodontitis and for introduction into the root canals in the treatment of chronic pulpitis, periodontitis. SA is also often used in the form of pastes (in combination with antibiotics) in the treatment of caries and pulpitis by the conservative method. It is advisable to use long-acting drugs. Side effects in the treatment of AS are observed in 3–10 % of cases and are expressed, first of all, in crystalluria, granulocytopenia, gastrointestinal disorders and allergic reactions.

3.14.5. Nitrofurans

Nitrofurans have a wide spectrum of action, covering both gram-positive and gram-negative microorganisms, anaerobes, many protozoa. In clinical efficacy, they are inferior to most antibiotics in clinical efficacy. The nature of the action is both bactericidal and bacteriostatic. Most often in clinical practice, furacilin, furazolidone, furadonin, furagin, nifuroxazide are used. In dental surgery, they are used for local treatment, which is associated with the preservation of antibacterial activity in the presence of pus and tissue decay products. So, furacilin in the form of 0.02 % solution is used for applications, irrigation, mouth baths, as well as for electrophoresis. Solutions of furadonin, furagin, furazolidone (respectively, at concentrations of 1:30,000; 1:3,000; 1:25,000) are also used locally. Nitrofurans are used for the manufacture of biological antiseptic pastes, which are introduced into periodontal pockets. To lubricate the affected areas, 0.2 %

furacilin ointment is prescribed. In the form of powders, nitrofuran preparations are prescribed for the treatment of aphthae, wounds, and ulcers.

Indications for the prescription of nitrofurans in a dental clinic are inflammatory and necrotizing ulcerative processes of the mucous membrane, periodontitis, burn injuries. Indications for clinical practice are infections of the UT and intestines. Side effects of nitrofurans are infrequent (dyspeptic phenomena, methemoglobinemia, allergies, inhibition of platelet aggregation, cholestasis, polyneuritis, hearing impairment, paresthesia, optic nerve damage, etc.), as usually do not require cancellation. Furacilin and furadonin are the most toxic. If necessary, drugs are combined with penicillins, AG, macrolides, and tetracyclines. The activity of nitrofurans decreases under the influence of FQ, SA. When used with chloramphenicol, the risk of inhibition of hematopoiesis increases. Nitrofurans should not be prescribed to pregnant women. Prescribing during breastfeeding and in newborns, due to the immaturity of the enzyme systems, can lead to the development of hemolytic anemia. Nitrofurans are characterized by a disulfiram-like reaction.

3.14.6. Hydroxyquinolines

Drugs of this group have activity mainly against gram-negative microorganisms, fungi and protozoa. Most often in clinical practice, nitroxoline (5-NOC) is used. Hydroxyquinolines in comparison with modern ABD (penicillins, CS, FQ) are not of interest for practice in dentistry. Nitroxoline can be prescribed orally for generalized periodontitis, inflammation of the mucous membrane, fungal stomatitis, and is also used in the form of applications and instillations. In the complex treatment of periodontitis, a mixture of nitroxoline with terrilytine, quinozole and chiniofon is locally used. With necrotizing ulcerative processes, the mucous membrane is irrigated with their solutions, lubricated with ointments, emulsions, pastes; with periodontal diseases – injected into the gingival pockets. With systemic use, the side effects of nitroxoline develop slowly in the form of headache, paresthesia, peripheral neuritis and atrophy of the optic nerve, dyspepsia, nausea, rashes, tachycardia, and a change in the color of urine (intensely yellow). Inhibition, retrograde amnesia sometimes occurs. Teratogenic effects are not ruled out. Hydroxyquinoline should not be prescribed to pregnant women, women who breastfeed and newborns.

3.14.7. Quinoxalines

The representative of this group, dioxidine, has a wide spectrum of action with a bactericidal effect. It is active against gram-positive and gram-negative, aerobic and anaerobic microorganisms. Dioxidine is prescribed i.v. dropwise (0.5 % solution on glucose) for severe bacterial infections caused by susceptible microorganisms. With this use, rapid and good penetration into the tissue is observed. Dioxidine is often used intravenously in purulent chronic infection (osteomyelitis, phlegmon), especially with symptoms of generalization of the process and in debilitated patients with torpid wounds, ulcers, burns. Dioxidin can be used topically in the form of a solution (ointment) for washing, lubricating, applying, and for introducing into the cavity. With surface processes, the drug is used on tissues moistened with 0.5–1 % solution. Deep wounds after treatment are loosened with tissues with 1 % solution of dioxidine. With osteomyelitis, it is possible to appoint bathing or washing for the cavity. With purulent-necrotic processes, 5 % dioxidin ointment is also used. Side effects: allergic reactions, dyspeptic symptoms, fever, and headache. There is evidence of a carcinogenic effect of the drug.

3.15
ANTIFUNGAL AGENTS

There are a large number of varieties of fungi. Under certain conditions, they can cause fungal diseases in humans – mycoses (local or systemic). Earlier, dermatologists were traditionally involved in fungal infections, but now, due to the clear localization and variety of clinical manifestations, they attract close attention of doctors of other specialties, including dentists. There are superficial mycoses (with damage to the skin, its appendages, mucous membranes), deep or systemic mycoses (with damage to internal organs, bones, brain, fungal septicemia). For dental practice, superficial mycoses, which are caused by yeast fungus Candida albicans, are relevant. Candidamycosis of the oral cavity, pharynx can occur in children and elderly people as a complication of various diseases and antibiotic therapy. For this infection, lesions of the intestines, bronchi, rectum, and external genitalia are also typical and, in an exceptional case, with a sharp inhibition of the body's resistance, fungal septicemia may develop. The choice of an antifungal drug is based on the clinical picture of the process, its localization and the results of laboratory studies (microscopy of native sputum preparations, stained biosubstrate preparations, cultural microscopic examination with inoculation of material on nutrient media, etc.). According to the pharmacological classification, which is based on the chemical origin, the following main groups of antifungal drugs are distinguished:

1) polyene antibiotics – nystatin, levorin, natamycin (pimafucin), amphotericin B (liposomal form – ambizom), amfoglucamine, mycoheptin;

2) azole derivatives:

- imidazoles – ketoconazole (nizoral), miconazole (klion-D, miconazole-Darnitsa, micogel-KMP), oxiconazole (myfungar), econazole (decalin);
- triazoles – fluconazole (diflucan, mycosyst), itraconazole (orungal), thioconazole (throside), sertaconazole (zalain);

3) pyrimidine derivatives – flucytosine (ancotil);

4) allylamines – terbinafine (lamisil);

5) other derivatives – undecylenic acid (undecime, mykoseptin), carboxylic acid (octicyl), chloro-nitrophenols (nitrofungin); non-quaternary ammonium bases (decamine).

Table 15

Spectra of antifungal action of antimycotic agents

Group	Drug	Antifungal spectrum
Polyenes	Nystatin Levorin Amphotericin B	Candida Candida, Trichomonas Candida, Aspergillus, Cryptococcus, Histoplasma, Blastomycetes, Sporotrichum, Mucoromycetes, Coccidiomycetes
Triazoles	Fluconazole Itraconazole	Onichomycetes, Histoplasma Candida, Cryptococcus, Blastomycetes, Aspergillus
Imidazoles	Ketoconazole Miconazole	Candida, Onichomycetes, Histoplasma Candida
Pyrimidine	Flucytosine	Candida, Cryptococcus, Cladosporium
Allylamines	Terbinafine	Candida, Aspergillus, Trichophyton, Blastomycetes, Microsporum, Criptococcus

3.15.1. Polyene antibiotics

Polyene antibiotics disrupt the functions of membranes (almost before they rupture), which occurs when they penetrate into the cell. At the same time, membrane permeability is selectively violated; a cell loses low molecular weight substances, primarily monovalent ions K^+, NH_4^+. All cells of fungi and mammals that contain sterol are sensitive to polyenes. They have a high affinity for estrogen and a significantly lower affinity for cholesterol – a component of human cells. Nystatin and levorin have a fungistatic effect on yeast-like fungi of the genus Candida and protozoa. When taken orally, they are poorly absorbed. For rinsing the mouth, irrigation, mouth baths, gum applications, use an aqueous suspension of levorin (1:500), transbuccal tablets that contain 500.000 IU of antibiotic. Levorin ointment is also used. Nystatin is prescribed orally in tablets – 500.000 IU,

which are effective in case of candidiasis of the digestive canal and locally – in the form of an ointment. Nystatin and levorin are low toxic drugs. They have a local irritant effect, which is an obstacle to their parenteral administration (in which toxicity increases significantly). Adverse reactions are rarely observed – dyspeptic disorders. With increased sensitivity, diarrhea, nausea, vomiting, fever, and dermatitis may occur. Mycoheptin is prescribed orally and externally in dentistry as an ointment for cheilitis, fungal stomatitis, interdigital erosion, lesions of the skin and genitals, visceral mycoses (coccidiomycosis, cryptococcosis, candidiasis, etc.). Side effects: headache, dizziness, dyspeptic symptoms, abdominal pain, nephrotoxicity, allergic reactions.

Amphotericin B has a wide spectrum of action. It is administered i.v. dropwise, due to its high toxicity. Side effects: nephrotoxicity, hypokalemia, hypomagnesemia, neurotoxicity (paresis, tremor, convulsions), anemia, fever, hypotension, allergic reactions, dyspeptic disorders, phlebitis. Amphoglucamine is less toxic than the previous drug, has similar pharmacological properties and indications for use. Most yeast fungi of the genus albicans are sensitive to pimafucin (natamycin) and dermatophytes are less sensitive. It is applied in dentistry for lesions of the oral mucosa in the form of a cream.

Due to the lack of systemic action, natamycin (solutions, suspensions, suppositories) is the drug of choice in the treatment of candida infection in children and pregnant women. When administered, dyspeptic symptoms may occur, with topical application – itching, heartburn. Pimafucin, along with neomycin and hydrocortisone, is a part of the pimafucort ointment, which is prescribed for superficial dermatoses infected with bacteria or fungi.

3.15.2. Azole derivatives

The mechanism of action of these antimycotic agents is based on their ability to suppress sterol synthesis in a fungal cell by blocking enzymes dependent on cytochrome P-450. The latter leads to a change in the lipid composition of the membrane, cessation of its functions, growth retardation and reproduction. With a high concentration in the blood, both fungistatic and fungicidal effects are provided. Ketoconazole (nizoral) is a drug that penetrates well into all tissues and organs, and therefore is

effective in superficial and systemic mycoses. The drug is effective against dermatophytes, mold fungi and the genus Candida. Ketoconazole is used externally and internally for mycoses of the skin, hair, nails, digestive canal, vaginal candidiasis, systemic mycoses, and fungal sepsis. Side effects: dyspeptic disorders, toxic hepatitis (if used for more than 14 days), neurotoxicity, headache, drowsiness, photophobia, gynecomastia, oligospermia, menstrual irregularities, thrombocytopenia, allergic reactions, etc. Clotrimazole (canesten) has a wide spectrum of action against yeast, mold, dermatophytes, trichomonads. The drug is prescribed for dermatomycosis, candidiasis, trichomoniasis, when applied to the skin, introduction to the vagina. For the treatment of candidiasis of the oral mucosa, a 1 % solution or cream is used topically. Side effects: local irritation, edema, heartburn, allergic reactions, itching. Miconazole is administered intravenously in case of systemic mycoses and is applied topically for fungal infections of the skin and mucous membranes. Gel or solution of miconazole is used, which treats the mucous membrane and dentures.

In dentistry, the most commonly used representative of triazole group is fluconazole (diflucan, fusys, medoflucan), which has a wide spectrum of action. It is effective against yeast fungi, cryptococci, microspores, trichophytons, etc. It has high bioavailability when administered orally. In dentistry, it is used for pseudomembranous and atrophic candidiasis of the oral cavity (including those associated with wearing dentures), oropharyngeal candidiasis in AIDS patients. Fluconazole is prescribed orally at a dose 50–400 mg once a day up to 15 days. It is also used to treat systemic mycoses. Side effects: headache, convulsions, leukopenia, thrombocytopenia, dyspepsia, liver damage, rash. Itraconazole (orungal) has a wide spectrum of action, is effective for candidiasis, dermatomycosis. In dentistry, with candidiasis of the mucous membrane, it is used once a day – 100 mg for 15 days for systemic therapy. Side effects: dyspepsia, abdominal pain, hepatitis, headache, peripheral neuropathy, dysmenorrhea, thrombocytopenia, leukopenia, angioedema, etc. It has cardiotoxicity, which limits its use in cardiovascular patients.

3.15.3. Antifungal agents of other groups

Terbinafine (lamisil) is an effective treatment for candidiasis and dermatomycosis. It accumulates in the skin, subcutaneous adipose tissue,

and nail plates. The drug is used internally and externally in the form of a cream. The indication for dentistry is oropharyngeal candidiasis, in which terbinafine is administered orally at a dose 250 mg once a day for 2 weeks. Side effects: dyspeptic symptoms, allergic reactions. Flucytosine (ancotil) affects yeast fungi, causative agents of cryptococcosis, aspergillosis, etc. It is usually prescribed i.v. dropwise, sometimes i.m. combination with amphotericin B. Side effects: toxic myocardial lesions, shortness of breath, apnea, skin allergic reactions, photosensitivity, dry mouth, dyspepsia, exacerbation of peptic ulcer, impaired liver function, acute renal failure, anemia, deafness, dizziness, convulsions, disorientation, psychosis. Griseofulvin has a narrow spectrum of activity on dermatophytes. The drug accumulates in keratin-containing tissues. It is prescribed for lesions of the feet, hands, scalp, hair, nails. Side effects: dizziness, headache, impaired liver function, allergic effects, photosensitivity, leukopenia.

Boric acid solution, iodine, decamine, decamethoxin, miramistin preparations are prescribed topically with various therapeutic forms for the treatment of fungal infections of the mucous membranes, skin, nails.

3.16
ANTIVIRAL AGENTS

Viral diseases account for most of the infectious pathology of humans. The amount of antiviral agents is limited, that depends on the close interaction between the reproduction of viruses and the synthesis processes in the cells of a macroorganism. Before entering the human cell, viruses are a nucleic acid that is surrounded by a protein shell and, therefore, during this period they are insensitive to chemotherapies. Penetrating into the cell, the virus discards the membrane and modifies its biosynthesis. The study of the molecular replication mechanisms of viruses has made it possible to selectively block viral enzymes. Antiviral agents influence at different stages of the development of viruses: adsorption or penetration of viruses into the cell, release of the viral genome, synthesis of proteins, nucleic acids, etc. In the treatment of viral pathology, diagnostic criteria play an important role – histological signs, the presence of virus antigens, antibodies to it, other antiviral agents are classified according to their mechanism of action and selective effect on certain diseases.

I. The mechanism of action distinguishes drugs that inhibit:

- virus adsorption on the cell and/or its penetration into the cell (immunoglobulin);
- release of the viral genome – protein deproteinization (midantan, rimantadine);
- synthesis of "early" viral proteins – enzymes (guanidine);
- synthesis of nucleic acids (zidovudine, acyclovir, idoxuridine, ribavirin, vidarabine, oxolin);
- synthesis of "late" viral proteins (saquinavir);
- "collecting" virions (metisazon);
- broad-spectrum drugs – IFN (laferon, reaferon, betaferon, etc.).

II. By appointment for certain diseases, drugs are distinguished:

- influenza (midantan, rimantadine, oseltamivir, oxolin, IFN, arbidol, adapromine, deutiforin, amixin, etc.);

- herpetic infections (acyclovir, valaciclovir, penciclovir, idoxuridine, vidarabine, bonaphton, IFN, proteflazide);
- AIDS (azidothymidine, didanosine, phosphonoformate, IFN).

3.16.1. Drugs prescribed to patients with influenza

Among this group of drugs, the most interesting are blockers of ionic M_2 channels (adamantane derivatives) and viral neuroaminidase blockers (oseltamivir, zanamivir). The blockade of the M_2 channel by midantan leads to the termination of the virus entry into the cell and the release of ribonucleotide. The midantan derivative, rimantadine, which inhibits the release of influenza virus RNA from protein and penetration into the cell nucleus, turned out to be more effective. A known analogue of rimantadine is deuteriforin. Indications for adamantane derivatives are the treatment and prevention of influenza A and respiratory infections. Close to the properties of rimantadine is the derivative of midantane – adaptromine, which has a wider spectrum of activity (active against influenza A and B virus).

The Russian drug arbidol (the Ukrainian analogue imustat) has found widespread use in the treatment of influenza and acute respiratory viral infections, which significantly enhances the humoral and cellular responses of the immune system, the phagocytic activity of macrophages, and has a direct antiviral effect by preventing the fusion of the lipid membrane of the virus with the cytoplasmic membranes externally and endosomes inside the cell. The therapeutic use of arbidol is from 50 to 200 mg 3–4 times a day. A drug is also prescribed for the purpose of prevention to those who are in contact with the patient. Oseltamivir is a highly effective drug in the treatment of influenza A and B. A blockade with a neuroaminidase drug leads to a cessation of the spread of the virus in the body due to inhibition of the ability of the virus to enter the cell and exit the virions from it. Recently, another representative of this group is also used – zanamivir (relenza). Oxolin (ointment) has virucidal and interferonogenic properties. It is used to lubricate the nasal mucosa in order to prevent flu and local treatment of viral diseases of the mucous membrane in the form of multiple applications. Undesirable effects of rimantadine, deutiforin, and adaptromin can occur in the form of allergic skin reactions, nausea, dizziness, ataxia, tongue disturbances, irritability, hallucinations, psychoses,

decreased blood pressure, and urinary retention. Oseltamivir can cause pain (headache, abdominal pain, sore throat), dizziness, insomnia, general weakness, vomiting, diarrhea, cough, and provoke bronchospasm in patients with bronchial asthma. Oxolinic ointment can cause burning sensation, sneezing, increased mucus separation.

For the prevention and treatment of many viral infections, interferons are widely used that do not have the disadvantages of chemotherapeutic agents, have a wide spectrum of action, and do not cause the development of virus resistance. IFN inhibit the reproduction of viruses at the stage of synthesis of virus-specific proteins, regulate immune responses, inhibit the development of malignant cells, etc. Three types of interferons are known: α-IFN produced by B lymphocytes, β-IFN produced by fibroblasts, γ-IFN synthesized by T lymphocytes. By origin, natural human leukocyte (1st generation) and recombinant (2nd generation) are distinguished. Viruses induce the synthesis of α- and γ-interferon. Under the influence of interferons, viral RNAs are cleaved in the cell, which interferes with the synthesis of viral proteins. Both DNA and RNA-containing viruses are sensitive to interferons. There are known different types of interferon preparations. The antiviral effect is more pronounced in α-IFN, antitumor – in β-IFN, immunostimulating – in γ-IFN. The following drugs are used at clinic: alpha-2A-IFN (reaferon, roferon), alpha-2B-IFN (intron-A, viferon), alpha-2C-IFN (berofor, egiferon), β-IFN (betaseron, fron), gamma IFN (gammaferon, immunoferon). In particular, recombinant preparations α_2-IFN – α-2α – roferon, α-2β – laferon, laferobion, etc. have been developed. Recombinant interferons are highly effective, more stable than natural ones, offer improved pharmacokinetics. In dentistry, viferon (contains human recombinant IFN (α-2)) is prescribed in the treatment of herpetic lesions of the mucous membranes in the form of an ointment. For the treatment of viral stomatitis, gingivitis, herpes zoster of the mucous membrane, applications of an aqueous solution or 50 % ointment of human leukocyte IFN are used. This drug is obtained from donor B lymphocytes (in 1 mg – 1000 IU), used only locally. Freshly prepared solution can be administered intranasally. Interferon is prescribed for influenza, CNS viral lesions, viral hepatitis B and C, herpetic lesions of the skin, eyes, genitals, some malignant neoplasms, etc. It can be used in combination with acyclovir and other drugs.

With parenteral administration of IFN, side effects can occur: fever, hematopoiesis, disorders of the central nervous system in the form of lethargy, fatigue, headache, myalgia, anaphylaxis, decreased blood pressure, arrhythmia, tachycardia, ventricular extrasystole, paresis, paralysis, loss of appetite, vomiting. Large doses of IFN can cause collagenosis and necrotic changes in the liver. Undesirable effects when applied topically.

The modern direction of prevention and treatment of influenza is the use of interferonogenesis inducers. These drugs are able to cause IFN synthesis, and also have antiviral, immunomodulatory and antitumor effects. All viruses, bacteria, rickettsiae, protozoa, natural double-stranded RNA, vitamin preparations, and others possess interferogenic effects. Among low-molecular substances, interferonogenic effects were found in amixin, neovir, megacin, mefenamic acid, amizon, arbidol, groprinosin, cycloferon, kagocel, proteflazide, etc. IFN inducers are used in the complex treatment of severe infections that are caused by the influenza virus, parainfluenza, herpes, encephalitis, HIV, hepatitis. Side effects of these drugs are rare. They combine well with ABD and other traditional treatments for viral diseases. Amixin is a synthetic inducer of IFN aromatic series. The drug stimulates bone marrow stem cells, enhances antibody production, reduces the degree of immunosuppression, and corrects the ratio of suppressors and helpers. In some cases, it can cause dyspeptic symptoms. The active inducer of IFN of high molecular weight is larifan, which is a double-stranded RNA of the phage. Sometimes it causes an increase in temperature and a drop in blood pressure. Cycloferon is a unique analogue of the plant alkaloid Citrus grandis, which has a prolonged antiviral, anti-inflammatory and immunomodulating effect and has the ability to cause the formation of α-, β-, γ-IFN. The drug has low toxicity, has no side effects. Kagocel is a high molecular weight aromatic compound that has antiviral activity in a wide range of pathogens. It also has immunomodulatory properties. Side effects are not pronounced. The therapeutic effect is observed with flu, hepatitis, and other diseases. Neovir is a synthetic IFN super-inductor that activates bone marrow stem cells, eliminates the imbalance in lymphocyte subpopulations, and activates T-cell immunity. In some patients, it can cause fever and joint aches.

3.16.2. Drugs used for herpetic infections

Antiviral agents are divided into groups:

- nucleoside analogues and compounds of a different structure that block the replication of viruses;
- direct virulocides;
- interferon and its inducers.

The first nucleoside analogue was idoxuridine, which in the process of metabolism turns into triphosphate, which contributes to the formation of defective populations of virions. The selectivity of the action of idoxuridine is low, and therefore, with herpetic keratitis, it is used only locally. The most important for dental practice among nucleoside analogues is acyclovir (herpevir, zovirax) – highly active against herpes simplex virus type 1 and 2, as well as herpes zoster virus, cytomegalovirus. Acyclovir suppresses viral DNA polymerase, is used instead of deoxyguanosine for viral DNA. The drug is prescribed for the treatment of gingivitis, primary and recurrent viral stomatitis, and herpes simplex of the skin. Depending on the nature of the course of the disease, acyclovir can be prescribed enterally, parenterally and topically. The drug is also used in the treatment of severe forms of genital herpes, recurrent infections caused by the herpes zoster virus, etc. Valacyclovir (valtrex) has a greater bioavailability compared to the latter. With cytomegalovirus infection, ganciclovir, foscarnet, famciclovir are effective. The new drug penciclovir (1 % cream) has an effect on herpes simplex with localization on the lips at the vesicle stage, helps to reduce the healing time (up to 4 days). Phosphonoformate (foscarnet) has antiviral activity against human herpes simplex viruses, cytomegalovirus, influenza A, hepatitis B. It is widely used for cytomegalovirus infections in AIDS patients, skin infections and lesions of the mucous membranes caused by human herpes virus. For herpetic encephalitis, keratitis and cytomegalovirus infections, vidarabine is used, which inhibits the replication of acyclovir-resistant herpes virus strains. In the treatment of herpetic encephalitis and other herpetic diseases, cytarabine is used, which stimulates the formation of a powerful inhibitor of the virus specific DNA polymerase. Ribavirin (ribamidil) has a wide spectrum of action; it inhibits the synthesis of viral nucleic acids in the cells infected with the virus. A significant therapeutic effect was obtained when using the drug during the flu and herpes.

Direct virulocides – gossypol, riodoxol, florenal, tebrophen adversely affect viruses outside the cells, where they are located for a limited time. They are applied topically for viral diseases of the skin, mucous membranes and cornea. The synthetic drug bonaphton and alpisarin, flacoside and helepin obtained from plants are used internally and locally for herpetic diseases of the skin, mucous membranes and cornea. Bonaphton acts on strains that are insensitive to nucleoside analogs and has an immunostimulating effect. Helepin may be effective for herpetic encephalitis. Metisazone is indicated for the prevention of smallpox (even when vaccination is ineffective), post-vaccination complications, and herpes. Side effects are associated with nausea and vomiting.

Acyclovir and valaciclovir can cause headaches, neurological disorders, lethargy, nausea, vomiting, diarrhea, fever, intestinal colic, skin rash, inhibition of blood formation and immunity, allergic lesions, irritation of the skin and mucous membranes. With i.v. administration, excitement, convulsions, psychosis, phlebitis, coma are sometimes observed. Ganciclovir can cause mutagenic, teratogenic and carcinogenic effects, reproductive disorders in men and women. Side effect of phosphonoformate can be manifested by inhibition of hematopoiesis, immunosuppression, nephrotoxicity (disappears after discontinuation of the drug). With an overdose of vidarabine, neurotoxicity may be observed. Cytarabine has a negative effect on the digestive tract, liver, kidneys, and blood cells. Ribavirin can cause bronchospasm, bradycardia, and respiratory arrest during inhalation, rash, conjunctivitis, nausea, abdominal pain, anemia. Bonaphton when administered orally can cause headache and diarrhea. Metisazon in some cases causes dizziness, nausea, and vomiting. To prevent the cytostatic effect, a blood test is necessary every 2 days, and if severe neutropenia and thrombocytopenia occur, the treatment is urgently stopped. It is also advisable to use drugs that stimulate hematopoiesis (for example, molgramostin).

In the complex treatment of herpetic infections, IFN (viferon, reaferon, fron, etc.), IFN inducers (cycloferon, proteflazide, poludan) and immunostimulating agents (isoprinosine, licopid, sodium nucleinate) are used. Cycloferon is a unique analogue of the plant alkaloid Citrus grandis, which has a prolonged antiviral, anti-inflammatory and immunomodulating effect, with the ability to cause the formation of α-, β-, γ-IFN. The drug is

well tolerated by patients, without causing serious complications. Indications for the use of cycloferon are AIDS, hepatitis, herpes and cytomegalovirus infection, chlamydia, rheumatoid arthritis, neuroviral infections, fungal diseases, secondary immunodeficiency states of various etiologies, etc. The drug has low toxicity, has no side effects, and goes well with traditional therapeutic agents, characterized by a prolonged immunomodulatory effect. Proteflazide is a liquid alcoholic extract obtained from wild cereal plants Deschampsia caespitosa L. and Calamagrostis epigeios L. The main biologically active substances of proteflazide are flavonoids like quercetin. The specific properties of the drug are determined by the induction of the synthesis of endogenous α-, γ-IFN, antiviral apoptosis modulating and antioxidant effects. The drug is used in the treatment and prevention of herpetic pathology. Among high molecular weight IFN inducers, poludan is used, which has a protective effect in case of herpetic and arbovirus infections. No side effects detected.

3.16.3. Drugs prescribed to AIDS patients

Drugs that are prescribed for AIDS are divided by the mechanism of action into 2 groups: 1) reverse transcription inhibitors – azidothymidine (zidovudine, retrovir), stavudine, didanosine, zalcitabine; 2) protease inhibitors – saquinavir, indinavir, ritonavir.

Acquired immunodeficiency syndrome caused by HIV has a complex genesis and various clinical manifestations, requires retroviral, immunomodulating, symptomatic therapy, etc. Azidothymidine, which is an antagonist of thymidine, is considered the first specific drug. It blocks reverse transcriptase and HIV DNA polymerase. The drug improves the immunological status of the patient, increases the number of T lymphocytes, prevents and facilitates the course of secondary infectious processes. Lamivudine, didanosine, zalcitabine are similar in action to azidothymidine. Protease inhibitors (saquinavir, indinavir) disrupt the cleavage of the polypeptide chain of the structural protein, that is, disrupt the formation of the structural elements of the viral capsid. Foscarnet sodium inhibits the DNA polymerase of viruses. The drug is prescribed for cytomegalovirus retinitis in patients with AIDS. For more effective action on HIV, specially developed antiviral drugs (combined) are used. In the complex treatment of AIDS patients, foscarnet, cycloferon, etc. are used.

3.17
IMMUNOTROPIC AGENTS

Immunotropic drugs inhibit or stimulate the body's immune response. These drugs share one common property – the presence of certain targets (immunological point of action) in the immune system. Drugs that increase the severity of the body's immune response are called immunostimulants. Immunosuppressants are used rarely to suppress the immune response. Immunity is a system of protecting the body from substances that carry signs of genetically foreign information. A specific immune system is immunocompetent cells (T and B lymphocytes). Non-specific immune systems include micro- and macrophages, complement system, lysozyme, IFN, etc. Against the background of a decrease in the immune response, superinfection (viral, bacterial, fungal) can develop, and tumors can occur. In medical practice, conditions are often observed that require the prescription of drugs that stimulate the body's immune system. This can be infectious processes with a torpid chronic course, postoperative complications, radiation injuries, pretumor and tumor processes, treatment with corticosteroids, etc. The greatest effectiveness from the prescription of IST should be expected with secondary or acquired immunodeficiencies, which manifest themselves as an infectious syndrome in 80–90 % of cases. The use of IST drugs simultaneously with ABD in purulent-inflammatory processes (in the early stages after surgery, etc.) and with proven secondary immune deficiency causes a double blow to the pathogen. In this case, ABD inhibit the functional activity of the pathogen and increase its sensitivity to the killer effect of the phagocyte, and IST accelerate their elimination. The use of drugs should be based on a preliminary examination of the immune status of a particular patient. It is necessary to carry out the selection of IST carefully, taking into account contraindications for administration and side effects.

In dental practice, IST are widely used in deseases accompanied by changes in the body's immune system. In surgical practice, indications for

the use of IST can be osteomyelitis, phlegmon, carbunculosis, in therapeutic practice – chronic generalized periodontitis, chronic recurrent aphthous stomatitis, acute radiation and herpetic stomatitis, exfoliative precancerous cheilitis, lichen planus, etc.). It is also advisable to prescribe IST in case of delayed tissue regeneration in the MFA, including mucous membrane of the oral cavity, with burns, radiation injuries, and in the postoperative period. There are two main methods of immunotherapy and immunoprophylaxis: specific (vaccines and immune sera) and non-specific, in which immunomodulators are used. Taking into account the purpose of the appointment, the following immunomodulating agents are distinguished:

- for replacement therapy (vaccines, sera, gammaglobulins);
- immunostimulants of various origin;
- immunosuppressants (glucocorticoids, cytostatics).

Means of substitution therapy are used for the prevention of infectious diseases, IST – for their treatment (along with ABD), ISU – for prevention of tissue rejection during organ transplantation, for the treatment of allergic, autoimmune diseases. Many IST distinguished by origin are used:

1) microbial origin (prodigiosin, pyrogenal, imudon, ribomunyl, bronchomunal, sodium nucleinate, preparations of purple coneflower, etc.);

2) animal origin:

- thymus preparations (tactivin, thymalin, thymoptin, thymactid, vilosen);
- preparations of bone marrow origin (B-activin, myelopid, etc.);

3) recombinant IST (filgrastim, molgramostin, neupogen, leukomax, reaferon, viferon, etc.);

4) synthetic and semi-synthetic IST (levamisole, diuciphone, polyoxidonium, immunofan, thymogen, licopid);

5) other drugs – cycloferon, immunomax.

The use of IST in infectious diseases is based on the following basic principles:

1) early prescription of IST – from the first day of the use of a chemotherapeutic etiotropic agent;

2) use of IST, acting on the phagocytic link of immunity, in patients with impaired immune status, i.e. based on the clinical picture;

3) inclusion of IST in the complex treatment of postoperative infectious complications;

4) use of IST in case of incomplete recovery after an acute infectious disease;

5) in order to use IST effectively and safely, it is advisable to conduct immunological monitoring.

3.17.1. Immunostimulants of microbial origin

Prodigiosin and pyrogenal belong to lipopolysaccharides of microbial origin, which promote the formation of antibodies, activate T lymphocytes, stimulate the phagocytic activity of macrophages, increase the content of endogenous IFN, etc. This group does not find application in connection with the presence of more modern drugs on the pharmaceutical market. Imudon is a lyophilized lysate of a number of microorganisms that are etiologically responsible for a number of lesions of the oral cavity: Lactobacillus acidophius, L. lactis, S. aureus, S. pyogenes, S. faecalis, S. faecium, Klebsiella pneumoniae, Fusiformis ftisiformis and Candida albicans, etc. Imudon has proven itself in dental practice with the resumption of local immunity, normalization of the microecology of the oral cavity, antirelapse effect. Under the influence of the drug, there is a sharp increase in the phagocytic activity of neutrophils and macrophages, an increase in the concentration of IgA in saliva, etc. The high clinical efficacy of mmudon in the treatment of diseases of the mucous membrane, periodontosis, gingivitis, aphthous stomatitis and glossitis, candidiasis is proved. Under the influence of the drug, there is an increase in immunity in all areas of the mucous membranes (the phenomenon of "mucosal solidarity"). Imudon is used in acute conditions – 6–8 tablets per day with an average duration of treatment of 10 days. In chronic processes, prolonged treatment is possible. Allergic phenomena and dyspepsia sometimes occur.

Ribomunyl contains bacterial ribosomes of 4 microorganisms (Klebsiella, pneumococci, hemophilic bacilli, pyogenic group A streptococcus and proteoglycans). It provides both specific immune defense of a macroorganism and stimulation of the synthesis of IFN, immunoglobulin A, increased activity of neutrophils and macrophages, etc. Bronchomunal is also a lyophilized bacterial lysate that enhances humoral and cellular immunity. Sometimes with the use of these drugs dyspeptic phenomena and fever are observed. Sodium nucleate represents sodium salt of a nucleic acid that is obtained from yeast. The drug stimulates leukopoiesis, helps

to accelerate the regeneration processes, increases phagocytosis, etc. In dentistry, it is used in the treatment of diseases of the oral mucosa and periodontal tissues, especially against the background of leukopenia and agranulocytosis. The drug is used in the complex treatment of a number of chronic infections, etc.

3.17.2. Immunostimulants of animal origin

Thymic factors (tactivin, thymalin, thymoptin, thymactid, vilosen) are complexes of polypeptide fractions isolated from the thymus gland of cattle. They mimic the effects of thymus hormones on the differentiation and stimulation of T lymphocytes, acting similarly to thymopoietin, enhance phagocytosis, etc. These drugs are widely used in chronic infections, surgical pathology, oncopathology, viral infections, etc. In dentistry, thymalin is prescribed for generalized periodontitis, periodontal disease, diseases of the oral mucosa, etc. It is prescribed as an immunomodulator in acute and chronic purulent infection, burn disease, intensive antibiotic therapy. Tactivin is used for infectious diseases, lymphogranulomatosis, tuberculosis, psoriasis and in the pre- and postoperative period.

3.17.3. Recombinant immunostimulants

Filgrastim and molgramostin is a human granulocyte colony stimulating factor obtained by the genetic engineering method. The drugs accelerate the formation of neutrophilic white blood cells, the growth and maturation of T lymphocytes, monocytes. They are used for the treatment of severe infections in patients with a decrease in the number of neutrophils, in combination with ABD, for the primary prevention of neutropenia after chemotherapy, etc. A promising direction in immunotherapy is the use of recombinant cytokines. Betaleukin and IFN are already being used. Among natural IFN, leukinferon is used (also in combination with tactivin (before surgery), sandoglobulin (after surgery).

3.17.4. Synthetic and semi-synthetic immunostimulants

Levamisole (decaris) is an imidazole derivative. The drug stimulates cell-mediated immune responses, potentiates the distribution and differentiation of T lymphocytes, increases the production of antibodies, and promotes the activation of phagocytosis, interferonogenesis. In dental

practice, the drug is prescribed orally for patients with reduced immunity in chronic recurrent infections in the MFA and on the mucous membrane of the oral cavity. With damage to the oral mucosa, levamisole can be administered topically, in the form of 0.01–0.05 % aqueous solution, oil emulsion or paste. Levamisole is used in primary and secondary immunodeficiency processes, rheumatoid arthritis, systemic lupus erythematosus, helminthic invasion, herpetic infection, etc. During general treatment with levamisole, it is necessary to monitor the status of peripheral blood, because leukopenia and agranulocytosis may develop. In connection with the latter it has a limited application. There is also a headache, fever, dyspeptic disorders, sleep disturbances, allergic skin manifestations.

Polyoxidonium has a wide range of immunopharmacological effects – stimulates the activity of three major leukocyte populations (mobile tissue macrophages, circulating blood phagocytes and sedentary phagocytes of the reticulo-endothelial system). It increases the functional activity of T and B lymphocytes, enhances their cooperative interactions, and increases the formation of antibodies. The drug restores the normal course of immune responses during aging, malignant tumors, exposure to ionizing radiation, GCS therapy, generalized surgical infections, and chemotherapeutics.

Licopid is a dosage form of a semisynthetic glucoprotein. The drug activates macrophages, increases the activity of lysosomal enzymes, absorption and killing of microbes, cytotoxic properties, expression of histocompatibility antigens, and synthesis of cytokines. In dental practice, licopid is successfully used for the prevention of purulent-septic complications in surgery, treatment of purulent-inflammatory processes of the skin and soft tissues, diseases of the mucous membrane of viral and fungal etiology. It is used in the treatment of chronic non-specific lung diseases, pulmonary tuberculosis, herpetic keratitis and dermatoses, cytomegalovirus infection. The chemical structure of immunofan is a hexapeptide that stimulates phagocytic immunity and the functional activity of neutrophils and macrophages. The drug is characterized by immunoregulatory, detoxifying, hepatoprotective effects. It is used for the prevention and treatment of immunodeficiency diseases in other areas of medicine.

Pyramidine derivatives – methyluracil, pentoxyl, sodium nucleinate, orotic acid activate the mechanisms of nonspecific and specific immune reactivity. They increase the synthesis and concentration of nucleic acids,

structural proteins, components of the complement system, lysozyme, IFN, immunoglobulins, stimulate the phagocytic activity of macro- and microphages. In dental practice, methyluracil is applied topically (applications, lubricants) to stimulate healing processes with necrotizing ulcerative stomatitis, generalized periodontitis in the form of instillations on the oral mucosa or in the gingival pockets. The drug is also introduced into the composition of pastes that contain antimicrobial agents. Sometimes 5–10 % methyluracil ointment is used. Side effects, as a rule, are not observed. Sometimes the toxic effect is detected by pentoxyl. Methyluracil positively affects the reparative tissue regeneration in case of burn and radiation injuries, leukopenia, hepatitis, colitis, gastric ulcer, chronic gastritis with secretory insufficiency, etc.

3.17.5. Interferons

The main producers of "own" endogenous IFN are immunocompetent cells – leukocytes, macrophages, fibroblasts, as well as epithelial cells. IFN (α, γ) – cytokines that regulate the differentiation, growth and reproduction of cells, which allows them to be attributed to the most important homeostatic agents and factors of nonspecific resistance of the body. IFN protect the body from infection with viruses, bacteria and protozoa, inhibit the growth of malignant cells, potentiate lymphotoxin.

Active production of IFN in the body is the basis of resistance to diseases and the rapid localization of the focus of infection. The decrease in the level of IFN production is due to a number of reasons: aggressive antibiotic and hormone therapy, surgery, alcoholism and drug addiction, burn disease, chronic infections, neoplasms, radiation, stress and excessive physical exertion. Antiviral, antibacterial, antimycotic and anti-chlamydial types of IFN actions are carried out through the cellular nucleic acid synthesis system using a number of enzymes and inhibitors, which leads to the degradation of foreign genetic information. IFN stimulate phagocytosis, activity of natural killer cells, and expression of antigens. On the other hand, IFN can suppress the formation of antibodies, development of AS, inflammation, delayed-type hypersensitivity, the complement bonding reaction, which makes IFN a valid IM, and the IFN system is the most important in the regulation of cellular homeostasis. γ-IFN has a more pronounced effect on immune cells.

Promising and highly active immunotropics are IFN preparations (reaferon, laferon, gammaferon, leukinferon). Reaferon is a recombinant (α-IFN) that is produced by a bacterial strain of pseudomonas. The drug is identical to human leukocyte α-IFN and has antiviral, immunomodulating and antitumor activity. Reaferon is prescribed locally and i.m. for viral hepatitis, conjunctivitis, keratitis, uveitis, leukemia, etc. Adverse effects: fever, allergic skin reactions, leukemia and thrombocytopenia.

3.17.6. Other drugs

Immunomax is an acidic peptidoglycan of plant origin. Enhances immune defense against viral and bacterial infections. It activates the following units of the immune system: NK cells, tissue macrophages, circulating monocytes, neutrophilic granulocytes, and the formation of antibodies. Immunomax enhances protection against infections caused by human papillomaviruses, herpes simplex or Escherichia coli, salmonella, staphylococcus, chlamydia, mycoplasma. The effect of the drug is manifested with the introduction of immunomax in various ways: intramuscularly, intravenously, intraperitoneally, orally. Diuciphone is a derivative of diaminodiphenyl sulfone and methyluracil, which has a pronounced stimulating effect on cellular immunity. They are used in the complex therapy of dermatoses (psoriasis, scleroderma, etc.), rheumatoid arthritis, tuberculosis, purulent-surgical diseases. Erbisol – a drug obtained from embryonic tissue of cattle. Its main immunomodulating effect is manifested due to the action on the macrophage link, which is responsible for the repair of damaged cells, as well as due to natural killer cells. In case of violations of the immunological status, the drug contributes to its normalization for the most part by activation of T helpers and T-killers. Sandoglobulin is a multivalent human immunoglobulin. The drug is used as a replacement therapy for hypoimmunoglobulinemia, as well as an immunomodulating agent. In patients with immunodeficiency diseases, sandoglobulin replenishes the amount of IgG class antibodies, thereby reducing the risk of infection. Subject to dosage recommendations, severe adverse reactions to sandoglobulin are rare. Herbal preparations (immunal, Eleutherococcus tincture, Ginseng tincture, Rhodiola rosea extract) have general tonic (adaptogenic) and anti-stress effects. They are able to side-increase the lysozyme activity of blood serum, stimulate the complement system, and contribute to the

production of antibodies. These drugs have found application as a means of preventing influenza and other viral infections during epidemics, as well as for adapting to harsh living conditions and stress.

3.18
BIOMEDICATIONS

Biological products are represented by biological substances that are used in medical practice for prevention, treatment and diagnostics of infectious and inflammatory processes. These include vaccines, protective antigens, enzymes, sera, gammaglobulins, native and disinfected toxins, bacterial waste products or suspensions of living and dead bacteria. This section discusses drugs that are used to resume physiological human microbiocenosis, have a positive effect on the physiological functions and biochemical reactions of the body by optimizing its microecological status, namely probiotics, prebiotics, synbiotics. Normalization of the microbial ecosphere of patients with these drugs significantly increases the effectiveness of treatment for infectious, oncological, gastroenterological, allergological, dermatological and gynecological pathologies. These groups of biological products have a definite perspective for modern dental practice. Three groups of drugs are used to correct intestinal microflora: probiotics, prebiotics and synbiotics.

3.18.1. Probiotics

The term "probiotics" was proposed by Richard Parker in 1974 to refer to a number of drugs containing live representatives of the normal microflora of the human intestine, which contribute to the normalization of its basic functions, general healing of the body and protection of infectious diseases. The human microflora ("microbial film") in terms of the number of microbial cells (1014–1015) exceeds the number of eukaryotic cells by 1–2 orders of magnitude. This invisible additional organ weighing 3–4 kg and with area of 400 m^2 contains more than 500 species of microorganisms (representatives of 17 families, 45 genera) and is a complex structure of a layer of mucus, immunoglobulins A, colonies of synbiotic microflora, etc. Up to 60 % of microbial biomass is concentrated in the ecosystem of the gut, in the oropharynx – 15–16 %, on the skin –15–20 %, in the vagi-

nal biotope – 9–10 %. Most of the bacteria that inhabit the intestines are classified as opportunistic. Indigenous (main, resident) microflora adds up to 95–99 % of the total microflora. It is represented by the most characteristic human symbiont – bifidobacteria, lactobacilli and propionic acid bacteria. Optional (additional) microflora adds up to 5 %. It mainly includes facultative aerobic bacteria of the species E. coli and S. faecium, which can cause severe infectious diseases under adverse conditions. The conditional pathogens of the genera Staphylococcus, Clostridium, Citrobacter, Enterobacter, Proteus, Klebsiella, Pseudomonas, Candida, etc. belong to the transient (residual) microflora.

The most common probiotics include the following bacteria: Bifidobacterium, Lactobacillus, Escherichia, Lactococcus, Eposterossus, Aerossossus or nonpathogenic spore-forming microorganisms and saccharomycetes. The physiological effects of probiotics include: a) protective – regulation of the composition of microflora, antimicrobial activity, increased barrier function; b) trophic – participation in the metabolism of dietary fiber, synthesis of cholesterol, bile acids, vitamins B and K; c) immunomodulatory – normalization of the number of β-lymphocytes, stimulation of the synthesis of immunoglobulins and production of cytokines, a change in the ratio of helpers and suppressors, stimulation of humoral immunity; d) detoxification – binding and destruction of toxins that enter the intestines with food, regulation of the detoxification function of the liver, inhibition of the growth of microorganisms that produce toxins; d) prevention of carcinogenesis and tumor growth, a change in allergic reactivity.

The main requirements for probiotics are associated with the presence of a sufficient number of live and active bacteria in the preparation that have antagonistic properties for pathogenic microbes and are resistant to antibiotics, acid and bile, and are safe for human health.

In recent years, biological products have become widely used not only in general medicine, but also in dental practice. A local method of daily use of bifidumbacterin forte in patients with phlegmon of the MFA is studied. In this case, faster wound cleaning, normalization of immunological, clinical and laboratory parameters are revealed. When prescribing probiotic preparations, there is a warning of postoperative complications in traumatic jaw fractures, as well as a reduction in the rehabilitation time

of these patients. In surgical practice, probiotics are also used in preparation for surgical interventions in order to reduce the risk of postoperative complications. In therapeutic dentistry, biologics are used to increase the effectiveness of treatment of periodontal tissue diseases. When using bifidumbacterin and acilact in the complex therapy of this pathology, the best result is achieved in patients with chronic catarrhal gingivitis and mild chronic generalized periodontitis. With pronounced destructive changes and the depth of the periodontal pocket of more than 6 mm, clinical indicators do not improve. In the complex treatment of chronic recurrent candidal stomatitis in combination with a fungal infection of the intestine, the use of pimafucin with bifiform was studied. Patients have a positive clinical effect and the absence of relapse of the disease after 10–12 months. An increase in efficiency occurs when probiotics are included in the treatment complex of lichen planus. Preparations bifilis and lactusan in combination with an immunomodulator (sodium nucleate) improve the results of treatment of various clinical forms of this disease.

A promising drug for the correction of microecological disorders and resumption of immunological resistance in the complex treatment of infectious-inflammatory diseases is probiotic of a new generation of synbiotic effects – vitaflor. A distinctive feature of the drug is the presence of Lactobacillus acidophilus synbiotic bioculture (strains D), which is characterized by an extended spectrum and a high level of antagonistic activity against clinical isolates of Gr(-) and Gr(+) bacteria and Candida yeast, expressed adhesive properties, and a high content of viable cells. To assess the effectiveness of the use of vitaflor in dental practice, we selected chronic periodontitis and alveolitis, which developed after tooth extraction. For the treatment of alveolitis, dry lyophilized powder is introduced into the alveolar socket, and, accordingly, for the treatment of periodontitis, a liquid adapted form of the drug is introduced into the root canal. In the complex treatment of patients with odontogenic sinusitis, a positive result was obtained when using the sinus rinses with lizodent probiotic preparation, lactovit-forte probiotic was prescribed enterally. The most developed method for the treatment of dysbiosis is the use of probiotics in dental practice after completing a course of antibacterial therapy. Preparations bifidumbacterin forte, bificol, linex, acilact are prescribed in

Table 16

Classification of probiotic preparations

Group	Original name
Monocomponent	Bifidumbacterin, probifor, lactobacterin, bactisporin, sporobacterin, gastropharm, bactisubtil, enterol, flonivin BS, colibacterin, biovestin
Multicomponent	Bifikol, biovestin-lacto, linex, lacidofil, acipol, bifiform, acilact, biosporin, lactiv-ratiopharm, lactovit-forte, lacium
Based on microorganisms atypical for microflora	Bactisubtil, biosporin, bion-3, enterol-250, A-bacterin

the usual dosage for 1–2 months. Then the prebiotic hylak forte is used according to the scheme for 1 month.

Treatment of intestinal dysbiosis should be comprehensive and aimed at certain links in its formation: improving digestion, resuming intestinal microbiocenosis, stimulating the body's reactivity. Improving digestion is facilitated by diet, the use of regulators of motility and absorption, antispasmodic, antidiarrheal, choleretic drugs, enzymes, etc. Selective decontamination of pathogenic microflora is carried out using intestinal antiseptics, bacteriophages. It is advisable to use enterosorbents (polyphepan, smecta, etc.). In case of III–IV degrees of dysbiosis, ABD are used (nitroxoline, furazolidone, nifuroxazide, ciprofloxacin, metronidazole, etc.). To increase the reactivity, eleutherococcus, ginseng, echinacea, sodium nucleinate, antioxidants, immunotropic drugs are prescribed. The course of treatment averages 4 weeks.

Bacterial biological products are prescribed without prior antibiotic therapy or after it. Enterol-250, enterogermina, bificol, bifiform, linex, hylak forte, lactuvit, etc. have proven themselves well. To increase the reactivity of the body, immunotropic drugs are used (licopid, derinat, immunofan, tactivin, etc.). These drugs are characterized by beneficial effects in stressful situations, irregular or poor-quality nutrition, and lack of benign drinking water, with diarrhea, flatulence, and climate change during travel. The effectiveness and reproducibility of the therapeutic effect of probiotics is not yet sufficiently confirmed. The widespread opinion is that when

ingested Lastobasillus, Bifidobacterium, bacterial spores of the species Vasillus, intestinal microflora disturbed by the action of ABD are restored. However, it is known that it is possible to cause long-term qualitative and quantitative changes in the intestinal microflora of an adult immunocompetent person only for a short time, and soon the initial composition will return.

The problems of biotherapy are the lack of effectiveness of many probiotics, as well as the safety of their use. For example, it is known that inactivation of the active substance of a drug can occur under the influence of acid, bile and enzymatic barriers of the gastrointestinal tract. Colonization of probiotic microorganisms in the colon may be interfered by opportunistic and resident microflora, the local immune system. It was found that the probiotic prescribed during antibiotic therapy to prevent dysbiosis may be incompatible with ABD due to the presence of antibiotic resistance. In patients with severe immunodeficiencies, the probiotic strain sometimes becomes an infectious agent or causes bacteremia. In such cases, antibiotic therapy using modern drugs (imipenem, piperacillin/tazobactam or clindamycin) is indicated. However, mortality in sepsis caused by lactobacilli reaches 39 %. A significant part of probiotics (Lactobacilli, Enterococci, Bacilli certus i Bifidobacteria)) are sensitive to such commonly used antibiotics as amoxicillin, doxycycline, FQ and CS. The prescription of drugs containing the latest microorganisms, simultaneously with antibiotic therapy is accompanied by their inactivation. The long-term consequences of probiotic therapy, which until recently had not been given attention, is the spread of antibiotic resistance genes among pathogenic microorganisms. When multiresistant probiotics are used simultaneously with antibiotics to prevent side effects from the gastrointestinal tract, there is a risk of transmission of plasmid resistance to pathogens. For example, many E. faecium strains have plasmids encoding resistance to various ABD, including vancomycin, which poses a risk in the treatment of drug-dependent diseases.

Along with acquired, there is also a fundamentally different type of bacterial antibiotic resistance – true (natural or primary). It limits the spectrum of bacterial activity of certain ABD. This resistance is chromosome-mediated, and without circumstances it can be transmitted to other bacteria. For example, a significant part of fungi, in particular yeast,

has a natural polyantibiotic resistance. In this aspect, the so-called bioenteroseptics, the microorganisms of which belong to the indigenous intestinal flora and are eliminated from the intestine on their own, are safe for use against antibiotic therapy. Among such preparations, yeast fungi Sassharomuses boulardii (Enterol-250) and saprophytic spore-forming anaerobes (subalin, enterogermina) were registered in Ukraine. The genetic difference between yeast prevents the possibility of the transition of a plasmid with an antibiotic resistance factor to the causative agents of acute intestinal infections. In addition, S. boulardii have a significant antagonistic effect on the pathogenic flora, increase immune defense and do not penetrate into the systemic circulation. After discontinuation of treatment, the intestines are released from them after 3–5 days.

3.18.2. Prebiotics

Prebiotics are products of microbial and non-microbial origin that contribute to the restoration of the biological environment in the intestine, necessary for the existence of normal microflora and inhibit the growth of pathogenic bacteria. The drugs are not split by enzyme systems of the gastrointestinal tract, but are utilized by the microflora of the colon, which contributes to the growth of bifidum and lactobacilli; change the pH of the environment in this section of the intestine.

Table 17

Classification of prebiotics

Group	Original name
Non-microbial origin	Lactulose, xylitol, sorbitol, soy oligosaccharide, paraaminomethylbenzoic acid, lysozyme, lecithin, calcium pantothenate, inulin, dietary fiber, amino acids, carotenes, microbial enzymes
Microbial origin	Hylak forte

Lactulose, oligosaccharides of breast milk and plants, and dietary fiber have a prebiotic effect. Dietary fibers include large molecular glucose polymers contained in the cell wall of plants, as well as inulin, chitin, pectin, mucus, brown algae alginic acids, etc. These substances are found in the largest quantities in dill, dried apricots, strawberries, tea, oat flour, and

wheat bran, roasted coffee, aronia melanocarpa, garlic. They retain water; affect the electrolyte composition and motility of the gastrointestinal tract, the mass of feces that carry out adsorbing, detoxification, and has cholesterol-lowering effects. Dietary fibers are not "ballast substances", their absence in the diet can lead to constipation, colon cancer, irritable bowel syndrome, gallstone disease, diabetes mellitus, atherosclerosis, etc. It is assumed that an adult should consume 20–35 g of dietary fiber per day, while the average European consumes about 13 g.

3.18.3. Synbiotics and preparations based on recombinant genetically engineered strains

Synbiotics are drugs of a combined composition, obtained by rational combination of probiotics and prebiotics. They have the properties of two components. The result of their interaction is to improve the properties of the drug with respect to normalizing the composition of microflora, increasing its protective qualities, including immunity, and neutralizing pathogenic representatives.

Table 18

Classification of synbiotics and preparations based on recombinant genetically engineered strains

Group	Original name
Combination of probiotics and prebiotics	Labix, extralact, bifilact-extra, bifacaps, yogurt, vitaflor, bifidumbacterin forte, bifilis, acipol, bioflor, probifor
Multiprobiotic	Symbiter, Allibact
preparations based on recombinant genetically engineered strains	Subalin

Multiprobiotics, which are created on the basis of a "living" mutualistic symbiosis of physiological saccharolytic bacteria, represent a separate subgroup. Their value is associated with high vitamin-synthesizing ability, which is important for the treatment of dysbiosis. Multicomponent preparations also contain a wide range of enzymes, important for the digestive function and metabolic processes of the macroorganism. The composi-

tion of the symbiter include selected bacteria that are resistant to gastric juice, digestive enzymes, and bile, because it has an advantage in comparison with drugs of a different composition that enter the body by the oral route. Symbiter has a natural antibiotic resistance, which is not transmitted to other microorganisms, which is the basis for its successful use simultaneously with antibiotic therapy.

A wide range of antibacterial, antifungal, antiviral, immunomodulating and antitumor activity is inherent in the new generation probiotic subalin, which was developed by genetic engineering by Russian microbiologists. Its basis is one of the strains of Bacillus subtilis, which contains a recombinant plasmid with the human interferon α-2 gene. They successfully started to use the drug in the treatment of purulent wounds, gastric ulcer, inflammatory diseases in gynecology, etc. A positive effect was achieved when using the multiprobiotic symbiter acidophilic concentrated in patients with chronic generalized periodontitis degrees I–II of severity. The effectiveness of multiprobiotics is achieved by oral and local administration. A multiprobiotic is injected in periodontitis patients for 22 days into the dentoalveolar mouthguards overnight using ultraform dental vacuum shaper made of polyethylene. Patients of all groups underwent professional oral hygiene, were prescribed local antibacterial therapy with Metrogyl Denta and local anti-inflammatory therapy with phytodent. The rationale for the clinical effectiveness of the use of multiprobiotics in the treatment of chronic generalized periodontitis degrees I–II of severity is microbiological studies of periodontal pocket. When comparing the microbiocenosis of the periodontal pocket before and after treatment, it was shown that the prescription of a multiprobiotic can increase the efficiency of eradication of pathogenic and conditionally pathogenic microflora. The results indicate that the drug is able to normalize the state of the microbiocenosis of the oral cavity, effectively stabilize colonization resistance and normalize the balance between the main types of obligate and conditionally pathogenic microflora.

An analysis of the numerous literature data on the use of biotherapy in clinical practice allows to note that the present is characterized by intensified research on the development of new biological products, further study of the mechanism of their therapeutic and prophylactic effect, features of their use in clinical practice and improvement of safety

of use. However, there are still many problems with the use of biological products. So, one of the reasons for the low efficiency may be the presence of a small number of living cells in freeze-dried probiotics. Mono- or 2–3-component preparations are not able to balance a microbial landscape similar to a natural one. Probiotics based on spore-forming, yeast-like opportunistic microorganisms can pose a risk of artificial infection for weakened people. Probiotics received from distant foreign producers may turn out to be ineffective (it is well known that the microbial landscape of Africans, Australians, Canadians differs from the same among Ukrainians). When using probiotics against antibiotic therapy in order to prevent the development of dysbiosis, it must be remembered that many of them are incompatible with antibiotics. Age restrictions that exist prior to the use of probiotics may also interfere with biotherapy.

There are more than 50 probiotic preparations on the Ukrainian market. The following drugs are most effectively used in treatment. Enterol-250 contains lyophilized culture of Saecharamyces boulardii. It is recognized as the No. 1 probiotic in the world. The drug is unique in that there are no similar generics on the world pharmacological market. Enterol has 7 ways of a unique mechanism of action (antitoxic, antimicrobial, metabolic, enzymatic, anti-inflammatory, antiviral, regenerative). This probiotic is used in the treatment of diarrhea of various geneses: chronic giardiasis, wandering, antibiotic-associated. A positive sign is the possibility of using the drug in parallel with antibiotic therapy. It should not be used by pregnant women, women who breastfeed, and children under 2 years of age, because there is no experience with this application. Normagut contains, like the previous preparation (Enterol-250), bacardi saccharomycelles. It has similar properties.

Symbiter contains living cells of the probiotic microflora from 14 to 24 strains of the most physiological bacteria for humans. A well-chosen stable symbiosis of a large number of guaranteed apatogenic beneficial microbes simulates a complete intestinal biofilm in composition and biological properties. This symbiotic product, combining friendly microflora with a large concentration of active cells that are not susceptible to freeze drying, has no analogues int he world. The drug is successfully used for purulent-inflammatory diseases, acute intestinal infections, liver disorders, allergies, superinfection, etc.

Enterogermina contains multiresistant spores of Bacillus clausii. It has bactericidal activity against most gram-positive bacteria, exhibits antagonism to pathogenic bacteria, and has a wide spectrum of antibiotic resistance. After taking the drug, Bacillus Clausii does not appear in the digestive tract after a month. It has been proven that it does not have the risk of transferring the atibiotic resistance gene to other microorganisms. It is included in a number of probiotic preparations with a known safety in the treatment of bacterial infections. Lactiv-ratiopharm contains a wide range of probiotics of the lactobacilli group, bifidobacteria and streptococcus, 7 vitamins of group B. It quickly and effectively restores the intestinal microflora balance and replenishes the deficiency of vitamins, which contributes to complete digestion. It is indicated for various disorders of the gastrointestinal tract (diarrhea, flatulence, discomfort, nausea), after acute intestinal infections, when using antibiotics, in stressful situations, etc.

Hylak forte contains a sterile concentrate of metabolic products of normal intestinal microflora, forms lactic acid, lactulose, amino acids, short-chain volatile fatty acids. The drug helps to restore the biological environment in the intestine, inhibits the growth of pathogenic bacteria, maintains the pH in the digestive tract, increases the synthesis of secretory immunoglobulins SIgA, normalizes the synthesis of vitamins, increases the survival of its own microflora and probiotic products, etc. Lactusan is a prebiotic based on lactulose. It selectively stimulates the growth and development of its own microflora of the gastrointestinal tract, participates in the suppression of toxic metabolites, stimulates liver function, softens feces, etc. It is prescribed to correct the effects of antibiotic therapy, for the treatment of dysbiosis of varying severity, candidiasis, salmonellosis, for the treatment of colitis, chronic constipation, toxicosis of pregnant women, renal failure, hypercholesterolemia, allergic diseases. The drug is very dangerous because it is not digested in the upper intestines and is not absorbed into the systemic circulation.

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