

Danylo Halytsky Lviv National Medical University  
Pediatric Dentistry Department

**Methodological Recommendations  
for Pediatric Therapeutic Dentistry  
for the 5<sup>th</sup> year students  
the 9<sup>th</sup> term**

Lviv 2021

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**Methodical recommendations were discussed, re-approved and confirmed at the meeting of the Department of Pediatric Dentistry of Lviv National Medical University named after Danylo Halytsky**

**Protocol №            from   «   » \_\_\_\_\_ 202**

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**Responsible for the issue  
Vice-Rector for Academic Affairs, Professor M.R. Grzegotskyy**

### The Practical Lessons Schedule

(Pediatric Dentistry)

(for the fifth year students of Dentistry Department, 9th term)

№	Topic of lessons	Hours
1	Clinic, diagnosis, differential diagnosis, treatment of gingivitis. The choice of medical drugs, methods of their application.	7
2	Periodontitis in children. Clinic, diagnosis. Principles of treatment of periodontitis in children.	7
3	Morphological and functional peculiarities of oral mucosa in children. Primary and secondary lesions. Oral cavity mucosa diseases in children. Classification. The main particularities of oral cavity mucosa injuring in acute infection diseases. Pedodontic's tactic.	7
4	Acute and recurrent herpetic stomatitis in children. Etiology, diagnosis, differential diagnosis, treatment, prevention.	6
5	Candidiasis. Etiology, pathogenesis, clinic, diagnosis, differential diagnosis, treatment and prevention of candidiasis in children. Cheilitis and tongue diseases in children. Independent and symptomatic cheilitis Clinical characteristics, diagnostics. Differential diagnostics. Treatment	7
6	Immediate allergic reactions (anaphylaxis, angioedema, urticaria) and delayed type (exudative erythema multiforme, Stevens-Johnson syndrome) and their manifestations in the oral cavity in children at different ages. Clinical manifestation, diagnosis, differential diagnosis and treatment.	7
7	Signs of gastric and endocrine system diseases in oral cavity. System diseases in children. Chronic Aphthous Recurrent Stomatitis. Etiology. Clinical characteristics, diagnostics, treatment.	7
8	Manifestations of the blood system diseases in children in the oral cavity. Pedodontic's tactic.	6
9	Medical card. Summary module control	6
	Whole	60

### The Independent Work Schedule

(Pediatric Dentistry)

(for the fifth year students of Dentistry Department, 9th term)

№	Topic of the lessons	Hours
1	Periodontal syndrome in children. Peculiarities of its clinical manifestations on the oral mucosa. Pedodontic's tactic.	3
2	Principles of treatment of periodontal disease in children. Professional oral hygiene. Basic medicines. Comprehensive approach to the treatment.	3
3	Viral diseases of the oral mucosa in children. Peculiarities of clinical manifestations in children. Differential diagnosis. Dentist's tactic. Prevention.	3
4	AIDS. Etiology, clinic, diagnosis, prevention. Peculiarities of the clinical manifestation in children. Dentist's tactics.	3
5	Laboratory methods of investigations of mucosa and periodontium of oral cavity in children.	3
6	Specific infection ( tuberculosis, syphilis, etc.) of the mucosa in children. Peculiarities of clinical manifestations of its appearance. Tactics of pedodontics.	3
7	Traumatic lesions of mucous membrane in children. Clinic, diagnosis, treatment and prevention.	3
8	First aid in child dentistry clinic.	3
9	Medical history	2
	Whole	26

## The Lecture Lessons Schedule

(Pediatric Dentistry)

(for the fifth year students of Dentistry Department, 9th term)

№	Topic of the lesson	Hours
1	Periodontal disease in children: etiology and pathogenesis. Gingivitis, periodontitis and periodontal syndrome in children: prevalence, clinical manifestations, diagnostics.	2
2	Morphofunctional particularities of mucosa of the oral cavity in children of different age periods. Viral diseases of mucosa of the oral cavity in children. Clinical appearance, diagnostics, treatment.	2
3	Candidiasis. Etiology, clinic, diagnostics, treatment and prevention of candidiasis in children.	2
4	Allergic diseases in children. Clinical features in the oral cavity, differential diagnostics and treatment.	2
5	Signs of blood system and infection diseases in the oral cavity in children. Clinical characteristics, diagnostics. Principles of treatment.	2
	<b>total</b>	<b>10</b>

## Practical class 1

### **Clinic, diagnosis, differential diagnosis, treatment of gingivitis. The choice of medical drugs, methods of their application.**

**Purpose of the lesson:** To study with student etiology of gingivitis in children and young person, peculiarities of clinical manifestation, diff.diagnosis and choice of the methods of treatment.

#### **Control of the initial level of knowledge**

1. What is periodontium?
2. Anatomy and physiology of the periodontium in the children in different age periods.
3. Prevalence of the periodontal disease.
4. The role of local and general factors in the development of the periodontal disease in children.
5. The choice of individual hygiene means for the children with periodontal disease.

#### **Content of the practical class**

*Periodontium* is a complex of morphologically and functionally related structures that surround the tooth and keep it in the alveolar bone. These are gums, periodontal ligament, cement of the tooth root and alveolar bone.

*Gums or gingiva* is an important structural unit of periodontium. It is divided into 3 parts, which are different in their structure: gingival interdental papillae, marginal and alveolar parts of gums.

*Gingival interdental papillae* have a triangular shape and they are localized in interdental space.

*Marginal gingiva* is adjacent to the neck of the tooth and it is separated from its surface by a narrow fissure-gingival sulcus.

*Alveolar part* of the gums is tightly connected with the periosteum and covers the alveolar bone.

The gingival mucosa in children has several features (Vinogradova T.F, 1983):

- thinner layer of cornified cells of the oral epithelium;
- more intensive vascularization of gums, which causes its bright red color ;
- low density of a connective tissue;
- gingival sulcus is more shallow;
- roundness of gingival margin with symptoms of its swelling and hyperemia during teeth eruption.

*Periodontal ligament* is a connective tissue formation, retaining the roots of teeth in the alveolar bone.

There are 2 parts in the *alveolar process*: the alveolar bone itself and supporting alveolar bone.

#### **Classification of periodontal diseases:**

1. **Gingivitis**- inflammation of gingival mucosa without affection of the dentogingival junction.  
Forms: catarrhal, hypertrophic, and ulcerative.  
Course: acute, chronic, aggravated, remission.  
Prevalence: localized, generalized.  
Degree of severity: mild, moderate, severe.
2. **Periodontitis**- the inflammatory destructive process in periodontal tissues with disturbed integrity of dentogingival junction.  
Course: chronic, aggravated, abscessed, remission.  
Prevalence: localized, generalized.  
Degree of severity: mild, moderate, severe.
3. **Periodontosis**: - adystrophic lesion of periodontal tissues.  
Course: chronic, remission.  
Prevalence: generalized.

Degree of severity: mild, moderate, severe.

4. Idiopathic diseases with progressive lysis of periodontal tissues (Papillon-Lefevre syndrome, histiocytosis, hereditary neutropenia, decompensated diabetes, etc).
5. Tumors and tumor-like diseases: epulis, gingival fibromatosis, etc.

**GINGIVITIS** is the inflammatory process in gingival mucosa, which isn't accompanied with the loss of integrity of the dento-gingival attachment.

Factors that can increase risk of gingivitis include:

- Poor oral health habits
- Tobacco use
- Diabetes
- Older age
- Decreased immunity as a result of leukemia, HIV/AIDS or other conditions
- Certain medications
- Certain viral and fungal infections
- Dry mouth
- Hormonal changes, such as those related to pregnancy, menstrual cycle or use of oral contraceptives
- Poor nutrition
- Substance abuse
- Ill-fitting dental restorations

**Classification of gingival diseases:**

1. Dental plaque-induced gingival diseases.
  1. Gingivitis associated with plaque only
  2. Gingival diseases modified by systemic factors
  3. Gingival diseases modified by medications
  4. Gingival diseases modified by malnutrition
2. Non-plaque-induced gingival lesions
  1. Gingival diseases of specific bacterial origin
  2. Gingival diseases of viral origin
  3. Gingival diseases of fungal origin
  4. Gingival diseases of genetic origin
  5. Gingival manifestations of systemic conditions
  6. Traumatic lesions
  7. Foreign body reactions
  8. Not otherwise specified

**Catarrhal gingivitis-acute course**

(by protocol)

**Diagnostic criteria:**

Anamnesis - complaints of pain and bleeding gums when brushing teeth and eating

**Clinical course:**

- Bright redness and swelling of the mucous membrane of the gums

Index assessment of periodontal tissues:

- PMA (papillary-marginally-alveolar index)

index to 20% - mild severity of gingivitis

from 25 to 50% - the average severity of gingivitis

above 51% - a severe severity of gingivitis

*Light form of severity*

- Hyperemia of gingival papillae;
- Swelling of the gingival papillae

*Average (middle form) of severity*

- Expressive hyperemia of gingival papillae and the gingival margin;
- Swelling of the gingival papilla and gingival margin;
- Pain on palpation of gingival papilla and gingival margin

*Severe degree of disease*

- Expressive hyperemia of gingival papillae, margin and alveolar part of the gums;
- Swelling of the gingival papilla, margin and alveolar part of the gums;
- Pain and bleeding on palpation of gingival papillae, margin and alveolar part of the gums

**Treatment**

- Professional oral hygiene
- Sanation of the oral cavity
- Orthodontic treatment –if there is the presence of an abnormal occlusion and occlusion anomalies.
- Surgical treatment - in the presence of anomalies of the structure and location of the soft tissues.

*Light form of severity*

- antibiotic therapy (topical) - taking into account the sensitivity of microflora;
- nonsteroidal anti-inflammatory drugs (local);
- antiseptic agents (local);

*Average severity*

- anesthetics (local);
- antibiotic therapy (topical) - taking into account the sensitivity of microflora;
- anty-trichomonas drugs (locally) - in the presence of trichomonas in the oral cavity;
- antiseptic agents (local);
- inhibitors of proteolysis (local);
- nonsteroidal anti-inflammatory drugs (local);

*Severe degree of disease*

- anesthetics(local);
- antibiotic therapy (topical) - taking into account the sensitivity of microflora;
- anty-trichomonas drugs (locally) - in the presence of trichomonas in the oral cavity;
- antiseptic agents (local);
- inhibitors of proteolysis (local);
- nonsteroidal anti-inflammatory drugs (local);

**Additional recommendations**

- hygienic education of the individual oral care;
- toothbrushing with soft or very soft bristle;
- therapeutic and prophylactic anti-inflammatory effect of toothpaste containing herbal extracts; paste containing antiseptics; paste containing macro and microelements - in case of radiological changes in periodontal tissues
- rinses containing antiseptics;
- elixir

**Performance criteria of treatment:**

- elimination of clinical manifestations of the disease.

**Catarrhal gingivitis, chronic course.**

(by protocol)

**Diagnostic criteria:**

Medical history - possible complaints of recurrent bleeding of gums during teeth brushing

**Clinical course:**



- Redness of the mucous membrane of the gums
- Cyanosis of the mucous membrane of the gums
- Moderate swelling of the mucous membrane of the gums

X-ray:

- Unclear contour of the cortical plate of the alveoli
- Osteoporosis of the spongy substance on the tops of the interdental septum

Index assessment of periodontal tissues:

- PMA (papillary-marginally-alveolar index)

index to 20% - mild severity of gingivitis

from 25 to 50% - the average severity of gingivitis

above 51% - a severe severity of gingivitis

- CPI (communal periodontal index)

0 - healthy gums

1 - bleeding of gums

2 - the presence of tartar

3 - pocket size 4-5 mm

4 - pocket size larger than 6 mm

### **Clinic manifestation:**

*Light form of severity*

- Moderate swelling of the gingival papilla and gingival margin;
- Stagnant hyperemia, cyanosis of gingival papillae

*Average severity*

- Moderate swelling of the gingival papilla and gingival margin;
- Stagnant hyperemia, cyanosis of gingival papilla and gingival margin

*Severe degree of disease*

- Moderate swelling of the gingival papilla and gingival margin, and alveolar part of gums
- Stagnant hyperemia, cyanosis of papilla and gingival margin, and alveolar part of gums.

### **Treatment**

*Light form of severity*

- antibiotic therapy (topical) - taking into account the sensitivity of microflora;
- nonsteroidal anti-inflammatory drugs (local);
- antiseptic agents (local);

Physiotherapy

hydrotherapy - water massage of the gums - in the absence of exacerbation in the gums

*Average severity*

- antibiotic therapy (topical) - taking into account the sensitivity of microflora;
- antiseptic agents (local);
- nonsteroidal anti-inflammatory drugs (local);

Physiotherapy

- hydrotherapy (locally)
- electrophoresis with calcium and fluoride preparations (topical) - in the presence of radiological changes in the periodontal tissues, electrophoresis with solutions of vitamins (in presence of the tendency to bleeding gums).

*Severe degree of disease*

- antibiotic therapy (topical) - taking into account the sensitivity of microflora;
- antibacterial agents of plant origin (local);
- antiseptic preparations (topical)
- anty-trichomonas drugs (locally)
- nonsteroidal anti-inflammatory drugs (local);

Physiotherapy

- hydrotherapy (locally)
- electrophoresis of calcium and fluoride preparations (topical) - in the presence of radiological changes in the periodontal tissues, electrophoresis solutions of vitamins (the tendency to bleeding gums).

### **Additional recommendations**

- hygienic education of the individual oral care;
- therapeutic and prophylactic toothpaste with anti-inflammatory effect containing herbal extracts; paste containing antiseptics; paste containing macro and microelements - in case of radiological changes in periodontal tissues
- rinses containing antiseptics

### **Dispensary care at the dentist:**

Light severity –1<sup>st</sup> dispensary group - clinical supervision 1 per year

Medium severity - II dispensary group - clinical supervision 2 times a year

Severe degree of disease - III dispensary group - clinical supervision 3 times a year

### **Performance criteria of treatment:**

- elimination of clinical manifestations of the disease.
- stabilization of radiological changes in alveolar process.

### **Comprehensive control:**

1. Classification of the periodontal disease.
2. Etiology of gingivitis in children.
3. Acute catarrhal gingivitis. Clinical course. Diagnosis. Treatment.
4. Chronic catarrhal gingivitis. Clinical course. Diagnosis. Treatment.
5. Prevention of the periodontal disease.
6. Hypertrophic gingivitis.. Clinical course. Diagnosis. Treatment

### **Test control:**

1. A 16-year-old teenager complains of halitosis, general weakness, body temperature rises up to 37, 6. These symptoms turned up 2 days ago; the boy has a history of recent angina. Objectively: oral cavity hygiene is unsatisfactory; teeth are covered with soft white deposit. Gums are hyperemic, gingival papillae are covered with grayish coating. What is the most likely diagnosis?

- A. Ulcero-necrotic gingivitis
- B. Acute catarrhal gingivitis
- C. Chronic catarrhal gingivitis
- D. Hypertrophic gingivitis
- E. Desquamative gingivitis

2. An 18-year-old patient complains of gingival enlargement, pain and haemorrhage during eating of solid food. Objectively: hyperaemia, gingival edema, hypertrophy of gingival edge up to 1/2 of crown height near the 12, 13, 14 teeth are noted. Formalin test is painless. What is the most likely diagnosis?

- A. Hypertrophic gingivitis
- B. Generalized II degree periodontitis, chronic course
- C. Exacerbation of generalized I degree periodontitis
- D. Ulcero-necrotic gingivitis
- E. Catarrhal gingivitis

3. Examination of an 11-year-old boy revealed thickened, somewhat cyanotic, dense gingival margin overlapping the crowns of all teeth by 1/2 of their height. Fedorov-Volodkina oral hygiene index is 2,6, PMA index is 20%. X-ray picture shows no pathological changes of periodontium. The child has a 2-year history of neuropsychiatric treatment for epilepsy. Make a provisional diagnosis:

- A. Chronic hypertrophic gingivitis
- B. Chronic catarrhal gingivitis

- C. Localized periodontitis
- D. Acute catarrhal gingivitis
- E. Generalized periodontitis

4. A 10-year-old child complains of gingival pain and haemorrhage which appeared two days ago after a cold. Objectively: the gingiva is edematous, hyperaemic, bleeds easily, painful on palpation. The tips of gingival papillae are dome-shaped. What is the most likely diagnosis?

- A. Acute catarrhal gingivitis
- B. Chronic catarrhal gingivitis
- C. Hypertrophic gingivitis
- D. Ulcerative gingivitis
- E. Generalized periodontitis

5. A 14-year-old teen complains of gingival haemorrhages during tooth brushing. Objectively: gingival mucosa is hyperemic, pastous, bleeds when touched. Schiller-Pisarev test is positive. PMA index - 70%. Hygienic index - 3,0. X-ray picture of the frontal area depicts no evident changes. What is the most likely diagnosis?

- A. Chronic catarrhal gingivitis
- B. Chronic periodontitis
- C. Acute catarrhal gingivitis
- D. Chronic hypertrophic gingivitis
- E. Exacerbation of chronic periodontitis

6. A 13,5 year old girl complains of gingival painfulness and haemorrhage during tooth brushing and eating, halitosis. She has been ill with angina for a week. Objectively: mucous membrane of gums in the area of frontal teeth of her upper and lower jaws is edematous, hyperemic. Apices of gingival papillae are necrotic, they also bleed when touched. There is a thick layer of soft tooth plaque. What is the causative agent of this disease?

- A. Anaerobic microflora
- B. Herpes virus
- C. Streptococci
- D. Staphylococci
- E. Yeast fungi

7. A 13-year-old patient complains about gingival haemorrhage during tooth brushing. Objectively: gums around all the teeth are hyperemic and edematous, PMA index (papillary marginal alveolar index) is 46%, Greene-Vermillion hygiene index is 2,5. Provisional diagnosis: exacerbation of chronic generalized catarrhal gingivitis. This patient should be recommended to use toothpaste with the following active component:

- A. Chlorhexidine
- B. Calcium glycerophosphate
- C. Monofluorophosphate
- D. Vitamins A, D, E
- E. Microelement complex

8. Parents of 10-years old patient turned to the dentist complaining about increasing of body temperature, to 37-38 c, weakness, headache, loss of appetite, sleep disturbance, gums bleeding,

that increases during food intake; putrid smell from the mouth, excessive salivation. During dental examination swelling, hyperemia and bleeding of gingival mucosa were revealed. On the surface of the gums dirty-gray necrotic coating is observed. Make the diagnosis.

- A. Ulcerative-necrotizing gingivitis
- B. Chronic catarrhal gingivitis
- C. Acute catarrhal gingivitis
- D. Hypertrophic gingivitis
- E. Desquamative gingivitis

9. The 9 -years-old child was diagnosed with ulcerative-necrotizing gingivitis. In which order should be the treatment conducted?

- A. Anesthesia, removal of necrotic tissues,antibacterial therapy,antiinflammatory therapy,stimulation of regeneration, hygienic education
- B. Removal of necrotic tissues,antibacterial therapy, anesthesia antiinflammatory therapy,stimulation of regeneration, hygienic education
- C. Hygienic education,removal of necrotic tissues,antibacterial therapy, anesthesia antiinflammatory therapy,stimulation of regeneration
- D. Antibacterial therapy, anesthesia antiinflammatory therapy,stimulation of regeneration,removal of local predisposing factors
- E. Removal of local predisposing factors,anesthesia, removal of necrotic tissues,antibacterial therapy,antiinflammatory therapy,stimulation of regeneration

10. 13-years-old patient was diagnosed with granulating form of hypertrophic gingivitis. Which group of medicine should be applied for the antibacterial therapy?

- A. Chlorhexidine
- B. Lydase solution
- C. "Kamistad"
- D. Maraslavine
- E. Mefenaminic paste

### **Recommended literature:**

Pediatric Therapeutic Dentistry: [textbook for students of dental faculties] / L. A. Khomenko, A. V. Savychuk, O. I. Ostapko [et al.]; ed. L. A. Khomenko. -Kiev: [s. n.], 2012. - 240 p.

## **Practical class 2**

### **Periodontitis in children. Clinic, diagnosis. Principles of treatment of periodontitis in children.**

**Purpose of the lesson:** To know the etiology of localized and generalized periodontitis in children and young person, peculiarities of clinical manifestation, diagnosis, diff.diagnosis and choice of the methods of treatment. To know the etiology, clinical manifestation, and diagnosis of periodontal syndrome in children.

### **Control of the initial level of knowledge**

1. Anatomy and physiology of the periodontium in the children in different age periods
2. Functions of periodontium.
3. Index assessment of the state of periodontal tissues.

4. The role of local and general factors in the development of the periodontal disease in children.
5. Methods of diagnostic of the periodontal disease in children.

**Content of the practical class:**

**Generalized Periodontitis**

*Diagnostic criteria:*

***Clinical course:***

- Symptomatic gingivitis
- Periodontal pocket
- Pathological tooth mobility
- Traumatic occlusion
- Progressive resorption of alveolar bone.

***X-ray:***

- Destruction of the cortical plate of tops of interalveolar septum
- Osteoporosis of the spongy substance between alveolar bony septa
- Resorption of the interalveolar septum
- Expansion of periodontal sulcus.

*Index assessment of periodontal tissues*

- PMA (papillary-marginally-alveolar index)

index to 20% - light severity of gingivitis

from 25 to 50% - the average severity of gingivitis

above 51% -severe severity of gingivitis

- PI (periodontal index)

index to 1.0 - initial degree of periodontitis

from 1.5 to 4.0 - the average degree of periodontitis

from 4.5 to 8.0 - severe degree of periodontitis

- CPI (communal periodontal index)

0 - healthy gums

1 - bleeding gums

2 - the presence of tartar

3 - pocket size 4-5 mm

4 - pocket size over 6 mm

Laboratory:

- Cytology of the content of gingival pockets with intact periodontium:

neutrophils - 2.0-3.0; epithelial cells - 4.0-5.0

Indicators of inflammation -more than 2.0-3.0; 4.0-5.0, respectively.

- Indicators of emigration of leukocytes in the oral cavity by Yasinovskiy

intact periodontium: 80-120 leukocytes in 1 ml (of which 90-98% are viable),

epithelial cells - 25-100

Values exceeding 80-120 leukocytes in 1 ml and epithelial cells of more than 100 indicate the inflammation in periodontal tissues.

***Clinical course:***

*Light form of disease*

- Chronic symptomatic gingivitis (catarrhal or hypertrophic)

- Periodontal pockets - 3-3.5mm

- Dental deposition

- Teeth are unmovable

*The average severity*

- Chronic symptomatic gingivitis (catarrhal or hypertrophic)

- Periodontal pockets - 3, 5-5 mm

- Pathological mobility of teeth (I and II degree)

- Traumatic occlusion

### Severe degree of disease

- Chronic symptomatic gingivitis
- Periodontal pockets - 5-6mm
- Pathological mobility of teeth (II-III)
- Single or multiple abscesses

#### **Treatment:**

- Elimination of local stimuli (dental deposition, cavities, traumatic occlusion, occlusion pathology, anomalies of attachment of soft tissues of the mouth, etc.)

### Light form of disease

- Treatment of symptomatic gingivitis.
- Antibiotic (locally) - taking into account the sensitivity of microflora pocket.
- Antifungal drugs (locally) - the presence of fungal flora in periodontal pockets.
- Anty-trichomonas drugs (locally) - in the presence of trichomonas in the oral cavity
- Natural compounds with sclerosing effect (locally) - in the presence of symptomatic hypertrophic gingivitis.

#### Physiotherapy.

- Electrophoresis of ascorbic acid (5%) and vitamin P (1%) or a 1% solution of nicotinic acid - with bleeding gums (locally).
- Hydrotherapy - in the absence of exacerbation in the gums.
- Electrophoresis with 10% solution of potassium gluconate or 10% solution of calcium chloride or 5% solution of calcium lactate or 2.3% solution of calcium glycerophosphate - in the presence of osteoporosis and resorption of the interdental septa (locally).

### The average severity of disease

- Antibiotic therapy - based on microflora pocket (locally).
- Proteolytic enzymes, enzymes and antibiotics based on sensitivity to certain microorganisms - in the presence of purulent exudates in periodontal pockets (locally).
- Surgical techniques: curettage, vacuum curettage - at a depth of periodontal pockets 4-5 mm, recurrent abscess.
- Physiotherapy: hydrotherapy or hydro massage or vibromassage - in the absence of aggravation in the gums.
- Electrophoresis with calcium and fluoride - in osteoporosis and progressive resorption of the interdental septa.

### Severe disease

- Surgical techniques: curettage - at a depth of periodontal pockets 4-5 mm, recurrent abscess.
- gingivectomy - at a depth of periodontal pockets more 4-5mm.
- gingivectomy - at a depth of pockets more than 4-5 mm and symptomatic hypertrophic gingivitis.
- Antibiotic therapy - based on microflora of pocket (locally).

### Exacerbation of generalized periodontitis

(light and medium severity form):

- Inhibitors of proteolysis (natural and synthetic) (locally).
- Nonsteroidal anti-inflammatory drugs (locally).
- Corticosteroids (topical).
- Essential oils - in periodontal pockets (locally).
- phytoncids drugs - in periodontal pockets (locally).
- Antibiotics of plant origin (locally).
- Physiotherapy (locally).
- UHF-therapy, or UV therapy or microwave therapy
- Aerosol antiseptics, non-steroidal anti-inflammatory drugs, enzymes and antibiotics - when indicated.

#### **General treatment:**

- Adequate rational nutrition.
- Calcium supplements (calcium gluconate or calcium glycerophosphate or calcium lactate or bicalcevit) - if necessary.

#### **Dispensary care at the dentist:**

Light severity –1<sup>st</sup> dispensary group - clinical supervision 1 per year

Medium severity - II dispensary group - clinical supervision 2 times a year

Severe degree of disease - III dispensary group - clinical supervision 3 times a year

**Performance criteria of treatment:**

- elimination of clinical manifestations of the disease.
- stabilization of radiological changes in alveolar process.

**Hand-Schuller-Christian Syndrome:**

A rare disease of unknown cause in which lipids accumulate in the body and manifest as histiocytic granuloma in bone, particularly in the skull; the skin; and viscera, often with hepatosplenomegaly and lymphadenopathy. Exophthalmos and diabetes insipidus may be present. Both sexes affected, with a slight male predominance. The disease is seen in children and young adults, seldom in elderly persons. Onset usually before the age of six years. As originally described, this syndrome included the classic triad of unilateral or bilateral exophthalmos, diabetes insipidus, and defects in the membranous bones of the skull. Clinical features may also include defects in the mandible, long bones, pelvis, ribs, and spine.

**In Letterer-Siwe disease** the lesions are widespread, the disease is severe and death likely within a short time. Aetiology unknown. Letterer-Siwe disease is a genetic disorder considered to be a type of histiocytosis (a condition where histiocytes proliferate in the body). It is sometimes classified as a form of Langerhans cell histiocytosis or as a form of histiocytosis X. It is most commonly seen in children less than two years old. The disorder is believed to be inherited in an autosomal recessive pattern. Signs :

1. Classic Triad (10%)
  1. Lytic bone lesions (esp. Skull defects)
  2. Diabetes Insipidus
  3. Exophthalmos
2. Oral Changes
  1. Gum swelling and necrosis
  2. Extrusion of teeth
3. Rash
  1. Papular, seborrheic or petechial rash
  2. Minute xanthomatous Nodules
  3. Raised yellow to brown lesions in neck and maxilla
4. Growth retardation
5. Developmental delay
6. Lung changes
2. Labs
  1. Complete Blood Count
    1. Hemoglobin or Hematocrit consistent with Anemia
    2. White Blood Cell Count consistent with Leukopenia
    3. Platelet Count consistent with Thrombocytopenia
  2. Chemistry panel and Serum osmolarity
1. Diabetes Insipidus changes
3. Diagnosis
  1. Skin biopsy
  2. Bone Marrow Biopsy

**Comprehensive control:**

1. Etiology and pathogenesis of periodontitis in children.
2. Clinical forms of periodontitis.

3. Clinical course of the localized periodontitis in children.
4. Clinical course of the generalized periodontitis in children.
5. Differential diagnosis of periodontitis in children.
6. Periodontal syndrome in children.
7. Hand-Schuller-Christian disease.
8. Papillon-Lefevre syndrome.

### **Test control**

1. A 12-year-old patient complains about gingival haemorrhage and tooth mobility. He has been suffering from this since the age of 4. Objectively: gums around all the teeth are hyperemic and edematous, bleed during instrumental examination. Tooth roots are exposed by 1/3 and covered with whitish deposit. II degree tooth mobility is present. Dentogingival pouches are 4-5 mm deep. External examination revealed dryness and thickening of superficial skin layer on the hands and feet, there are also some cracks. What is the most likely diagnosis?

- A. Papillon-Lefevre syndrome
- B. Hand-Schuller-Christian disease
- C. Generalized periodontitis
- D. Letterer-Siwe disease
- E. Localized periodontitis

2. A young patient complains of gum bleeding and pain during mastication, unpleasant smell from the mouth. During the examination the hypertrophy of marginal gums in the areas of 11, 12, 13, 21, 22, 23, 34, 33, 32, 31, 41, 42, 43, 44 teeth on 1/3 of their crown's height was found. Dental calculus and periodontal pockets of 3-4 mm of depth were present as well in mentioned areas. What is the most probable diagnosis?

- A. General periodontitis of I degree
- B. General periodontitis of II degree
- C. Hypertrophic gingivitis, fibrous form
- D. Hypertrophic gingivitis, granulated form
- E. Local periodontitis of I degree

3. Parents of a 5-year-old child complain of tooth mobility and bleeding of the gums in a child. During the examination - the mucous membrane of the gums is swollen, hyperemic, bleeds easily, the mobility of the teeth is I-II degree. What additional examination of the oral cavity the doctor should prescribe?

- A. Radiography
- B. Determination of the depth of periodontal pockets
- C. Electroodontometry
- D. Blood test
- E. Determination of tooth mobility

4. The 13-year-old child complains of bleeding of the gums during brushing of the teeth for several years. Objectively: gingival margin in the region of the 31 and 41 teeth is swollen, hyperemic, and cyanotic. There is a shortening of the lower lip frenulum. Radiological in this area osteoporosis of the interdental septum and cortical plate destruction of the alveoli are defined. Clarify the diagnosis:

- A. Chronic localized periodontitis
- B. Chronic atrophic gingivitis



- C. Chronic generalized periodontitis
- D. Chronic catarrhal gingivitis
- E. Chronic hypertrophic gingivitis

5. A 14-year-old girl appealed to the dentist with complaints of bleeding of the gums, bad odor from the mouth. Objectively: gingival mucosa in the area of the frontal teeth of the upper and lower jaws is hyperemic, pasty, bleeding is noted. Schiller - Pisareva test is positive, PMA index is 70 %, GI by Fedorov-Volodkina is 3. On the frontal radiograph of both jaws - extension of periodontal sulcus, disturbance of the sharpness of interdental tops, and its starting resorption in the area of the central teeth are present. What is the most likely diagnosis?

- A. Acute localized periodontitis
- B. Generalized chronic catarrhal gingivitis
- C. Exacerbation of chronic generalized periodontitis
- D. Chronic generalized hypertrophic gingivitis
- E. Chronic generalized periodontitis

6. The 16 year-old girl complains of bleeding and painfull of the gums. The patient is ill on diabetes about 5 years. Objectively: there are cyanotic gums, the depth of periodontal pockets in the region of the 34, 35, 36, 37 teeth is 3 mm, with a sero- purulent exudates. On radiographs - the resorption of the alveolar bone is within 1 /4 of their height. What is the most likely diagnosis?

- A. Generalized periodontitis I degree, exacerbative course
- B. Generalized periodontitis I degree, chronic course
- C. Generalized periodontal II degree, chronic
- D. Chronic catarrhal gingivitis
- E. Generalized periodontitis II degree, exacerbative course

7. The 15 years-old patient was diagnosed with generalized periodontitis. With what diseases is it necessary to make the diff. diagnosis?

- A. With catarrhal gingivitis, periodontal syndrome in hereditary neuropenia, eosinophilic granuloma
- B. With acute catarrhal gingivitis, periodontitis marginal papillitis
- C. With catarrhal and hypertrophic gingivitis, odontogenic abscess
- D. With hypertrophic gingivitis, periodontitis
- E. With hypertrophic gingivitis, gingival fibromatosis, papillitis

8. The 12 years-old patient turned to the dentist for the checkup. During the examination patient was diagnosed with acute localized periodontitis. As an anti-inflammatory therapy the doctor used:

- A. 0.1% solution of sodium mefenamin
- B. 5% solution of ascorbic acid
- C. 1% solution of nicotinic acid
- D. 2% sodium fluoride
- E. 2.5% solution of calcium glycerophosphate

9. The parents of the 3 year-old girl complain of falling out of all teeth in their child. The blood test revealed a complete absence of neutrophils with normal total leukocyte count and a slight increase in the red cells of blood and platelets. What disease is characterized with such results of the test?

- A. Permanent neutropenia
- B. Letterer-Siwe disease

- C. Cyclic neutropenia
- D. Hand-Schuller Christian disease
- E. Papillon -Lefevre syndrome

10. What disorder is characterized by reduced of number of neutrophils in bone marrow and periphery blood?

- A. Hereditary neutropenia
- B. Letterer-Siwe disease
- C. Hand-Schuller Christian disease
- D. Niemann-Pick Disease
- E. Eosinophilic granuloma

### **Recommended literature:**

Pediatric Therapeutic Dentistry: [textbook for students of dental faculties] / L. A. Khomenko, A. V. Savychuk, O. I. Ostapko [et al.]; ed. L. A. Khomenko. -Kiev: [s. n.], 2012. - 240 p.

## **Practical class 3**

**Morphological and functional peculiarities of oral mucosa in children. Primary and secondary lesions. Oral cavity mucosa diseases in children. Classification. The main particularities of oral cavity mucosa injuring in acute infection diseases. Pedodontic's tactic.**

**Purpose of the lesson:** To study with student morphological and functional peculiarities of oral mucosa in children. The main particularities of oral cavity mucosa injuring in acute infection diseases.

### **Control of the initial level of knowledge**

1. The main methods of examination of the patient with oral mucosa pathology.
2. Additional methods of examination of the patient with oral mucosa pathology.
3. Pathomorphologic manifestation of oral mucosa diseases.

### **Content of the practical class**

Oral mucosa has three layers - epithelium, mucosa and submucosa. The ratio of these layers in different parts of the oral cavity is different. In some layers - epithelium (dorsum of the tongue, hard palate, gums), in others - actually mucous membrane (lips and cheeks), in the third - submucosal layer (transitional fold the bottom of the mouth) is more pronounced.

The structure of oral mucosa clearly varies depending on age. It is divided into three age periods:

- neonatal period (up to 10 days after birth)
- breast feed period (1 year);
- early childhood period (1-3 years);
- primary period (4-7 years) and secondary child (8-12 years) period.

Each of the age periods corresponds the inherent features of the structure of the mucous membrane, which should be considered when analyzing the pathological condition.

Epithelium and connective tissue of the newborns is less differentiated, and consists only of the basal and spicular cells. The epithelium consists of a large number of glycogen and RNA, basal membrane is thin and tender. Fibrous structure of its proper layer are slightly differentiated, there is

a big number of the cellular elements (fibroblasts, histiocytes, lymphocytes) in the submucosal layer. Mucosa at this age is easily injured and quickly heals.

Breast period is characterized by an increasing of thickness of epithelium and appearing of parakeratosis in the masticatory regions (gums, palate, and dorsum of the tongue). Glycogen disappears in the epithelium. The number of cellular elements and blood vessels is decreased. The basal membrane is thin and loose. Immunological capacity of the tissues is decreased if compare to the antenatal period. Infants period is characterized by resistance of the mucous membrane to the viral and bacterial (except fungi) flora.

Early childhood period is characterized by such features of the regional structure of the oral mucosa: there is a lower amount of glycogen in the epithelium of the tongue, lips and cheeks; the basal membrane is mainly loose, soft and delicate. Decreased level of immune response and increased levels of tissue permeability are characteristic, which leads to higher frequency of viral infection.

The primary childhood period is characterized by the slight increase of the epithelium and of glycogen and RNA in it. The reduction of the number of cellular elements, blood vessels and of reduction of metabolic processes in tissues is also observed.

The secondary childhood period is characterized by decreasing of glycogen levels and an increasing number of protein structures in the epithelium of the oral mucosa. The number of reticular and elastic structures increases. Changes in cellular composition are characterized by overgrowth of lymphoid-histiocytic elements that stabilize the immunological changes. The number of mast cells decreases and the permeability of vascular walls decreases as well. Glycogen appears in the epithelium of the gums and hard palate. This age is more vulnerable to the acute and chronic inflammation, which are based on allergic reactions.

**Functions** of oral mucosa:

- protective,
- plastic,
- sensitive,
- absorptive.

Protective function is provided by:

- impermeability of the mucous membrane of bacteria and viruses,
- removing bacteria from the surface,
- the desquamation of the epithelium,
- the protective effect of oral leukocytes, which penetrate the gingiva.

High activity of the epithelium provides the plastic function.

Sensitive function of the oral mucosa is achieved due to the receptors of pain, touch, taste, cold and heat.

Oral mucosa has the ability to absorb a number of protein and mineral compounds, including drugs.

### **Measles (Rubeola)**

Measles, also known as rubeola, is an acute, infectious, highly contagious disease that frequently occurs in children. The incidence of measles has dramatically decreased as a result of the measles vaccine; however, it remains a significant problem.

#### *Pathophysiology*

The measles virus is a paramyxovirus belonging to the Morbillivirus genus. The paramyxovirus can survive for as long as 2 hours in the air and on surfaces. Measles is spread by direct contact via droplets from respiratory tract secretions in patients who are infected. It is considered one of the most communicable infectious diseases.

The initial site of infection is the respiratory tract epithelium. Multiplication of the measles virus in the respiratory tract epithelium and regional lymph nodes is followed by a primary viremia, with spread to the reticuloendothelial system. A secondary viremia occurs upon breakdown and necrosis of the reticuloendothelial cells, and the virus infects the leukocytes. During the secondary viremia, infection may spread to the thymus, spleen, lymph nodes, liver, skin, and lungs.

#### *Frequency*

Measles generally occurs in late winter and spring. Prior to the use of the measles vaccine in 1963, approximately 500,000 cases and 500 deaths were reported each year. Epidemic cycles occurred every 2-3 years. Greater than 50% of the population had measles by age 6 years, and greater than 90% were reported to have had it by age 15 years. After licensure of the vaccine in 1963, the number of reported cases of measles dropped by more than 98%, and the 2- to 3-year epidemic cycles no longer prevailed.

#### *Clinical history*

The incubation period for measles is the time from exposure to the prodrome. This period is approximately 10-14 days and is longer in adults than in children.

The prodrome phase lasts for several days and likely coincides with the secondary viremia phase. It is manifested by malaise, fever, anorexia, conjunctivitis, and respiratory symptoms. Toward the end of the prodrome and just prior to the appearance of the rash, Koplik spots are observed. The skin eruption of measles lasts approximately 5-6 days. The period of uncomplicated illness from the late prodrome to disappearance of skin lesions and fever lasts 7-10 days.

The fever in affected individuals can peak as high as 38-39C. Patients also experience respiratory symptoms, such as cough and coryza (runny nose), which may resemble a severe upper respiratory tract infection.

Koplik spots are pathognomonic for measles. They are located on the buccal mucosa in the premolar and/or molar area. Occasionally, in severe cases of measles, several areas of the oral cavity may be affected by the enanthem. The intraoral lesions may persist for several days and begin to slough with the onset of the rash.

Koplik spots consist of bluish-gray specks against an erythematous background. They have been compared to grains of sand. As few as 1 spot and as many as 50 spots may occur. The lesions are plaque-like or nodular and oval or round. The measles rash often begins near the hairline and then involves the face and the neck; over the next few days, it progresses to the extremities and finally to the palms and the soles. The rash is erythematous and maculopapular and may become confluent as it progresses. It lasts approximately 5 days and resolves in the same order it appeared, from the face and the neck to the extremities.

#### *Differentials*

Koplik spots - Cheek chewing keratotic lesions

Large Fordyce granules

#### *Laboratory studies*

The measles virus can be isolated from blood, urine, or nasopharyngeal secretions. Clinical specimens and serologic specimens should be obtained at the same time and preferably within 7 days of the onset of the rash. The easiest method that aids in confirming the diagnosis is to test for immunoglobulin M (IgM) antibody levels in a single specimen from an individual who is infected. A person who is infected or has received the vaccine initially has an IgM response followed by an immunoglobulin G (IgG) response. IgM antibodies are present for 1-2 months after exposure to the measles virus, and IgG antibodies are present for many years.

#### *Medical care*

No specific treatment is necessary for Koplik spots.

Patients should be referred to an appropriate physician for care. Supportive treatment is recommended. Appropriate antibiotic therapy is necessary for secondary bacterial infections.

The World Health Organization has recommended that vitamin A supplementation be provided for children with measles living in areas that have a documented vitamin A deficiency problem.

Intravenous and aerosol administration of ribavirin has been used to treat severe cases of measles in patients who are immunocompromised; however, the FDA has not approved this drug for the treatment of measles.

The measles vaccine is currently used. This vaccine is combined with the rubella and mumps vaccines and is administered as the MMR vaccine. Antibodies to measles virus develop in approximately 95% of children vaccinated at age 12 months and in 98% of children vaccinated at age 15 months. The vaccine induces long-term, if not lifelong, immunity to measles in 99% of individuals who receive 2 doses. Two doses of the measles vaccine in the form of MMR are recommended for all children.

### *Complications*

No oral complications are reported from measles. Diarrhea, otitis media, and pneumonia are the more common complications encountered from measles infection.

One case of acute encephalitis occurs in every 1000-2000 cases of measles. Acute encephalitis begins 6 days after the onset of the rash; symptoms include high-grade fever, headache, stiff neck, convulsions, and coma. The fatality rate is approximately 15%.

Subacute sclerosing panencephalitis is a previously unexplained disease that occurs months to years after the initial measles infection. Progressive deterioration of intellect, convulsive seizures, motor abnormalities, and, eventually, death characterize subacute sclerosing panencephalitis.

When measles infection occurs during pregnancy, the likelihood of early labor, spontaneous abortion, and low birth weight increases. Whether birth defects are caused by measles infection is questionable.

### *Prognosis*

The prognosis is good in well-nourished children.

### **Diphtheria**

is an upper respiratory tract illness caused by *Corynebacterium diphtheriae*, a facultative anaerobic Gram-positive bacterium. It is characterized by sore throat, low fever, and an adherent membrane (a *pseudomembrane*) on the tonsils, pharynx, and/or nasal cavity. A milder form of diphtheria can be restricted to the skin. Uncommon consequences include myocarditis (about 20% of cases) and peripheral neuropathy (about 10% of cases).

Diphtheria is a contagious disease spread by direct physical contact or breathing the aerosolized secretions of infected individuals. Historically quite common, diphtheria has largely been eradicated in industrialized nations through widespread vaccination. The DPT (*Diphtheria–Pertussis–Tetanus*) vaccine is recommended for all school-age children.

The current definition of diphtheria is based on both laboratory and clinical criteria.

Laboratory criteria

- Isolation of *Corynebacterium diphtheriae* from a clinical specimen, or
- Histopathologic diagnosis of diphtheria

Clinical criteria

- Upper respiratory tract illness with sore throat
- Low-grade fever
- An adherent pseudomembrane of the tonsil(s), pharynx, and/or nose.

Empirical treatment should generally be started in a patient in whom suspicion of diphtheria is high.

### **Comprehensive control:**

1. Peculiarities of the clinical course and diagnosis of measles in children.
2. Peculiarities of the clinical course and diagnosis of diphtheria in children.
3. Peculiarities of the clinical course and diagnosis of scarlet fever in children.
4. Peculiarities of the clinical course and diagnosis of chickenpox in children.
5. Peculiarities of the clinical course and diagnosis of infectious mononucleosis in children.
6. Pediatric dental tactics during acute infections in children.

### **Test control:**

1. A 9-year-old child complains of the fever, sore throat and presence of the rash which firstly appeared on the face and then spread all over the body. Objectively: the body temperature is 38°C, the mucosa of soft palate, tonsils and pharynx is hyperemic. There is the spotty pale-pink rash on the soft palate. Retroauricular and occipital lymph nodes are enlarged. The skin is covered with the spotty rash of the body. Define the preliminary diagnosis.

- A. Rubella
- B. Scarlet fever
- C. Chickenpox

- D. Measles
- E. Mononucleosis

2. Preventive examination of a 7-year-old schoolboy revealed unremovable grey-and-white layerings on the mucous membrane of cheek along the line of teeth joining. Mucous membrane is slightly hyperaemic, painless on palpation. The boy is emotionally unbalanced, bites his cheeks. What is the most likely diagnosis?

- A. Mild leukoplakia
- B. Chronic recurrent aphthous stomatitis
- C. Chronic candidous stomatitis
- D. Lichen ruber planus
- E. Multiform exudative erythema

3. A 10-year-old child complains of sore throat, cough, fever (up to 38°C). These presentations turned up 2 days ago. Objectively: acute catarrhal stomatitis is present. Tonsils are swollen, hyperemic, covered with yellow-gray friable film which can be easily removed. Submandibular and cervical lymph nodes are significantly enlarged, painful on palpation. Laboratory analysis revealed leuko- and monocytosis. What is the most likely diagnosis?

- A. Infectious mononucleosis
- B. Diphtheria
- C. Scarlet fever
- D. Rubella
- E. Measles

4. A 12-year-old child complains about sore throat, headache, body temperature rise up to 38,5°C, rhinitis, cough in summer period. Objectively: mucous membrane of oral cavity is hyperemic, edematous. There are 10-15 erosions up to 0,5 mm large on the palate and palatine arches, that aren't covered with deposit and have red floor. Regional lymph nodes are enlarged and painful on palpation. What is the most likely diagnosis?

- A. Herpetic angina
- B. Acute herpetic stomatitis
- C. Erythema multiforme
- D. Chronic recurrent aphthous stomatitis
- E. Infectious mononucleosis

5. A 7 month old child was brought to a dentist because of an ulcer in the oral cavity. The child was born prematurely. She has been fed with breast milk substitutes by means of a bottle with rubber nipple. Objectively: on the border between hard and soft palate there is an oval ulcer 0,8x1,0 cm large covered with yellowish-grey deposit and surrounded with a roll-like infiltration. Make a provisional diagnosis:

- A. Bednar's aphtha
- B. Setton's aphtha
- C. Tuberculous ulcer
- D. Acute candidous stomatitis
- E. Acute herpetic stomatitis

6. A 14-year-old boy complains of rash on the lips, pain while talking and eating. These presentations showed up three days ago. Similar rash has appeared 1-4 times a year for three years. Objectively: general condition is satisfactory, the body temperature is of 36,9°C. On the vermilion border of the lower lip and the skin below there are multiple small grouped vesicles with serous content, and crusts. What is the etiology of the disease?

- A. Herpes simplex virus
- B. Coxsackie virus
- C. Streptococc
- D. Herpes zoster Virus
- E. Staphylococci

7. According to the mother, a 5-year-old child complains about pain during swallowing, weakness, body temperature rise up to 39,5°C, and swelling of submental lymph nodes. Objectively: the child's condition is grave, body temperature is 38,8°C. Mucous membrane of the oral cavity is markedly hyperaemic and edematous with haemorrhages and ulcerations. Pharynx is markedly hyperemic, lacunae are enlarged and have necrosis areas. Regional, cervical, occipital lymph nodes are painful, enlarged and dense. What is the most likely diagnosis?

- A. Infectious mononucleosis
- B. Acute herpetic stomatitis
- C. Herpetic angina
- D. Necrotizing ulcerative gingivostomatitis
- E. Lacunar tonsillitis

8. A 4, 5-year-old child presents with eruptions on skin and in the mouth which appeared on the previous day. Objectively: the child is in medium severe condition, body temperature is 38,3 °C. Scalp, trunk skin and extremities are covered with multiple vesicles with transparent content. Mucous membrane of cheeks, tongue, hard and soft palate exhibits roundish erosion covered with fibrinous film. Gums remain unchanged. Submandibular lymph nodes are slightly enlarged. What diagnosis can be assumed?

- A. Chicken pox-induced stomatitis
- B. Acute herpetic stomatitis
- C. Exudative erythema multiforme
- D. Measles-induced stomatitis
- E. Scarlet fever-induced stomatitis

9. A 9-year-old child complains of increase of body temperature to 38, 5 ° C, sore throat, weakness. There is an acute catarrhal stomatitis in the mouth. Tonsils are swollen, hyperemic, coated with yellow-gray coating that is easy to remove. Submandibular, cervical, occipital lymph nodes are significantly enlarged, slightly painful to palpation. It was revealed leukocytosis and atypical mononuclear cells in blood. Define the causative agent.

- A. Epstein-Barr virus
- B. Herpes simplex virus
- C. Streptococcus haemolytica
- D. Coxsackie virus
- E. Herpes simplex virus

10. A 10 year-old child has been complaining of pain in the throat, cough, and increase of temperature to 38 C for 2 days. An objective examination revealed an acute catarrhal stomatitis. Tonsils are swollen, hyperemic, coated with yellow-gray coating. The coating is crumbly and easy to remove. Submandibular, cervical lymph nodes are significantly enlarged, painful to palpation. The laboratory study found leucocytosis and monocytosis. Define the most likely diagnosis.

- A. Infectious mononucleosis
- B. Varicella
- C. Measles
- D. Scarlet fever
- E. Diphtheria

**Recommended literature:**

Pediatric Therapeutic Dentistry: [textbook for students of dental faculties] / L. A. Khomenko, A. V. Savychuk, O. I. Ostapko [et al.]; ed. L. A. Khomenko. -Kiev: [s. n.], 2012. - 240 p.

**Practical class 4**

**Acute and recurrent herpetic stomatitis in children. Etiology, diagnosis, differential diagnosis, treatment, prevention.**

**Purpose of the lesson:** To study with student clinical course, diagnosis and treatment of the acute and recurrent herpetic stomatitis in children.

**Control of the initial level of knowledge**

1. The main methods of examination of the patient with oral mucosa pathology.
2. Additional methods of examination of the patient with oral mucosa pathology.
3. Pathomorphologic manifestation of oral mucosa diseases.
4. Classification of the mucous diseases.

**Content of the practical class**

**Herpetic stomatitis** is a viral infection of the mouth that causes ulcers and inflammation. Herpetic stomatitis is a contagious viral illness caused by *Herpes virus hominis* (also herpes simplex virus, HSV). It is seen mainly in young children. This condition is probably a child's first exposure to the herpes virus. An adult member of the family may have a cold sore at the time the child develops herpetic stomatitis. More likely, no source for the infection will be discovered.

**HHV (Herpes hominis virus)** infections are common in the oral cavity. They may be primary or recurrent infections. Eight types of HHV have been linked with oral disease. These types have 1 different disease patterns in their hosts.

**HHV-1**, also known as **herpes simplex virus (HSV)–1**, causes primary herpetic gingivostomatitis, or oral herpes. In some hosts, it becomes latent and may periodically recur as a common cold sore.

**HHV-2**, also known as HSV-2, causes genital herpes and occasionally causes oral disease that is clinically similar to that of HHV-1 infection.

**HHV-3**, also known as **varicella-zoster virus (VZV)**, causes the primary infection chickenpox and the secondary reactivation disease herpes zoster.



**HHV-4**, also known as **Epstein-Barr virus** (EBV), causes the primary infection infectious mononucleosis, and it is implicated in various diseases, such as African Burkitt lymphoma, other immunoproliferative disorders, and nasopharyngeal carcinoma. HHV-4 causes oral hairy leukoplakia in patients who are immunosuppressed.

**HHV-5**, also known as **cytomegalovirus** (CMV), causes a primary infection of the salivary glands and other tissues, and it is believed to have a chronic form.

**HHV-6**, which can produce acute infection in CD4+ T lymphocytes, causes **roseola infantum**, a febrile illness that affects young children. It is believed to chronically persist in salivary gland tissue in some hosts, and oral shedding is the probable route of disease transmission.

**HHV-7** has been isolated from the saliva of healthy adults and has been implicated as one cause of roseola infantum and febrile seizures in children.

**HHV-8** is associated with **Kaposi sarcoma** (KS), and evidence links it with body-cavity lymphomas and Castleman disease.

### **Pathophysiology**

Herpesvirus family members are DNA viruses. HHVs replicate in the host cell nucleus. Infected saliva or droplets spread the viruses in the oral cavity. The viruses also may be transmitted via oral-genital contact. Viral shedding has been detected before, during, and after the appearance of clinical lesions in patients with recurrent HHV-1 and HHV-2 infections; therefore, lack of visible lesions does not correlate with lack of potential infectivity. In a localized primary infection, the virus penetrates the mucosal epithelium and invades the cells of the basal layer, where the viral DNA inserts into the host DNA.

In HHV-1 and HHV-2 oral infections, viral replication within the oral epithelium may cause lysis of epithelial cells, with vesicle formation. Shallow ulcers with scabs that then heal without scarring follow the formation of vesicles. Herpesviruses establish latent permanent infections in their hosts, although clinical signs of disease may not be detected.

In children and adults who are immunocompetent, primary herpetic infections may be annoying and uncomfortable, but they rarely cause significant morbidity or mortality.

In individuals who are immunosuppressed, primary herpetic infections can be severe, and, occasionally, they can cause esophagitis, encephalitis, keratoconjunctivitis, and other diseases. The other forms of HHV can result in death. Herpes infections occasionally trigger erythema multiforme.

Primary herpes infections typically occur during childhood or youth, although occasional cases are observed in older individuals. Recurrent HHV-1 infections typically occur throughout life and are particularly triggered by stress, illness, immune compromise, or other factors. Herpes zoster usually affects patients older than 40 years.

### **Clinical history**

#### **HHV-1**

When HHV-1 infection recurs, it has different and distinct oral and perioral presentations from primary herpetic gingivostomatitis.

Primary herpes infection (primary herpetic gingivostomatitis) usually occurs in children or adolescents who have not been previously exposed to the virus. Many primary infections are asymptomatic. Symptomatic primary infection, with multiple, small, clustered vesicles in numerous locations, can occur anywhere in the oral cavity, on the perioral skin, on the pharynx, or on the genitalia. Headache, fever, painful lymphadenopathy, and malaise are common. Antibody

production follows, and the virus may become latent in sensory ganglia, often the trigeminal ganglion. Primary herpetic gingivostomatitis usually resolves within approximately 14 days. Recurrent herpes lesions are commonly referred to as cold sores. Recurrent herpes occurs in approximately one third of patients who have experienced primary herpetic gingivostomatitis. When the disease manifests extraorally, prodromal burning or itching often precedes vesicle formation. Recurrent herpes is a more limited disease than primary herpes. Unlike primary herpes, it occurs on keratinized mucosa (usually the lips, attached gingiva, and/or the hard palate). Vesicles are present in one discrete area, typically the same site every time in any given patient. Such sites include the vermilion border of the lips, the perioral skin, the hard palate, or, occasionally, the gingiva or the dorsal aspect of the tongue. Because vesicles can easily rupture intraorally, only an ulcer may be observed in some cases. Lymphadenopathy and systemic manifestations are much milder than in the primary disease.

Triggers for recurrence may include sunlight exposure, physical or emotional stress, or systemic illness for extraoral lesions and trauma (eg, a dental procedure) for intraoral lesions.

In immunosuppressed individuals, recurrent herpes lesions may occur on any oral mucosal surface, including nonkeratinized sites. They also may manifest solely as lesions on the dorsal aspect of the tongue. Such a presentation has been variously reported as red or white nodules, painful nonvesicular ulcerations, fissured, and, rarely, as a tongue mass. Herpes lesions in immunocompromised individuals are often severe. Such atypical presentations in an individual who is immunocompetent may lead the clinician to further investigate the patient's immune status.

### **HHV-2**

HHV-2 infection is less common in the oral cavity than HHV-1 infection; however, its oral manifestations are clinically indistinguishable from HHV-1 infection. Assessment of HSV-2 shedding by polymerase chain reaction has detected oral HSV-2 shedding in the absence of an oral lesion, but concurrent with genital HSV-2 reactivation. This was more common in HIV-positive males.

### **HHV-3**

HHV-3 is responsible for chickenpox and shingles.

**Primary varicella, or chickenpox**, usually occurs in children aged 3-6 years who are not immunized at the time of their first exposure to the virus. Itchy vesicles begin on the skin of the trunk and spread to the skin of the head. Intraoral and pharyngeal vesicles may occur. Antibody production follows, and the virus usually becomes latent in the dorsal root ganglia. Healthy children usually recover uneventfully, with a mortality rate of fewer than 2 deaths per 100,000 cases. However, older patients may experience more severe symptoms, and, in patients who are immunocompromised, the mortality rate may approach 18%.

**Recurrent varicella, also known as herpes zoster or shingles**, usually occurs in adults, and its incidence increases with age. It can occur in any patient who has had chickenpox and only rarely occurs in patients who have received chickenpox immunization. Recurrent varicella may occur when cellular immunity decreases. It results in a vesicular rash that usually affects a single dermatome. Inside the oral cavity, this may be observed as vesicles or ulcerations that stop sharply at the midline. A prodrome of pain, burning, or itching that mimics a toothache may occur. After resolution of the rash, postherpetic neuralgia may linger for a month or longer, especially in patients who are immunosuppressed or in those older than 50 years.

Unusual complications can include devitalization of teeth, root resorption, osteonecrosis.

Ramsay-Hunt syndrome arises when the virus emerges from latency in the geniculate ganglion. It involves cranial nerve VII (facial nerve), which has both motor and sensory functions.

Manifestations may include paralysis that involves the levator palati muscle and the face; hoarseness; loss of secretory function (eg, dry mouth, loss of taste); vertigo; tinnitus; pain; and vesicles involving the pharynx, the eardrum, the external ear, or the tympanic membrane. Persistent facial nerve weakness or deafness may follow.

### **HHV-4**

HHV-4 is most commonly known as the agent that causes infectious mononucleosis, although it has been linked to Burkitt lymphoma, other lymphoproliferative diseases, and some nasopharyngeal carcinomas.

Primary infection, infectious mononucleosis occurs on first exposure to the virus, usually during young adulthood. It is often a subclinical infection. The virus (usually acquired from infected saliva) replicates in the cells of the mucosa and salivary glands and spreads to B lymphocytes and the bloodstream. If the patient is immunocompetent, cytotoxic T cells become activated and a characteristic lymphadenopathy (notably involving the posterior cervical nodes) accompanies tonsillitis and hepatosplenomegaly. Tonsillitis may be severe and may encroach on the airway. Thrombocytopenia may complicate the infection, and petechiae may be noted at the junction of the hard and soft palates. The patient may report headache, fever, malaise, myalgia, and fatigue. Severe abdominal pain may indicate splenic rupture.

Hairy leukoplakia, caused by EBV, primarily occurs in adults who are immunosuppressed. Hairy leukoplakia manifests as asymptomatic white lesions on the lateral border of the tongue, often bilaterally. The lesions may be observed on the adjacent dorsal or ventral surface of the tongue. Occasionally, lesions are present in other sites, such as the buccal mucosa near the commissures. The lesions have a corrugated, linear appearance and may appear granular or nodular or may have hairlike projections. Hairy leukoplakia may be the first manifestation of immunosuppression and may prompt the clinician to test the patient's HIV status. The presence of hairy leukoplakia is significantly associated with an HIV viral load of at least 3000 copies/ $\mu$ L.

EBV has been detected in aggressive periodontal lesions more often than in less diseased periodontal tissues, and EBV has also been detected in periapical lesions. The significance of these findings is unclear.

### **HHV-5**

Primary CMV infection is usually asymptomatic in patients who are immunocompetent. The virus is shed by glandular secretions, including saliva. It occasionally is shed in urine. Primary CMV infection can be asymptomatic, but it can also mimic mononucleosis. Clinical disease is more common in neonates and in patients who are immunosuppressed than in other individuals.

CMV can persist indefinitely in the host. Reactivation of latent infection can occur in patients who are immunosuppressed, including most patients who have undergone organ transplantation and as many as 90% of patients with AIDS. Latent CMV infection may cause esophagitis, which is occasionally accompanied by oral ulcerations or erythema. The disease can also affect many other body systems, including the colon, eyes, liver, lungs, or brain. The oral ulcerations are clinically nonspecific, and a biopsy is required for definitive diagnosis. A patient with HIV infection who develops CMV oral ulcerations is at high risk for progression to AIDS.

Congenital CMV infection affects 0.5-2.2% of newborns. It is frequently asymptomatic, but oral manifestations may include enamel hypoplasia of the primary teeth.

### **HHV-7**

HHV-7 infection has been associated with roseola infantum, acute hemiplegia of childhood, respiratory tract infections, and hepatitis. It has also been linked to seizures in children with febrile illnesses. HHV-7 has been identified in the saliva of adults, and this is most likely where the virus persists chronically.

### **HHV-8**

DNA sequences of HHV-8 have been identified in persons with KS. HHV-8, also termed KS-associated herpesvirus, may be important in causing and/or maintaining KS lesions. KS in the oral cavity follows the same disease pattern as KS in other body sites, and, initially, the lesion may appear as a red, purple, or dusky patch that enlarges into a plaque and later progresses into a tumorous mass. It is observed most frequently in immunosuppressed patients and rarely occurs in children. In the oral cavity, early KS may mimic an amalgam tattoo. The palate is the initial site of

intraoral KS in approximately half the cases; other favored sites include the gingiva, the tongue, and the tonsillar area.

**Diagnosis** is often made based on the clinical findings alone, especially for HHV-1, HHV-2, and HHV-3. A smear of an intact viral vesicle may be helpful to confirm the clinical diagnosis. Smear results may reveal virally altered epithelial cells. Direct immunofluorescence antibody tests and culturing help identify the causative virus. Biopsy is usually required to confirm a diagnosis of KS, and it may be required to confirm the diagnosis of other conditions.

### **Histologic findings**

Herpes simplex infection is characterized by an acantholytic intraepidermal vesicle with epithelial giant cells. The cells exhibit nuclear molding and peripheral accentuation of the nucleoplasm. Underlying leukocytoclastic vasculitis is typically present. Zoster has similar findings, but the leukocytoclastic vasculitis is more pronounced.

CMV infection manifests as enlarged endothelial cells. The cells have ample cytoplasm and an owl's eye nucleus.

KS is typically a neoplastic spindle cell proliferation with erythrocytes in slit like spaces and extravasation between the neoplastic cells.

### **Medical care**

Establishing the diagnosis is important because the differential diagnoses include diseases that are conventionally treated with immunosuppressive agents. Immunosuppressive therapy may not be prudent for an active herpetic infection because it could promote dissemination.

Herpesvirus infections may trigger erythema multiforme. If recurrences are common and debilitating, long-term suppressive antiviral therapy may reduce the recurrence of herpes and thus erythema multiforme.

### **Primary HHV-1/HHV-2**

The goals of treatment are to make the patient comfortable and to prevent secondary infections or worsening systemic illness. The patient should maintain fluid intake and a balanced diet with the use of liquid food replacement if necessary. Analgesics, such as acetaminophen, may make the patient more comfortable. **Aspirin should be avoided in pediatric patients because of the possibility of Reye syndrome.** Topical anesthetics and coating agents may make the patient more comfortable and may aid in the consumption of food; however, they do not speed healing. Patients should be advised about the potential for autoinoculation if they touch the herpetic lesion and then touch a mucous membrane or an eye. Controlling autoinoculation can be a challenge if the patient is a young child.

### **Recurrent orofacial HHV-1/HHV-2**

Some patients find that sunburn triggers the recurrence of labial lesions. Sun avoidance with the use of hats or shading or the application of a sunscreen or sunblock may reduce the frequency of recurrences.

If the decision is made to use systemic antiviral treatment, it should be initiated as early as possible in the prodromal stage to reduce the size, severity, and duration of the lesions. Topical antiviral medications are minimally useful in treating recurrent HHV-1 infection in healthy patients.

Emollient preparations may make the patient more comfortable. Systemic prophylactic antiviral medication may be indicated for patients who experience 6 or more recurrences a year or for patients who experience repeated bouts of erythema multiforme induced by herpes.

### **HHV-3 (varicella-zoster virus)**

Antiviral therapy is most effective in limiting the area of involvement and the duration of the symptoms if instituted within the first 48-72 hours. Acyclovir may control the size of the lesions, but it is less effective than valacyclovir or famciclovir in reducing pain and in lessening the risk of postherpetic neuralgia. Postherpetic neuralgia is especially common in older patients, and it may be appropriately managed with short-term, high-dose corticosteroid prophylaxis in conjunction with or following antiviral therapy. The pain of postherpetic neuralgia can also be managed with anticonvulsants, antidepressants, painkillers, or topical anesthetics.

Prevention of chicken pox/varicella infection can be accomplished via vaccination. Two vaccines are available for the prevention of varicella infection. The first is a single-antigen varicella vaccine (Varivax; Merck & Co). It is indicated for use in healthy children older than 12 months, adolescents, and adults. The second vaccine is a combination of the measles, mumps, rubella, and varicella components (ProQuad; Merck & Co) for use in children aged 12 months to 12 years. Persons with either varicella or zoster may benefit from oral antiviral drugs.

#### **HHV-4 (EBV)**

Topical tretinoin gel may be used to manage oral hairy leukoplakia, but it often is not necessary. Topical podophyllin applications (a keratotic agent) may help to control EBV-associated hairy leukoplakia. Repeated treatment may be necessary to obtain satisfactory results. Management of the underlying immunosuppressed status may be a more useful strategy. Occasionally, the use of systemic antiviral medication may be warranted. Potential toxicity, adverse effects, and complications of systemic therapy combined with a high risk of lesion reappearance and the benign nature of hairy leukoplakia support a conservative approach in the management of hairy leukoplakia.

#### **HHV-5 (CMV)**

Similar to HHV-1/HHV-2, CMV-related ulceration of the oral cavity requires immediate referral to an ophthalmologist if ocular involvement is of concern. Systemic antiviral treatment (ie, with ganciclovir or valganciclovir) is the treatment of choice for oral lesions.

#### **HHV-8**

Patients diagnosed with HHV-8-associated KS should be referred to a health care provider experienced in the treatment of this disease. The best results in the treatment of KS are achieved by improving systemic immune functions. When limited to the oral cavity, low-dose radiation therapy, intralesional injections of vinblastine and/or sodium tetradecyl sulfate (Sotradecol), and/or interferon alfa (IFN- $\alpha$ ) have been reported to result in the resolution of the lesions.

#### **Consultations**

Patients with ocular lesions should be immediately referred to an ophthalmologist.

Patients with KS are commonly referred to an appropriate subspecialist for treatment.

Patients with confirmed hairy leukoplakia or KS should undergo a thorough investigation of their immune status.

#### **Comprehensive control:**

1. Peculiarities of the clinical course and diagnosis of acute herpetic stomatitis in children.
2. Peculiarities of the clinical course and diagnosis of recurrent herpetic stomatitis in children.
3. Etiology and pathogenesis of AHS and RHS.
4. Differential diagnosis of acute herpetic stomatitis in children.
5. Differential diagnosis of recurrent herpetic stomatitis in children.
6. Scheme of local treatment of AHS and RHS depending from the stage of disease.
7. Scheme of general treatment of AHS and RHS depending from the stage of disease.
8. Antiviral remedies.
9. Prevention.

#### **Test control:**

1. The parents of an 8-year-old child complain of the presence of a sore formation in the child's oral cavity that makes food consumption difficult. Similar complaints were first made 2 years ago. The erosion of 0,7cm in size, of oval shape covered by a grayish yellow plaque is found on the lateral surface of the tongue, on a background of the hyperemic and swollen mucous membrane. The erosion has hyperemic margins and is painful during the palpation. The medical history includes a record of chronic cholecystocholangitis and biliary dyskinesia. Define a provisional diagnosis.

1. A. Stomatitis aphthous chronica recurring
2. B. Stevens-Johnson syndrome

3. C. Bechchets syndrome
4. D. Multiform exudative erythema
5. E. Traumatic erosion

2. A 12-year-old child complains of body temperature rise up to 39,8°C, weakness, headache and pain in throat getting worse when swallowing. Objectively: mucous membrane of gums is edematous, hyperemic. Tonsils are bright red, hypertrophic, covered with yellow-gray deposit which does not extend beyond the lymphoid tissue and can be easily removed. Submandibular, occipital lymph nodes are significantly enlarged, slightly painful on palpation. Hepatosplenomegaly is present. Identify the causative agent of this disease:

- A. Epstein-Barr virus
- B. Bordet-Gengou bacillus
- C. Coxsackie virus
- D. Herpes virus
- E. Loeffler's Bacillus

3. During dental examination of 13-year-old patient acute herpetic stomatitis was revealed. Which group of medicine should be applied for the dissolution of fibrinous coating?

- A. Proteolytic enzymes
- B. Anti-viral
- C. Antibiotic
- D. Anti-inflammatory
- E. No correct answer

4. During dental examination of 11-year-old patient acute herpetic stomatitis was clarified. Which medicines of anti-viral action should be applied for the local treatment?

- A. Acyclovir (zovirax)
- B. Solcoseryl
- C. Trypsin
- D. Deoxyribonuclease
- E. All mention above

5. During dental examination of 11-year-old patient acute herpetic stomatitis was revealed. What is the etiological agent of this disease?

- A. DNA-containing herpes simplex virus
- B. Groups A coxsackieviruses
- C. Groups B coxsackieviruses
- D. Chickenpox virus
- E. Shingle's virus

6. The parents of 13-year-old child turned to the dentist with complaints of weakness, hyperemia, gums bleeding, loss of appetite, increasing of salivation in their child. Objectively: there are 5-15 round erosions with yellowish fibrinous coating and thin red halo on the oral mucosa of lips, cheeks, tongue, angles of mouth. There are areas of superficial epithelial necrosis or vesicles (1-30 mm) with the muddy content. The erosions are sharply painful while touched. The relapses occur 4 times per year. Make the diagnosis.

- A. Recurrent herpetic stomatitis (severe form)

- B. Acute herpetic stomatitis, (mild form)
- C. Acute herpetic stomatitis, (mild form)
- D. Recurrent herpetic stomatitis (medium form)
- E. Recurrent herpetic stomatitis (moderate form)

7. The parents of 3, 5-years- old child turned to the pediatrician complaining about raise of body temperature to 39 - 40 C, weakness, hyperemia, bleeding gums, refuse from eating, increasing of salivation and unpleasant smell. Objectively: significant area of oral mucosa of lips, cheeks tongue, soft and hard palate are covered with yellowish fibrinous coating and thin red halo. The erosions are sharply painful while touched. Make the diagnosis.

- A. Acute herpetic stomatitis, (severe form)
- B. Acute herpetic stomatitis, (mild form)
- C. Generalized periodontitis
- D. Acute catarrhal gingivitis
- E. Recurrent herpetic stomatitis

8. The parents of 4-years- old boy turned to the dentist complaining about raise of body temperature to 37,5-39 C, weakness, hyperemia, bleeding gums, refuse from eating, increasing of salivation. Objectively: there are 3-5 round erosions with yellowish fibrinous coating and thin red halo on the oral mucosa of lips and cheeks. The erosions are sharply painful while touched. Acute herpetic stomatitis (mild form) was diagnosed. What is the first step of treatment of this disease?

- A. Pain control
- B. Prevention of relapses of new elements
- C. Stimulation of epithelization
- D. Hygienic education
- E. Anti-bacterial therapy

9. During dental examination of 4-years-old patient was diagnosed with acute herpetic stomatitis (mild form). Which medicine should be applied for the etiological therapy?

- A. Antiviral medication
- B. Anti-bacterial medication
- C. Pain control
- D. Stimulation of epithelization
- E. Hygienic education

10. During dental examination of 13-years -old patient recurrent herpetic stomatitis was revealed. Which methods should be use for the diagnostics of this disease?

- A. Virologic
- B. Immunofluorescence
- C. Cytological
- D. All mention above
- E. Blood test

**Recommended literature:**

Pediatric Therapeutic Dentistry: [textbook for students of dental faculties] / L. A. Khomenko, A. V. Savychuk, O. I. Ostapko [et al.]; ed. L. A. Khomenko. -Kiev: [s. n.], 2012. - 240 p.

## Practical class 5

**Candidiasis. Etiology, pathogenesis, clinic, diagnosis, differential diagnosis, treatment and prevention of candidiasis in children.**

**Cheilitis and tongue diseases in children. Independent and symptomatic cheilitis Clinical characteristics, diagnostics. Differential diagnostics. Treatment**

**Purpose of the lesson:** To study with student etiology, pathogenesis, clinical course, diagnosis and treatment of the mycotic lesions of the mucosa of the oral cavity in children. To study classification, clinical course, diagnosis and treatment of the cheilitis and glossitis in children.

### **Control of the initial level of knowledge**

1. The main methods of examination of the patient with oral mucosa pathology.
2. Additional methods of examination of the patient with oral mucosa pathology.
3. Pathomorphologic manifestation of oral mucosa diseases.
4. Classification of the mucous diseases.
5. Mycosis, general understanding.

### **Content of the practical class**

**Oral candidiasis** (also known as "thrush") is an infection of yeast fungi of the genus *Candida* on the mucous membranes of the mouth. Although candida is present in 50% of healthy mouths, it causes infection (candidiasis) when increased numbers of yeast cells invade the mucosa. It is frequently caused by *Candida albicans*, or less commonly by *Candida glabrata* or *Candida tropicalis*. Oral thrush may refer to candidiasis in the mouths of babies, while if occurring in the mouth or throat of adults it may also be termed *candidosis* or *moniliasis*.

By tradition, the most commonly used **classification** of oral candidosis divides the infection into 4 types including:

- 1) acute pseudomembranous candidosis (thrush),
- 2) acute atrophic (erythematous) candidosis,
- 3) chronic hyperplastic candidosis was further subdivided into 4 groups based on localization patterns and endocrine involvement including:
  - chronic oral candidosis (candidal leukoplakia),
  - endocrine candidosis syndrome,
  - chronic localized mucocutaneous candidosis,
  - chronic diffuse candidosis.
- 4) chronic atrophic (erythematous) candidosis.

### **Pathophysiology**

*C. albicans* is the predominant causal organism of most candidosis. Other species, including *Candida krusei*, have appeared in persons who are severely immunocompromised. *Candida glabrata* is an emerging cause of oropharyngeal candidosis in patients receiving radiation for head and neck cancer. In patients with HIV infection, new species, such as *Candida dubliniensis* and *Candida inconspicua*, have been recognized.

*C. albicans* is a harmless commensal organism inhabiting the mouths of almost 50% of the population (carriers); persister cells are clinically relevant, and antimicrobial therapy selects for high-persister strains in vivo. Under certain circumstances, *C. albicans* can become an opportunistic pathogen. Such a suitable circumstance for it to become an opportunist may be a disturbance in the oral flora or a decrease in immune defences.



## **Acute pseudomembranous candidosis (thrush)**

Thrush may be observed in healthy neonates or in persons in whom antibiotics, corticosteroids, or xerostomia disturb the oral microflora. Oropharyngeal thrush occasionally complicates the use of corticosteroid inhalers. Immune defects, especially HIV infection, immunosuppressive treatment, leukemias, lymphomas, cancer, and diabetes, may predispose patients to candidal infection.

## **Erythematous candidosis**

Erythematous candidosis may cause a sore red mouth, especially of the tongue, in patients taking broad-spectrum antimicrobials. It also may be a feature of HIV disease. Median rhomboid glossitis is a red patch occurring in the middle of the dorsum in the posterior area of the anterior two thirds of the tongue and especially is observed in smokers and in those with HIV disease.

## **Chronic mucocutaneous candidosis**

Chronic mucocutaneous candidosis (CMC) describes a group of rare syndromes, which sometimes include a definable immune defect, in which persistent mucocutaneous candidosis responds poorly to topical treatment.

## **Symptoms**

While it can sometimes occur without symptoms, the most common are discomfort and burning of the mouth and throat and an altered sense of taste (often described as “bad”). Oral infections by *Candida* species usually appear as thick white or cream-colored deposits on mucosal membranes. The infected mucosa of the mouth may appear inflamed (red and possibly slightly raised). Creamy white or yellowish spots on the mouth and throat that can be removed by light scraping are also common. When the cream-colored deposits are scraped, there is slight bleeding. These may be accompanied by cracking, redness, soreness and swelling at the corners of the mouth. A bad case can include mouth sores. In babies the condition is termed thrush. Adults may experience discomfort or burning.

## **Risk factors**

- Newborn babies.
- Diabetics with poorly controlled diabetes.
- As a side effect of medication, most commonly having taken antibiotics. Inhaled corticosteroids for treatment of lung conditions (e.g., asthma) may also result in oral candidiasis: the risk may be reduced by regularly rinsing the mouth with water after taking the medication.
- People with an immune deficiency (e.g. as a result of AIDS/HIV or chemotherapy treatment).
- Women undergoing hormonal changes, like pregnancy or those on birth control pills.
- Denture users.
- Other factors that may stimulate *Candida* to grow include iron, folate, vitamin B12 or zinc deficiency and using antihistamines. Cancer chemotherapy, stress and depression can also cause candidiasis.

## ***Clinical features***

*Candida* may arise suddenly as an acute infection or persist for long periods as a chronic infection.

- Acute pseudomembranous candidiasis. There are white patches on gums, tongue & inside the mouth that can be peeled off leaving a raw area.

- Acute atrophic candidiasis. There are smooth red shiny patches on the tongue. The mouth is very sore.
- Chronic atrophic candidiasis. This is common in those with dentures. The underlying mucosa is red and swollen.
- Angular cheilitis. There are sore red splits at each side of the mouth, more likely if there is overhang of the upper lip over the lower lip causing a moist deep furrow. Angular cheilitis due to candida and/or *Staphylococcus aureus* arises frequently in those taking the medication isotretinoin for acne; this medication dries the lips.
- Chronic hyperplastic candidiasis. This is a type of oral leukoplakia (white patch) inside the cheeks or on the tongue with persistent nodules or lumps. It usually affects smokers and is pre-malignant. Red patches (erythroplakia) as well as white patches may indicate malignant change.
- Chronic mucocutaneous candidiasis presents as a chronic pseudomembranous infection. The skin and nails are also affected.
- Median rhomboid glossitis - there is diamond-shaped inflammation at the back of the tongue.
- Candida can cause secondary infection of other skin conditions such as lichen planus or geographic tongue.

Severe infections may extend down the throat (oesophageal infection).

## **Diagnosis**

Oral conditions are usually diagnosed by appearance and symptoms. Microscopy and culture of skin swabs and scrapings aid in the diagnosis of candidal infections. However, candida can live on a mucosal surface quite harmlessly. It may also secondarily infect an underlying disorder.

## **Prevention**

Using antifungal drugs to prevent fungal infections is approached with great care and is generally discouraged, especially using fluconazole this way. This makes treating newer and more aggressive infections more difficult and often unsuccessful. However, this may not be possible in some people with recurrent infections who must remain on long-term therapy to prevent them.

Overall, the best way to naturally prevent fungal infections is to eat healthfully and regularly, avoid excessive sugar intake, and avoid or decrease alcohol, caffeine, dairy and cigarettes.

- Decrease or avoid sugars (syrup, glucose, fructose and sucrose)
- Decrease or avoid alcohol.
- Drink milk or eat yogurt that contains acidophilus bacteria.
- Eat larger amounts of food that may keep yeast from growing. Some nutritionists believe garlic has natural antifungal properties. Fresh garlic is considered best, although commercial garlic “pills” help reduce the odors. (NOTE: Large amounts of garlic may interfere with HIV meds, especially Norvir (ritonavir).

## **Treatment**

Oral candidiasis can be treated with topical anti-fungal drugs, such as nystatin, miconazole, Gentian violet or amphotericin B. Topical therapy is given as an oral suspension which is washed around the mouth and then swallowed by the patient.

Patients who are immunocompromised, either with HIV/AIDS or as a result of chemotherapy, may require systemic treatment with oral or intravenous administered anti-fungals.

### Drugs used to treat oral candidiasis

Drug Name	Dose	Side effects	Notes
<b>TOPICAL THERAPIES</b>			
Clotrimazole (Mycelex) troches	10mg 4–5 times daily for 1–2 weeks	May cause altered taste and stomach upset	Suck slowly; do not chew or swallow whole
Nystatin (Mycostatin) Pastille	1–2 pastilles 4–5 times daily	May cause irritation in the mouth; nausea	Suck slowly; do not chew or swallow whole
Nystatin (Mycostatin) oral suspension	5ml four times daily for 7–14 days	May cause stomach upset	Swish around mouth before swallowing
<b>SYSTEMIC THERAPIES</b>			
Ketoconazole (Nizoral) tablet	200mg a day, 7–14 days; 400mg day, 14–21 days*	Nausea, vomiting, stomach pain; liver toxicity	Monitor liver function; Take with food
Itraconazole (Sporanox)	100mg a day, 7–14 days; 200mg a day, 14–21 days*	Nausea, vomiting, stomach pain; liver toxicity	Monitor liver function
Fluconazole (Diflucan)	200mg a day, 7–14 days; 200mg a day, 14–21 days*	Nausea, vomiting, stomach pain; liver toxicity	Monitor liver function
Amphotericin B (Fungizone) Amphotericin B lipid complex (Abelcet)	100mg a day four times daily (oral suspension); 0.5mg/kg a day, 14–21 days (intravenous)*	For intravenous form: kidney toxicity, electrolyte losses, fever, chills, sweats	For oral suspension, swish around mouth before swallowing; monitor kidney function
<b>OTHER THERAPIES</b>			
Gentian violet (1% solution in water)	Applied to affected areas twice a day for three days	May cause swelling	Available over-the-counter. May be useful for recurrent infections when applied every 7 days for 1 month; messy application.

#### **Comprehensive control:**

1. Classification of the mycotic diseases.
2. Etiology and pathogenesis of candidosis in children.
3. Acute pseudomembranous candidosis. Clinical course. Diagnosis.
4. Acute atrophic (erythematous) candidosis. Clinical course. Diagnosis.
5. Chronic forms of candidosis. Clinical course. Diagnosis.
5. Prevention of the mycotic diseases.
6. Treatment of the mycotic diseases.

#### **Test control:**

1. A 10-month-old child fell ill 2 days ago and refused to eat. He was treated by a pediatrician on the occasion of pneumonia. He got antibiotics, sulfanilamide. Objectively: the mucous membrane of the oral cavity is hyperemic, swollen. There is white plaque on the mucous of cheeks, lips, soft and

hard palate that is removed in some areas with formation of erosions. Submaxilla lymphatic nodes are enlarged. What is the most probable diagnosis?

- A. Acute Candida stomatitis
- B. Acute herpetic stomatitis
- C. Soft form of leucoplakia
- D. Chronic Candida stomatitis
- E. Allergic stomatitis

2. An 8.5 -year- old boy complains of dryness and itching of lips during the last days. The boy has a harmful habit to retain a pen in the mouth. Objectively: the red contour and skin of the lips are swollen, brightly hyperemic. The moderate peeling of the staggered area is found. What is the most probable diagnosis?

- A. Contagious allergic cheilitis
- B. Atopic cheilitis
- C. Eczematous cheilitis
- D. Meteorological cheilitis
- E. Exfoliate cheilitis

3. During the prophylactic examination of the 6-year-old child the areas of epithelium desquamation with oval red spots have been found out on the back of a tongue with the areas of hyperkeratinization of papillae filiformes. The papillae fungiformes are hypertrophied. The subjective feelings are absent. The child's anamnesis shows the disbacteriosis of intestine. What is the most probable diagnosis?

- A. Desquamative glossitis
- B. Acute catarrhal glossitis
- C. Herpetic affect of tongue
- D. Mycotic glossitis
- E. Rhomboidal glossitis

4. A 5-year-old patient visited the doctor with complains of painful swelling of lips. He suffers from biliary dyskinesia. The anamnesis shows a postvaccination allergy. The illness lasts for a year. In summer the patient felt health improvement. Objectively: a red contour of the lips is hyperemic, on the contour there are small blisters, in the corners of the mouth there are perleches. What is the most probable diagnosis?

- A. Allergic cheilitis
- B. Meteorologic cheilitis
- C. Bacterial cheilitis
- D. Exfoliative cheilitis
- E. Traumatic cheilitis

5. Parents of a child of 4 months complain of the appearance of a white plaque in the mouth cavity of their child and it refusal to eat. Objectively: general condition is satisfactory, the T-37, 1C. The cheesy white plaque on the mucosa of the cheeks, lips and the hard palate is determined. Coating is easily removed, the mucous underneath is hyperemic. What additional method of investigation will confirm the diagnosis?

- A. Microbiological
- B. Immunofluorentcent

- C. Cytological
- D. Immunological
- E. Virology

6. Child of 6 years is complaining of soreness and dryness of the lips. The disease developed two days ago after a long stay in the open air. There is slight edema, hyperemia of the lips, light infiltration, scales on red rim lip. The surface of lips is dry. Put the diagnosis of the disease:

- A. Meteorological cheilitis
- B. Actinic cheilitis
- C. Eczematous cheilitis
- D. Exfoliative cheilitis
- E. Glandular cheilitis

7. An 1 year old child is restless, refuses to eat, the body temperature is 37.7 C. Objectively: mucosa of cheeks, vestibulum oris, and tongue is hyperaemic and covered with cheesy white coating. What medications should be prescribed firstly?

- A. Antifungal
- B. Antibiotics
- C. Antiviral
- D. Antiallergic
- E. Antiseptic

8. Parents of 6 months child complain of the presence of plaque in the oral cavity in their child. Objectively: oral mucosa is hyperemic, covered with white coating that resembles clotted milk; the coating can be easily withdrawn. Clarify the diagnosis:

- A. Acute candidous stomatitis
- B. Chronic candidous stomatitis
- C. Acute herpetic stomatitis
- D. Recurrent herpetic stomatitis
- E. Soft form of leukoplaky

9. Parents of 6 months child complain of the presence of plaque in the oral cavity in their child. Objectively: oral mucosa is hyperemic, covered with white coating that resembles clotted milk; the coating can be easily withdrawn. What is the causative agent of this disease?

- A. Candida
- B. Herpes simplex virus
- C. Lefler's rod
- D. Koksaki virus
- E. Epstein-Barr virus

10. Parents of 6-year-old child appeared with complaints of child's refusal of food and presence of gray-yellow plaque in the mouth during the year. The child marks a sharp dryness and burning in oral cavity. Objectively: the yellowish-gray coating is present on the hyperemic and swollen mucosa of lips, cheeks. Plaque on the tongue is associated with tissue, is fixed with surface and is located on infiltrated basis. A child suffers of chronic bronchitis and receives systematic treatment with antibiotics. What is the most likely diagnosis?

- A. Chronic candidous stomatitis

- B. Acute herpetic stomatitis
- C. Chronic recurrent aphthous stomatitis
- D. Multiform exudative erythema
- E. Acute candidous stomatitis

**Recommended literature:**

Pediatric Therapeutic Dentistry: [textbook for students of dental faculties] / L. A. Khomenko, A. V. Savychuk, O. I. Ostapko [et al.]; ed. L. A. Khomenko. -Kiev: [s. n.], 2012. - 240 p.

**Practical class 6**

**Immediate allergic reactions (anaphylaxis, angioedema, urticaria) and delayed type (exudative erythema multiforme, Stevens-Johnson syndrome) and their manifestations in the oral cavity in children at different ages. Clinical manifestation, diagnosis, differential diagnosis and treatment.**

**Purpose of the lesson:** To study with student clinical course, diagnosis and treatment of the medicamentall allergy, Erythema multiforme, Stevens-Johnson syndrome in children.

**Control of the initial level of knowledge:**

1. What is allergy?
2. Classification of the allergens.
3. Stages of the development of allergic reactions.
4. Types of the allergic reactions
5. Mechanism of the development of immediate allergic reactions.
6. Mechanism of the development of delayed type of allergic reactions.

**Content of the practical class**

Allergy is an epidemic which overcame all countries in the world and has a tendency to increase in 21st century. An **allergic reaction** is a hypersensitivity of the immune system at the repeated influence of allergen on before sensitized organism. The symptoms usually are eye's pang, edema, rheum, hives, sneezing etc.

**Anaphylaxis** refers to a rapidly developing and serious allergic reaction that affects a number of different areas of the body at one time. Anaphylaxis is often triggered by substances that are injected or ingested and thereby gain access into the blood stream. An explosive reaction involving the skin, lungs, nose, throat, and gastrointestinal tract can then result. Although severe cases of anaphylaxis can occur within seconds or minutes of exposure and be fatal if untreated, many reactions are milder and can be ended with prompt medical therapy.

**The causes of anaphylaxis are divided into two major groups:**

- **IgE mediated:** This form is the true anaphylaxis that requires an initial sensitizing exposure, the coating of mast cells and basophils (cells in the blood and tissue that secrete the substances that cause allergic reactions, known as mediators) by IgE, and the explosive release of chemical mediators upon re-exposure.
- **Non-IgE mediated:** These reactions, the so called "anaphylactoid" reactions, are similar to those of true anaphylaxis, but do not require an IgE immune reaction. They are usually caused by the direct stimulation of the mast cells and basophils. The same mediators as occur with true anaphylaxis are released and the same effects are produced. This reaction

can happen, and often does, on initial as well as subsequent exposures, since no sensitization is required.

The terms anaphylaxis and anaphylactoid (meaning "like anaphylaxis") are both used to describe this severe, allergic reaction. Anaphylaxis is used to describe reactions that are initiated by IgE and anaphylactoid is used in reference to reactions that are not caused by IgE. The effects of the reactions are the same, however, and are generally treated in the same manner. Often, they can not be distinguished initially.

### **Anaphylaxis symptoms:**

The symptoms of an anaphylactic reaction may occur within seconds of exposure, or be delayed 15 to 30 minutes, or even an hour or more after exposure (typical of reactions to aspirin and similar drugs). Early symptoms are often related to the skin and include:

- Flushing (warmth and redness of the skin),
- itching (often in the groin or armpits), and
- hives.

These symptoms are often accompanied by:

- a feeling of "impending doom,"
- anxiety, and
- sometimes a rapid, irregular pulse.

Frequently following the above symptoms, throat and tongue swelling results in hoarseness, difficulty swallowing, and difficulty breathing.

Symptoms of rhinitis (hay fever) or asthma may occur causing:

- a runny nose,
- sneezing, and wheezing, which may worsen the breathing difficulty,
- vomiting, diarrhea, and stomach cramps may develop.

About 25% of the time, the mediators flooding the blood stream cause a generalized opening of capillaries (tiny blood vessels) which results in a drop in blood pressure, lightheadedness, or even loss of consciousness. These are the typical features of anaphylactic shock.

The most distinctive symptoms of anaphylaxis include:

- Hives
- Swelling of the throat, lips, tongue, or around the eyes
- Difficulty breathing or swallowing

Other common symptoms of anaphylaxis may include:

- Metallic taste or itching in the mouth
- Generalized flushing, itching, or redness of the skin
- Abdominal cramps, nausea, vomiting, or diarrhea
- Increased heart rate
- Sudden decrease in blood pressure (and accompanying paleness)
- Sudden feeling of weakness
- Anxiety or an overwhelming sense of doom
- Collapse
- Loss of consciousness

### **Emergency treatment**

- to stop introduction of the medicine, that caused the shock
- to put child on a side, to prevent aspirate asphyxia
- introduction of 0,1 % sol. Epinephrine (adrenalin) or 1% sol. Mezatone (0.2-0.5 ml) around the place of injection and hypodermic ( 0,01 ml/kg)
- antihistaminic medication ( diphenhydramine hydrochloride, benadryl or suprastin (1 mg/kg)
- corticosteroids – hydrocortisone( 4-8 mg/kg) intramuscular, or 3% Sol. Prednisolone ( 0,1-0,2 mg/kg)
- 2,4 % sol. ephiline ( 5-7 mg/kg) i/v when bronchospasm is observed

Once anaphylaxis begins, the treatment of choice is an immediate injection of epinephrine, sometimes called adrenaline, which is effective for 10 to 15 minutes. With no result it is necessary to repeat introduction of epinephrine each 15 minutes. Epinephrine rapidly constricts the blood vessels, relaxes the muscles in the airway, reverses swelling, and stimulates heartbeat, thereby reversing the most dangerous effects of an anaphylactic reaction. The sooner a patient receives epinephrine, the better that patient's chance of survival. Extra vigilance is also essential after an episode of anaphylaxis.

Regarding the patients with higher risk of anaphylactic reaction relapse (e.g. patients that have experienced anaphylactic reaction to insect venom or food), it is necessary to instruct them to always carry with them self-aid set (e.g. EPI-PEN, ANA-KIT). EPI-PEN consists of a syringe with a needle and adrenaline for singular intramuscular application. ANA-KIT contains two doses of adrenaline and chlorpheniramine (antihistamine) chewing tablets. Patients with anaphylactic reaction to insect venom must undergo hyposensitization.

Side effects may include an increase in heart rate, a stronger or irregular heartbeat, sweating, nausea and vomiting, difficulty breathing, paleness, dizziness, weakness or shakiness, headache, apprehension, nervousness, or anxiety. These side effects usually go away quickly.

There are three possible **outcomes**:

1. The signs and symptoms may be mild and fade spontaneously or be quickly ended by administering emergency medication. In this outcome, the symptoms do not subsequently recur from this particular exposure.
2. After initial improvement, the symptoms may recur within 4 to 12 hours (late phase reaction) and require additional treatment and close observation. Recent evidence suggests that a late phase reaction occurs in fewer than 10% of cases.
3. Lastly, the reaction may be persistent and more severe, thus requiring intensive medical treatment and hospitalization. This may occur up to 20% of the time with certain exposures.

### **Quincke's Disease**

Nettle rash and Quincke's edema are widespread. It is statistically proven that each fifth person on Earth had allergic edema once in his life.

This disease got its name for characteristic displays: blisters as though they appear after nettle's burn. These blisters are accompanied by reddening, edema, itching. A fervecence, weakness and headache are also possible. Hives can be local or generalized, acute or chronic. Depending on the reason of allergic reaction's origin we can separate physical - warm, cold, pressure, solar radiation; mechanical - in the place of skin's irritation; antheriferous etc. When the reason can not be found - hives are named idiopathic.

Quincke's edema is an angioneurotic edema or giant hives that differs from ordinary hives in skin defeat depth. The giant edema mostly appears in places with loose cellulose - on lips, eyelids, cheeks, mucous membrane of mouth and on genital organs. In typical cases edema disappears in few hours (2/3 to 24 hours), if not - those patients must be hospitalized. A special form of inherited angioneurotic edema is distinguished - it is related to insufficiency of specific inhibitor. Men have allergy more frequently, it is characterized by positive family anamnesis, microtraumas and stress. Predisposing factors can be parasitogenic and viral infections or endocrine system's diseases.

In addition serious Quincke's edema may complicate as an immediate allergic reaction - anaphylactic shock.

**Treatment of Quincke's edema is the first aid** - eliminate the action of allergen, quiet the patient, provide access to fresh air ( take off tie/belt, unbutton collar, open the window), get a cold compress and lay it on the staggered area for diminishing of itch and edema, begin to drip into nose vasoconstrictor drops (for example Naphthyzinum).

The first medical aid consists of antihistamine injection (for example Suprastinum or Dimedrolum) to remove the edema. If edema spreads very quickly and violations of breathing appear,



glucocorticoid hormones are indicated.

To those who ever had Quincke's edema a hypoallergic diet is appointed - exception of food allergens as eggs, milk, wheat, fish, nuts, tomatoes, chocolate, citrus. A prophylaxis of Quincke's edema is to cure all types of chronic infections – carious teeth or adenoids, because they assist general allergization of organism. Periodically, courses of antiallergic medicine can be appointed, for example, in the period of plants flowering.

In the past few years an expressed number of morbidity is marked as an allergy. There are different theories explaining this phenomenon: a hygiene hypothesis by David P. Strachan which says that observance of norms of hygiene prevents organism's contact with antigens, that causes the insufficient loading of the immune system (in particular case for children). Nowadays, genetically modified food can cause pre-conditions for development of allergic reaction by means of parafunction of the nervous and endocrine system.

However, in spite of numerous attempts to explain an increase of allergic diseases influenced by technogenic environment, until now there were no explanations given.

### **Erythema exsudativum multiforme (EEM), Erythema multiforme (EM)**

**Erythema multiforme (EM)** was initially described in 1866 by Ferdinand von Hebra as an acute self-limited skin disease, symmetrically distributed on the extremities with typical and often recurrent concentric "target" lesions. The term EM minor was proposed later to differentiate the mild cutaneous syndrome from the more severe form, EM major, which involves several mucous membranes.

**Stevens-Johnson syndrome (SJS)** was considered an extreme variant of EM for many years, while **toxic epidermal necrolysis (TEN)** was considered a different entity. However, in 1993, a group of medical experts proposed a consensus definition and classification of EM, SJS, and TEN based on a photographic atlas and extent of body surface area involvement. According to the consensus definition, SJS was separated from the EM spectrum and added to TEN. Essentially SJS and TEN are considered severity variants of a single entity. The two spectra are now divided into (1) EM consisting of erythema minor and major (EMM) and (2) SJS/TEN. The clinical descriptions are as follows:

*EM minor* - Typical targets or raised, edematous papules distributed acrally

*EM major* - Typical targets or raised, edematous papules distributed acrally with involvement of one or more mucous membranes; epidermal detachment involves less than 10% of total body surface area (TBSA).

*SJS/TEN* - Widespread blisters predominant on the trunk and face, presenting with erythematous or pruritic macules and one or more mucous membrane erosions; epidermal detachment is less than 10% TBSA for SJS and 30% or more for TEN.

#### **Pathophysiology**

Pathophysiology of EM is not completely understood but appears to involve a hypersensitivity reaction that can be triggered by a variety of stimuli, particularly bacterial, viral, or chemical products.

A recent international prospective study showed that the major cause of EM is herpes virus. It appeared to play a smaller role in SJS/TEN. In fact, recent or recurrent herpes was the principle risk factor for EMM. Drugs were found to be a more common trigger for SJS/TEN.

Histopathologic characteristics include a lymphocytic infiltrate at the dermal-epidermal junction and around dermal blood vessels, dermal edema, epidermal keratinocyte necrosis, and subepidermal bullae formation. Histology and immunochemistry studies have shown that inflammatory infiltrates of EM and SJS/TEN are strikingly different in density and nature. EM has a high density of cell infiltrate rich in T-lymphocytes. By contrast, SJS/TEN is characterized by a cell-poor infiltrate of macrophages and dendrocytes with strong TNF-alpha immunoreactivity. Immune complex

deposition is variable and nonspecific. In severe cases, fibrinoid necrosis can occur in the stomach, spleen, trachea, and bronchi.

### **Physical**

- Symmetrically distributed, erythematous, expanding macules or papules evolve into classic iris or target lesions, with bright red borders and central petechiae, vesicles, or purpura.
- Lesions may coalesce and become generalized.
- Vesiculobullous lesions develop within preexisting macules, papules, or wheals.
- Rash favors palms and soles, dorsum of the hands, and extensor surfaces of extremities and face.
- Postinflammatory hyperpigmentation or hypopigmentation may occur.
- Eye involvement occurs in 10% of EM cases, mostly bilateral purulent conjunctivitis with increased lacrimation.
- Mucous membrane blistering occurs in about 25% of cases of EM, is usually mild, and typically involves the oral cavity.

Eruptions occur symmetrically on the extensor aspects of the joints (e.g., the dorsal hands, elbows, knees) as erythematous papules or edematous erythema, and they spread centrifugally in about 48 hours to form sharply circumscribed, round or irregularly shaped erythema. The center of the erythema is concave, presenting either as a target lesion or iris formation, also called exudative erythema. The affected area simultaneously shows new and old lesions that may fuse into map-like patterns. EM may be accompanied by blistering (bullous EM) and erosions of the oral mucosa. EM frequently occurs in the young and middle-aged, and it tends to appear during the spring and summer. Infectious symptoms including high fever and pharyngodynia may precede the onset. In cases caused by herpes simplex infection, EM tends to occur 1 to 3 weeks after the onset of the herpes simplex symptoms (post-herpetic EM).

### **Pathogenesis**

EM is caused by various factors, such as viral or bacterial infections (by herpes simplex or *Mycoplasma pneumoniae*), and drugs and malignant tumors. It is estimated that EM is a cell-mediated immune reaction leading to the destruction of keratinocytes expressing various antigens. However, the underlying pathomechanism is not known.

### **Pathology**

In the early stages of epidermal EM, there is lymphocytic infiltration into the dermo-epidermal junction and vacuolar degeneration of basal cells. As the disease progresses, lymphocytes (CD8+T cells) infiltrate into the epidermis and necrosis of epidermal cells and subepidermal blistering are found.

### **Laboratory findings**

Because of inflammation, CRP may be positive and the erythrocyte sedimentation rate is elevated. The herpes simplex virus antibody titer, *Mycoplasma* antibody titer and antistreptolysin O (ASO) titer may be elevated in some cases. In cases involving bacterial infection, there is an increase in neutrophils.

### **Diagnosis, Differential diagnosis**

EM is relatively easy to diagnose by its characteristic clinical features and by the distribution of the eruptions. History of previous diseases, such as infectious diseases, supports the diagnosis.

#### *Differential diagnosis*

**Urticaria**- Itching is more severe. Each lesion usually disappears within 24 hours.

Dermographism rubrum occurs.

**SLE - Systemic** symptoms occur (renal, arthritic, etc.). Laboratory findings of antinuclear antibodies, etc. Erythema multiforme sometimes occurs in association with SLE.

**Bullous pemphigoid** - Direct/indirect immunofluorescence reveals antibodies against basement membrane.

### **Treatment, Prognosis**

*Emergency Department Care*

Mild cases of erythema multiforme (EM) require only symptomatic treatment, which may include analgesics or NSAIDs; cold compresses with saline or Burrow's solution; topical steroids; and soothing oral treatments such as saline gargles, viscous lidocaine, and diphenhydramine elixir. Administer empiric antibiotics if clinical evidence of secondary infection exists. Most authorities advise against routine use of prophylactic antibiotics.

Use analgesics as needed to control pain, which may be severe.

Avoid systemic corticosteroids in minor cases. In severe cases, their use is controversial because they do not improve prognosis and may increase risk of complications.

*Symptomatic treatment for mild cases*

Oral lesions: Oral rinsing with warm saline or a solution of diphenhydramine, Xylocaine, and Kaopectate for symptomatic relief.

Steroid use is controversial. Patients who have herpes-induced erythema multiforme (EM) may benefit from acyclovir.

### **Stevens-Johnson syndrome (SJS)**

Synonyms: Mucocutaneous ocular syndrome, EM major

SJS is a severe acute mucocutaneous reaction with systemic symptoms such as fever and arthralgia. It may develop into toxic epidermal necrolysis (TEN). When the symptoms are severe, systemic corticosteroids is administered. Steroid pulse therapy and systemic management may also be adopted.

#### **Classification**

Stevens-Johnson syndrome (SJS) is EM major with oculomucous lesion and systemic symptoms including liver and renal dysfunction. Nevertheless, well-defined findings on the differences between EM major and SJS have not been obtained. Drugs are clearly the leading causative factor of SJS. The disease occurs 1 to 6 cases per million populations per year. It is sometimes difficult to draw an absolutely clear distinction between SJS and toxic epidermal necrolysis (TEN).

#### **Clinical features**

EM occurs suddenly, with systemic symptoms such as high fever, general fatigue, arthralgia, myalgic pain, chest pain and gastrointestinal distress. Intense edematous EM major accompanied by blistering and bleeding, develops and tends to be severe. The extensor surface of the extremities and the entire body surface including the face and trunk are affected. Mucosal sites are involved and may be severe. Erythema, hemorrhagic bullae, and erosions accompanied by pus and bloody crusts occur in the eyes, oral cavity, nose, perineal regions, and genital mucosa. Patients sometimes cannot eat or excrete because of severe pain. Systemic treatment is essential for cases with involvement of hepatopathy and renal dysfunction. Conjunctival inflammation, adhesion, corneal opacity and ulceration occur in the eyes. When it heals, SJS may leave serious aftereffects, such as loss of eyesight. Dense fibrous adhesion (symblepharon) between the conjunctival linings is also seen. Ocular involvement in SJS requires early consultation with an ophthalmologist.

#### **Pathology**

Refer to the section on erythema multiforme. Necrotic degeneration is found mostly in the epidermis. Vacuolar degeneration of the basal membranes and dermal edema are also present.

#### **Diagnosis, Differential diagnosis**

SJS is characterized by severe lesions in the mucocutaneous junction, erythema over the entire body surface, blisters, erosions and systemic symptoms, and histopathologically by epidermal necrotic degeneration. A detailed medical history is needed to identify the cause. Antibody titers of HSV, Mycoplasma, pharynx culture and chest X-ray are performed. Sudden enlargement on the entire body suggests progression to TEN.

#### **Treatment**

Early diagnosis and treatment are important for improving the prognosis. Systemic steroid administration (orally or by pulse therapy) is especially important in the early stages. The causative drug should be discontinued immediately. The skin and mucous membranes should be protected by ointment application.

**Toxic epidermal necrolysis** (also known as "**Lyell's syndrome**") is a rare, life-threatening dermatological condition that is usually induced by a reaction to medications. It is characterized by

the detachment of the top layer of skin (the epidermis) from the lower layers of the skin (the dermis) all over the body.

There is broad agreement in medical literature that TEN can be considered a more severe form of Stevens-Johnson syndrome, and debate whether it falls on a spectrum of disease that includes erythema multiforme. Some authors consider that there is an overlap between the two syndromes (usually between 10% and 30% of skin detachment).

The incidence is between 0.4 and 1.3 cases per million each year.

The mortality for toxic epidermal necrolysis is 30-40 per cent. Loss of the skin leaves patients vulnerable to infections from fungi and bacteria, and can result in sepsis, the leading cause of death in the disease. Death is caused either by infection or by respiratory distress which is either due to pneumonia or damage to the linings of the airway. Microscopic analysis of tissue (especially the degree of dermal mononuclear inflammation and the degree of inflammation in general) can play a role in determining the prognosis of individual cases.

### **Pathogenesis**

Microscopically, TEN causes cell death throughout the epidermis. Keratinocytes, which are the cells found lower in the epidermis, specializing in holding the skin cells together, undergo necrosis (cell death).

### **Etiology**

Toxic epidermal necrolysis is a rare and usually severe adverse reaction to certain drugs. History of medication use exists in over 95% of patients with TEN. The drugs most often implicated in TEN are antibiotics such as sulfonamides, nonsteroidal anti-inflammatory drugs, allopurinol, antimetabolites (methotrexate), antiretroviral drugs, corticosteroids, chlormezanone (anxiolytic) and anticonvulsants such as phenobarbital, phenytoin, carbamazepine, and valproic acid.

The condition might also result from infection with agents such as *Mycoplasma pneumoniae* or the herpes virus; and transplants of bone marrow or organs.

### **Symptoms**

TEN affects many parts of the body, but it most severely affects the mucous membranes, such as the mouth, eyes, and vagina. The severe findings of TEN are often preceded by 1 to 2 weeks of fever. These symptoms may mimic those of a common upper respiratory tract infection. When the rash appears it may be over large and varied parts of the body, and it is usually warm and appears red. The dermal layer fills with fluid being deposited there by the body's immune system, usually as a result of a negative reaction to an antibiotic. The skin then begins to sag from the body and can be peeled off in great swaths. The mouth becomes blistered and eroded, making eating difficult and sometimes necessitating feeding through a nasogastric tube through the nose or a gastric tube directly into the stomach. The eyes are affected, becoming swollen, crusted, and ulcerated and blindness may occur.

### **Diagnosis**

Often, the diagnosis can be made clinically. Generally, if the clinical history is consistent with Stevens-Johnson syndrome, and the skin lesion covers greater than 30% of the body surface area, the diagnosis of TEN is appropriate. Sometimes, however, examination of affected tissue under the microscope may be needed to distinguish it between other entities such as staphylococcal scalded skin syndrome. Typical histological criteria of TEN include mild infiltrate of lymphocytes which may obscure the dermoepidermal junction and prominent cell death with basal vacuolar change and individual cell necrosis.

Nikolsky's sign is almost always present in toxic epidermal necrolysis

### **Practical approach to treatment**

*Treatment of the condition has three primary goals:*

- haemodynamic stability
- pain management
- infection control policy

With regard to this last goal, isolation of the patient in a burns unit greatly improves infection control as well as guaranteeing adequate skin coverage.

The management protocol consists of:

- monitoring of various parameters used in burn patients: pulse rate, arterial pressure, body temperature, central venous pressure, percentage of oxygen-haemoglobin saturation, urine output, etc.
- laboratory tests to check fluid requirements
- periodic surface cultures of the regions affected and blood cultures if there is fever above 38.5 °C (101.3 °F)
- management of the patient on an air-fluidized bed in order to avoid decubitus ulcers and to obtain an adequate temperature and humidity state
- intravenous access through a central line for fluid therapy
- enteral nutrition if oral feeding is impaired, or parenteral feeding if mucosal damage is present
- intravenous narcotics for pain control, such as morphine 0.1 mg/kg/24 h
- oral antiacids for gastric stress ulcer prophylaxis
- no empirical antibiotherapy is indicated, either systemic or topic. If any infectious process is present, a specific therapy is applied by means of cultures and antibiograms
- in the light of numerous articles that have found a relationship between a higher mortality rate and the initiation of the steroid therapy, it is contraindicated to initiate the steroid therapy for the patients with TEN.
- the management of the wound is performed under sedation and analgesia, with Midazolam and Fentanyl, in adequate doses, in relation to the patient's body weight. Skin cultures are taken, loose devitalized epidermis and blisters are removed, and the resulting wound is covered with cryopreserved allografts if the damaged skin exceeds 15% of the body surface.

#### *Wound management*

First of all a calculation is made of the affected surface area, reckoning that 1% equals 150-180 cm<sup>2</sup>. It is advisable to calculate the injured area periodically, as the initial erythema may develop into exfoliative lesions, thus becoming an injured area susceptible to coverage.

The cryopreserved allografts proceed from the skin bank and are unfrozen by immersion in warm water. The allografts are applied on the de-epithelialized areas using an aseptic technique. For fixation of the allografts employs a xerofonn and soft gauze dressing.

The use of an airfluidized bed is advised for the patient's comfort and in order to facilitate wound epithelialization.

The external dressings are changed periodically in relation to clinical evaluations. The allografts remain attached to their bed until they peel off after about 10-12 days, by which time the epithelial layers have been restored. If there is any sign of infection, the allografts must be removed and replaced.

#### **Comprehensive control:**

1. Allergic reactions of immediate and delayed type.
2. Anaphylactic shock, classification, clinical course, diagnosis, first aid.
3. Erythema multiforme, classification, clinical course, diagnosis, treatment.
4. Stevens-Johnson syndrome, clinical course, diagnosis, treatment
5. "Lyell's syndrome". Clinical course, diagnosis, treatment.
5. Local treatment of Erythema multiforme.
6. General treatment of Erythema multiforme.

#### **Test control:**

1. A 12-year-old boy complains of fever up to 38 C, weakness, headache, pain in the mouth, presence of vesicles and ulcers. The acute condition developed three days ago. The patient has a history of recent pneumonia treated with antibiotics. Objectively: oral mucosa is hyperemic and edematous. The mucosa of lips, tongue and cheeks has large erosions covered with fibrinous

pellicle. The lips are covered with thick brown crusts. The back of the hand has papules of double-contour colour. Which of the listed agents should be primarily used in the topical treatment?

- A. Painkillers
- B. Antiinflammatory
- C. Antiviral
- D. Antimicrobial
- E. Antifungal

2. A 10-year-old child complains of itching, dryness and burning lips. A week ago the child started to use the new toothpaste. Objectively: a red border of lips and skin are hyperemic, there are the small blisters on this background. These blisters burst in some areas. What is the basis of this disease?

- A. Delayed-type allergic reaction
- B. Immediate type allergic reaction
- C. Chronic inflammation of the lips
- D. Reduction of the immune reactivity
- E. Allergic stomatitis

3. In a minute after torus anaesthesia was introduced with 2% solution of novocaine of 4 ml on the occasion of the 17 tooth extraction, a patient complained of a difficult breathing. Objectively: upper and lower lips, mucous membrane of larynx and oral cavity are swelled and hyperemic. What complication occurred in the patient?

- A. Quincke's edema
- B. Intoxication by anaesthetics
- C. Anaphylactic shock
- D. Collapse
- E. Coma

4. A 10-year old boy complains of swelling of the lower lip, which appeared suddenly after wasp sting and difficult breathing. Objectively: lower lip is in three times bigger than normal, the skin in the area of edema is pale. There is swelling of the tongue in the mouth. Oral mucosa of the soft palate is swollen. What drugs should be used firstly?

- A. Antihistamines
- B. Corticosteroids
- C. Anti-inflammatory drugs
- D. Antibacterials
- E. Analgesics

5. A 16-year-old patient appealed to the dentist to extract the tooth 27. After anesthesia of 2% lidocaine she complained of a throbbing headache, stuffiness in the ears, nausea, itching skin. Wheezing, drop in blood pressure, tachycardia, thready pulse were observed in the patient. What is the most likely diagnosis?

- A. Anaphylactic shock
- B. Hyperglycemic coma
- C. Angioedema
- D. Urticaria
- E. Hypertensive crisis

6. A 12-year-old girl is under clinical observation in gastroenterologist in case of biliary dyskinesia. The girl appealed to the dentist with complaints of pain while eating, the presence of lesions on the oral mucosa. An objective examination of the mucosa of the oral cavity revealed erosion, red border of lips is covered with hemorrhagic crusts. Forearms are covered with cyanotic papules with vesicles in center. Define diagnosis.

- A. Exudative erythema multiforme, infectious- allergic form
- B. Acute herpetic stomatitis, severe form
- C. Stevens-Johnson syndrome
- D. Exudative erythema multiforme, toxic- allergic form
- E. Chronic recurrent aphthous stomatitis, severe form

7. A 16-year-old girl appealed to the dentist to remove the tooth 16. After anesthesia with 2% lidocaine she complained of a throbbing headache, tinnitus, nausea, itchy skin. Wheezing, drop in blood pressure, tachycardia, thready pulse were observed. The diagnosis is anaphylactic shock.

What are the possible causes of death in anaphylactic shock?

- A. All answers are correct
- B. Swelling of the brain
- C. Acute heart failure
- D. Acute renal failure
- E. Acute respiratory failure

8. In an 11-year old boy weakness, cough, body itching, headache, increasing of the body temperature to 38-39 ° C appeared immediately after taking the medications. Objectively: there is rash on the skin that looks like the nettle burns. Define the diagnosis.

- A. Urticaria
- B. Lyell's syndrome
- C. Recurrent herpetic stomatitis
- D. Stevens-Johnson syndrome
- E. Chronic recurrent aphthous stomatitis

9. A 14-year-old boy complains of fever, pain in the joints. There are bluish-pink spots with a diameter of 1-2cm with bubbles in the center on the skin of the upper and lower extremities. There are sharp painful erosions on the oral mucosa against erythema and edema and hemorrhagic crusts on lips. Symptom of Nicholsky is negative. Select the most probable diagnosis.

- A. Exudative erythema multiforme
- B. Chronic recurrent aphthous stomatitis
- C. Ulcerous-necrotic stomatitis
- D. Chronic recurrent herpetic stomatitis
- E. Pemphigus

10. A 7- years- old girl became ill 3 days ago. Objectively: the temperature is 39, 3°C. On the skin of a face, neck, breasts, back, forearms, shins there is papular rash and single vesicles of 4-5 cm in size, filled by serous maintenance. In the oral cavity there are large erosions, covered with a white plaque, severely painful at the touch. Lips are swollen, hyperemic, covered with bleeding crusts. Conjunctivitis is present. What is the most probable diagnosis?

- A. Stevens-Johnson's syndrome

- B. Infectious mononucleosis
- C. Layela syndroms
- D. Multiform exudative erythema
- E. Acute herpetic stomatitis

**Recommended literature:**

Pediatric Therapeutic Dentistry: [textbook for students of dental faculties] / L. A. Khomenko, A. V. Savychuk, O. I. Ostapko [et al.]; ed. L. A. Khomenko. -Kiev: [s. n.], 2012. - 240 p.

**Practical class 7**

**Signs of gastric and endocrine system diseases in oral cavity. System diseases in children.  
Chronic Aphthous Recurrent Stomatitis. Etiology. Clinical characteristics, diagnostics,  
treatment.**

**Purpose of the lesson:** To study the etiology, clinical course, diagnosis and treatment of the chronic aphthous recurrent stomatitis in children.

**Control of the initial level of knowledge:**

1. Morphologic peculiarities of the structure of mucosa in children.
2. Structure and functions of digestive system.
3. Anatomy of tongue and papillar apparatus of the tongue.
4. Peculiarities of the structure and functions of the endocrinic glands.

**Content of the practical class**

**Recurrent aphthous stomatitis (RAS).**

An aphthous ulcer also known as a canker sore, is a type of oral ulcer, which presents as a painful open sore inside the mouth or upper throat characterized by a break in the mucous membrane. Its cause is unknown, but they are not contagious. The condition is also known as aphthous stomatitis, and alternatively as Sutton's Disease, especially in the case of major, multiple, or recurring ulcers. The term aphtha means ulcer; it has been used to describe areas of ulceration on mucous membranes.

**Aphthous stomatitis** is a condition which is characterized by recurrent discrete areas of ulceration which are almost always painful. Recurrent aphthous stomatitis (RAS) can be distinguished from other diseases with similar-appearing oral lesions, such as certain viral exanthems or herpes simplex, by their tendency to recur, and their multiplicity and chronicity. Recurrent aphthous stomatitis is one of the most common oral conditions. At least 10% of the population has it, and women are more often affected than men. About 30–40% of patients with recurrent aphthae report a family history.

**Classification**

*-Minor ulceration.* "Minor aphthous ulcers" indicate that the lesion size is between 3 mm-10 mm. The appearance of the lesion is that of an erythematous halo with yellowish or grayish color. Extreme pain is the obvious characteristic of the lesion. When the ulcer is white or grayish, the ulcer will be extremely painful and the affected lip may swell. They may last about 1 week.

*-Major ulcerations.* Major aphthous ulcers have the same appearance as minor ulcerations, but are greater than 10 mm in diameter and are extremely painful. They usually take more than a month to heal, and frequently leave a scar. These typically develop after puberty with frequent recurrences. They occur on movable nonkeratinizing oral surfaces, but the ulcer borders may extend onto keratinized surfaces. They may last about 10 to 14 days.

*-Herpetiform ulcerations*



This is the most severe form. It occurs more frequently in females, and onset is often in adulthood. It is characterized by small, numerous, 1–3 mm lesions that form clusters. They typically heal in less than a month without scarring. Supportive treatment is almost always necessary.

### **Signs and symptoms**

Aphthous ulcers usually begin with a tingling or burning sensation at the site of the future aphthous ulcer. In a few days, they often progress to form a red spot or bump, followed by an open ulcer. The *aphthous ulcer* appears as a white or yellow oval with an inflamed red border. Sometimes a white circle or halo around the lesion can be observed. The gray-, white-, or yellow-colored area within the red boundary is due to the formation of layers of fibrin, a protein involved in the clotting of blood. The ulcer, which itself is often extremely painful, especially when agitated, may be accompanied by a painful swelling of the lymph nodes below the jaw, which can be mistaken for toothache; another symptom is fever. A sore on the gums may be accompanied by discomfort or pain in the teeth.

### **Causes**

The exact cause of many aphthous ulcers is unknown but citrus fruits (e.g. oranges and lemons), physical trauma, stress, lack of sleep; sudden weight loss, food allergies, immune system reactions and deficiencies in vitamin B12, iron, and folic acid may contribute to their development. Nicorandil and certain types of chemotherapy are also linked to aphthous ulcers. One recent study showed a strong correlation with allergies to cow's milk. Aphthous ulcers are a major manifestation of Behcet disease, and are also common in people with Crohn's disease.

Trauma to the mouth is the most common trigger. Physical trauma, such as that caused by toothbrush abrasions, laceration with sharp or abrasive foods (such as toast, potato chips or other objects), accidental biting (particularly common with sharp canine teeth), after losing teeth, or dental braces can cause aphthous ulcers by breaking the mucous membrane. Other factors, such as chemical irritants or thermal injury, may also lead to the development of ulcers. Using toothpaste without sodium lauryl sulfate (SLS) may reduce the frequency of aphthous ulcers but some studies have found no connection between SLS in toothpaste and aphthous ulcers. Celiac disease has been suggested as a cause of aphthous ulcers; small studies of patients (33% or 1 out of 3) with Celiac disease did demonstrate a conclusive link between the disease and aphthous ulcers vs control group (23%) but some patients benefited from eliminating gluten from their diet.

Stress can provoke episodes of RAS, but the association is not invariable.

There is no indication that aphthous ulcers are related to menstruation, pregnancy and menopause.

There are a few patients whose RAS remits with oral contraceptives or during pregnancy.

Smokers appear to be affected less often.

There often is a genetic basis for RAS. More than 42% of patients with RAS have first-degree relatives with RAS. The likelihood of RAS is 90% when both parents are affected, but only 20% when neither parent has RAS. It also is likely to be more severe and to start at an earlier age in patients with a positive family history than in those without.

### **Diagnosis**

The diagnosis of RAS is made on the basis of history and clinical criteria, since there are no specific laboratory tests available. A medical history should be taken to rule out other ulcerative disorders and conditions such as Crohn's disease, celiac disease, neutropenia, HIV infection and Behcet's syndrome.

### **Prevention**

#### *Oral and dental measures*

Regular use of non-alcoholic mouthwash may help prevent or reduce the frequency of sores. In fact, informal studies suggest that mouthwash may help to temporarily relieve pain.

In some cases, switching toothpastes can prevent aphthous ulcers from occurring with research looking at the role of sodium dodecyl sulfate (sometimes called sodium lauryl sulfate, or with the acronyms SDS or SLS), a detergent found in most toothpastes. Using toothpaste free of this compound has been found in several studies to help reduce the amount, size and recurrence of ulcers.

Dental braces are a common physical trauma that can lead to aphthous ulcers and the dental bracket can be covered with wax to reduce abrasion of the mucosa. Avoidance of other types of physical and chemical trauma will prevent some ulcers, but since such trauma is usually accidental, this type of prevention is not usually practical.

### **Nutritional therapy**

Zinc deficiency has been reported in people with recurrent aphthous ulcers. The few small studies looking into the role of zinc supplementation have mostly reported positive results particularly for those people with deficiency, although some research has found no therapeutic effect.

**Treatment** is symptomatic, the goal being to:

- decrease symptoms;
- reduce ulcer number and size;
- increase disease-free periods.

The best treatment is that which will control ulcers for the longest period with minimal adverse side effects. The treatment approach should be determined by disease severity (pain), the patient's medical history, the frequency of flare-ups and the patient's ability to tolerate the medication. In all patients with RAS, it is important to rule out predisposing factors and treat any such factors, where possible, before introducing more specific therapy.

Perhaps surprisingly, few randomized controlled clinical trials have been conducted to determine the best treatments for RAS. Those that exist showed that chlorhexidine gluconate mouthwashes and topical corticosteroids both can reduce the severity and duration of RAS ulcers, but that neither significantly influences the frequency of RAS episodes.

To help determine management strategies, the practitioner may find it useful to classify RAS in three clinical presentations: type A, type B and type C.

**Type A.** RAS episodes lasting for only a few days, occurring only a few times a year, are classified as "type A."

In this scenario, pain is tolerable. The clinician should try to identify what precipitates the ulcers, what the patient uses to treat them, and how effective that treatment is. If it is effective and safe, the health care providers should encourage the patient to continue it. If a precipitating factor(s) is identified, the dentist should try eliminating it first. For example, if trauma-induced RAS is suspected, the dentist can suggest a softer toothbrush and gentler brushing. Medication may not be indicated.

**Type B.** Painful RAS each month, lasting between three and 10 days, is "type B".

In this scenario, the patient may have changed diet and oral hygiene habits because of the pain. If a precipitating factor can be identified—for example, oral hygiene, stress trauma or diet—alternatives or remedies should be discussed with the patient. It is imperative to identify patients who experience prodromal symptoms, such as tingling or swelling, because the patient can use corticosteroids (if they are indicated for him or her) at the prodromal stage to abort the attacks. Treatment often includes the use of a chlorhexidine mouthwash (without alcohol base), and a short course of topical corticosteroids as soon as the ulcers appear. Because of the consistent recurrent pattern, these patients may need a maintenance treatment protocol.

Alternative regimens include dexamethasone 0.05 milligrams/ 5 mL (rinse and spit three times per day) or a high-potency topical corticosteroid such as clobetasol ointment 0.05 % in Orabase (1:1) (Colgate Oral Pharmaceuticals, Canton, Mass.) or fluocinonide ointment 0.05 % in Orabase (1:1) if the ulcer(s) recur on the same site, used three times daily. If corticosteroids are used, patients should be monitored for yeast superinfection. In patients with poor oral hygiene, professional help from a dental hygienist should be considered once ulcers heal.

In patients with recalcitrant RAS, a short course of systemic corticosteroid therapy may be required, never exceeding more than 50 mg per day (preferably in the morning) for five days. This course of treatment is best left to a physician or oral medicine specialist.

**Type C.** Type C RAS involves painful, chronic courses of RAS in which by the time one ulcer heals, another develops.

These patients are best treated by an oral medicine specialist, who often will use potent topical corticosteroids (such as betamethasone, beclomethasone, clobetasol, fluticasone or fluocinonide),

systemic corticosteroids, azathioprine or other immunosuppressants such as dapsone, pentoxifylline and sometimes thalidomide.

In addition, oral medicine specialists may administer intralesional injections of a corticosteroid such as betamethasone, dexamethasone or triamcinolone to enhance or boost the local response, thus allowing for shorter systemic treatment. In patients with poor oral hygiene, professional help from a dental hygienist should be considered.

**Comprehensive control:**

1. Etiology, pathogenesis, diagnosis of CRAS. Elements of lesion.
2. Differential diagnosis of CRAS with chronic recurrent herpetic stomatitis.
3. Treatment and prevention of CRAS.

**Test control:**

1. Parents of a 5-month-old baby complain of food refusal, ulcers on the palate. The infant was born prematurely, is now artificially fed. Objectively: at the junction of hard and soft palate there is an oval well-defined ulcer, covered with yellow-gray film and limited by a hyperemic swelling, protruding above the surface of oral mucosa. Which group of drugs should be administered for the aphtha epithelization?

- A. Keratoplastic agents
- B. Antiviral drugs
- C. Antimycotic drugs
- D. Antiseptics
- E. Antibiotics

2. Parents of an 8-year-old child complain about a painful formation in the child's oral cavity that obstructs food intake. The same complaints were registered two years ago. Mucous membrane of lateral tongue surface is hyperemic and edematous. There is an oval erosion over 0,7 cm large covered with yellow greyish deposit. Erosion edges are hyperemic and painful on palpation. The child has a history of chronic cholecystocholangitis. What is the most likely diagnosis?

- A. Chronic recurrent aphthous stomatitis
- B. Erythema multiforme
- C. Behcet's syndrome
- D. Stevens-Johnson syndrome
- E. Traumatic erosion

3. A child of 12 years old complains on pain during chewing. Anamnesis morbi: every six months, sometimes more often, an "ulcers" appear in various parts of the mucous oral mucosa, which spontaneously heal for 7-10 days. The boy complains on intermittent pain in the abdomen, frequent constipation. The child is under clinical supervision of a gastroenterologist. Objectively: there are small oval in form erosions, surrounded by flushing rim, covered with fibrinous coating on the mucous membrane of the cheeks and lips. Define the diagnosis.

- A. Chronic recurrent aphthous stomatitis
- B. Acute herpetic stomatitis
- C. Recurrent herpetic stomatitis
- D. Exudative erythema multiforme
- E. Acute respiratory viral infections

4. A girl of 12 years old complains of pain and the presence of ulcers in the mouth cavity. The painful sensation is evident especially during eating. Objectively: there are three aphthous elements with 5 mm in diameter, covered with a yellowish coating, surrounded by inflamed red border on the transitional fold of mucous membrane in the region of the frontal teeth of the lower jaw. The aphtae are sharply painful. The chronic recurrent aphthous stomatitis is diagnosed. What group of medicines should be prescribed for the child for general treatment before consultation and diagnostic procedure in allergist?

- A. Hyposensibilization
- B. Antiviral
- C. Antifungal
- D. Nonsteroidal anti-inflammatory
- E. Antibiotics

5. The patient of 14 years old is being treated in hospital with exacerbation of chronic colitis. Objectively: there are four round-shaped erosions in the area on the lateral surface of flushed tongue and in the area of transitional fold near by tooth 45. What drugs should be used for the treatment of elements during first visit of the dentist?

- A. Anesthetics, antiseptics
- B. Painkillers, antiviral drugs
- C. Painkillers, antifungal drugs
- D. Painkillers, antibiotics
- E. Keratoplastyc substances

6. An 8 years old child complains of the presence of painful lesion in the mouth cavity which hurts during eating. Similar complaints were seen 2 years ago. There is an erosion of up to 0.6 cm of oval shape, covered with a grayish and yellowish coating and surrounded by hyperemic rim on the lateral surface of the tongue. Erosion is painful on palpation. Anamnes of disease: chronic cholecystocholangitis was diagnosed. Clarify the diagnosis.

- A. Chronic recurrent aphthous stomatitis
- B. Traumatic erosion
- C. Multiforme exudative erythema
- D. Behcet's syndrome
- E. Stevens-Johnson's syndrome

7. The 15 years old child complains of the presence of several painful erosions in the mouth cavity. The erosions appear and disappear during several days, and in 3-4 months period they appear again. Objectively: there are round-shaped erosive elements on the mucosa of lower lip sized 6.5 mm with sharp edges, surrounded by flushing rim, covered with a grayish coating, sharply painful on palpation. After the examination, diagnosis was clarified: HRAS. What drugs for topical treatment should be applied to reliae swelling and inflammation in the early stage of treatment?

- A. Corticosteroids
- B. Anesthetics
- C. Keratoplastic substances
- D. Antimicrobial drugs
- E. Hyposensibilization medicines

8. Child of 10 years old complains of presence of painful element in the mouth cavity which prevents of normal food intake. The same symptoms were observed for the first time 2 years ago. Anamnes of disease: chronic colitis. Objectively: there is a small painful erosion of oval shape, with clear hyperemic rim, covered with grayish-white coating on the vestibulum oral area. Lymph nodes are not enlarged. Clarify the diagnosis.

- A. Chronic recurrent aphthous stomatitis
- B. Aphtha Settona
- C. Chronic recurrent herpetic stomatitis
- D. Syphilitic ulcer
- E. Acute herpetic stomatitis

9. A child of 11 years old complains of presence of painful lesion in the mouth cavity which makes eating difficult. Similar symptoms were observed for the first time 2 years ago. There is an painful small-sized oval erosion, covered with grayish-white color on the bottom of the mouth. The erosion is hyperemic and has infiltrated edges. What local treatment scheme should be chosen for treatment of this pathology?

- A. Anesthesia, antiseptics, keratoplastics
- B. Anesthesia, causal therapy, keratoplastics
- C. Removal of traumatic factor, suturing damage
- D. Elimination of irritating factor, antiseptics, analgesics, keratoplastics
- E. Hyposensitization, keratoplastics

10. The parents of an 8-year-old child complain of the presence of a sore formation in the child's oral cavity that makes food consumption difficult. Similar complaints were first made 2 years ago. The erosion of 0,7cm in size, of oval shape covered by a grayish yellow plaque is found on the lateral surface of the tongue, on a background of the hyperemic and swollen mucous membrane. The erosion has hyperemic margins and is painful during the palpation. The medical history includes a record of chronic cholecystocholangitis and biliary dyskinesia. Define a provisional diagnosis.

- A. Stomatitis aphtous chronica recurring
- B. Styvens-Johnsons syndrome
- C. Bechchets syndrome
- D. Multiform exudative erythema
- E. Traumatic erosion

**Recommended literature:**

Pediatric Therapeutic Dentistry: [textbook for students of dental faculties] / L. A. Khomenko, A. V. Savychuk, O. I. Ostapko [et al.]; ed. L. A. Khomenko. -Kiev: [s. n.], 2012. - 240 p.

## Practical class 8

### **Manifestations of the blood system diseases in children in the oral cavity. Pedodontic's tactic.**

**Purpose of the lesson:** To study clinical manifestation of the blood system diseases in children in the oral cavity.

#### **Control of the initial level of knowledge:**

1. Anemia. Types of anemia.
2. Iron deficiency anemia. Etiology.
3. Hemophilia in children.
4. Classification of leucosis.

#### **Content of the practical class**

**Anemia** is a decrease in normal number of red blood cells (RBCs) or less than the normal quantity of hemoglobin in the blood. However, it can include decreased oxygen-binding ability of each hemoglobin molecule due to deformity or lack in numerical development as in some other types of hemoglobin deficiency.

Anemia is the most common disorder of the blood. There are several kinds of anemia, produced by a variety of underlying causes. Anemia can be classified in a variety of ways, based on the morphology of RBCs, underlying etiologic mechanisms, and discernible clinical spectra, to mention a few. The three main classes of anemia include excessive blood loss (acutely such as a hemorrhage or chronically through low-volume loss), excessive blood cell destruction (hemolysis) or deficient red blood cell production (ineffective hematopoiesis).

#### **Iron Deficiency Anemia**

Iron deficiency is the most common cause of anemia and usually results from blood loss. Symptoms are usually nonspecific. RBCs tend to be microcytic and hypochromic, and iron stores are low as shown by low serum ferritin and low serum iron levels with high serum total iron binding capacity. If the diagnosis is made, occult blood loss is suspected. Treatment involves iron replacement and treatment of the cause of blood loss.

#### **Pathophysiology**

Iron is distributed in active metabolic and storage pools. Total body iron is about 3.5 g in healthy men and 2.5 g in women; the difference relates to women's smaller body size, lower androgen levels, and dearth of stored iron because of iron loss with menses and pregnancy. The distribution of body iron in an average man is Hb, 2100 mg; ferritin, 700 mg (in cells and plasma); hemosiderin, 300 mg (in cells); myoglobin, 200 mg; tissue (heme and nonheme) enzymes, 150 mg; and transport-iron compartment, 3 mg.

The average diet, which contains 6 mg of elemental iron/kcal of food, is adequate for iron homeostasis. Of about 15 mg/day of dietary iron, adults absorb only 1 mg, which is the approximate amount lost daily by cell desquamation from the skin and intestines. In iron depletion, absorption increases, although the exact signaling mechanism is not known; however, absorption rarely increases to > 6 mg/day unless supplemental iron is added. Children have a greater need for iron and appear to absorb more to meet this need.

Deficiency develops in stages. In the first stage, iron requirement exceeds intake, causing progressive depletion of bone marrow iron stores. As stores decrease, absorption of dietary iron increases in compensation. During later stages, deficiency impairs RBC synthesis, ultimately causing anemia.

Severe and prolonged iron deficiency also may cause dysfunction of iron-containing cellular enzymes.

#### **Etiology**

Because iron is poorly absorbed, dietary iron barely meets the daily requirement for most people. Even so, people who eat a typical diet are unlikely to become iron deficient solely as a result of

dietary deficiency. However, even modest losses, increased requirements, or decreased intake readily produces iron deficiency.

Blood loss is almost always the cause. In men, the most frequent cause is chronic occult bleeding, usually from the GI tract. In premenopausal women, cumulative menstrual blood loss (mean, 0.5 mg iron/day) is a common cause. Another possible cause of blood loss in men and women is chronic intravascular hemolysis. Vitamin C deficiency can contribute to iron deficiency anemia by producing capillary fragility, hemolysis, and bleeding.

Increased iron requirement may contribute to iron deficiency. From birth to age 2 and during adolescence, when rapid growth requires a large iron intake, dietary iron often is inadequate. During pregnancy, the fetal iron requirement increases the maternal iron requirement (mean, 0.5 to 0.8 mg/day) despite the absence of menses. Lactation also increases the iron requirement (mean, 0.4 mg/day).

Decreased iron absorption can result from gastrectomy and upper small-bowel malabsorption syndromes. Rarely, absorption is decreased by dietary deprivation from undernutrition.

#### Symptoms and Signs

Most symptoms of iron deficiency are due to anemia. Such symptoms include fatigue, loss of stamina, shortness of breath, weakness, increased heart rate (tachycardia), enlarged spleen, dizziness, sore or swollen tongue and pallor. Fatigue also may result from dysfunction of iron-containing cellular enzymes.

In addition to the usual manifestations of anemia, some uncommon symptoms occur in severe iron deficiency. Patients may have pica, an abnormal craving to eat substances (eg, ice, dirt, paint). Other symptoms of severe deficiency include glossitis, cheilosis, concave nails (koilonychia), and, rarely, dysphagia.

#### Diagnosis

- CBC (complete blood count), serum iron, iron-binding capacity, and serum ferritin
- Rarely, bone marrow examination

Iron deficiency anemia is suspected in patients with chronic blood loss or microcytic anemia, particularly if pica is present. In such patients, CBC, serum iron and iron-binding capacity, and serum ferritin are obtained.

Iron and iron-binding capacity (or transferrin) is usually both measured, because their relationship is important. Various tests exist; the range of normal values relates to the test used. In general, normal serum iron is 75 to 150  $\mu\text{g/dL}$  (13 to 27  $\mu\text{mol/L}$ ) for men and 60 to 140  $\mu\text{g/dL}$  (11 to 25  $\mu\text{mol/L}$ ) for women; total iron-binding capacity is 250 to 450  $\mu\text{g/dL}$  (45 to 81  $\mu\text{mol/L}$ ). Serum iron level is low in iron deficiency and in many chronic diseases and is elevated in hemolytic disorders and in iron-overload syndromes. Patients taking oral iron may have normal serum iron despite a deficiency; in such circumstances, a valid test requires cessation of iron therapy for 24 to 48 h. The iron-binding capacity increases in iron deficiency. Serum transferrin receptor levels reflect the amount of RBC precursors available for active proliferation; levels are sensitive and specific. The range of normal is 3.0 to 8.5  $\mu\text{g/mL}$ . Levels increase in early iron deficiency and with increased erythropoiesis.

Treatment may include:

- **iron-rich diet**

Eating a diet with iron-rich foods can help treat iron-deficiency anemia. Good sources of iron include the following:

- meats - beef, pork, lamb, liver, and other organ meats
- poultry - chicken, duck, turkey, liver (especially dark meat)
- fish - shellfish, including clams, mussels, and oysters, sardines, anchovies
- leafy greens of the cabbage family, such as broccoli, kale, turnip greens, and collards
- legumes, such as lima beans and green peas; dry beans and peas, such as pinto beans, black-eyed peas, and canned baked beans
- yeast-leavened whole-wheat bread and rolls
- iron-enriched white bread, pasta, rice, and cereals

- **iron supplements**

Iron therapy without pursuit of the cause is poor practice; the bleeding site should be sought even in cases of mild anemia.

Iron can be provided by various iron salts (eg, ferrous sulphate-Some Trade Names FEOSOL, FERGENSOL, FERINSOL, gluconate, fumarate) or saccharated iron 30 min before meals (food or antacids may reduce absorption). A typical initial dose is 60 mg of elemental iron (eg, as 325 mg of ferrous sulfate) given 1 or 2 times/day. Larger doses are largely unabsorbed but increase adverse effects, especially. Ascorbic acid either as a pill (500 mg) or as orange juice when taken with iron enhances iron absorption without increasing gastric distress. Parenteral iron causes the same therapeutic response as oral iron but can cause adverse effects, such as anaphylactoid reactions, serum sickness, thrombophlebitis, and pain. It is reserved for patients who do not tolerate or who will not take oral iron or for patients who steadily lose large amounts of blood because of capillary or vascular disorders (eg, hereditary hemorrhagic telangiectasia). The dose of parenteral iron is determined by a hematologist. Oral or parenteral iron therapy should continue for  $\geq 6$  mo after correction of Hb levels to replenish tissue stores.

### **Aplastic Anemia**

Aplastic anemia occurs when the bone marrow produces too few of all three types of blood cells: red blood cells, white blood cells, and platelets. A reduced number of red blood cells cause hemoglobin to drop. A reduced number of white blood cells makes the patient susceptible to infection. And, a reduced number of platelets causes the blood not to clot as easily.

#### Etiology

Aplastic anemia has multiple causes. Some of these causes are idiopathic, meaning they occur sporadically for no known reason. Other causes are secondary, resulting from a previous illness or disorder. Acquired causes, however, may include the following:

- history of specific infectious diseases such as infectious hepatitis
- history of taking certain medications, such as antibiotics and anticonvulsants
- exposure to certain toxins such as heavy metals
- exposure to radiation
- history of an autoimmune disease
- inherited condition

#### Symptoms of aplastic anemia

The following are the most common symptoms of aplastic anemia. However, each individual may experience symptoms differently. Symptoms may include:

- headache
- dizziness
- nausea
- shortness of breath
- bruising
- lack of energy or tiring easily (fatigue)
- abnormal paleness or lack of color of the skin
- blood in stool
- nosebleeds
- bleeding gums
- fevers
- sinus tenderness
- enlarged liver or spleen
- oral thrush - white patches on a red, moist, swollen surface, occurring anywhere in the mouth.

The symptoms of aplastic anemia may resemble other blood disorders or medical problems. Always consult your physician for a diagnosis.

#### Diagnosis

In addition to a complete medical history and physical examination, diagnostic procedures for anemia include additional blood tests and a bone marrow biopsy.

#### Treatment

Specific treatment for aplastic anemia will be based on:

- age, overall health, and medical history
- extent of the disease



- tolerance for specific medications, procedures, or therapies
- expectations for the course of the disease

Treatment and supportive therapy may include:

- blood transfusion (both red blood cells and platelets)
- preventative antibiotic therapy
- meticulous handwashing
- special care to food preparation (such as only eating cooked foods)
- avoiding construction sites which may be a source of certain fungi
- medications (to stimulate the bone marrow to produce cells)
- immunosuppressive therapy
- hormone therapy

### **Hereditary hemorrhagic telangiectasia**

also known as **Osler-Weber-Rendu disease** and **Osler-Weber-Rendu syndrome**, is a genetic disorder that leads to abnormal blood vessel formation in the skin, mucous membranes, and often in organs such as the lungs, liver and brain.

It may lead to nosebleeds, acute and chronic digestive tract bleeding, and various problems due to the involvement of other organs. Treatment focuses on reducing bleeding from blood vessel lesions, and sometimes surgery or other targeted interventions to remove arteriovenous malformations in organs. Chronic bleeding often requires iron supplements and sometimes blood transfusions. HHT is transmitted in an autosomal dominant fashion, and occurs in one in 5,000 people.

#### Signs and symptoms

Telangiectasia (small vascular malformations) may occur in the skin and mucosal linings of the nose and gastrointestinal tract. The most common problem is nosebleeds (epistaxis), which happen frequently from childhood and affect about 90–95% of people with HHT. Lesions on the skin and in the mouth bleed less often but may be considered cosmetically displeasing; they affect about 80%. The skin lesions characteristically occur on the lips, the nose and the fingers, and on the skin of the face in sun-exposed areas. They appear suddenly, with the number increasing over time.

### **Thrombocytopenic Purpura**

Thrombocytopenic purpura is a hematological disorder characterized by a decrease in platelets in the peripheral blood.

Etiology Presumably a nonspecific viral infection, myelotoxic agents.

Clinical features The oral manifestations consist of red lesions in the form of petechiae, ecchymoses, or even hematomas, usually located on the palate and buccal mucosa. Spontaneous gingival bleeding is a constant early finding. Purpuric skin rash, epistaxis, and bleeding from the gastrointestinal and urinary tract are common.

Laboratory tests Peripheral platelet count, bone-marrow aspiration, bleeding and clotting times.

Differential diagnosis Aplastic anemia, leukemias, polycythemia vera, agranulocytosis, macroglobulinemia, drug reactions.

Treatment Steroids, platelet transfusions, cessation of drug treatment if it is drug-related.

## **LEUKEMIA**

Malignancy is second only to accidents as the leading cause of death in children. Leukemias are hematopoietic malignancies in which there is a proliferation of abnormal leukocytes in the bone marrow and dissemination of these cells into the peripheral blood. The abnormal leukocytes (blast cells) replace normal cells in bone marrow and accumulate in other tissues and organs of the body.

Leukemia is classified according to the morphology of the predominant abnormal white blood cells in the bone marrow. These types are further categorized as acute or chronic, depending on the clinical course and the degree of differentiation, or maturation, of the predominant abnormal cells.

**Acute leukemia** is the most common malignancy in children, with about 2500 new cases diagnosed annually. Thus acute leukemia accounts for about one third of all childhood

malignancies; of these, approximately 80% are lymphocytic (acute lymphocytic leukemia, or ALL). **Chronic leukemia** in children is rare, accounting for less than 2% of all cases. Leukemia affects about 5 in 100,000 children. The peak incidence is between 2 and 5 years of age. Although the cause of leukemia is unknown, ionizing radiation, certain chemical agents, and genetic factors have been implicated.

The clinical manifestations of acute leukemia are caused by the infiltration of leukemia cells into tissues and organs. Infiltration and proliferation of leukemia cells in the bone marrow lead to anemia, thrombocytopenia, and granulocytopenia. Because these cytopenias develop gradually, the onset of the disease is frequently insidious. The history at presentation may reveal increased irritability, lethargy, persistent fever, vague bone pain, and easy bruising. Some of the more common findings on initial physical examination are pallor, fever, tachycardia, adenopathy, hepatosplenomegaly, petechiae, cutaneous bruises, gingival bleeding, and evidence of infection. In approximately 90% of the cases of acute leukemia a peripheral blood smear reveals anemia and thrombocytopenia. In about 65% of cases the white blood cell count is low or normal, but it may be greater than 50,000 cells/mm<sup>3</sup>.

When a new case of leukemia is diagnosed, the patient is hospitalized and therapy is directed toward stabilizing the patient physiologically, controlling hemorrhage, identifying and eliminating infection, evaluating renal and hepatic functions, and preparing the patient for chemotherapy.

These interventions proceed while the definitive studies to determine the exact type of leukemia are undertaken. These include obtaining bone marrow for microscopic analysis, special cytochemical staining, immunophenotyping by flow cytometry, and cytogenetic analysis. The goal of treatment is to induce and maintain a complete remission, which is defined as resolution of the physical findings of leukemia (e.g., adenopathy, hepatosplenomegaly, petechiae) and normalization of peripheral blood counts and bone marrow (less than 5% blasts).

In all, **the treatment** regimens vary considerably depending on prognostic factors and the parameters being evaluated by the strategists' cooperative group (e.g., children's oncology group). The initial phase of treatment, induction, incorporates the use of a combination of antileukemic drugs at staggered intervals during a 4-week regimen. This combination of drugs should rapidly destroy the leukemic cells, yet maintain the regenerative potential of the non-malignant hematopoietic cells within the bone marrow. About 95% of patients with ALL will be in complete remission at day 28 of therapy. The second phase of ALL treatment, consolidation, attempts to consolidate remission and intensify prophylactic central nervous system (CNS) treatment.

Prevention of CNS relapse uses intrathecally administered chemotherapy (methotrexate with or without cytosine arabinoside and hydrocortisone) to destroy leukemic cells within the CNS. This chemotherapeutic agent is instilled directly into the lumbar spinal fluid because antileukemic drugs do not readily cross the blood-brain barrier. Intensive intrathecal chemotherapy to prevent CNS relapse has replaced cranial irradiation for patients in the good and intermediate-risk groups of ALL patients. However, both cranial irradiation and intrathecal chemotherapy are still used to prevent CNS relapse in high-risk ALL patients.

The third phase of treatment, interim maintenance, uses a combination of agents that are relatively nontoxic and require only monthly visits to the outpatient clinic. In most cases, another phase, delayed intensification, follows interim maintenance. This serves to intensify antileukemic therapy again after a short period of less intensive therapy. The addition of a late phase of intensive therapy substantially improves survival in patients with ALL. Following delayed intensification, therapy continues for 2 years for girls and 3 years for boys (maintenance phase), with chemotherapeutic agents given as in interim maintenance.

The prognosis for a child with acute leukemia has improved dramatically over the past 30 years. Thirty-five years ago, there would have been little need to discuss dental treatment for a child with leukemia because the disease was invariably fatal, in most cases within 6 months of diagnosis.

Today, with the development of new and better antileukemia drugs, the use of intensive combination drug therapy, the incorporation of radiation therapy, and improvements in diagnostic techniques and general supportive care, complete cures are being achieved in the

majority of patients. Pre-treatment prognostic factors identify patients who are likely to benefit from either standard or more intensive therapy. Factors that identify patients who are likely to benefit from the type of therapy just outlined, which causes relatively minimal toxicity, are patient age between 1 and 10 years, a white blood cell count of less than 50,000/mm<sup>3</sup>, lymphoblast morphology that is not of the Burkitt type, and absence of certain cytogenetic abnormalities.

Children with ALL who are at particularly high risk are those who are younger than 1 year of age at diagnosis, have a high white blood cell count, or have the cytogenetic abnormalities just mentioned. More intensive treatment regimens are used for these patients.

The prognosis for children with ANLL has improved significantly over the past several years, with event-free survivals of approximately 50% (at least 3 years) for children receiving chemotherapy and somewhat higher percentages for patients undergoing allogeneic bone marrow transplantation after achieving remission with chemotherapy. The treatment regimens are intensive and result in profound bone marrow suppression. These patients have severe prolonged neutropenia and often have severe mucositis.

### **ORAL MANIFESTATIONS OF LEUKEMIA**

The most frequently reported oral abnormalities attributed to the leukemic process include regional lymphadenopathy, mucous membrane petechiae and ecchymoses, gingival bleeding, gingival hypertrophy, pallor, and nonspecific ulcerations.

Manifestations seen occasionally are cranial nerve palsies, chin and lip paresthesias, odontalgia, jaw pain, loose teeth, extruded teeth, and gangrenous stomatitis.

Each of these findings has been reported in all types of leukemia. Regional lymphadenopathy is the most frequently reported finding. Gingival abnormalities, including hypertrophy and bleeding, are more common in patients with nonlymphocytic leukemia, whereas petechiae and ecchymoses are more common in those with ALL.

Like the systemic manifestations of leukemia, oral changes can be attributed to anemia, granulocytopenia, and thrombocytopenia, all of which result from the replacement of normal bone marrow elements by undifferentiated blast cells, or to direct invasion of tissue by these leukemic cells. Very high circulating white blood cell numbers in the peripheral blood can lead to stasis in small vascular channels. The subsequent tissue anoxia results in areas of necrosis and ulceration that can readily become infected by opportunistic oral microorganisms in patients with neutropenia. A person with thrombocytopenia, having lost the capacity to maintain vascular integrity, is likely to bleed spontaneously. Clinical manifestations of this are petechiae or ecchymoses of the oral mucosa or frank bleeding from the gingival sulcus. The propensity for gingival bleeding is greatly increased in persons with deficient oral hygiene, because accumulated plaque and debris are significant local irritants.

Direct invasion of tissue by an infiltrate of leukemic cells can produce gingival hypertrophy. Such gingival changes can occur despite excellent oral hygiene. Infiltration of leukemic cells along vascular channels can result in strangulation of pulpal tissue and spontaneous abscess formation as a result of infection or focal areas of liquefaction necrosis in the dental pulp of clinically and radiographically sound teeth. In a similar fashion, the teeth may rapidly loosen as a result of necrosis of the periodontal ligament. Skeletal lesions caused by leukemic infiltration of bone are common in childhood leukemia. The most common finding is a generalized osteoporosis caused by enlargement of the Haversian canals and Volkmann canals. Osteolytic lesions resulting from focal areas of hemorrhage and necrosis and leading to loss of trabecular bone are also common. Evidence of skeletal lesions is visible on dental radiographs in up to 63% of children with acute leukemia.

Manifestations in the jaws include generalized loss of trabeculation, destruction of the crypts of developing teeth, loss of lamina dura, widening of the periodontal ligament space, and displacement of teeth and tooth buds. Because none of the oral changes is a pathognomonic sign of leukemia and all can be associated with numerous local or systemic disease processes, a diagnosis of leukemia cannot be based on oral findings alone. Such changes should, however, alert the clinician to the possibility of malignancy as the underlying cause.

**Comprehensive control:**

1. Oral manifestations of iron deficiency anemia.
2. Agranulocytosis.
3. Aplastic anemia.
4. Hereditary hemorrhagic telangiectasia.
5. Thrombocytopenic Purpura.
6. Leukemia.
7. Oral manifestation of leukemia.

**Test control:**

1. Parents of 3.5 years old child complain of frequent nosebleeds, bleeding under the skin and mucous membranes in their child. Objectively: on the pale skin and oral mucosa the multiple petechiae are present. There is spontaneous bleeding of gums. What additional tests should be undertaken for the diagnosis?

- A. Complete blood test
- B. Biochemical examination of blood
- C. Immunological examination of blood
- D. Blood test for sugar
- E. Urine test for sugar

2. Child of 14 years old appealed to the dentist for dental sanitation. Objectively: the skin of the face is pale, the rim of the lips is dry. The lips are covered with flakes. There are cracks in the corners of the mouth. The mucous membrane of the mouth is pale, the tongue is hyperemic and smooth, filiform papillae are atrophied. There is swelling and cyanosis of the gingival margin in the frontal area. MDF = 10. Enamel of the teeth is without brilliance. Clarify the diagnosis:

- A. Iron deficiency anemia
- B. Hemophilia
- C. Werlhof's disease
- D. Acute leukemia
- E. Vitamin B12 Deficiency Anemia

3. The patient complains of headache, muscle ache and joint pain, fatigue, lack of appetite for a month. There is a massive bleeding of gums during teeth brushing. Also the patient complains of gingival overgrowth, its burning and sore, pain during eating. Objectively: paleness of the skin and mucous membrane. There are teeth imprints on the mucous membrane of the cheeks. There are petechial hemorrhage on the tongue and palate?existing bleeding. The gums are hyperemic, edematous and loose in the frontal teeth area. Teeth are intact. Clarify the diagnosis:

- A. Acute leukemia
- B. Chronic leukemia
- C. Hypertrophic gingivitis
- D. Hypovitaminosis C
- E. Werlhof disease

4. The patient appealed to the dentist with complaints of frequent bleeding of the mucous membrane of the mouth and nose. The patient specifies that the same problems have been observed in his father. Objectively: multiple existing telangiectasia and anhiomatous formations on skin and

mucous membrane of cheeks, lips and tongue are noted. Blood test is within normal limits. What is the most likely diagnosis?

- A. Osler-Weber-Rendu disease
- B. Werlhof's disease
- C. Schoenlein-Henock disease
- D. Anemia
- E. Von Willebrand disease

5. 15 years old girl complains of deteriorating of the health condition ( fatigue, dizziness, headache, loss of appetite, nausea) during the last year. From history of disease revealed long (5-6 days) massive menstruation. Objectively: paleness and dryness of the skin, brittleness of the hair. Intraoral examination: cracks in the corners of the mouth, mucous membrane is pale and dry, filiform papillae of the tongue are atrophied. Blood test: Hb - 80 g/l, color index - 0,75, anisocytosis, hypochromia of erythrocytes. Preliminary diagnosis:

- A. Iron deficiency anemia
- B. Vitamin B 12 deficiency anemia
- C. Hypoplastic anemia
- D. Chronic leukemia
- E. Hypovitaminosis of vitamin C

6. The boy of 17 years old complains of frequent nosebleeds, gums bleeding, positive braid symptom. Werlhof's diseases was diagnosed previously. Which index of blood test will confirm the diagnosis?

- A. The number of platelets
- B. Number of reticulocytes
- C. The number of leukocytes
- D. The amount of hemoglobin
- E. ESR

7. Patient of 15 years old complains of gums bleeding. From history: frequent nosebleeds, weakness. Objectively: paleness of the skin and oral mucosa. On the mucous membrane of the cheeks, tongue and soft palate there are numerous petechiae. Blood test: red blood cells - 3.1 million, hemoglobin - 94 g/l, color index - 0.9, clotting time - 9 min, ESR 18 mm/h. What is the most likely diagnosis?

- A. Iron deficiency anemia
- B. Leukemia
- C. Vaquez Osler disease
- D. Addison - Birmer anemia
- E. Werlhof's disease

8. A girl of 16 years old complains of burning, soreness of the tongue tip, impaired taste sensation, dry mouth. She suffers from antacid gastritis. Objectively: mucous membrane is pale and yellowish color. Cracks in the corners of the mouth are noted. There are teeth imprints on the mucous membrane on the cheek and filiform papillae are absent on the tip of the tongue. The back of the tongue is red. Blood test: Hb -80 g/l, color index - 0.7. What is the most likely diagnosis?

- A. Folic and vitamin B12 deficiency anemia
- B. Acute leukemia

- C. Iron deficiency anemia
- D. Werlhof's disease
- E. Von Willebrand 's disease

9. The 7 years old boy's parents complained of the spontaneous night-time bleeding from the gums and nose in their son. The presence of small and large hemorrhages of different colors (from red to blue-green-yellow) in the mouth and on the skin of the child are noted. Blood test: significant decreasing of platelets and the presence of giant platelets in peripheral blood is observed. Clarify the diagnosis:

- A. Werlhof's disease
- B. Acute leukemia
- C. Chronic leukemia
- D. Hemophilia
- E. Iron deficiency anemia

10. For what disease the following symptoms are significant: small symmetrical hemorrhages on the feet, legs, hips, painful symmetric polyarthritis, abdominal pain, hemorrhagic rash in the mouth, violation of the permeability of vascular walls?

- A. Hemorrhagic vasculitis
- B. Hemophilia C
- C. Osler-Weber-Rendu syndrome
- D. Werlhof's disease
- E. Hemophilia A

**Recommended literature:**

Pediatric Therapeutic Dentistry: [textbook for students of dental faculties] / L. A. Khomenko, A. V. Savychuk, O. I. Ostapko [et al.]; ed. L. A. Khomenko. -Kiev: [s. n.], 2012. - 240 p.