Task 1. Patient of 52 years old consulted a doctor concerning the eruptions on face and extremities and strong pruritus in dedicated areas. *On examination*: numerous of bulla on skin of jowls, metope, antibrachium, inguinal and axillary folds on extremely reddened background sized from usual grain to pea. There are grouped papulovesicles observed.

a) Which disease corresponds to the clinical presentation being described above:
- **A.** Lichen acuminatus
- **B.** Psoriasis
- **C.** Duhring disease
- **D.** Herpetic fever
- **E.** Weeping dermatitis

b) What special dermatological tests should be performed for confirmation of diagnosis?

Task 2. Patient of 55 years old was hospitalized by air medical service. General state of the patient on examination is critical, active movements are embarrassed because of pain, the temperature is 38.3 °C, mouth opens hard, and there are residues of hemorrhagic crusts on vermilion surface. The numerous of major anabrosis covered by dirty pellicle are observed at skin of alvus, axillary, femoroinguinal folds and folds under inframammary crease; there are papillomatous proliferations noticed on its surface. The perilesional vesicles and bulla are on the background of healthy skin. The Nikolsky's sign is positive.

a) What dermatosis should be thought about in this case:
- **A.** Weeping dermatitis
- **B.** Pemphigus vera
- **C.** Herpes zoster
- **D.** Herpetic fever
- **E.** Lichen acuminatus

b) What diseases the differential diagnostics should be performed with?

Task 3. Patient of 47 years old was hospitalized to dermatological department after infection disease specialist's advice. From antecedent history: complains for skin pruritus, sleep paralysis, performance decrement, sourness. Patient notices the occurrence of symptoms mentioned above after disposal of courses from sea-water fish. The state is significantly getting worse and whole body and extremities eruptions after lubrication of skin by 5% iodine tincture. Dermatologic status: on skin of body and extremities the strained small vesicles, bulla, papule having tend to grouping are determined. The Nikolsky's sign is negative.

a) What diagnosis and on which grounds could be made:
- **A.** Pemphigus vera
- **B.** Duhring disease
- **C.** Allergodermia
- **D.** Lichen acuminatus
- **E.** Mycosis of mucous membranes

b) What the patient surveillance will be?

Task 4. Patient of 40 years old has got anabrosis month ago on oral mucosa and bulla on the sternum skin, which were transformed into anabrosis fast. He used antibiotics during two weeks but there was no mend. *Unbiased*: the bright round-shaped anabrosis of 2-3 cm in diameter and several soft bullae on oral mucosa and on the sternum. At drawing by patient of edge of tegmentum the lamination of epidermis is observed.

a) Which disease corresponds to the clinical presentation being described above:
- **A.** Pemphigus vera
- **B.** Duhring disease
- **C.** Herpes zoster
- **D.** Herpetic fever
- **E.** Weeping dermatitis

b) What else symptoms are typical for this disease?

Task 5. Patient of 57 years old complains for appearance of numerous of bullae on skin of body, dorsum and sternum. The bullae are soft, big and with serosal content. Then the anabrosis appears which epithelized gradually. The anabrosis are also observed on

oral mucosa because of which the chewing is painful. The acantholytic cells are discovered in impression smears taken from the bottom of the anabrosis.

a) What the most possible nature of this disease is:

A. Weeping dermatitis
B. Pemphigus vera
C. Allergodermia
D. Lichen acuminatus
E. Leukokeratosis

Answers for first level self-control questions
1 – E; 2 – C; 3 – D; 4 – A; 5 – A; 6 – A; 7 – A; 8 – C; 9 – B; 10 – B
Answers for second and third level self-control questions
1a – C; 2a – B; 3a – B; 4a – A; 5a – B

11 TOPIC

Viral infections of skin and mucous membranes

Viral infections of skin and mucous membranes are the diseases caused by infection of cells with the subsequent proliferation of viruses, which are small non-cellular particles consisting of a nucleic acid (DNA or RNA) and protein shell. Depending on a leading clinical sign, there are two groups of viral diseases of skin and mucous membranes:

1) Viral infections whose main symptom is blistering (herpes simplex and herpes zoster);

2) viral infections whose main symptom is verruca (verruca vulgaris, flat wart, condyloma acuminatum, molluscum contagiosum.

Both types are caused by a viral infection of epidermis. In addition, there is a fairly large group of *systemic viral infections*, in which skin rash is caused by viremia and various systemic allergic reactions (measles, rubella, etc.).

TRAINING AND EDUCATIONAL PURPOSES

- Know the current views on etiology, prevalence, pathogenesis, and the course of viral infections of skin and mucous membranes
- Explain epidemiological features and ways of transmission of viral skin diseases
- Determine clinical symptoms and the course of skin viral infections, to understand their place in the overall morbidity patterns
- Understand the role of sexually transmitted viral infections as uncontrolled and socially dangerous
- Learn to distinguish the features of the course (clinical signs) of a simple and herpes zoster, which testify of immune deficiency and may serve as markers of life-threatening or significantly reducing life quality conditions
- Recognize the role of a general practitioner and pediatrician in early diagnosis, treatment, primary and secondary prevention of skin viral diseases
- Understand the principles of rational, safe and pathogenetically substantiated therapy of viral diseases of skin and mucous membranes

11.1 Viral infections whose main symptom is blistering

The group of skin viral infections characterized by formation of blisters (vesicles), which appearance is caused by the degeneration of epidermal cells, includes herpes simplex and herpes zoster.

Herpes simplex

Herpes simplex (*herpes simplex*) is a viral disease of skin and mucous membranes caused by herpes simplex virus (HSV).

TO KNOW:

- etiology, pathogenesis and transmission of herpes simplex;
- classification and features of clinical manifestations of herpes simplex;
- histopathological features and differential diagnosis of the disease;
- principles of general and local treatment of herpes simplex;
- factors that cause exacerbation or progression of the disease;
- methods of primary and secondary prevention.

TO BE ABLE TO:

- properly collect medical history of a patient with herpes simplex;
- put a diagnosis based on symptoms and signs;
- apply additional studies to confirm the diagnosis;
- make a differential diagnosis with the diseases that have similar clinical picture;
- justify and prescribe adequate treatment.

Etiology and pathogenesis. Herpes simplex virus belongs to the family of *Herpesviridae,* subfamily *Alphaherpesvirinae* type *Simplexvirus*. There are two antigenic serotypes of HSV: first (HSV-1) and second (HSV-2).

Transmission of HSV-1 usually occurs in childhood, through a direct contact with a HIV-sick or infected person. This causes frequent localization of orofacial herpes lesions caused by HSV-1, in particular on skin areas around mouth (herpes labialis), nose (herpes nasalis), seldom on cheeks, eyelids and ears. In addition to skin, mucous membranes of the mouth (herpes stomatitis) may also be affected. Transmission of HSV-2 occurs mainly through sexual contact. HSV-2 is dominant in causing genital herpes infection (*herpes genitalis*) with the localization of lesions on skin and mucous membranes of the external genital organs of men and women. However, there is no stable relationship between antigen serotypes of HSV and localization of herpetic lesions on skin and visible mucous membranes (genital, extragenital). This is confirmed by the fact that about 20% of cases of genital herpes are caused by HSV-1.

In the pathogenesis of herpes simplex virus, the development of chronic persistent infection in sensory ganglia is crucial. Penetrating through the mucous membranes of the oropharynx, conjunctiva, urethra, cervix, rectum, or skin micro-cracks in the process of initial infection, HSV reaches nerve endings and moves to sensory ganglia through the retrograde axon, where there occurs an acute infection, when the virus replicates in the cells of sensitive ganglion. Further, virus enters into the state of persistence, which provokes the latent course of herpes. Under certain conditions (primarily, due to the lack of immune control), there occurs activation of the virus; from ganglion, the activated virus migrates along the axon of the peripheral nerve and replicates in the epithelial cells. Except general weakening of the immune control,

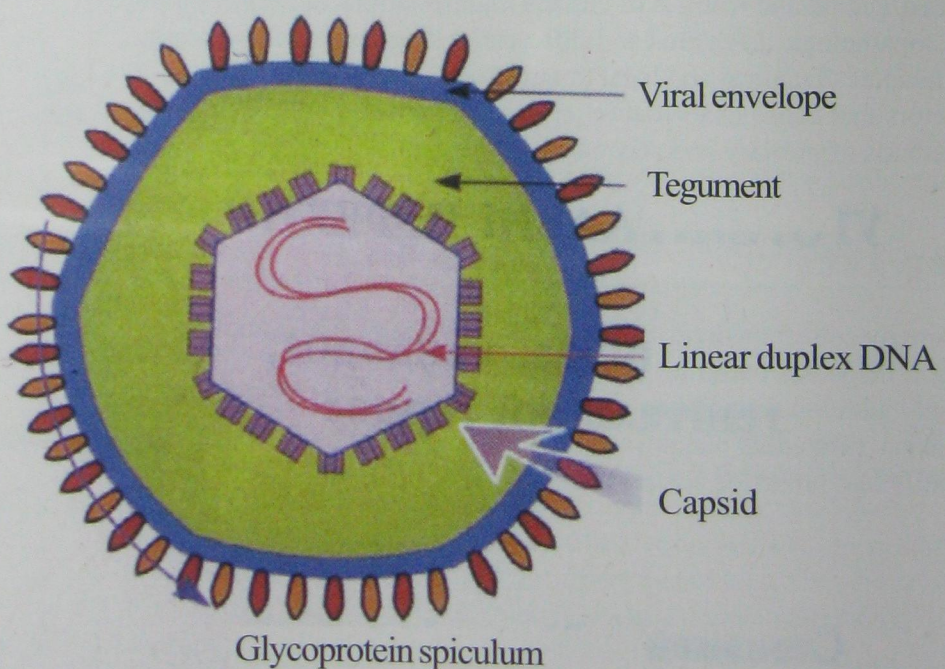

Fig. 11.1. Schematic representation of herpes simplex virus structure (HSV).

reproduction of virus is caused by a violation of local immunity in the area of the epidermis.

Epidemiology. At the present stage, herpes simplex is one of the most common uncontrolled human infections (uncontrolled human infections involve the inefficiency of vaccination or treatment methods, which allow achieving the complete elimination of the pathogen from the host's body). More than 50% of the population of developed countries and 100% of the population of developing countries are seropositive to HSV presense.

The disease features pandemic nature. Genital herpes ranks first in the list of common human infections transmitted primarily through sexual contact. The problem of herpetic infection is aggravated by the growth of cases of abortive and atypical clinical course of the disease. There is an essential difference between the number of persons seropositive to HSV and the number of people with clinical manifestations of herpes simplex.

Clinic. Herpes can be primary and simplex recurrent.

The disease begins with itching or burning, accompanied by the formation of groups of small strained vesicles amid a slightly edematous limited congested spot. The content of vesicles is transparent, becomes thick in 2-3 days. Vesicles feature a tendency to merge. After 3-5 days, vesicles dry up and form yellowish-gray crusts. After 6-8 days, crusts fall off, while secondary pigmentation is left in their place, which then disappears with no trace.

Primary herpes simplex. Primary infection with HSV-1 occurs mainly in young children. In most cases, the primary manifestations of herpes simplex are minor (redness, itching) and remain undetected. However, children infected with HSV-1 may develop primary herpetic gingivostomatitis. The disease is developed suddenly, with an increase in body temperature to 39-40 ° C and intoxication. Mucous membranes of cheeks, gums, lips, tongue, and throat are tonsils are covered with painful grouped vesicles. After their destruction, there occur painful erosions prone to a merge. Clinical manifestations of the inflammation subside in two to three weeks.

Primary genital herpes. The primary episode of genital herpes occurs after an incubation period of 1-7 days. In men, herpes rash is usually localized on the head and shaft of the penis and foreskin, while in women it is localized on small and large labia, vagina, clitoris, cervix, perineum, thighs and buttocks. On the background of significant erythema and edema, there develop grouped vesicles, first with clear, and then thick contents. On the ruins of vesicles, erosions, sometimes ulcers and cracks are formed. Subjectively, the rash is accompanied by a sensation of pain and itching. There develops painful bubonadenitis. Unlike further relapses, primary clinical episode of genital herpes features more severe and prolonged course (4-5 weeks).

Recurrent herpes simplex and recurrent genital herpes. In most cases, the initial clinical episode of herpes simplex is followed by clinical recovery. However,

virus (HSV-1, HSV-2) is stored in the body in a latent form throughout a person's life, not causing any clinical symptoms. Approximately 90% of people infected with HSV are virus carriers. Under the influence of a series of factors that reduce protective capacity of the body, which include hypothermia, overheating, infectious diseases, especially colds, etc., there occur recurrences of herpes simplex. Unlike primary clinical episode of the disease, clinical episode of recurrent herpes simplex virus features milder course. In recurrent herpes simplex, typical location of the lesion includes lips, face, cornea and conjunctiva of the eye, buttocks. At these sites, there develop grouped vesicles with clear content, accompanied by itching and burning. In further, painful erosions are formed, which may merge. On the surface of the erosion, exudate dries in the form of a crust. After the removal of crust, secondary spots are left. Clinical recurrences of herpes simplex may occur over many years and decades, with varying frequency – from one or two a year to two to four per month.

Compared with the initial episode, recurrences of genital herpes are also characterized by a mild course. Rash on skin and mucous membranes is rather sparse. Typical for herpes, lesions are located on skin and mucous membranes of the vulva.

Genital herpes can cause diverse complications, including reproductive disorders, miscarriage, intrauterine infection of fetus, and be transmitted to a baby during childbirth. In case of transplacental infection, a newborn may develop growth retardation, encephalitis, chorioretinitis. In addition, due to chronic recurrent genital herpes patients may experience significant psychosomatic disorders.

Diagnosis of herpes simplex is simple and based on presence of typical clinical symptoms: itching, grouped vesicular eruption, formation of erosions and crusts. The recurrent nature of the lesion is testified by:

1) similar clinical manifestations in the past;

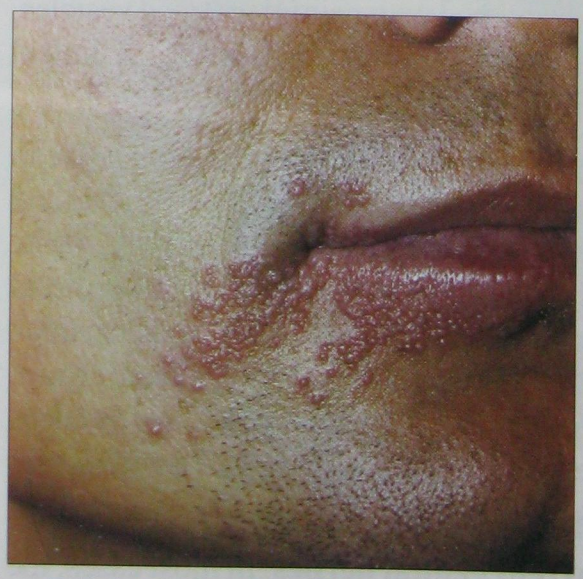

Fig. 11.2. Labial herpes simplex.

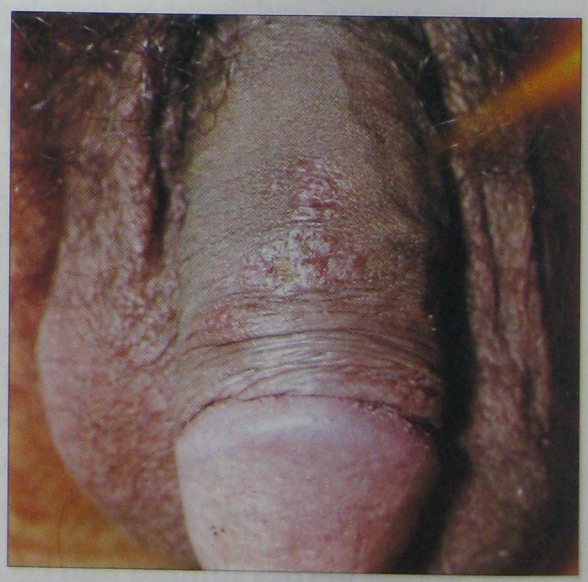

Fig. 11.3. Genital herpes simplex.

2) identification of high titers of antibodies to HSV during relapse;
3) identification of antigen in the focus of clinical manifestation.

The coincidence of the type identified from the source of HSV and type of HSV, to which the antibodies in a patient's serum are found, is the condition for diagnosis of recurrent herpes. However, it should be noted that serology and identification of viral antigen are not routine methods in the diagnosis of herpes simplex. They are applyied only in specific cases, when there is considerable doubt as to the clinical diagnosis of herpes simplex. In addition, high titers of antibodies to HSV with no clinical manifestations (recurrent episodes) are not the reason for the diagnosis of herpes simplex.

Differential diagnosis. In case of localization in the mouth mucosa, herpes simplex is to be distinguished from acantholytic pemphigus and polymorphous exudative erythema. In pemphigus, erosions are localized on a visually normal mucous membrane, they are not subject to epithelialization, Nikolsky's symptom is positive, acantholytic cells are found in the impression smears from the surface of erosions. Unlike herpes, polymorphous exudative erythema is characterized by seasonality index (spring and autumn), significant size of bubbles and erosions on a dramatically inflamed background, layering of bloody crusts on the red border.

Clinical manifestations of genital herpes localized on the genitals should be differentiated from syphilitic chancre. Unlike herpes, syphilitic erosion is characterized by smooth edges, saucer-like shape, hard bottom, indolence and peculiar regional lymphadenitis. In doubtful cases, the issue is finally resolved by microscopy examination of the material from erosions to detect the agent of syphilis – Treponema Pallidum.

Treatment. All currently existing methods and tools for treatment of herpes do not allow achieving complete elimination of pathogens (HSV-1, HSV-2) from the human body. Approaches to treatment of herpes simplex are determined by a clinical picture of the disease, severity of clinical course, frequency of relapses, as well as availability of comorbidity. In the antiviral therapy of herpes infections, preparations of acyclic nucleotides that have an ability to disrupt interaction of virus and cells, in particular inhibit reproduction of the virus through its virostatic action, play the major role.

For treatment of infections caused by herpes simplex viruses, the drugs from a group of acyclic purine nucleosides are used: acyclovir, valacyclovir (valine a e t h e r of acyclovir) and famciclovir (pro-forma of penciclovir). In the form of topical preparations (cream), acyclovir is prescribed to reduce the intensity and duration of the recurrent episode of herpes simplex. Systemic prescription of purine nucleoside analogs (internal or parenteral) is used for treatment of primary manifestations of herpes simplex virus, as well as treatment of relapse (for active clinical manifestations). With frequent recurrences of skin herpes and genital herpes, acyclovir and valacyclovir may be prescribed in long continual courses (so-called long-term suppressive therapy). For a healthy sexual partner of a patient with

recurrent herpes, prophylactic or preventive treatment has no medical meaning, since existing antiviral drugs are unable to eliminate the virus from a human body. In some countries, particularly Ukraine, Russia and Belarus, recombinant interferons and interferon inducers are used as a part of comprehensive treatment of the disease.

Prevention. Preventive measures against primary HSV infection in children are reduced to avoidance of contacts with adults that have active clinical signs of infection. Compliance with the principles of safe sexual behavior (monogamous sexual relationships, the use of barrier protection equipment) is the only way to prevent infection with HSV. Secondary prophylaxis involves the avoidance of hypothermia or excessive sun exposure, as well as the appointment of prolonged systemic antiviral therapy.

Forecast. The recurrence rate depends on a patient's sex, duration of the initial episode and the disease itself. In women, the recurrence rate is slightly higher than that of men. The longer the primary clinical episode of herpes is, the shorter the period prior to the first recurrence is, and the higher the frequency of further recurrences is. It was also found that the younger a person is at the first sign of herpes, the higher the recurrence rate of future infection is. With age, the recurrence rate is gradually reduced. It should also be noted that the majority of people infected with HSV experience no recurrences. This is explained by the proper state of their immune system, which is able to block the replication of virus in the nerve ganglia and epithelial cells.

HERPES ZOSTER

Herpes zoster (shingles) is an acute infectious disease of skin and mucous membranes caused by a neurotropic virus (*varicella zoster*), which is also a pathogen of chickenpox. The disease is characterized by the occurrence of unilateral grouped vesicular lesions within one to two dermatomes and accompanied by neurological pain.

TO KNOW:

- etiology and pathogenesis of herpes zoster;
- ways of contamination with varicella infection (herpes zoster);
- characteristics of clinical manifestations and potential complications of the disease;
- histopathologic features and differential diagnosis of herpes zoster;
- characteristics of postherpetic neuralgia;
- principles of local and general therapy for the disease;
- factors that cause exacerbation or progression of the disease;
- methods for prevention of herpes zoster.

TO BE ABLE TO:

- properly collect the history of a patient with herpes zoster;
- put a diagnosis based on clinical picture;
- identify additional studies to confirm the diagnosis;
- make a differential diagnosis with the diseases that have similar clinical picture;
- prescribe pathogenetic therapy.

Etiology and pathogenesis. Shingles and chickenpox are both caused by is the varicella-zoster virus, which belongs to the family of *Herpesviridae*.

There is a hypothesis saying that after the primary attack of varicella (manifested in the symptoms of chickenpox), the virus penetrates into the cells of dorsal root ganglion, where it is stored in an asymptomatic condition (persistent) until the moment of reactivation caused by certain factors (hypothermia, stress, cancer, immune incompetence and others). Under the influence of these factors that weaken the body immune reactivity, the virus is activated, multiplies, causing inflammation of the ganglia. In further, the virus enters the sensory nerves, causing neuritis and neuralgia, spreads around sensory nerve endings in skin and causes formation of a characteristic rash, which is located along one of the nerves. Recurrences of herpes zoster are rare; occur mainly in the background of a significant immune suppression, particularly in HIV infection and malignancy. People of any age may suffer from shingles, while elderly people are at a higher risk.

Clinical picture. The disease may begin suddenly or be precededed by a general malaise, headache, fever, neuralgia or paresthesia in the areas that are to be subject to rash. The most frequent localization of lesions includes the area of intercostal nerves, hence the name «shingles», while the rash is always localized on one side of the body (unilateral localization), rarely covers a little area on the opposite side (due to anastomotic innervation). The second most common place of the lesion is the area of trigeminal nerve. The lesion of the first and third branches of the trigeminal nerve causes the emergence of rash in the mouth mucosa. The eruption emerges in a paroxysmal way: on congested skin, there appear clusters of vesicles with clear serous contents, which quickly becomes cloudy and shrinks in serous crusts. The rash of vesicles on each individual spot occurs simultaneously, but stains emerge sequentially, with an interval of several days. Foci of the lesions may be located fairly closely, forming almost a continuous line along the nerves. After rejection of crusts, there remain brownish-red spots, which gradually disappear. In typical cases, the disease continues for two to three weeks. Burning and pain along the affected nerve are observed subjectively, especially when the rash is localized on face and mucous membrane of the mouth cavity. In herpes zoster, mucous membranes are rarely affected; typically, simultaneously with a skin lesion of a certain area. Against the background of edematous (from one side) oral mucosa, there emerge vesicles, which are rapidly destroyed, forming painful erosions, often covered with gray-white pellicle. Subjectively, burning is marked in the affected areas. Very rarely, shingles can affect vaginal mucosa and bladder.

The most common complication of herpes zoster is the development of a persistent pain syndrome, prone to a prolonged and persistent course after dermatological recovery (postherpetic neuralgia). Postherpetic neuralgia occurs in older patients, which significantly affects the quality of life. Timely administration of systemic antiviral therapy during the first 72 hours from the moment of rash emergence (erythema and vesicles) reduces the risk of this complication in a few

times. Other complications of shingles include facial paralysis, meningitis, meningoencephalitis, arachnoiditis, vestibular disorders, pneumonia, paralysis of the diaphragm, bladder paralysis, paresis of the lower extremities, myelitis with the disorder of pelvic organs, etc.

Diagnostics. Diagnosis of herpes zoster is usually based on clinical manifestations. Presence of a neurological pain syndrome preceding and accompanying rash, unilateral localization of lesions located along the corresponding nerve and herpetiform grouped localization of vesicles are considered.

Differential diagnosis. In some cases, shingles should be differentiated from bullous form of erysipelas, atopic dermatitis, and sometimes impetigo. Pain syndrome that precedes formation of rash can resemble chest pain and pain in myocardial infarction, pain with bowel obstruction, etc.

Treatment. In the antiviral therapy of both herpes zoster and herpes simplex, an important place is given to the drugs of the group of acyclic nucleosides that feature a virostatic action. Acyclovir, 800 mg orally, 4-5 times a day for 7-10 days is used. Given poor bioavailability of acyclovir, the valacyclovir, 1000 mg orally 3 times a day for 7-10 days, and famciclovir, 250 mg 3 times a day orally for 7 days are widely used in treatment of herpes.

In severe cases of herpes zoster, systemic corticosteroids in high doses (40-60 mg of prednisone per day, with a gradual reduction of the dose) are prescribed. Topical preparations of acyclovir and penciclovir (creams) are applied locally. The need for analgesics depends on pain intensity. Usually, paracetamol or indomethacin is enough. In some cases, the need to use opioids or epidural anesthesia may arise.

Expressed pain that occurs prior to or simultaneously with herpetic eruption indicates a possibility of prolonged neuralgia in the future. In prolonged neuralgia that

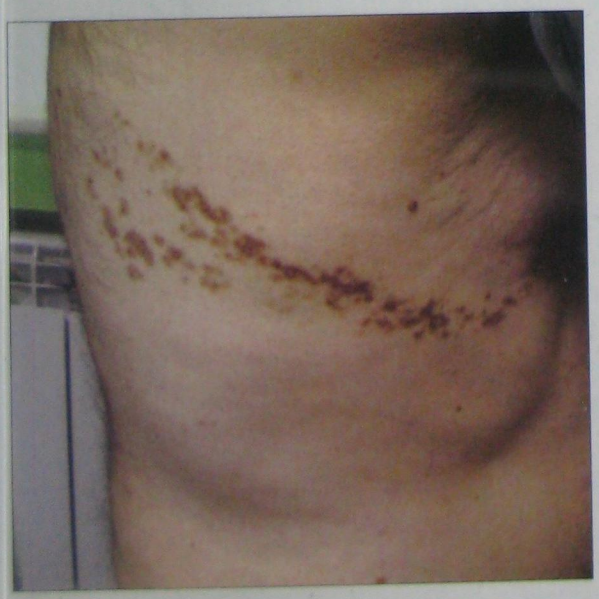

Fig. 11.4. Herpes zoster.

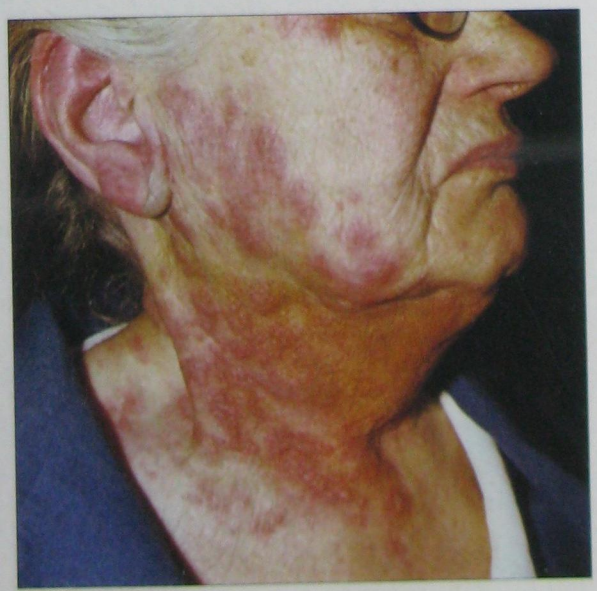

Fig. 11.5. Herpes zoster.

persists after the rash recourse, analgesics and non-steroidal anti-inflammatory drugs (infometatsin etc.) are prescribed. Patients with herpes zoster should avoid exposure to cold, exercise and stress situations.

Prevention. Primary prevention of chicken pox (and later, herpes zoster) involves a specific vaccine immunization in childhood. Patients with active manifestations of herpes zoster should avoid contact with people (especially children) that have not had chickenpox. If shingles is diagnosed in a hospitalized patient, he is to be immediately isolated to prevent nosocomial infection.

Prognosis. Shingles belongs to a group of diseases that are treated independently and feature no tendency to relapse (except in patients with immune deficiency). Elderly patients that received improper treatment may experience persistent pain syndrome, which leads to a deterioration in the life quality. Recurrences of herpes zoster testify significant violations of immune status. Such patients must be carefully examined for the presence of malignant neoplasms and HIV infections.

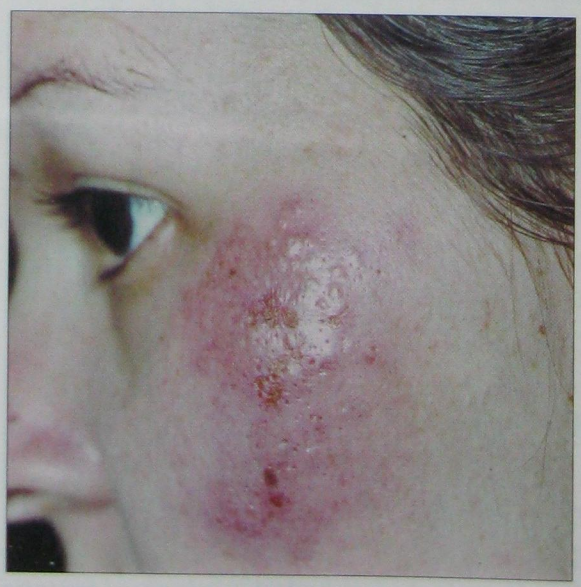

Fig. 11.6. Herpes zoster.

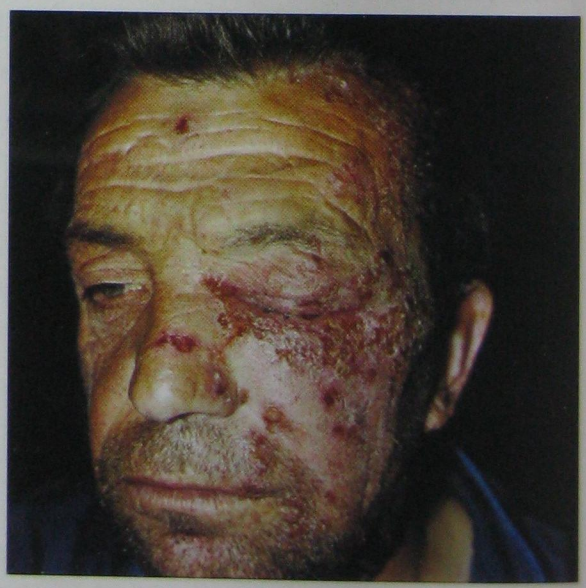

Fig. 11.7. Herpes zoster (eye form).

11.2 VIRAL INFECTIONS OF SKIN AND MUCOUS MEMBRANES THAT CAUSE THE GROWTH OF THE EPIDERMIS

The group of viral infections of skin that manifest themselves in the growth of the epidermis involves molluscum contagiosum, warts, condyloma acuminatum.

TO KNOW:

- etiological factors and epidemiology of viral infections of skin that manifest themselves in the growth of the epidermis (molluscum contagiosum, warts, condyloma acuminatum);
- features of the pathogenesis and clinical course of these viral infections of skin;
- pathogenesis, clinical manifestations and complications of molluscum contagiosum, warts, condyloma acuminatum;
- role of viral infections of skin as a marker of immunodeficiency (HIV infection, cancer pathology, etc.);
- clinical and laboratory diagnosis of these viral infections of skin;
- approaches to treatment of viral infections.

TO BE ABLE TO:

- properly collect medical history of patients with viral infections of skin that manifest themselves in the growth of the epidermis;
- differentiate clinical forms of viral infections of skin;
- identify the markers of acquired or congenital immune deficiencies;
- make a plan of the investigation of patients with viral infections of skin that manifest themselves in the growth of the epidermis;
- choose the right tactic of treatment of viral infections of skin, particularly in elderly patients;
- carry out differential diagnosis of these viral infections.

Molluscum Contagiosum

Etiology and pathogenesis. *Molluscum contagiosum* is a viral disease of skin caused by a specific virus of the *Poxviridae* family. The infection is spread by a direct contact with a patient or everyday objects used by people sick with molluscum contagiosum. Sexual route of transmission is also possible. The disease can occur in people of all ages, but is more common in children. The incubation period can last from two weeks to several months.

Clinical picture. The disease is characterized by formation of tight, hemispherical flesh-colored papules (nodules) with a waxy tint, the size of a millet grain to pea. In the center of nodules, a navel-shaped cavity is formed; at squeezing from the two sides, white curd mass is excreted from the cavity. Nodules can be solitary or multiple, may merge, forming conglomerates up to 2-3 cm in diameter. There is a selective localization of the lesion: on face, anterior abdominal wall, pubis, vulva, perineum, thighs. The rash can remain for months. Subjective feelings are absent.

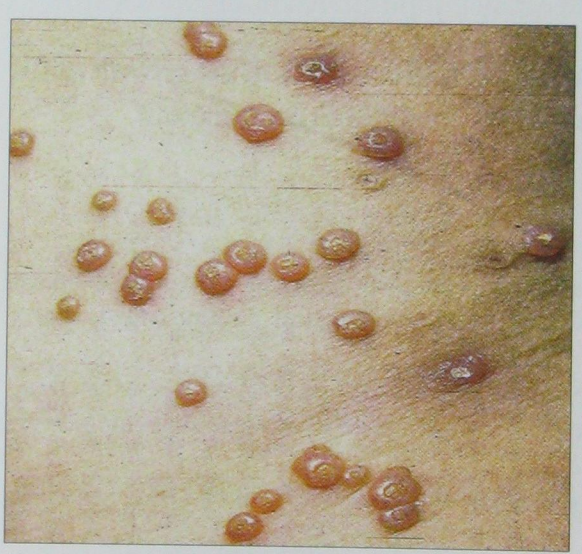

Fig. 11.8. Molluscum contagiosum.

Atypical clinical manifestations of molluscum contagiosum are also known. The disease can be warty; keratotic; cystic; furunculus; giant; solitary (with no central navel-shaped cavity); inflammatory (resembles pyogenic granuloma, prone to bleeding).

Diagnostics. The diagnosis creates no problems and is based on clinical signs.

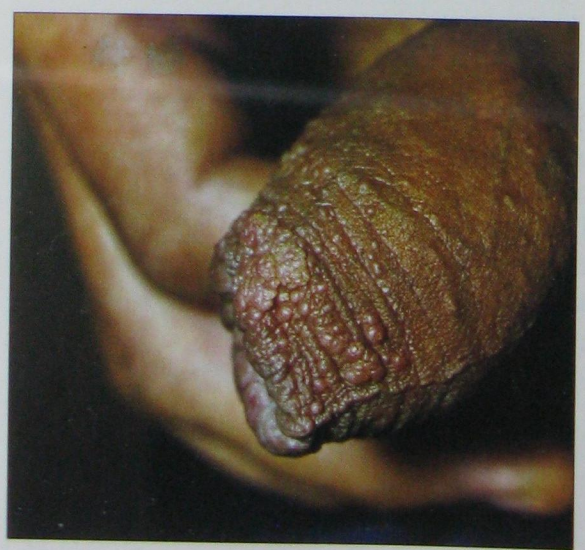

Fig. 11.9. Molluscum contagiosum.

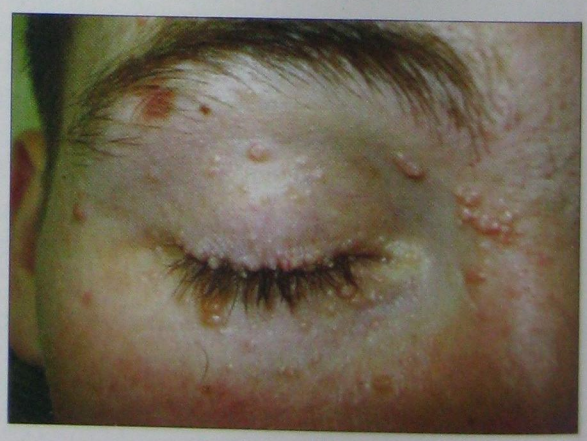

Fig. 11.10. Molluscum contagiosum.

Differential diagnosis. Differential diagnosis of molluscum contagiosum is carried out with warts, basalioma, keratoacanthoma.

Treatment. With few elements of the rash, nodules are first rubbed with alcohol, squeezed from both sides by means of forceps, and then lubricated with the alcoholic solution of iodine. Cryotherapy, curettage and retinoids in the form of a cream are also applied.

Warts

Etiology. Warts (*verrucae*) are benign epidermal growths caused by the human papillomavirus (HPV). There are more than 70 types of HPV. Most of them are caused by different clinical forms of warts of skin and mucous membranes. Some serotypes of the virus are considered carcinogenic (HPV-16, HPV-18) and can cause cervical cancer and skin cancer (Table 11.1).

Table 11.1
Types of human papillomavirus and associated clinical manifestations

HPV type	Clinical manifestations
2, 4, 7, 26–29	Verruca vulgaris (common warts)
3, 10	Plantar warts (flat warts)
5, 8, 9, 12, 14, 15, 17, 19–26, 36, 47, 50	Epidermodysplasia verruciformis
6, 11	Condyloma acuminatum
16, 18, 31, 33-35, 39–41, 51–60	Cervical dysplasia, endocervical cancer
13, 32	Oral focal epithelial dysplasia
30, 40	Pharyngeal carcinoma

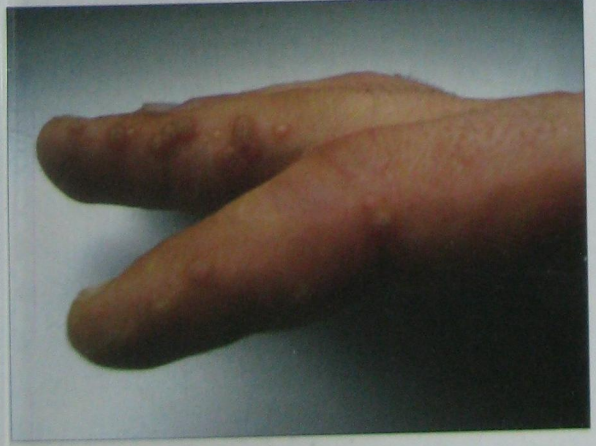

Fig. 11.11. Plantar warts.

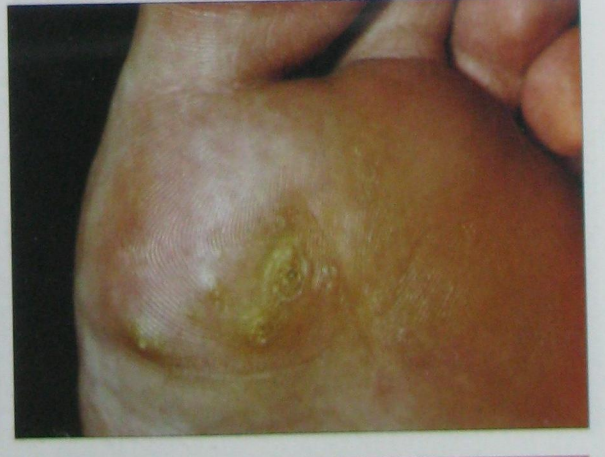

Fig. 11.12. Plantar warts.

Pathogenesis. Infection occurs through a direct contact with a patient or household items. Regardless of symptoms, familial cases are reported for all forms of warts. The occurrence of warts is caused by mechanical trauma, immune-suppression (including induced nuclear radiation, cytotoxic drugs, HIV infection, common serious diseases, etc.). HPV replication occurs in the basal layer of the epidermis. Warty growths are formed in the stratum corneum in loci of the maximum viral persistence. The infection process is limited to the outer layers of skin and mucous membranes. The incubation period is very variable: from one week to a year.

Clinical picture. Clinical features of warts depend on the species. There are common warts, plantar and flat (youthful), as well as condyloma acuminatum (condylomata).

Common warts represent one of the most common skin diseases that arise in children and adolescents. With age, the incidence is significantly reduced. Common warts are clinically manifested with hyper-keratotic papules that feature small papillae on the surface, reminiscent of the «cauliflower», common focalization involves hands and feet, seldom - skin of the forearms and legs. Warts can be located individually or in groups; often around nail plates.

Plantar warts can be single, multiple or grouped (so-called «mosaic» warts). Plantar warts are flat; a typical sign is skin thickening. If thickened skin is cut off, numerous black dots, which are thrombosed capillaries, are seen. Plantar warts are characterized with soreness.

Flat (plane) warts are most often localized on face and the dorsa of hands. They are flesh-colored, very small, with a flat surface. Often, arranged linearly as a result of viral inoculation, in a place of a random scratch.

Differential diagnosis. Diagnosis of ordinary, flat and plantar warts is clinically uncomplicated. In some cases, common warts require differential diagnosis with tuberculosis cutis verrucosa, while plantar warts are to be differentially diagnosed with calluses that are characterized by a distinct skin pattern and lack of pain.

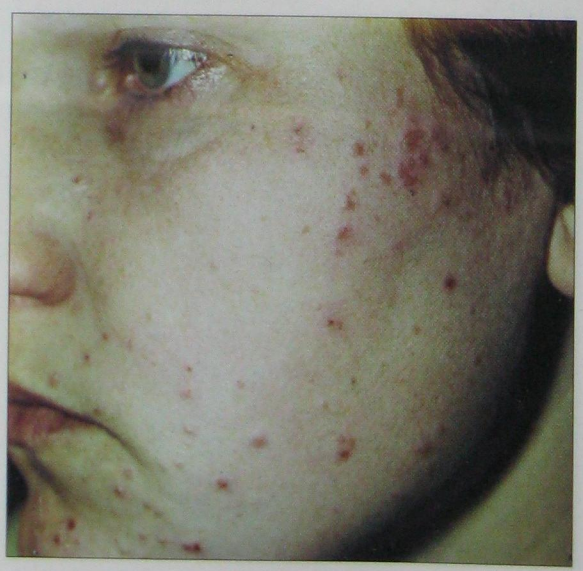

Fig. 11.13. Verrucas plantar.

Treatment. For treatment of common and flat warts, applications of topical drugs and substances that contain salicylic acid, formaldehyde, or silver nitrate are applied. In treatment of warts, the drug called «Kollomak» (10 ml solution contains 2.0 g salicylic acid, 0.5 g lactic acid, 0.2 g polidocanol) is fairly effective. Cryotherapy with liquid nitrogen is appointed when applications of topical drugs provide no effect. Since the

procedure of cryotherapy is rather painful, it should not be used in children. Multiple warts require more than one procedure of cryotherapy, with an optimum interval of two-three weeks. Treatment of plantar warts is similar to that of common warts; though, before applying topical drugs or cryotherapy, the superficial horny layer is to be removed. It should be noted that the viral propensity to persistence may provoke relapses of warts. Effective methods of preventing the occurrence of warts are still unknown.

Genital warts (Condyloma acuminatum)

Etiology. condyloma acuminatum, Most cases of condyloma acuminatum are caused by human papillomavirus (HPV) types 6 and 11.

Pathogenesis. Genital warts are related to infections transmitted by sexual contact The incubation time lasts from two to three months. The virus enters the epidermis through minor and subtle mechanical damages, infects cells of the basal layer and provokes their abnormal proliferation.

Clinical picture. Single or multiple papules of papillary form (thin leg) or resembling cauliflower represent clinical manifestation of condyloma acuminatum. Color of papules varies from flesh (or the color of mucous membrane) to various shades of dark, in case of pigmentation. Condyloma acuminatum feature soft consistency. The rash is localized on genital skin and periproctic area. In case of infection of epithelial cells of the mucous membranes, papules appear on the mucous membrane of the mouth, urethra, vagina, rectum, cervical canal.

Diagnosis and differential diagnosis. Condyloma acuminatum are diagnosed by clinical signs: thin legs and soft consistency. However, histological examination (biopsy) may be required for the differential diagnosis with Bowenoid papulosis, which

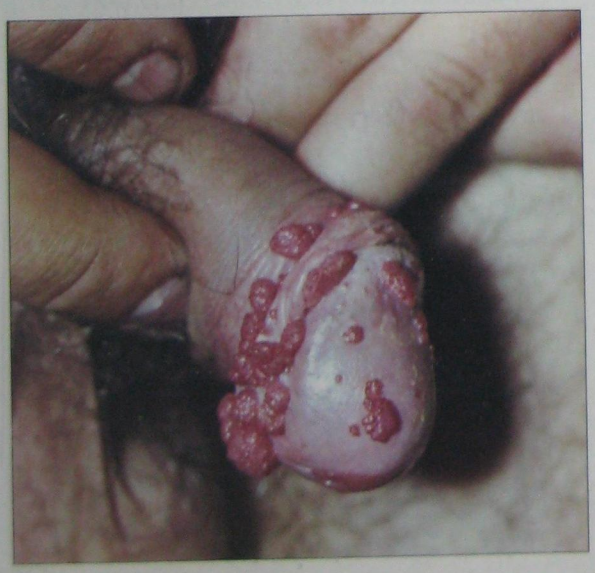

Fig. 11.14. Condyloma acuminatum.

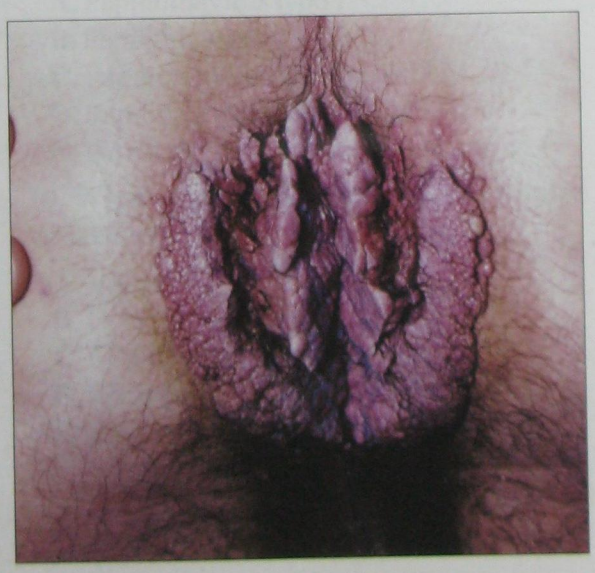

Fig. 11.15. Condyloma acuminatum.

is morphologically similar to dermoid cancellation and clinically characterized by the appearance of spots, papules and plaques. Condyloma acuminatum are also to be differentiated with syphilitic mucous papules.

Treatment. For treatment of condyloma acuminatum, cryotherapy with liquid nitrogen, as well as surgical removal by means of electric scalpel or carbon dioxide laser are applied. The latter method is used, if the warts are located in the vagina and cervix. Applications with 20-25% solution of podophyllin (for the full effect, 2-4 repeated applications at a certain period of time are required) are also quite efficient. However, podophyllin treatment should be carried out under a physician's supervision, since the drug features potent neurotoxicity in case of systemic absorption. The use of local applications with a solution of the Kollomak is highly efficient (the main active ingredients are salicylic acid, lactic acid, polidocanol).

1. Identify an erroneous statement:

A. Herpes simplex is a viral disease
B. Herpes simplex virus is transmitted by contact
C. Herpes simplex can be a triggering factor of pemphigus acantholytic
D. Herpes simplex virus replication occurs in the cells of ganglia
E. Manifestations of herpes simplex can disappear with no medical intervention

2. Herpes simplex virus causes the following disease:

A. Genital Herpes
B. Chickenpox
C. Shingles
D. CMV infection
E. Measles

3. Which of the following medications are not used for treatment of herpes simplex virus?

A. Acyclovir
B. Benzyl benzoate
C. Valacyclovir
D. Oxolinic ointment
E. Interferon ointment

4. What type of pathogen causes herpes zoster?

A. Herpes simplex virus
B. Cytomegalovirus
C. Varicella zoster virus (*varicella zoster*)
D. HIV
E. Gardnerella

5. Unusual features for herpes zoster are:

A. Asymmetric process
B. Grouped vesicular eruption on an erythematous base
C. Contagious pathogen
D. Expressed subjective sensations
E. Lack of subjective sensations

6. Which of the following statements is correct?

A. Warts are caused by human papillomavirus
B. Warts have a bacterial etiology
C. Warts are an air-communicable disease
D. Teenagers are not subject to warts
E. Warts resolve to form lichenification

7. Which of the following criteria are not important for the diagnosis of molluscum contagiosum?

A. Papular (nodular) lesions
B. Navel-shaped cavity in the center of the rash element
C. The disease is more common in children
D. Papules-vesicular elements
E. When squeezed, nodules excrete pultaceous mass

8. What method of therapy is used to treat molluscum contagiosum?

A. Squeezing pimple content by means of tweezers and smearing it with an alcoholic solution of iodine
B. Antibiotic treatment
C. Steroid therapy
D. UFO
E. Antifungal therapy

9. What type of pathogen causes genital warts?

A. Papillomavirus type 1
B. Papillomavirus type 2
C. Papillomavirus types 6 and 11
D. Papillomavirus types 16 and 18
E. Papillomavirus types 3 and 10

10. What complication can occur in women with chronic course of genital warts?

A. Vesiculitis
B. Cystitis
C. Cervical cancer
D. Epididymitis
E. Balanoposthitis

Answers to the questions of the first level of complexity
1 – C; 2 – A; 3 – B; 4 – C; 5 – E; 6 – A; 7 – D; 8 – A; 9 – C; 10 – C
Answers to the questions of the second and third levels of complexity
1a – B; 2a – E; 3a – E; 4a – C; 5a – A

Task 1. Parents of a two-year boy visited a doctor. Two days ago, a child's red lip border got covered with a rash of small grouped vesicles, accompanied by severe itching. The next day, parents observed a gradual increase in temperature at the end of the day, and rapid spread of the rash on skin of both cheeks. On examination, an abundant vesicular facial rash, erosions with severe oozing lesion amid lichenoid skin are detected. Oral mucosa is covered with erosion. The general condition of a child is violated, the body temperature is 38,0 ° C. A child has atopic dermatitis, moderately severe course.

a) Put a provisional diagnosis:
- **A.** Shingles
- **B.** Herpes simplex
- **C.** Streptococcal impetigo
- **D.** Vulgar impetigo
- **E.** Duhring disease

b) Make a schedule for evaluation and treatment of the patient.

Task 2. A 23 y. o. man applied to a physician with complaints of itchy rashes in the foreskin area. The rash elements appeared after a lengthy stay on the beach. When collecting the history, doctor found out the symptoms occurred in a patient previously. On examination, grouped rash of small vesicles is detected: some of vesicles opened with the formation of erosions, the bottom is bright pink and soft. Lymph nodes are not changed.

a) Put a preliminary diagnosis:
- **A.** Streptococcal impetigo
- **B.** Shingles
- **C.** Candidiasis
- **D.** Secondary syphilis
- **E.** Herpes simplex

b) Conduct a differential diagnosis and compose a treatment plan.

Task 3. Parents of a 5 y.o. boy visited a doctor with complaints that a child has a rash on his hands. On examination, grouped papular rash on the proximal part of the back of the right hand is detected. The surface of papules features marked hyperkeratosis, covered with small papillae and resembles a cauliflower. The rash is painless, with no inflammation.

a) Put a diagnosis:
- **A.** Condyloma acuminatum
- **B.** Syphilitic extensive warts
- **C.** Vegetating pyoderma
- **D.** Squamous epithelioma
- **E.** Common warts

b) Work out a treatment schedule.

Task 4. A 24 y.o. patient visited a doctor complaining of a rash on the foreskin. On examination, foreskin and perianal region featured a few small flesh-colored papules with a thin leg. Papules are soft and painless.

a) Put a preliminary diagnosis:
- **A.** Genital herpes
- **B.** Erosive chancre
- **C.** Condyloma acuminatum
- **D.** Chancroid
- **E.** Candidal balanoposthitis

b) Conduct a differential diagnosis.

Task 5. A 72 y.o. patient came to a doctor complaining of severe pain in the left chest, as well as redness of skin in the area. In the anamnesis, angor pectoris and myocardial infarction are detected. On examination, grouped vesicular rash (in the setting of erythema) is found in the dermatome Th5 to the left.

a) Put a preliminary diagnosis:
- **A.** Shingles
- **B.** Streptococcal impetigo
- **C.** Pemphigus acantholytic
- **D.** Pityriasis rosea
- **E.** Atopic dermatitis

b) Work out a schedule for examination and treatment.

12 TOPIC

Acne and Acneiform Erruptions

12.1 Acne

Acne is a multifactor multiform long-term illness of oil glands.

TRAINING AND EDUCATIONAL GOALS

- Determine classification and common characteristics of acneiform rash
- Explain role of different factors favored for development of blotches
- Understand general course of disease and clinical findings of acneiform rash
- Determine typical clinical findings of disease and distinguish the blotches different by origin.
- Know the principles of therapy and preventive treatment of acneiform rash

TO KNOW:

- modern views of causation and pathogenic mechanism of different clinical types of blotches;
- factors favored for development and advance of acne;
- principles of classification of blotches;
- symptomatology of major clinical types of acne;
- main approaches for general and topical treatment and particularities of preventive treatment of blotches.

TO BE ABLE TO:

- carry out an examination correctly and interview the patient with acne;
- place on additional examinations for the purpose of diagnosis confirmation;
- carry out differential diagnosis with diseases having similar clinical findings;
- give advices as for treatment and preventive treatment of acne.

Epidemiology. Acne is one of the most widespread long-term illnesses of skin. According to variety of researchers acne is diagnosed over 60–80% persons of growing and young age. The incidence of acne is quite high also among persons of adult and advanced years.

Causation and pathogenic mechanism. Leading factors of development of acne are compositional and production disorder of sebum, changes of hormonal and immune status of body, failure of keratinization of follicular canal, intensive colonization of aqueducts of *Propionibacterium acnes* oil glands, development of inflammatory response in perifollicular areas, and genetic disposition.

Change of composition of sebum plays certain role in formation of comedones. The deficit of keratinosomes is observed during acne and lowering of content of epidermal lipids, linolenoic acid, ceramids, and free sterols. Simultaneously on the background of lowering of epidermal lipids level the secretion of lipids in oil glands increases and the contents of follicular cholesterol sulphate in it. It increase the adhesion epithelial cells and is one of the factors of follicular retentional hyperkeratosis i.e. facilitates to abnormal keratinization of follicular ceruminous' opening.

Except qualitative changes of sebum the increase of its quantity occurs at acne. At this the hypersecretion of sebum is an important condition for acne's forming.

Important value in acne's development the microbial hyper colonization has. In particular, it was established that skin liable to be damaged by acne is colonized by three types of microorganisms – *Staphyllococcus epidermis*, *Malassezia furfur*, and *Propionibacterium acnes*. It is considerable at this that *P. acnes* plays most role in overall stage of disease.

The significant role in pathogenic mechanism of women's acne plays hormonal dysfunctions, particularly, concerned with imbalance of testosterone and other androgens levels, menstrual disorders and different gynaecological problems.

There is also the opinion regarding opportunity of certain value in acne's pathogenic mechanism for Demodex folliculorum, Demodex brevis.

Nosology and different clinical presentations of different forms of acne. There are many nosologies of acne. They are based either on clinical presentations of disease or on assessment of its severity.

Taking into consideration the severity of clinical presentations the following is separated:

- *mild disease* when up to 20 comedones are observed or up to 15 inflammatory components or up to 30 components of hives on the skin of damaged areas totally;
- *heavy-medium acne disease* which is characterized by presence of from 20 to 100 comedones or from 15 to 50 inflammatory components or from 30 to 125 components of hives totally;
- *heavy disease* is determined at presence of 5 nodes or 5 cystophorous components or 100 comedones or 50 inflammatory components or more than 125 components of hives on the skin of damaged areas totally.

With that there is no standard classification of acne till now.

The more complete clinical classification is the one proposed by G.Plewig, F.Kligman:

1. *Childhood acne*
   Acne neonatorum
   Acne infantum
2. *Acne juveniles, acne vulgaris*
   Acne comedonica
   Acne papulopustilosa
   Acne nodulocystica
   Acne furminans
3. *Acne adultorum*
   Acne tarda
   Acne inversa
   «Bodybuilding acne»
   Acne conglobate
4. Acne precipitated by external causes (*acne venenata, cosmetic acne, contact acne*)
5. Acne precipitated by mechanical agents (*acne mechanica*)
6. Acne-typed eruptions

Acne neonatorum. Occurrence of these eruptions is connected with eyesore of hormonal crisis or supersecretion of testosterone in the antenatal life. The hormonal crisis is associated by fast decrease of theelol in blood of newborns during first week of life. The hives is mostly represented by closed comedones on cheeks, metope and mentum. Closed comedones are also called as lardaceous cyst encapsulations. These components appear after born of 50% of newborn infants and have a form of pointed papule of nacre-white or yellowish color. The eruptions could be individual or multifocal, often grouped. They have been destroyed unprompted during one or two weeks and rarely require care delivery.

Acne infantum. This acne could occur of children at third to sixth month of life and progress causing sometimes quite serious injuries. As a rule, this acne exists till five-year old. Corresponding eruptions could be concerned with congenital adrenal hyperplasia or with androgen-producing space-occupying process. In connection with this child with acne requires meticulous examination.

Acne juveniles, acne vulgaris. Juveniles or vulgaris acne is the most widespread dermatosis which occurs at the beginning of adolescence, reaches top of development in ephebic age and slowly regresses during first adult period. It is considered that ephebic acne (vulgaris, adolescent) reflects natural age particularities of developmental physiology and regresses of most persons spontaneously.

60-80% of persons suffered by ephebic acne forms have spontaneous regress of dermatosis' clinical implications at the age of up to 20 years. Overwhelming majority of adolescents has acne localized on the face only and part of them have it on face, sternum and dorsum.

Comedones (*acne comedonica*). This form is characterized by predominance of comedones which are the sealed cells of hair follicles in clinical presentation. Inflammatory component is franked incompletely. Further the so called close comedones appear which have no free fenestration with surface of skin. They represented by compacted noninflammatory papule with diameter of up to 2 mm. Gradual enlargement of these papule in volume with respect to continuous production of sebum creates conditions for transformation of some of them into open comedones (black-pointed acne).

Papulopustular acne (*acne papulopustulosa*). At this clinical form the fire of different intensity appears around the open or closed comedones. Clinically it is evidenced as formation of papule and pustule. At mild case the acne papulopustulosa are resolved without cicatrization. At significant expression of inflammatory response which is accompanied by damage of dermis structures the cicatricial tissues appear on places of inflammatory components.

Nodular cystophorous acne (*acne nodulocystica*). This form is characterized by formation of deep infiltrations and cystophorous cavities filled with purulence, which could interlock between each other. At opposite development of these components of hives the cicatricial tissues always appear.

Acne furminans. It is a heavy form of acne which occurs rarely. The disease appears mostly of juveniles at age of from 13 to 18 years who suffers from acne papulopustulosa or acne nodulocystica and is characterized by spontaneous beginning of ulcerated necrotizing components appearance on skin of dorsum and sternum mostly.

Acne adultorum. This acne could persist since ephebic age or could appear in adult age for the first time.

Acne tarda. This form is observed of women mostly. 20% of adult women have regular appearance of acne on the mentum in 2-7 days before the beginning of periods. In some cases acne are permanent. Such patients have appearance of acne papulosa and papulopustular components, sometimes the acne nodulocystica could appear. Patients who suffer from acne tarda should be examined meticulously. They

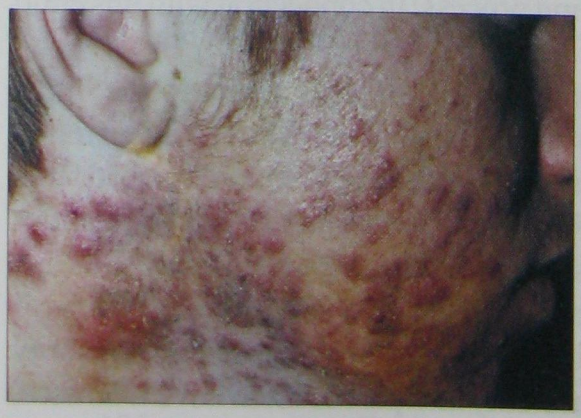

Fig. 12.2. Acne juveniles (papulopustular form).

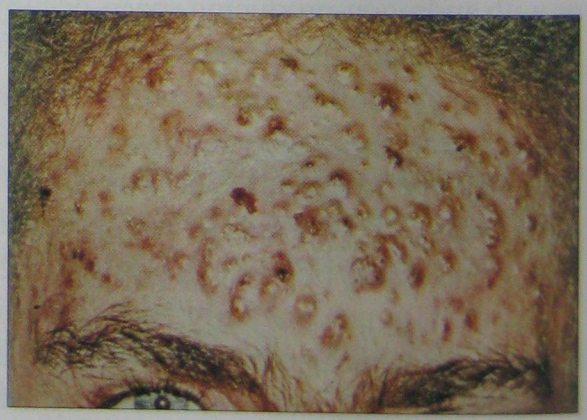

Fig. 12.3. Acne juveniles (papulopustular form).

often being discovered the sclerocystic disease of the ovary or polycystic ovarian syndrome. Adult women suffered from acne should be also excluded the growth of butterfly adrenals.

Acne inversa. This form concerned with secondary affection of apocrine sweat glands. At first, the obstruction and abruption of hair follicle's wall appears and then inflammatory infiltrate is being formed around the follicle's residues. Apocrine sweat glands are involved in process recurrently. This disease appears after adulthood and often combined with heavy forms of acne as well as with fatty degeneration. The disease begins from appearance of painful bosselated infiltrates which are open to the surface of the skin by fistulose openings. The content of infiltrates is suppurative or sanguinopurulent. The course of disease is chronicity with tend to backsets.

«Bodybuilding acne». This form of acne is concerned with abuse of anabolic steroids. The most reason of corresponding pathology is hyperandrogenism which enforces the production of sebum. The similar effect is caused also by glucocorticosteroids at chronic ingestion. Clinically, it is evidenced as appearance of acne nodulocystica.

Acne conglobate. According to the data of some researchers this heavy form of acne is most frequently observed of men with ctetosome (XYY). Clinically, the acne conglobate are characterized by gradual appearance of numerous nodular cystophorous components which are connected with each other as well as with large grouped comedones. Evidences of this disease, as usual, are not retracted after completion of adulthood and they could anticipate as long as life endures.

Acne precipitated by external causes (*acne venenata, cosmetic acne, contact acne*). The term origins from Latin word "venenum" which means "poison" and indicates on fact that comedones are formed in oil glands after epicutical influence. Comedonic and genic substances are mostly in beauty preparations. (wool fat, petroleum butter, some of vegetable greases)

Acne precipitated by mechanical agents (*acne mechanica*). Appearance of this acne is connected with pressure and friction (usual dermatosis) which causes

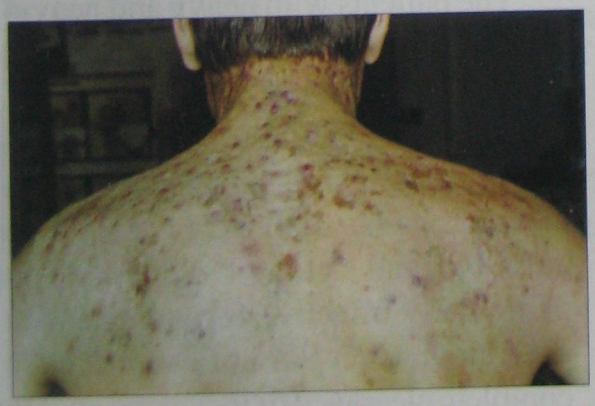

Fig. 12.4. Acne in dorsum area.

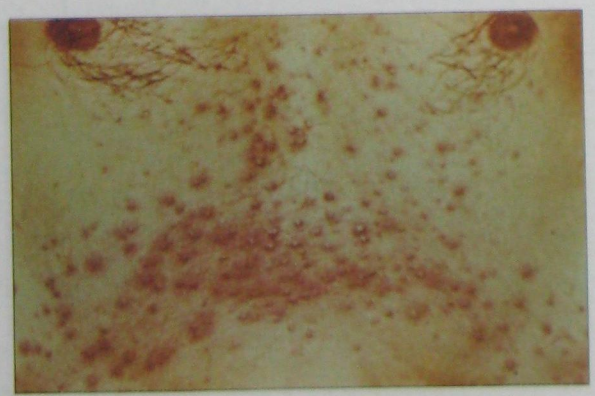

Fig. 12.5. Acne in sternum area.

mechanical blocking of follicles openings. The example could be continuous wearing of head wears, sport helmets, and plaster bandages together with excessive hidrosis.

Diacrisis. The acne's diagnostics is based on past medical history, course and clinical presentation of inflammatory process.

Differential diagnostics. The rule out is often carried out with diseases similar to acne (rosacea, demodicosis, perioral dermatitis and others) as well as with medicamental acne (iodic, bromatus, steroidal).

Curing. There are systemic and topical antiacneic solutions used in curing of acne which is assigned for breaking of main acne's pathogenetic mechanism's links, in particular, of abnormal keratinization and differentiation of keratocytes in ducts and openings of oil glands as well as hyperseborrhea, excessive activity of bacterial population in the oil glands, oil glandular obstruction and fire.

Treatment of acne should be commenced early to prevent scarring. Patients should be counseled that an improvement may not be seen for at least a couple of months. The choice of treatment depends on whether the acne is predominantly inflammatory or comedonal and its severity.

Mild to moderate acne is generally treated with topical preparations. Systemic treatment with oral antibacterials is generally used for moderate to severe acne or where topical preparations are not tolerated or are ineffective or where application to the site is difficult. Another oral preparation used for acne is the hormone treatment co-cyprindiol (cyproterone acetate with ethinylestradiol); it is for women only.

Severe acne, *acne unresponsive to prolonged courses of oral antibacterials, scarring, or acne associated with psychological problems calls for early referral to a consultant dermatologist who may prescribe isotretinoin for administration by mouth.*

Systemic treatment of acne involves using of antibiotics, 13-cis retinoic acid (isotretinoin) and cyproterone acetate.

The most effective are considered to be an antibiotics of tetracycline range (tetracycline, doxycycline) and macrolides erythromycin, josamycin and azithromycin.

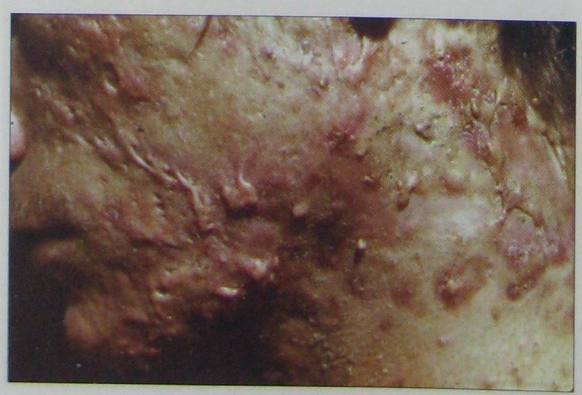

Fig. 12.6. Acne (nodular cystophorous form).

The patients with heavy and heavy-medium forms of acne are being assigned the isotretinoin per os.

Combined administration of «Diane-35» drug containing progesterone with antiandrogenic activity (cyproterone acetate) and ethinyl estradiol is particularly effective for women with acne tarda. Over 90% of patients have complete clearance of their acne and up to 80% there is no relapse. It has several

side-effects: dry lips, eyes and skin, mild alopecia, aches and pains. It also raises blood fat levels and may affect liver functions tests. The most serious problem is teratogenicity.

The group of pathogenetic remedies of acne's external therapy include topical retinoids, azelaic acid, topic antibiotics and bacterial agents as well as benzoyl peroxide. The most sebosuppressive and comedolythic effectiveness among existent remedies the local retinoids have (tretinoin, retene-A and others). According to existent algorithm of therapy of acne the topic retinoids are used for curing of different stages of severity of this disease. At acne of severity I the curing is limited by topic retinoid and benzoyl peroxide only, at acne of severity II-III the topic retinoids with benzoyl peroxide are assigned and system therapy by the means of oral antibiotics or hormonal medications, at acne of severity IV – isotretinoin, topic retinoids and hormonal androgen-deprivation therapy.

Azelaic acid is also effective anticomedogenic drug. At this, azelaic acid in contradistinction from retinoids has no sebosuppressive effect.

The existent for the now local anticomedogenic drugs containing antibiotics include «Zynerit» (erythromycin-zinc complex in form of wash).

The existent local antimicrobial drugs for curing of acne vulgaris also include benzoyl peroxide.

Individual researchers are also doubts regarding to expedience of number of cosmetic measures while acne, in particular, in sense of boosted clearing of skin by detergents, brushes, alcohol as well as carrying out the mechanical and chemical pilling, and deep cleaning of skin.

12.2 Acne-typed diseases

The term «Acne-typed diseases» is quite often occurred in modern special literature. The rosacea, perioral dermatosis, and demodicosis are considered to be placed in this group of diseases. The provisional union of these diseases into one group is conditioned by existence of a range of similar and interconnected factors which have been given a certain meaning in development of corresponding dermatosis. The common signs of rosacea, perioral dermatosis and demodicosis are location of inflammatory process on the skin of face, morphological components of exanthema as well as nature of clinical progression. At this, separate assumptions of origin and particularities of clinical presentation for this dermatosis, in particular, the type of location of inflammatory process on certain parts of face, are show for specialties of each from corresponding nosologies. Taking into account the proven leading role of acarian demodecydes in occurrence of demodicosis this dermatosis is considered in textbook in "Parasitic diseases of skin – dermatozoonosis" chapter.

Rosacea

Rosacea, symptoms: acne erythematosus – chronic dermatosis with incompletely discovered causation, which is characterized by occurrence of fixed eruption, telangiectasia, papule, and pustule on the face.

TRAINING AND EDUCATIONAL GOALS

- Publicize modern representations of rosacea's aetiopathogenesis
- Determine factors which are facilitate the disease establishment
- Know the classification particularities of dermatosis
- Determine its typical clinical presentations
- Carry out the differential diagnostics of rosacea
- Know general principles of medical and preventive measures at rosacea

TO KNOW:

- etiological and pathogenetic particularities of rosacea;
- clinical sorts of this disease;
- principles of therapy and preventive measures at rosacea.

TO BE ABLE TO:

- carry out an examination correctly and interview the patient with rosacea;
- carry out the laboratory diagnostics and determine additional examination technics with respect to discovering of acarian demodecydes, *H. pylori*;
- carry out the differential diagnostics with diseases having similar clinical performance and prove the diagnosis;
- make up a plan of advices regarding to curing and prevention of this disease.

Aetiopathogenesis. Causation and pathogenetic mechanism of rosacea are discovered incompletely. Among possible factors of occurrence of this chronic dermatosis the numerous of external and internal causes are separated.

The external causes of rosacea's progression include alimentary and meteorological factors, activity of acarian demodecydes (*Demodex folliculorum*), presence of infection which includes *H. pylori*. The range of alimentary factors (alcohol, hot drinks, spices) take stimulating effect on mucous coat of stomach which calls face hemahgiectasia reflectory. Some of authors count that excessive intake of food from meat and spices are facilitating the appearance of rosacea.

Certain role on rosacea's progression also have influence of physical agents, particularly, solar irradiation, heat and cold. It is clearly known that solar irradiation together with subsequent responses of reddening provokes the progression of erythematic form of rosacea.

The background of inflectional theory of appearance and progression of rosacea is presence of pustular components of patients' exanthema as well as effectiveness of antibacterial drugs in therapy of dermatosis.

Possible external causes of occurrence and progression of rosacea include also presence of Demodex folliculorum in pilosebaceous follicles of skin of face. At this in virtue of morphological and biological particularities of Demodex folliculorum the discussions regarding possible mechanisms of its pathogenetic effect still are. There are two types of acarian demodecydes separated (*Demodex folliculorum, Demodex brevis*) which are conditionally considered to be pathogenetic exophytes and have famous specificity regarding to human. *Demodex folliculorum* are parasitized in openings of hair follicles and *Demodex brevis* are parasitized in oil glands. The pathogenic properties of these acarian demodecydes include their ability to mechanical destroying of epithelial cells lining the follicles as well as initiate forming of granulomas and inflammatory lymphohysteocytic infiltrations in derma.

For the now one of the most pathogenetic external causes of origin of rosacea is considered to be an angioneurosis with dominating damage of vessels of face.

Clinical findings. The typical for rosacea is following location of damages – on cheeks, metope, mentum as well as sometimes in postaural areas, on hairy part of the head, front surface of neck, concha of auricles, ear lobes, and blepharons.

With due regard to clinical and morphological characteristics of rosacea there are different classifications o this dermatosis offered.

Classification on the basis of nature of morphological components and prevalence rate of inflammatory process determines six clinical forms of rosacea – smooth, localized and spreading as well as deep forms – localized with deep papular and pustular components, localized with transformation into hammer nose, spreading with deep papular and pustular rash.

On the basis of clinical course of rosacea and pathomorphological changes the classification was created according to which there are four forms of dermatosis separated – erythematic, papular, pustular and infiltrative-productive.

In addition, there is a classification of rosacea which takes into consideration the ethiopathogenetic factors of progression of dermatosis. In accordance with this classification there are four stages of progression of inflammatory process separated: prerosacea – corresponds temporary responses of skin's reddening, vascular rosacea – characterized by fixed eruption and telangiectasia, inflammatory rosacea – accompanied by occurrence of papules and pustules, delayed rosacea – corresponds to progression of hammer nose. The specialized form of rosacea is a rosacea of eyes.

Classical progression of rosacea is characterized by occurrence of tidal erythema. At first the duration of reddening varies from several minutes to several hours and is accompanied by fever sensation or warmth sense and then disappears without leaving a trace. After quite short time interval under influence of different provoking factors (insolation, atmospheric and temperature oscillations, abuse of hot or spicy food, alcohol) the tidal erythema appears again. Its location is mostly limited by central part of the face and nasal-cheek folds. The process of change of quite often erythema backsets by remissions could continue for months and even years. With this after some time the duration of backsets is increased and duration of remission between them becomes less. Erythema gradually becomes more marked, gets cyanochroic tone and goes to cheeks, metope and mentum. Subjectively the patients complain for fever sensation as well as heat and pruritus. Occurrence of pruritus is explained by range of researchers as a result of increasing of *Demodex folliculorum* population. Maybe, the pruritus is also a result of raised activity of acarian demodecydes on the background of favorable conditions for its life activity. At histological examination of this stage of rosacea there are only enlarged blood vessels and lymphangions observed in affected areas.

Later on the background of erythema and thickness of affected areas of skin the isolated or grouped inflammatory pink-red papules are occur covered by furfur. The persistence is characteristic for papules during quite long period of time (several weeks). Gradually, most of nodes are suppurate forming a papule-pustules and pustules with sterile content.

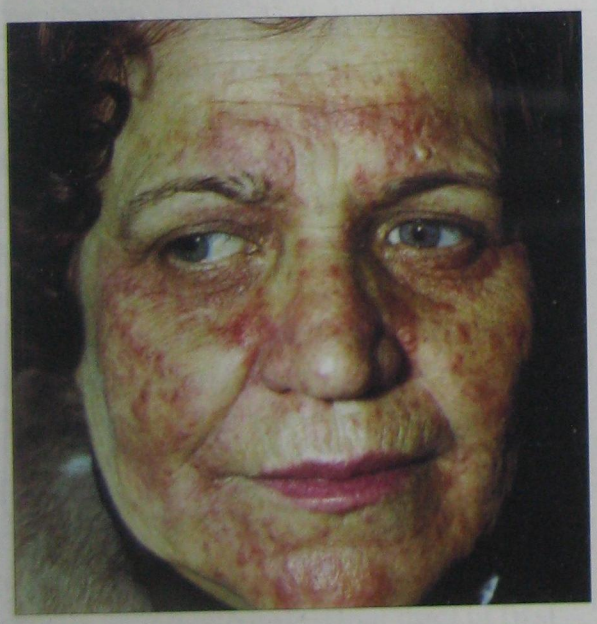

Fig. 12.7. Rosacea.

Pathomorphology. The inflammatory disorder with follicular orientation is observed in pustules at presence of lymphocytes, clasmatocytes, and neutrophils in follicle's opening. Histologically the hammer nose is a hyperplasia of oil glands and hypertrophia of connective tissue.

Diagnostics. At determination of rosacea diagnosis it is necessary to take

into account an anamnestic data, clinical presentation of damage, in particular, special clinical signs characteristic for this dermatosis in complex as well as results of microscopic investigation for presence of acarian demodecydes.

Differential diagnostics. At opposite to rosacea:

Demodicosis (*rosacea-typed form*) is characterized by fact that at progression of this disease the most etiological value have an acarian demodecydes; it begins from occurrence of follicular papules, pustules and only after some time the diffuse erythema and infiltration of skin occur.

Sebborheal dermatosis is localized on hairy part of head; its characteristic is a fatty furfur; at microscopic investigation the numerous cryptococcus of Malassezia are discovered;

Acne appears before rosacea by age criteria, in ephebic, begins from appearance of comedones, its transformation into papules and pustules and after some time only the spread erythema could progress;

Erythema centrifugum (*discoid form*) is characterized by limited discoid locuses, symptoms of follicular keratosis and progression of cicatricial;

Perioral dermatitis has typical location of process (perioral), nature of papules is non-follicular, there are no pustules and desquamation, the pruritus is observed.

Bourneville-Pringle disease (adenomatosis of oil glands) is characterized by fact that progression of adenomatosis infiltrates being started in childhood, there is no diffuse erythema;

Perniosis of nose (freezing injury) leads to uniform cyanochroic-red color in nasal area.

Menopause is accompanied by tides with hyperhidrosis.

Curing. The pustules and papules of rosacea respond to topical metronidazole or to topical azelaic acid Alternatively, oral administration of oxytetracycline or tetracycline 500 mg twice daily, or of erythromycin 500 mg twice daily, can be used; courses usually last 6-12 weeks and are repeated intermittently. Doxycycline 100 mg once daily can be used if oxytetracycline or tetracycline is inappropriate (e.g. in renal impairment). A modified-release preparation of doxycycline is licensed in low doses of 40 mg once daily for the treatment of facial rosacea (section 5.1.3). Isotretinoin is occasionally given in refractory cases [unlicensed indication]. Camouflagers (section 13.8.2) may be required for the redness.

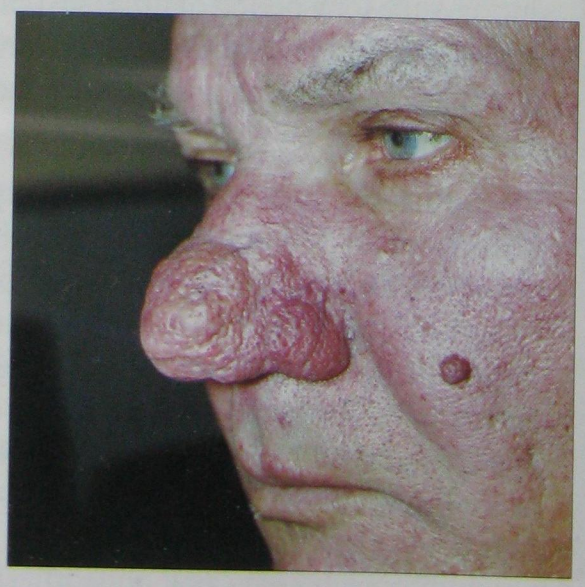

Fig. 12.8. Hammer nose.

Perioral dermatitis

Perioral dermatitis is a chronic dermatosis located on the face's skin, mostly nearby mouth, with possible spreading of inflammatory process to the area of nosolabial triangle, mentum, and cheeks. This dermatosis is mostly registered of young and middle-age women.

Causation and pathogenetic mechanism. Perioral dermatitis is often occurs of persons with burdened allergic anamnesis, in particular, with neurodermatitis accompanied by xerodermia. Many of patients with perioral dermatitis were discovered connection of it with long-lasting abuse of outer therapeutic agents containing fluorinated corticosteroid medicinal products. Progression of this dermatosis could be provoked by cosmetic creams, washes, paints, some of teeth pasts as well as long-term staying under solar irradiation (perioral dermatitis is often recrudesces in spring and summer). According to the data of some researchers the certain role in occurrence and progression of perioral dermatitis play *Demodex folliculorum* and *Demodex brevis* acarians.

Clinical findings. The most typical clinical presentation of perioral dermatitis is occurrence of numerous small papules of red color located on the face's skin mostly around the mouth and nosolabial triangle, as well as on mentum, cheeks, bridge of the nose and periorbital areas. Later on the background of erythema these papules interlocked into largest components part of which transforms into painful pustules and nodes. The specialty of perioral dermatitis is saving of narrow strip of undamaged skin around the vermilion surface.

Clinical course of perioral dermatitis is characterized by periods of recrudescence and remission. With this even during remission period there are always separate papule-pustule components of exanthema.

Diagnosis and differential diagnostics. The differential diagnostics is carried out most often with rosacea. In contradistinction from rosacea at perioral dermatitis there are no telangiectasis, true pustulation, and nodes; the thin strip of undamaged skin is left around the vermilion surface.

Curing. The therapy of perioral dermatitis should include complex measures. In particular, the curing of concurred conditions is recommended (diseases of gastrointestinal tract at first instance), sanitation of locus of chronic

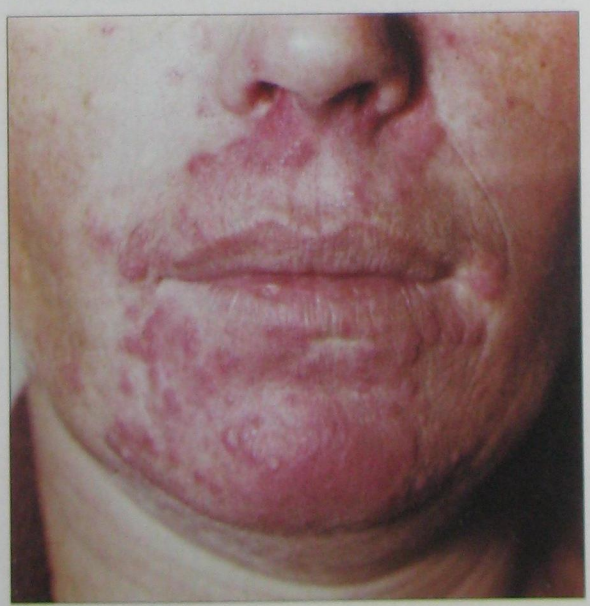

Fig. 12.9. Perioral dermatitis.

infection; if possible normalize functioning of endocrine system. The immunomodulators are used by indications, bracing and analeptic medicines as well as drugs normalizing the operation of excitatory system. There are alcohol drinks, spicy food, chocolate, and citrus should be excluded from nutrient budget as well as limit the abuse of carbohydrates and salt.

At presence of postulant exanthema it is necessary to use an antibiotics of tetracycline range, in particular, minocycline or doxycycline during 4-6 months.

The metronidazole is also used in quantity of 0.25 g twice a day during 2-3 weeks. The significant place in curing of perioral dermatosis the local therapy takes. At first instance, the patients are recommended to withdraw from cosmetic remedies. The shaken blend is used locally with 1-3% of sulphur and ichthammol (in case of fat skin) or pasts with these agents (in case of dry skin), as well as 1-2% salicylic acid, 1-2% boric acid, 2% mixture of resorcin, and 2% mixture of metronidazole. At expressed inflammatory process the cold packs are assigned with 1% solution of resorcin, 3% boric acid, 3% tetraborate sodium, as well as statutory unctures with corticosteroid medical agents.

At discovering of acarian demodecydes of patients with perioral dermatosis it is recommended to treat the skin of face by 20% suspension of benzyl benzoate or by 33% sulfur ointment during 20 days.

Prognostication. The prognosis is laudable, at condition of balanced therapy the ultimate recovery occurs.

1. Clinically the following is not included in types of acne juveniles:

A. *Acne tarda*
B. *Acne comedonica*
C. *Acne papulopustolosa*
D. *Acne nodulocystica*
E. *Acne fulminans*

2. For acne's occurrence the important thing is:

A. Pathological follicular hyperkeratosis
B. Excessive production of sebaceous matter
C. Influence of *Propionbacterium acnes*
D. Inflammation
E. All of mentioned above

3. For acne of medium severity the presence of the following is typical:

A. From 20 to 100 comedones
B. From 15 to 50 inflammatory components
C. From 30 to 125 components on skin totally
D. All of mentioned above is wrong
E. All of mentioned above is right

4. What stage of inflammatory process' progress could not be at rosacea:

A. Erythematic (Erythrosis of face)
B. Lichenificated
C. Papulopustule
D. Nodular
E. Erythematic-papular

5. The differential diagnostic of rosacea is most often carried out with:

A. Demodicosis
B. Seborrheal dermatosis
C. Erythema centrifugum
D. Bourneville-Pringle disease
E. All answers are correct

6. The following are not the types of rosacea:

A. Lupiform acne
B. Acne congolobata
C. Acne furminans
D. White acne
E. Rosacea-leukophlegmasia

7. The drugs assigned at acne have no any effect on:

A. Normalization of flake off of dead cells of skin
B. Antimicotic influence
C. Anti-inflammatory effect
D. Destroying of *Propionibacterium acnes*
E. Hormonal influence

8. What of specified drugs is not recommended for curing of rosacea:

A. "Metrogyl-gel"
B. Metronidazole
C. Glucocorticosteroid unctures
D. Antibiotics of tetracycline range
E. Azelaic acid

Task 1. The female patient of 19 years old seek advice with complains for rash on skin of face, sensation of tightness of skin after washing and stipulated by disease necessity of often washing a head. *Unbiased*: the yellow-red spots with relatively clear borders and peeling on surface are observed on the skin of hairy part of head, eyebrows, blepharons, and nasal wings. Affected skin is calloused, with rugged surface, flare. The hair is fat, flare, gummed. Rash is accompanied by pruritus, especially at excessive hyperhidrosis.

a) What the provisional diagnosis is:

A. Liquid seborrhea
B. Professional seborrheal weeping dermatitis
C. Dry seborrhea
D. Mixed seborrhea
E. Seborrheal pemphigus

b) Determine the management of examination and managing of patient.

Task 2. The male patient of 16 years old seeks medical advice for dermatologist regarding to rashes on skin of face and sternum. It is known from anamnesis that patient is sick during five years, was cured periodically using only drying medical agents and medicaments of different action (antibiotics, antifungal, exfoliating) for local abuse. Clinically the variety of rash components is observed located on skin of face, upper half of sternum and dorsum in form of acne, papules, pustules, there are crusts and cyanochroic-pink cicatricial tissues in some places.

a) Determine the provisional diagnosis:

A. *Acne inversa*
B. *Acne papulopustulosa*
C. *Acne infantum*
D. *Acne nodulocystica*
E. *Acne comedonica*

b) Make the complete clinical diagnosis with determination of severity of disease's course.

Task 3. The male patient of 20 years old came to the outpatient attendance to the dermatologist with complains for rashes in area of dorsum, sternum, neck (except face), which appear spontaneously, rising of body temperature up to 38 °C, pain in articulations, sickliness. It is known from anamnesis that rashes in form of acne and nodes were noticed during six years. The patient have not been examined and curried. *Unbiased*: there are numerous inflammatory painful nodes, pustules with suppurative and hemorogic content which destroyed in some places forming anabrosis and ulcerations are observed. The hematologic state is leukocytosis, and accelerated ESR.

a) Determine the provisional diagnosis:

A. *Acne tarda*
B. *Acne comedonica*
C. *Acne papulopustulosa*
D. *Acne nodulocystica*
E. *Acne fulminans*

b) Determine the management of examination and curing of patient.

Task 4. The female patient of 36 years old is on institutional treatment in gastroenterology department regarding to duodenal ulcer, the advice of dermatologist is recommended in connection with presence of rashes on skin of nose, cheeks and mentum. On the basis of anamnesis and dermatological examination it was determined that disease at first observed periodically and then fixed erythema of face and telangiectasia appear. Later on the background of erythema the milliar follicular papules and pustules appear.

a) Determine the provisional diagnosis:

A. Demodicosis
B. Sebborheal dermatosis
C. Steroid acne
D. Rosacea
E. Perioral dermatosis

b) Determine the management of patient.

Task 5. The woman of 34 years old complains for presence of rash without subjective sensations located around mouth. It is known from anamnesis that patient has often disorders of gastrointestinal tract. During dermatological examination the symmetric rash in form of locus

erythema of pink color is discovered around the mouth. There are grouped milliar papules, micro vesicles, micro pseudo pustules located on its background and not connected with follicles. *Demodex folliculorum* is not discovered.

a) Determine the provisional diagnosis:
A. Demodicosis
B. Sebborheal dermatosis
C. Perioral dermatosis
D. Acne adultorum
E. Rosacea

b) Cary out differential diagnostics of specified disease.

Answers for first level self-control questions
1 – A; 2 – E; 3 – E; 4 – B; 5 – E; 6 – D; 7 – B; 8 – C
Answers for second and third level self-control questions
1a – A; 2a – B; 3a – E; 4a – D; 5a – C

13 TOPIC

Cutaneous tuberculosis

Lupus (*tuberculosis cutis*) is a chronic infectious disease caused by tuberculosis bacteria. Cutaneous tuberculosis is often a manifestation of a single process of tuberculosis in the whole organism and is combined with a lesion of the upper respiratory tract, lungs, bones, joints, and other forms of tuberculosis.

TRAINING AND EDUCATIONAL PURPOSES

- Disclose the relevance of the problem of lupus, as well as ways and conditions of infection
- Have an idea of the main points of etiology and pathogenesis of lupus
- Classify typical symptoms
- Understand characteristic clinical features of lupus
- Identify principles of treatment and prevention of cutaneous tuberculosis

TO KNOW:

- current status of the theory of etiology and pathogenesis of cutaneous tuberculosis;
- classification of cutaneous tuberculosis;
- characteristic clinical and diagnostic features of the main types of skin tuberculosis (lupus, scrofuloderma, tuberculosis cutis verrucosa, tuberculosis cutis lichenoides, lichenoid, papulonecrotic tuberculid, erythema induratum, etc.);
- methods of examination of patients with cutaneous tuberculosis (dermatology, laboratory, general therapeutic);
- differential diagnosis of the diseases with similar symptoms;
- modes of treatment and principles of clinical examination in cutaneous tuberculosis;
- prevention of tuberculosis infection.

TO BE ABLE TO:

- properly interview a patient with cutaneous tuberculosis;
- formulate a complete clinical diagnosis with characteristic clinical form of the disease;
- perform differential diagnosis based on a clinical form of skin tuberculosis;
- prescribe laboratory tests to confirm the diagnosis;
- prescribe a rational therapy for a patient with skin tuberculosis, depending on a clinical form of the disease;
- prescribe a rational therapy for a patient with skin tuberculosis based on the disease case.

Etiology. The causative agent of tuberculosis is Mycobacterium tuberculosis belongs to the group of acid-fast bacilli, related to lower plants – actinomycetes, or ray fungi. Mycobacterium tuberculosis is characterized by considerable polymorphism and a strand, bacillary, granular, filter stage of development. It is a thin stick, sometimes straight, often curved, with slightly rounded ends, length of 0,8-3-5 microns and width of 0.2-0.5 mm. It is aerobic, but can also be a facultative anaerobe. Temperature limits of the growth of this bacteria are within the temperature from 29 to 42 ° C (optimum temperature is 37-38 ° C), vital activity is stored at very low temperatures, while the temperature rise to 80 ° C is stood within 5 minutes. Under intense solar radiation, vital functions of the mycobacterium are sharply reduced, while darkness and dampness allows survival for a significant number of bacteria.

In the course of phylogenetic development, the three types of human pathogens Mycobacterium tuberculosis formed: human (*typus humanus*), bovine (*typus bovinus*) and avian (*typus avium*).

Pathogenesis. Lupus represents a group of skin diseases different in clinical and histological picture, caused by a single cause: penetration of Mycobacterium tuberculosis of one of these types into skin.

For the pathogenesis of lupus, a single causative agent of the disease is not enough. It is believed that the development of the disease requires the impact of at least three factors, which include: getting of a sufficient number of virulent mycobacterium tuberculosis into skin, reduced skin reactivity to them, which is characterized by an increased content of sodium salts and water in skin, adverse effects of the environment.

Penetrating into skin, Mycobacterium tuberculosis gives rise to abnormal focal inflammation. Initially, epithelioid, and then mixed (predominantly lymphocytic) tubercle are formed. Phospholipid fractions of Mycobacterium tuberculosis are responsible for appearance of epithelioid cells, while protein fractions of Mycobacterium tuberculosis form lymphoid cells.

Classification. Numerous forms of the disease are divided into two groups: localized (focal) and scattered (disseminated) lupus.

Localized forms of skin tuberculosis include:

- primary skin tuberculosis (tuberculous chancre);
- TB erythematosus;
- tuberculosis cutis colliquativa (skrofuloderma) and tuberculosis of mucous membranes;
- verrucous tuberculosis of skin and mucous membranes;
- military-ulcerative tuberculosis of skin and mucous membranes.

Diffuse (metastatic) forms of skin tuberculosis include:

- miliary tuberculosis of skin;
- tuberculosis papulonecrotica;
- indurative (callous) erythema Bazen;

- moniliformis scrophulosorum.

In typical cases, all clinical forms of skin tuberculosis are characterized with gradual development, lack of acute inflammation and severe pain, chronic undulating course, remission and relapse in spring and fall.

Clinical picture. A variety of clinical forms of skin tuberculosis depends on many factors, which principally include immunobiological reactivity, age and sex of patients. Generally, tuberculous lupus, skrofuloderma, lichen scrofulous appear in childhood or adolescence, while verrucous and ulcerative tuberculosis, as well as erythema induratum Bazen, develop mainly in adults. Warty tuberculosis is more common in men, whereas indurative form is typical only for women.

Tuberculous skin lesions are predominantly secondary, as they develop in the body, which is infected with mycobacterium tuberculosis in one way or another. In most cases, penetration of Mycobacterium tuberculosis into the body occurs through the respiratory tract.

Localized (focal) forms of lupus

TB erythematosus *(lupus vulgaris, tuberculosis cutis luposa)*, ***synonyms: tuberculosis cutis luposa, or lupus,*** are most common cases. It is characterized by a slow chronic progressive course with a tendency to dissolution of tissues. The disease usually begins in childhood or adolescence; often in adults.

The primary element of tuberculous lupus rash is a tubercle (lyupoma), the size of a pinhead to a pea, somewhat above the skin level. Tubercle is of brownish-reddish color and soft (doughy) consistency. When pressed with the object carrier (diascopy), by squeezing blood from dilated blood vessels the bump turns yellowish-brown and translucent (*apple jelly symptom*); when pressed with a blunt probe, a fossa is formed (*probe symptom*) due to a significant reduction of the amount of collagen and elastic fibers in the tuberculum. The fossa remains for five to ten seconds. In some cases, its surface is easily pierced, while being accompanied by bleeding.

In further, the tuberculum decays to ulcer. Ulcers feature shall depth, grainy bottom, red surface with a predisposition to bleeding, and soft edges. After healing of the ulcer, a scar with smooth white surface is formed; new tuberculums may develop.

Most often, the process is localized on face, nose, cheeks, upper lip, ears, seldom on the neck, trunk and extremities. Mucous membranes and skin areas bordering them mainly feature ulcerous forms.

Clinical picture of tuberculous lupus features a number of varieties. Initially, the bumps are grouped closely, in the future, they slowly increase as a result of peripheral growth, merging into a diffuse infiltration, which barely rises above the skin surface, and then we talk about a flat variety of tuberculous erythematosus (*lupus vulgaris planus*). Sometimes, bums feature a significant lamellar peeling that leaves barely visible scar atrophy. This type is defined as *lupus vulgaris exfoliativus*. In long-term existence of the focal point of plane lupus, ulcers may prevail.

In this case, we talk about *lupus vulgaris exulcerosus*. If on the surface of the lesion featueres a large number of crusts, the type is called *lupus vulgaris crustosus*. If papulose elements reach the size of a pea and significantly overhang above skin surface, this form of is called *lupus vulgaris tuberosus*. If there are large soft infiltrates in the form of tumor mass formed by a merging of bumps, the type is called *lupus vulgaris tumidus*. Frequently, with the localization of the pathological process in face, upper and lower extremities and buttocks a peripheral increase of the infiltration with simultaneous decay, ulceration and scarring in the center is observed. Such state is defined as *lupus vulgaris serpiginosus*. The process has a creepy character, covers more skin area.

Destructive ulcerative changes involve the deep tissues in the process (cartilages, bone, joints) with spontaneous amputation, formation of fibrotic scars and keloids, deformation of nose, ears, fingers, eyelids and limbs (*lupus vulgaris mutilans*). With the destruction of cartilage nasal septum, nose becomes shortened and flat, there occur lid eversion and narrowing of the mouth, which greatly disfigures a patient (*lupus vulgaris vorax*).

Lesions of mucous membranes of nose and mouth are sometimes isolated. In the mouth, the process is more often localized in the mucosa of the gum and palate. Initially, there appear small bumps of bluish-red color and the size of a millet seed. Formed ulcers bleed easily; they are covered with a yellowish fur.

Diagnosis is based on clinical signs of the disease, characteristics of lupoma (apple jelly and probe symptoms), ulcers, scars, pathologic behavior and localization.

Differential diagnosis is to consider the following aspects.

Papulose syphilide. The characteristics involve the dense texture of bumps, focal localization, formation of a not solid, but mosaic scar, which consists of individual small scars with no conjugation (see «Tertiary syphilis»).

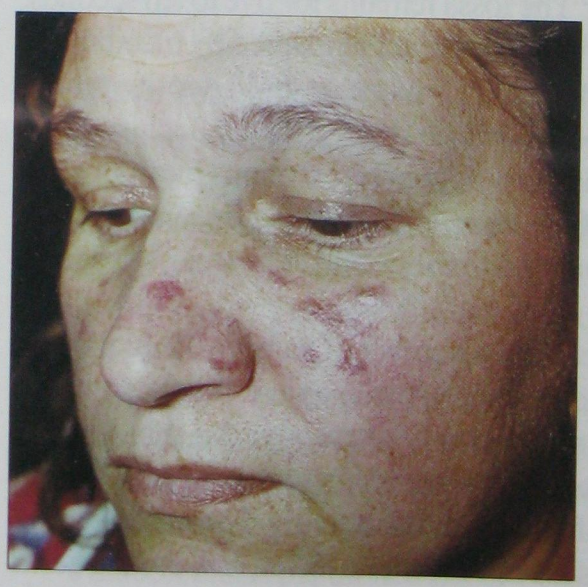

Fig. 13.1. Tuberculous lupus.

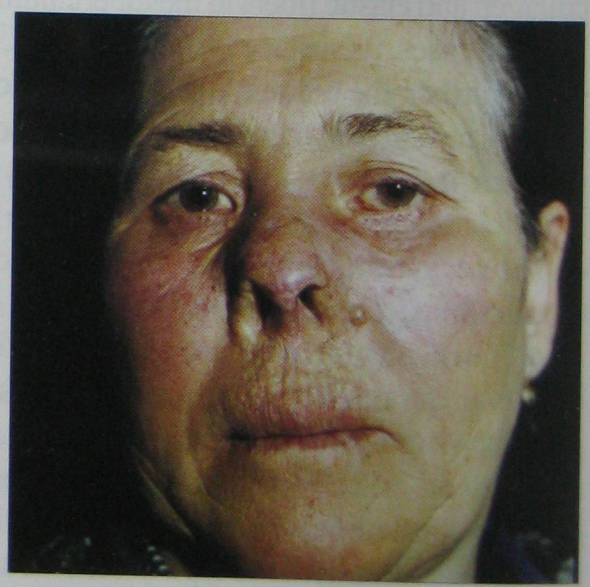

Fig. 13.2. Tuberculous lupus.

Tuberculoid form of leprosy. Unlike tubercular lupus, it features the absence of temperature and pain sensitivity in the affected skin area (see «Leprosy»).

Tuberculoid form of leishmaniasis. For differential diagnosis, history is important (a patient's staying in an endemic area), placing of bumps around the scar, their localization in the open skin areas, rapid formation of ulcers with thick copious purulent discharge, identification of Leishmania (see «Leishmaniasis»).

Some forms of tuberculous lupus (with scaling and hyperkeratosis in the cheeks and nose) may resemble erythematosus. In severe cases, biopsy and histology are applied.

Strumoderma (*tuberculosis cutis colliguativa*) or **skrofuloderma** (*scrofuloderma*). Skrofuloderma is one of the most common forms of skin tuberculosis. It is usually observed in children and adolescents, but can also develop in older people.

The lesion is the result of hematogenous infection of skin with Mycobacterium tuberculosis (*primary skrofuloderma*); more often, it occurs as the result of transition of the infection per contituitatem from the infected lymph nodes (*secondary skrofuloderma*).

The disease begins with the appearance of one or more sharply limited dense nodes the size of a hazelnut in the subcutaneous tissue. Nodes gradually increase in size. Over time, they are soldered with the covering skin. The skin over the nodes is of a bluish-red color. In further, nodes soften and turn into a cold abscess. Skin becomes thinner and then breaks. From small openings, rare liquid pus with lumps and bits of dead tissue is discharged. Then, the holes widen and form ulcers with soft deep overhanging cyanotic edges. The bottom of the ulcer is covered with yellowish flabby granulations, which bleed easily with a slight touch. After some time, typical inverted

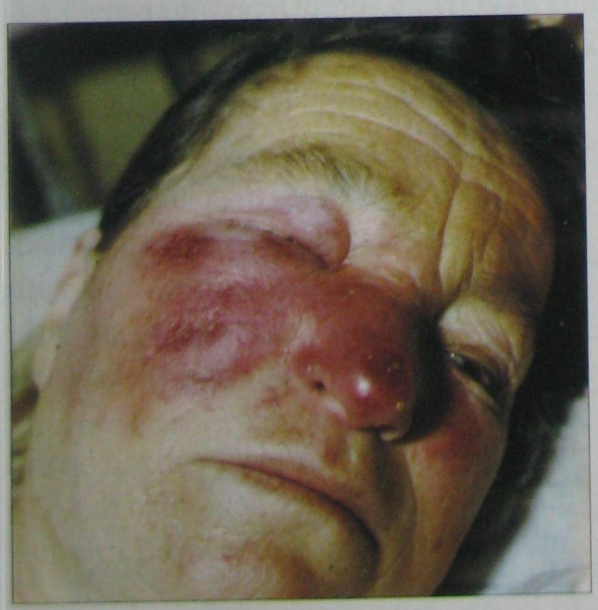

Fig. 13.3. Tuberculous lupus complicated by erysipelas.

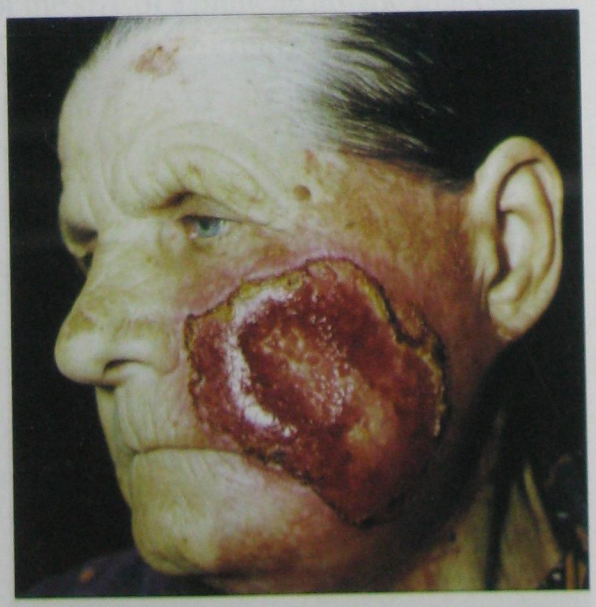

Fig. 13.4. Tuberculous lupus complicated by carcinoma.

jagged disfiguring scars resembling bridges with the intersections of unaffected skin and fibers are formed on the site of ulcers.

In secondary skrofuloderma caused by the lesion of lymph nodes, sores are deeper and penetrate into the tissue of the lymph node. After healing, a bumpy tight retracted scar is left.

Diagnosis. Diagnosis is based on clinical symptoms, results of Pirquet's reaction (in older children, it is strong positive with a benign course of the process, while giving versatile results in younger children). Clinical history, the results of clinical, radiological and histological studies are considered.

Differential diagnosis. It is carried out with gummatous syphilides, gummy-knotted actinomycosis, chronic ulcerative pyoderma, erythema indurativum Bazin.

Gummatous syphilides are only subject to central decay, form sores similar to a crater, surrounded by the dense infiltrated shaft, which heal in a test specific treatment.

Chronic ulcerative pyoderma develops in adults and is characterized by polymorphism of superficial and deep ulcers, not related to the location of lymph nodes and presence of the inflammatory reaction around ulcers.

Localized in the neck and under the jaw areas, gummy-knotted actinomycosis is characterized by formation of large knots of dense consistency. After they merge, there develops a solid dense infiltrate, similar to a tree, with a zone of softening in the center. Discharged pus is liquid with crumbly yellowish inclusions (nodules).

When skrofuloderma is localized on shanks, the differential diagnosis with erythema indurativum Bazin is required. It is located on symmetric parts of skin, less prone to ulcers, occurs more often in girls at puberty.

In mild cases, temporary treatment leads to the formation of a single node and a patient's recovery. In cases of persistent ulcers, the prognosis is less favorable.

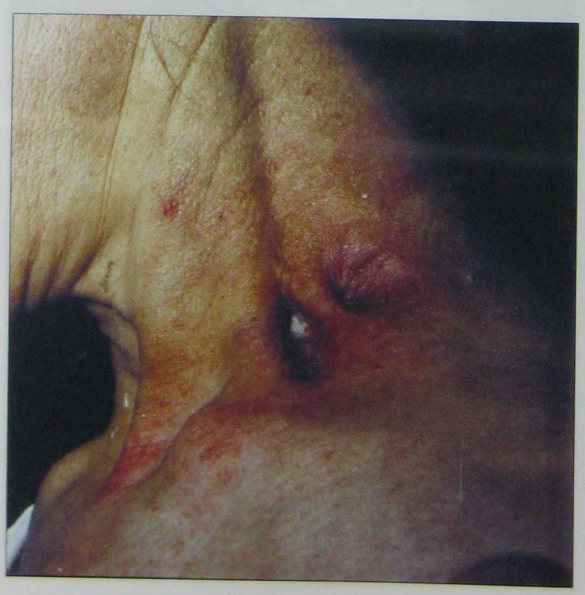

Fig. 13.5. Skrofuloderma.

Warty tuberculosis (*tuberculosis cutis verrucosa*). The disease mostly occurs in people who deal with the corpses of people sick with tuberculosis, as well as in workers of slaughterhouse and leather industries, which are in contact with meat and skin of animals sick with tuberculosis. Infection may be not only exogenous, but also autoinoculation and hematogenous.

The disease is often localized on the dorsum of the fingers, seldom in feet and ankles; the lesion is observed in other parts of skin.

The disease begins with the formation of a bluish-red lentil-sized

tubercle, dense to the touch. Tubercle increases in size, the stratum corneum thickens, and the surface becomes rough, gradually turning into warty papillary ecphymas, separated by cracks. In the formed foci behind the central zone of warty mass, there is an infiltration zone, covered with scales and crusts, and finally peripheral zone of the inflammatory rim.

This is one of the most benign skin tuberculosis, slowly evolving and relatively easy to treat. With no treatment, the process can occur for months or even years, with a gradual peripheral increase in the focus (usually single), scarring or atrophy in the center.

Differential diagnosis. Differential diagnosis is to consider a simple wart. The difference is that the wart is a non-inflammatory tumor and has no peripheral inflammatory corolla. Unlike *lupus verrucosus*, tuberculosis cutis verrucosa features the enhancing mass and lack of tubercles in atrophic areas.

Acute hyperkeratosis with acanthosis is the histopathological feature of warty tuberculosis. Epidermal scallops are thickened, lengthened and go deep into the dermis. The dermis contains a significant infiltrate consisting of epiteioid cells, a small number of giant cells and lymphoid cells.

Ulcerative tuberculosis of skin and mucous membranes, or miliary tuberculosis, ulcerative skin (*tuberculosis ulcerosa cutis et mucose*). This is a rare form of tuberculosis, found in patients with active tuberculosis of the internal organs (lungs, larynx, colon, urinary tract) caused by the autoinoculation with Mycobacterium tuberculosis. The lesion is often localized near the natural openings, at the junctions of skin transition into the mucous membranes: mouth, nose, genitals, and anus. In these patients, mycobacteria are excreted with sputum, urine, and penetrate into skin or mucous membranes.

Dense spherical lumps of red light color the size of a pinhead are the first clinical manifestation of the disease. They are rapidly destroyed, forming small painful ulcers with scalloped soft slightly undermined edges and uneven grainy bottom with limp grayish bleeding granulations.

Diagnosis. The diagnosis is based on presence of active tuberculosis of the internal organs, Thrall's grainules, typical clinical picture and identification of mycobacteria in bacterioscopic study.

Differential diagnosis. When recognizing tuberculous ulcers, a differential diagnosis with ulcerative syphilides of the secondary period of syphilis is primarily required. For this purpose, thefirm texture of their edges

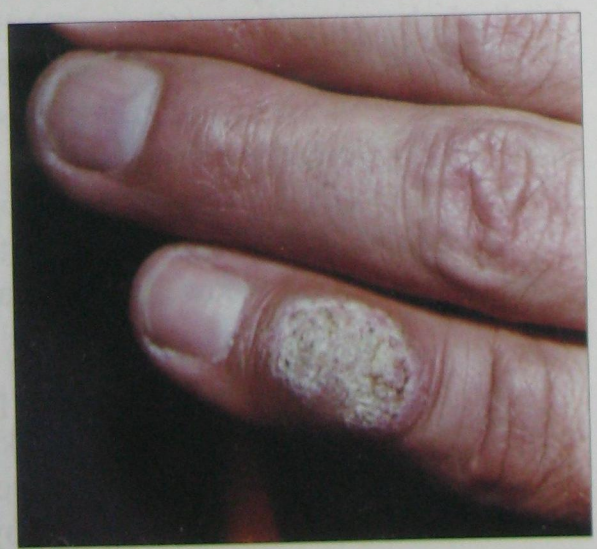

Fig. 13.6. Verrucous lupus.

and bottom, detection of pale treponemes, positive serological tests and the availability of other clinical signs of secondary syphilis are considered. In papulose tertiary syphilis, ulcers are deep, right round, with thick cushion edges, nontender. In gastric form of tuberculous lupus, the characteristic lupomas with positive probe and apple jelly symptoms are observed on the periphery of ulcers. Positive tuberculin skin tests, as well as general good condition are considered. Epitheliomas are characterized by thick edges of ulcers, presence of pearl-gray «pearls» on the periphery of ulcers, lymph node density.

The prognosis depends on the course of tuberculosis.

Disseminated forms of skin tuberculosis

Lichenoid tuberculosis (*tuberculosis cutis lichenoides*) **or shingles scrofulous** (*lichen scrofulosorum*). Scrofulous lichen is a disease that occurs most often in children. It develops in people who have other symptoms of active tuberculosis: lesions of lymph nodes, bones, internal organs and skin. The rash is localized on the lateral body surfaces, abdomen, and consists of miliary nodules with color from pale pink to reddish-yellow, covered with scales. The elements are disseminated, but mostly in groups.

Differential diagnosis. The disease is to be differentiated with miliary syphilides, in which the rash has bluish-red color, while its tendency to grouping and, sometimes, formation of various shapes (rings, half rings) is more pronounced; and finally, positive serological reactions decide the issue of *lichen syphiliticus*.

Histopathological features lie in the fact that a perifollicular infiltrate composed of lymphoid, epithelioid and giant cells is formed the upper layers of the dermis. Areas of infiltration feature quite expressive contours.

Tuberculosis papulonecrotica (*tuberculosis cutis papulonecrotica, acnitis, folliclis*). Tuberculosis papulonecrotica is caused by the contact of mycobacteria with skin by the hematogenous pathway. The disease begins with the appearance of knots the size of a lentil seed, of firm texture and bluish-red color. After some time, nodules in the center get necrotized and a pustule is formed, which soon is covered with a tight brownish crust. After removing the crust, a small ulcer is formed. When healing, the crust falls away, while leaving a bluish-purple scar. Gradually, it becomes colorless.

The lesions are located on the extensor surfaces of the upper and lower extremities, knee and elbow joints, ears and face (*acnitis*) and not accompanied by subjective sensations.

Differential diagnosis. Tuberculosis papulonecrotica is to be differentiated with oil folliculitis, which develop from blackheads. **Erythema induratum** (*erythema induratum Basin*). This form of skin tuberculosis is characterized by formation of nodes in the subcutaneous tissue caused by penetration of mycobacteria into skin by a hematogenous pathway. At the beginning of the disease, nodes of bluish-purple color, different sizes and dense texture appear most frequently on legs. Nodes feature

round or oval shape, sometimes are elongated in the form of a band, not sharply separated from the surrounding tissue, project above the skin level and are usually painful. Skin over them turns dark red with a bluish tint, gradually turning into a color of the surrounding tissue. Nodes split, forming rounded ulcers with undermined edges.

Diagnosis. It is based on clinical and histological data. The greatest difficulty appears during the differential diagnosis with erythema nodosum and skrofuloderma with its localization in legs. Erythema nodosum is characterized by severe inflammation, fever and soreness, localization across the front surface of the lower leg, with no predisposition to frequent relapses, disintegration and formation of ulcers. Pirquet's reaction is negative. In clinically severe cases, the effectiveness of a specific treatment is considered. Skrofuloderma is characterized by soft texture of the nodules and presence of fistulas.

Miliary tuberculosis of skin, or miliary disseminated lupus of face (*tuberculosis luposa miliaris cutis, lupus miliaris disseminatus faciei*). The disease affects almost exclusively adults aged 20-40 years, mostly women. The disease is characterized by facial enanthesis in the form of scattered non-homogenous brownish-pink bumps, the size of a pinhead to lentil seed. Existing for several months, bumps leave a faint pigmentation or superficial atrophic scars («stamped ribs»). Pirquet's reaction is generally positive.

Pathohistological study of the lesion focus reveals the accumulation of epithelioid cells in the loops of argyrophilic fibers in the center, and on the periphery – a zone of lymphoid and some plasma cells. Multinucleated giant Langerhans cells are an indispensable companion of the specific inflammation.

Diagnostics. In addition to histological examination, lupus can be confirmed by carrying out tuberculin tests (Mantoux and Pirquet's reaction), thanks to positive results of instilling pathological material in experimental animals (mostly guinea pigs, which are very sensitive to Mycobacterium tuberculosis), detection of Mycobacterium tuberculosis when plated on nutrient media.

Treatment. For treatment, different tuberculostatic drugs in combination with pathogenic agents (vitamins, anabolic steroids, therapeutic feeding and the use of physical therapy methods) are applied.

For therapeutic effect, tuberculostatic drugs are divided into the following groups:

- the first group includes most effective drugs (isoniazid, rifampicin, etc.);

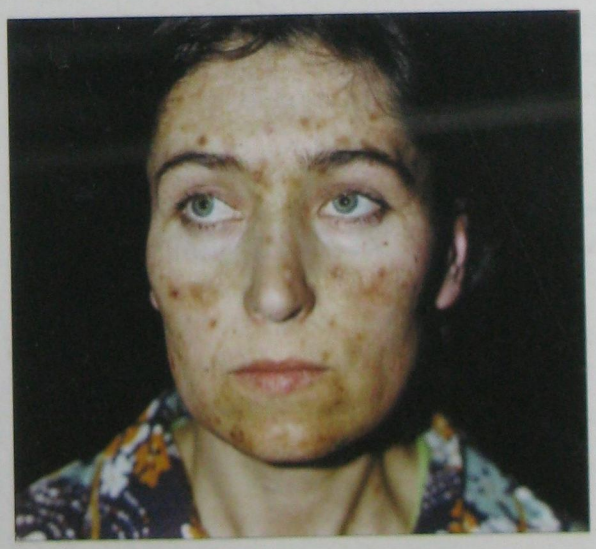

Fig. 13.7. Tuberculosis papulonecrotica.

- the second group includes the drugs of average efficiency (ethambutol, streptomycin, kanamycin, pyrazinamide, and so on);
- the third group includes preparations of moderate activity (paraaminosalicylic acid, tibon or tiotsetazin etc.).

Treatment with tuberculostatic drugs is carried out in two stages. In the first phase, at least three drugs for three months are prescribed, in the second phase two drugs daily or two to three times a week (intermittent mode) are prescribed. After three or four months, a combination of drugs is changed to prevent drug resistance.

In dermatological practice, treatment begins with the application of a combination of tuberculostatic drugs of the first group (e.g. rifampicin and isoniazid), sometimes pyrazinamide or tiotsetazin are added. Further, these drugs are replaced with streptomycin, ethambutol, paraaminosalicylic acid. The main course of treatment is carried out in a specialized (but not lung) hospital (luposorium) for 5-7 months, then a question of the appointment of anti-relapse treatment is decided individually (3-4 courses with an interval of 3-6 months). In resistant cases of tuberculosis papulonecrotica and miliary tuberculosis of skin, as well as some of its other forms an additional treatment with corticosteroids is required.

Prevention. Preventive measures are the same as in the general tuberculosis infection. They are based on improved living and health conditions of the population, early detection and treatment of early forms of tuberculosis.

1. Of the listed factors, following contribute to the emergence of skin tuberculosis:

A. Long-term exposure to the sun
B. Gastrointestinal diseases
C. Tuberculosis of other organs
D. Vascular disorders
E. Frequent colds

2. What are the skin manifestations characteristic of tuberculous lupus?

A. Spots
B. Telangiectasia
C. Pustules and papules
D. Tubercles
E. All of the above, except for tubercles

3. Which of the following symptoms is detected in tuberculous lupus herpes?

A. Symptom of a woman's heel
B. Biett's collarette
S. Koebner's Phenomenon
D. Apple jelly symptom
E. Nikolskiy's symptom

4. The most common penetration route of tubercle bacilli into skin is:

A. Insect bites
B. Hematogenous or lymphogenous
C. Sexual
D. All of the above is not true
E. All of the above is true

5. Lupus is caused by mycobacteria:

A. Human type
B. Bird type
C. Bull type
D. All of the above types
E. All of the above is not true

6. Optimal temperature for the growth of Mycobacterium tuberculosis is:

A. 37-38 degrees
B. 40 degrees
C. 42 degrees
D. 29 degrees
E. 0-15 degrees

7. Ulcerative tuberculosis of skin and mucous membranes is most often observed on:

A. Extremities
B. Trunk
C. Hairy part of the head
D. Mucosa of the mouth and around the natural orifices
E. Toes

8. Tuberculous lupus is often complicated with:

A. Erysipelas
B. Elephantiasis
C. Eczematization
D. Epithelioma
E. All true, except eczematization

9. Skrofuloderma is characterized by:

A. Ulceration of the nodes often in the submandibular region
B. Availability of chronic inflammatory sites
C. Presence of fistulas between ulcers
D. Hypertrophic scars with papillary growths and bridges of healthy tissue
E. All versions are possible

10. Treatment of skin tuberculosis:

A. Should not last more than three months
B. Is not significantly different from treatment of tuberculosis of the internal organs
C. Should not exceed five months
D. All of the above is true, except that treatment should not last more than three months
E. Should not exceed one month

Task 1. A female patient aged 35 years visited a doctor complaining of spot eruption on the extensor surfaces of the upper arms and thighs, within a period of about one year. At these sites, there are nodules the size of a small pea, of brownish-bluish color. Near the nodules, hollow, as if stamped, ribs surrounded by a pigmented border are observed.

a) The described eruption is characteristic of:
- **A.** Tuberculosis lupus
- **B.** Psoriasis
- **C.** Planus
- **D.** Skrofuloderma
- **E.** Tuberculosis papulonecrotica

b) What diseases require differential diagnosis?

Task 2. A female patient aged 43 years has single tight tubercules on legs, not soldered to the underlying tissues. Skin over the tubercules is red with a bluish tinge. Subjectively, slight soreness is detected. In history, pulmonary tuberculosis is diagnosed.

a) Put the initial diagnosis:
- A. Miliary tuberculosis of skin
- B. Acnitis
- C. Erythema indurativum Bazin
- D. Verrucous lupus
- E. Miliary-ulcerative tuberculosis of skin.

b) Determine the therapeutic approach.

Task 3. A patient works as a veterinarian; on the dorsum of the right hand, an infiltration with warty layers is observed. Peripheral part of the infiltrate is free of warty layers and features a reddish rim.

a) Put the diagnosis:
- **A.** Primary tuberculosis of skin
- **B.** Tuberculosis lupus
- **C.** Strumoderma
- **D.** Verrucous lupus
- **E.** Miliary-ulcerative tuberculosis of skin

b) Determine the methods of treatment and prevention.

Task 4. A 30-year-old patient has the papules the size of a sesame seed of reddish color with a bluish tinge and dense texture on the extensor surfaces of the upper and lower extremities. In the central part of some papules, tight brown crusts are observed, after their removal an ulcer with steep edges is opened. At the site of ulcers, «stamped» scars are formed.

a) What kind of disease is this?
- **A.** Miliary tuberculosis of skin
- **B.** Acnitis
- **C.** Indurativnyy erythema Bazin
- **D.** Verrucous lupus
- **E.** Miliary-ulcerative tuberculosis of skin

b) What additional tests are required to put the diagnosis?

Task 5. A 12-year-old patient has a brown-red tubercule of dense texture, the size of a walnut, in the right submandibular region, within a period of four weeks. A few days ago, an irregularly shaped ulcer with undermined edges formed on the site. *Subjectively*: pain.

a) Put the initial diagnosis:
- **A.** Acnitis
- **B.** Strumoderma
- **C.** Tuberculosis lupus
- **D.** Verrucous lupus
- **E.** Miliary-ulcerative tuberculosis of skin

b) Identify ways to clarify the diagnosis.

Answers to the questions of the first level of complexity
1 – C; **2** – E; **3** – D; **4** – B; **5** – D; **6** – A; **7** – D; **8** – E; **9** – E; **10** – B
Answers to the questions of the second and third levels of complexity
1a – E; **2a** – C; **3a** – D; **4a** – A; **5a** – B

14 TOPIC

Lepra

Lepra *(lepra),* ***synonyms: leprosy, Hansen's disease, St. Giles' disease, Saint Lazarus disease,*** – a chronic generalized infection with an indefinite duration of the incubation period, a variety of clinical manifestations, involvement of numerous organs and systems in the pathological process. In leprosy, ectoderm derivatives – skin and the peripheral nervous system, the organ of vision, as well as internal organs, bones and joints are involved in the pathological process.

TRAINING AND EDUCATIONAL OBJECTIVES

- To describe the urgency of the problem of leprosy, ways and conditions of infection
- To identify key issues of the etiology, pathogenesis and epidemiology of leprosy
- To identify typical clinical manifestations of leprosy
- To understand characteristic clinical features of different types of leprosy
- To determine general principles of diagnosis, differential diagnosis, therapy and prevention of leprosy

TO KNOW:

- current state of knowledge about the etiology and pathogenesis of leprosy;
- epidemiology and incidence of leprosy in the world and in Ukraine;
- classification and typical clinical and diagnostic characteristics of the main types of leprosy (lepromatous, tuberculoid and undifferentiated);
- principles of diagnosis and treatment of leprosy.

TO BE ABLE TO:

- correctly collect medical history of a patient with suspected leprosy;
- formulate a complete clinical diagnosis with characterization of the clinical form of the disease;
- perform diagnostic tests to assess the level of sweating (Minor's test), peripheral nervous sensitivity disturbance;
- perform differential diagnosis depending on the clinical form;
- prescribe laboratory studies confirming the diagnosis;
- prescribe rational therapy of leprosy patients depending on the type of the disease;
- undertake preventive actions in the infection focal point.

Epidemiology. Lepra is one of the most ancient diseases known to the humanity long before our era. Lepra was most widely distributed in the European countries in the 11th-12th centuries. Since then, a number of European countries started to create special detention centers for lepers (leprosariums). These special buildings were built outside the cities, and their inhabitants (leprosy patients) were isolated from the outside world. Due to the isolation of these patients in the 17th century, the incidence of leprosy has decreased significantly, and at the end of 19th century the infection almost disappeared in the European continent, except for some countries. Now there are about 15 million leprosy patients, mainly among the poor population in the countries of Africa, Asia, Indochina and South America. In economically developed countries, there are only isolated cases of lepra.

Etiology. The causative agent of lepra (*Mycobacterium leprae hominis*) was discovered in 1874 by Norwegian doctor G. Hansen. He found it in a scraping from the surface of the node cut of a leprosy patient, and in 1879 German microbiologist A. Neisser proposed a method of staining lepra bacteria. Therefore, in the literature, the causative agent of lepra is sometimes described as Hansen-Neisser mycobacterium. The causative agent of lepra to some extent resembles that of tuberculosis; this is a gram-positive and alcohol-and acid-resistant mycobacterium, 1.5-6 мм long and 0.2-0.5 мм wide. Usually mycobacteria are found in fresh leproma in large numbers. Like other mycobacteria, lepra mycobacterium are stained red by Ziehl-Neelsen; they are found in tissue cells as clusters of spherical form in which separate mycobacteria are arranged parallel to each other, resembling cigarettes in a pack («cigarette packs»).

Pathogenesis. Once in the body, the causative agent of lepra overcomes the mucocutaneous barrier, enters the nerve endings, the lymphatic and circulatory system, and gradually spreads throughout the body, without causing any significant changes (hidden generalization). In cases of sufficient immune resistance of the body, lepra mycobacteria pass into the latent stage of indefinite duration or die (cases of self-healing have been reliably established in paucibacillary lepra).

The pathogenetic mechanism in leprosy is the formation of immunocompetent granulomas. These granulomas occur when pathogens entering the body are not completely destroyed by macrophages. This leads to the induction of cellular and humoral immune response. «Leproma» (leprous tubercle, granuloma lepromatous) is the general name of specific granules observed in leprosy.

The incidence of leprosy among the population in different countries depends primarily on socio-economic factors, the standard of living, and the general health culture. Lepra is a low-contagious disease; it is believed that the main, and perhaps the only source of infection is a patient excreting mycobacteria with sputum, saliva, urine, breast milk, semen.

The problem of bacilli carriage in leprosy needs to be clarified. Thus, detection of Hansen mycobacteria on mucosae in healthy individuals, particularly medical personnel of leprosariums and family members of leprosy patients is not a sign of the

disease by itself. A precondition for confirm the diagnosis of latent lepra in such mycobacteria hosts is their multiple detection in nasal scrapings.

Incubation period and precursors. The incubation period in lepra can range from 2-3 to 10-20 years or more. At the end of the incubation period, which is sometimes referred to as the latent phase of the disease, there are various, poorly characteristic symptoms of this disease.

In a number of cases, the disease begins with rapidly progressing anemia, general weakness, drowsiness, joint pain. Paroxysmal neuralgia in the extremities, paresthesia, acroasphyxia, impaired sweating, and later sensitivity precede the development of explicit polyneuritis. There are frequent cases of rhinitis, nasal bleeding. After some time (from several weeks to several years), the disease enters a phase of marked clinical manifestations of a certain type.

Classification. In practice, there are three types of lepra – the lepromatous (lepra L.), tuberculoid (lepra T.) and undifferentiated (lepra J.) type.

Clinic. The most characteristic symptoms in lepra are lesions of the skin and nervous system; they are often combined, but primarily, as a rule, there are cutaneous manifestations, which are later supplemented with neurological disorders.

Lepromatous type of lepra. This is the most severe form of lepra, affecting the skin, mucous membranes, eyes, lymph nodes and many visceral organs. Patients emit large amounts of mycobacteria. At this stage they are the most dangerous to others. The lepromatous type of lepra develops independently or is formed on the basis of other types and is characterized by polymorphism of clinical manifestations.

Typically, the process begins with appearance of red spots of different sizes on the skin, with a purple or cherry shade; they are round or irregular in shape and have

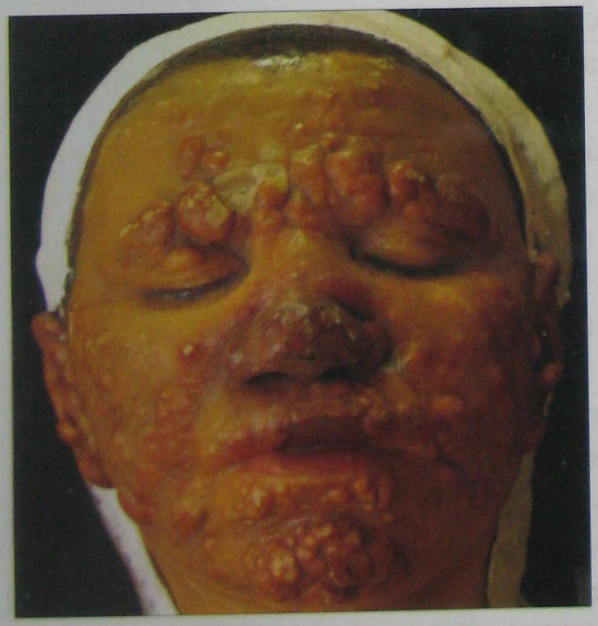

Fig. 14.1. Lepromatous type of lepra – *«facies leonine»*.

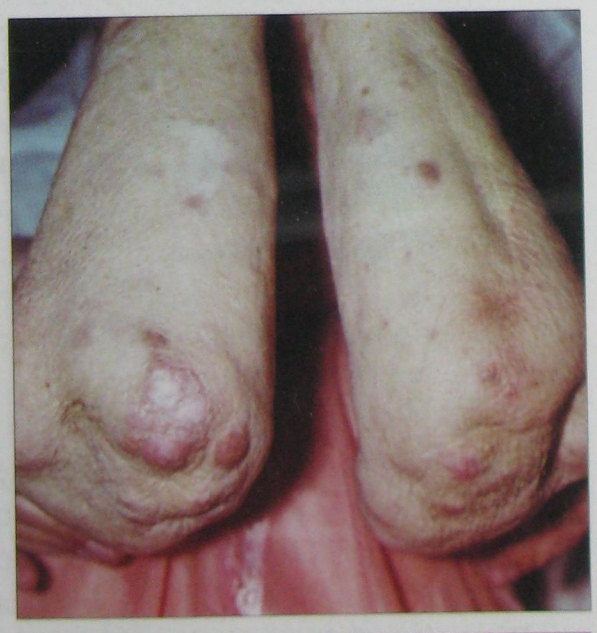

Fig. 14.2. Lepromatous type of lepra (elbow lepromas).

distinctive shiny surface. At initial stages, the sensitivity within the spots may be preserved, but sometimes their hyperesthesia is observed. Over time, the sensitivity decreases and then disappears. Gradually, the spots become more dense, form massive infiltrates becoming rusty in color; along with the skin the process involves the subcutaneous fatty tissue. Lepromas are formed. Spotted infiltrates may be observed anywhere on the skin. On the face this leads to mimic disorders and distortion: development of an angry expression (lion's muzzle symptom – facies leonine), which caused the emergence of one of the synonyms of lepra – «leontiazis».

With further progress, bundles are formed. The fusion results in a large infiltrate with an uneven bumpy surface. Palpation can detect infiltrations, even conglomerates of tumors consisting of separate lepromas. Infiltration of the superciliary archs leads to permanent hair loss in the lateral part of the brows.

On the mucous membranes, as well as the skin, the process may begin with appearance of separate lepromas or diffuse lepromatous infiltration. Typical signs of lesions of the mucous membranes of the nose are dryness and the presence of stubborn crusts. In the course of evolution and spread of infiltration on the cartilage and nasopharyngal bone tissue, nasal septum perforation may appear. When the epiglottis is involved, voice becomes hoarse (aphonia) and even respiration may be compromised.

Another typical sign of the lepromatous of lepra is injury of the vision organ. Conjunctivitis, keratitis, episcleritis, iritis, iridocyclitis, damaged lens may develop. Leprosy lesions often result in blindness.

Among the internal organs, the lepromatous infection mostly affects the spleen in the form of splenomegaly. Impairments of the renal, hepatic and pulmonary function are observed.

Noticeable changes occur in the genital area. In men, the testis, prostate, and especially the scrotum organs may be affected. In women, due to sclerotic changes in the ovaries there occurs strong disturbance of the menstrual cycle, leading to premature menopause.

The lymph nodes are affected very early. Mycobacteria of lepra are found almost always in their punctates. Lepra in general and its lepromatous type in particular is characterized by recurrent exacerbations, or leprosy reactions (usually in spring and autumn).

The peripheral nervous system is affected relatively late and is rare, usually in the form of symmetrical polyneuritis.

Tubercuoid type of lepra. This is the most benign clinical form of lepra, which develops in subjects with frank resistance and confirms high resistance of the body (positive lepromin test). In the tuberculoid type of lepra the pathological process involves mainly the skin and nerves, seldom – other organs, and there are no express clinical symptoms. Due to scarcity of the rash, it is difficult to determine the pathogen.

Diversity of skin rash depends on the depth of the eruption, its nature (acute, subacute, chronic), and the phase of the disease. The basic elements of skin rash in

the tuberculoid type of lepra are small reddish-bluish flat polygonal papules that tend to merge. A characteristic feature of this type of lepra is presence of a cushion along the periphery, whose outer edge is somewhat elevated, clearly defined and is reddish-bluish. The inner edge is indistinct and imperceptibly merges into the central pale part of the lesion. Elements of rash are localized anywhere on the skin and can be isolated or multiple, but the scalp is never affected.

Lepromas are characterized by cacesthesia, which is especially clearly expressed in the central part of the rash element. As always in lepra, at first thermal, then pain and finally tactile sensitivity disappears. In addition to full anesthesia, occurring during a more or less prolonged period, hyperesthesia, various paresthesias can be observed. Sweating in the tuberculoid type of lepra, as in lepromatous, around rash elements disrupts, then disappears. Hair become dull, often fall.

A monotonous and steady course of the tuberculoid type of lepra can sometimes be violated by acute reaction.

Tuberculoid neuritis occur manifest themselves through thickening of skin branches in the area of skin rashes, damage of major nerve stems can occur.

Undifferentiated or nondescript type of lepra. This type of lepra is intermediate between the lepromatous and tuberculoid types. It often develops in either tuberculoid (more favorable outcome), or lepromatous type with decrease of immunobiological resistance and body defenses.

Undifferentiated type of lepra is characterized by frank neurological symptoms and absence of typical lesions on the skin. A patient with this type of lepra is less dangerous to others than those with the lepromatous type.

With this type of lepra neurological symptoms are presented with leprous neuritis, which develop gradually. In addition to loss of sensitivity, reflexes impairment is

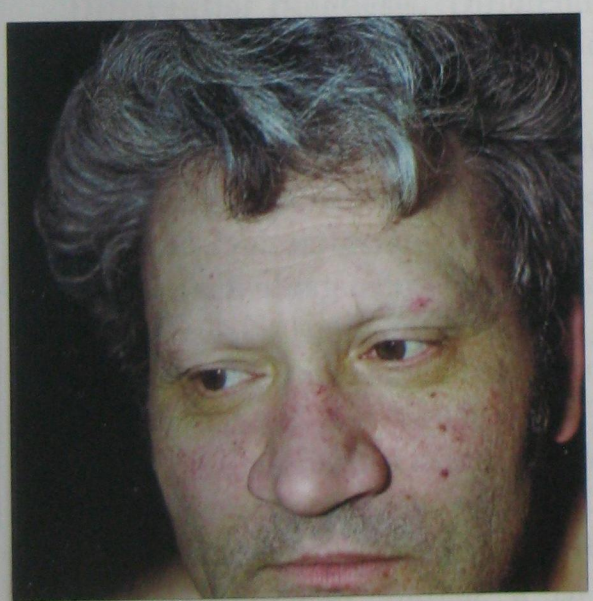

Fig. 14.3. Undifferentiated type of lepra (eyebrow and eyelash loss).

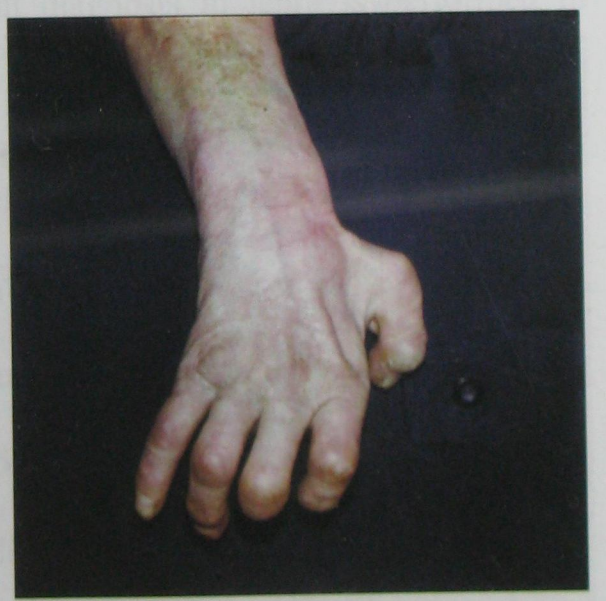

Fig. 14.4. Lepra (deformation of the hand joints and muscle atrophy).

observed. Amyotrophies of different muscle groups develop. Amyotrophies of facial muscles cause development of «St. Anthony's mask» (face becomes sad and resembles a mask), palm amyotrophies – formation of the «monkey paw».

Diagnosis. For diagnosis of lepra, in addition to typical clinical picture (taking into account appropriate anamnestic data about stays in endemic areas) special methods are of particular importance. This is primarily microscopy and a series of clinical and functional tests.

After a thorough inspection of the skin and mucous membranes, determining the state of nerve stems and lymph nodes and sensitivity testing, it is necessary to perform a bacterioscopic examination, which is very important for early diagnosis.

Laboratory diagnostics. For bacteriologic examination, scrapings from the mucous membranes of the nose and from the affected area of skin and skin of the superciliary arch, earlobes, chin, distal parts of the limbs are taken. To take skin scrapings, pinch the crease with two fingers and make a small 1-2 mm deep incision using a scalpel, then scrape the section walls material to be transferred on a microscope slide and stained by Ziehl-Neelsen to detect mycobacteria.

Functional tests. Pharmacodynamic tests help to identify very early lesions of the peripheral nervous system, manifesting (in addition to sensory) through vasomotor, secretory and trophic disorders. At first, perform tests using histamine, morphine and dionin. Apply one drop of 0.1% aqueous solution of histamine (or 1% morphine, 2% dionin) on the test area of the skin (both affected and unaffected). Pierce the skin through these drops without affecting the capillaries. In a healthy person, in 1-2 minutes a limited erythema should appear on the injection site, replaced with a reflex erythema several centimeters in diameter, with a blister or pimple in the center, in another minute or two. In leprosy lesions, there is no or mild reflex erythema.

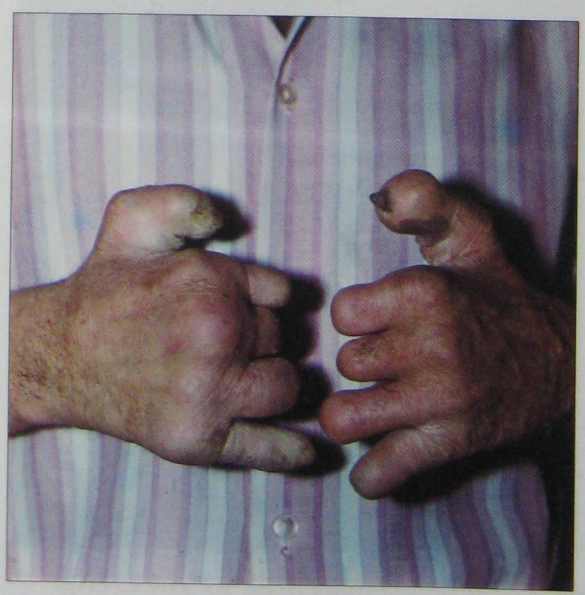

Fig. 14.5. Lepra (mutilation of finger phalanges).

In order to detect leprosy process, nicotine test is used (flash phenomenon). After one to three minutes after administration of 5.8 ml of 1% aqueous solution of nicotinic acid, an erythema appears and gradually increases, disappearing after 10-15 minutes. The affected areas remain bright red and swell; sometimesblisters appear on the surface.

Lepromin test. A specific antigen (lepromin) derived from lepromas is used as a starting material. The test is performed by intradermal injection of lepromin into the skin of the forearm

flexion. «Orange peel» should appear at the site of lepromin injection. In healthy people, swelling and redness appear at the injection site on day 2 or 3.

Interpretation of lepromin test findings

1. Negative reaction: after injection a papule is formed, less than 3 mm in diameter, and disappears in the end of day 2.

2. Mildly positive reaction: a swollen nodular infiltrate is formed, 3 to 5 mm in diameter, surrounded by a barely noticeable sore rim.

3. Positive reaction: an infiltrate is formed, 5 mm to 10 mm in diameter; the swelling is expressly elevated above the skin level and is surrounded by an inflamed aureola.

4. Acutely positive test: a sappy papule appears that turns into a node of more than 10 mm in diameter; inflammations are frank; often an ulcer is formed.

The said allergy test is very important to differentiate the type of lepra, as well as to determine the course of the disease, effectiveness of treatment and prognosis. The transition of lepromin test from negative to positive always means improvement, and the transition from positive to negative – decreased immunobiological reactivity of the body. This test may help forecasting in the undifferentiated type of lepra, especially in an exacerbation reactions (in this case, the transition of lepromin test from positive to negative evidences the transformation of lepra in the lepromatous type). In healthy people who never contacted with leprosy patients, the lepromin test is positive. This is important when examining the population in endemic areas, as well as families of patients and staff of leprosariums. The diagnostic value of this reaction is relative. It can be considered in conjunction with other data obtained in the patient examination. As is known, in all infants it is negative. The vaccine of Calmette and Guerin may be used for transition of negative lepromin test into positive.

Differential diagnosis. Differential diagnosis in lepra is performed in accordance with the symptoms as dermatological, neurological and special (with eye and upper respiratory tract diseases).

Dermatological differential diagnosis is performed with:

- erythematous dermatoses (erysipelas, erythema multiforme, secondary and tertiary syphilitic roseola);
- erythematous-squamous dermatoses (psoriasis, parapsoriasis, lupus erythematosus, pityriasis rosea);
- dyschromias (syphilitic leucoderma, leucoderma after pityriasis versicolor, vitiligo);
- papulose and nodular dermatitis (skin tuberculosis, tertiary syphilides, mycosis fungoides);
- ulcerative dermatosis (Raynaud's disease, varicose ulcers and hypertonic).

Treatment and prevention.

The main etiotropic means at the time are several groups of drugs. These are sulfone class drugs: diaminodiphenylsulfone(DDS), dapsone, avlosulfone,

diuciphonum, diazonium, etc.; thiourea derivatives (tibon, diamide, Ciba-1906 or thiambutosine), antibiotics and anti-tuberculosis drugs – rifampicin, izoprodian, klofamizin, ethionamide, isoniazid, tubazid, protionamide; fluoroquinolones – ofloxacin, pefloxacin. Several etiotropic medicines are prescribed concurrently, as each of them in monotherapy is not sufficient to inhibit sulfone mycobacteria, which are used for many decades, so that a lot of drug-resistant strains of Mycobacterium have developed.

Until now, the form of leprosy patients' isolation (and more recently – its necessaity after all) has been questionable.

Prognosis. Prognosis in lepra depends on the type of disease, stage of the process at the time of treatment and proper selection of drugs. With the tuberculoid type of lepra, the prognosis is more favorable than in undifferentiated and especially lepromatous. After treatment in leprosariums, subject to resorption of clinically visible manifestations on the skin and mucous membranes, repeatedly negative results of lepra mycobacteria (Mycobacterium lepre) tests in scrapings from the nasal mucosa and lymph node punctate, patients can be discharged for outpatient treatment with dispensary control of a leprologist or dermatologist.

1. Mark a wrong definition of lepra:

A. General infectious disease
B. Skin infectious disease
C. Skin and mucosae infectious disease
D. Toxico-allergic disease
E. Chronic infectious disease of the skin and internal organs

2. The following are skin manifestations in lepra:

A. Macula
B. Tubercle
C. Nodules
D. Bulla
E. All of the above

3. The causative agent of lepra is:

A. Protozoa
B. Mycobacteria
C. Treponema
D. Myceliums
E. Viruses

4. The following is characteristic of the tuberculoid type of lepra:

A. Polymorphic rash bothering the patient
B. Benign course
C. Early desensitization
D. Erythematous spots and hypopigmentation
E. All of the above

5. The lepromatous type of lepra develops:

A. Independently
B. Based on other types
C. As a result of new infection
D. All of the above is false
E. Independently and forms from other types

6. The following is characteristic of undifferentiated lepra:

A. Severe neurological symptoms (paresis, paralysis)
B. Absence of typical rash on the skin
C. Continued stabilization process
D. All of the above is true

7. The following type of staining is performed when examining materials for the presence of lepra causative agent:

A. Argentation
C. Ziehl-Nielsen
D. Methylene blue
E. Romanovsky-Giemsa

8. The following is used to treat lepra:

A. Dapsone
B. Rifampicin
C. Ofloxacin
D. Thiambutosine
E. All of the above

Task 1. A 47-year old patient consulted a doctor. In the past this patient worked for several years in the Middle East, and complained of rash in the form of skin nodes, replacing spots that appeared several months ago. Examination showed multiple nodes on the face, body and extremities, merging into tumor infiltrates with uneven surface. Some nodes break down to ulcers. There is no reaction to touch, pain, heat and cold.

a) Which disease is best characterized by these symptoms:
A. Spinal gliosis
B. Scrofuloderma
C. Syphiloma
D. Lepra
E. Lupus

b) Which additional studies are necessary to establish a definitive diagnosis?

Task 2. A 30-year old patient has numerous small reddish-blue flat polygonal papules on the skin of the body and limbs that merge to form elements of shaped as rings, semicircles, ovals, with elevated outer edges, clearly defined, of reddish-bluish color. There is no thermal and tactile sensitivity in the central part of the rash elements.

a) Which disease is characterized by this clinical picture:
A. Lichen acuminatus
B. Papule necrotizing tuberculosis
C. Tuberculoid type of lepra
D. Leishmaniosis
E. Tuberculous chancre

b) This is the dermatologist's tactics in this case?

Task 3. A patient consulted a doctor complaining of deformation of the face and the limb phalanges, and skin rashes. There is dyschromic erythematous skin rash with clear boundaries on the body and upper extremities, amyotrophy of different groups of facial muscles. There is no mimic («St. Anthony's mask»). As a result of mutilation the palm resembles a seal's paw.

a) This clinical picture is typical for:
A. Undifferentiated type of lepra
B. Lepromatous type of lepra
C. Tuberculoid type of lepra
D. Syphiloma
E. Lupus

b) What is the prognosis for the disease?

Task 4. A 45-year old patient consulted a doctor complaining of skin rash. There is rash in the form of hyper- and depigmented spots on the skin of the body, upper and lower extremities, as well as amyotrophy of different groups of facial muscles, and atrophy of the majority of small phalange bones. There is no or reduced pain, temperature and tactile sensitivity within the spots. From past history it is known that the patient lived in Yemen for five years.

a) Which disease can be suspected?
A. Lupus
B. Lepromatous type of lepra
C. Tuberculoid type of lepra
D. Syphiloma
E. Undifferentiated type of lepra

b) Make up a plan of rehabilitation measures.

Answers to the questions of the first level of complexity
1 – D; 2 – E; 3 – B; 4 – B; 5 – E; 6 – E; 7 – C; 8 – E
Answers to the questions of the second and third levels of complexity
1a – D; 2a – C; 3a – A; 4a – C

15 TOPIC

Leishmanioses

Leishmanioses (*leishmanioses*), ***synonym: Borovsky's disease*** is a group of vector-borne protozoan diseases of humans and animals, whose pathogens (Leishmania) are transmitted by winged insects – mosquitoes.

TRAINING AND EDUCATIONAL OBJECTIVES

- To disclose the urgency of the problem of leishmaniosis, routes and conditions of infection
- To identify key aspects of etiology and pathogenesis, and epidemiology of leishmaniosis
- Identify typical symptoms of this disease
- To distinguish characteristic clinical features of dermal leishmaniosis
- To summarize the principles of treatment and prevention of skin leishmanioses

TO KNOW:

- modern views of etiology and pathogenesis of dermal leishmaniosis;
- factors that trigger the development of this disease;
- classification and characteristic clinical and diagnostic features of the main varieties of dermal leishmaniosis;
- principles of diagnosis and treatment of dermal leishmaniosis;
- measures to prevent dermal leishmaniosis.

TO BE ABLE TO:

- to correctly collect past history of patient with dermal leishmaniosis;
- to formulate a complete clinical diagnosis of the disease;
- to perform diagnostic tests to confirm the diagnosis;
- to perform differential diagnosis with diseases that have a similar clinical picture;
- to prescribe rational therapy to patient with dermal leishmaniosis.

Epidemiology. According to the WHO, more than 400 million people around the world have leishmaniosis every year.

Etiology. The causative agent of leishmaniosis *Leischmania tropika* is a *Protozoa*, found and first described in 1898 by P.F. Borovsky. The life cycle of Leishmania occurs in two stages with change of the host – amastigote and promastigote. The amastigote form (nonflagellate stage) parasite intracellularly in the body of vertebrate animals and humans. The promastigote form (flagellate stage) parasites in the intestinal lumen of the invertebrate pathogen mediator – Mosquito.

Pathogenesis. Leishmania as intracellular parasites multiply in the mammalian body in cells of the reticuloendothelial system, or in free macrophages. Mosquitoes become infected by sucking blood of an animal or person with leishmaniosis. After sucking the blood a female mosquito is contagious for 6-8 days. Parasites persist in the insect's body throughout its life. A patient with leishmaniosis is not hazardous for others in absence of a carrier.

The parasite is abundant in macrophages as well as skin lesions. NNN (Novi Nicole Nicole) medium is widely used to cultivate Leishmania, on which their growth is observed on day 7-21. Leishmania have common antigens with mycobacteria, which can cause diagnostic errors when performing serological tests.

Classification. There are two forms of human leishmaniosis.

Visceral leishmaniosis (synonyms: internal leishmaniosis, children leishmaniosis, kala azar) is characterized by impairment of the lymphohistiocytic system with relapsing fever, cachexia, progressive anemia, leukopenia, abrupt spleen enlargement.

Dermal leishmaniosis (synonyms: pendin ulcers, Ashgabat disease, Kokand disease and many others) which predominantly affects the skin (mucous) includes Old World and New World dermal leishmaniosis.

Both forms have different geographical and clinical and epidemiological variants.

Dermal leishmaniosis

Dermal leishmaniosis it is a transmissible protozoan disease with typical clinical symptoms and clear endemic nature of spread in many tropical and sub-tropical climates, where there are mosquitoes. There are a great number of local names of this disease, which originate, as a rule, from geographical names.

Pathogenesis. After a mosquito bite (Leishmania carrier), promastigote (flagellated) forms of the parasite get in the skin, which quickly penetrate into macrophages, acquire the amastigote (nonflagellate) form and begin to proliferate. In the area of Leishmania penetration there is accumulation of a large number of macrophages, «stuffed» with amastigotes. They are surrounded by lymphocytes and plasma cells, whose number tends to increase. As a result, granuloma begins to form. Further there is elimination of parasitic cells, epithelioid and giant Langerhans cells

appear. During the period of active decay of parasites its products directly affect the surrounding skin, thus causing swelling of the surface layer of the dermis, damage of collagen and elastin fibers (often their necrosis).

In dermal leishmaniosis there is early formation of increased delayed cellular sensitivity. Gradual increase of its activity promotes development of diffuse dermal leishmaniosis. The pathological process caused by *leischmania panamiensis et brasiliensis* is characterized by damage of not only the skin but also the mucosa of the nose and pharynx (mucocutaneous leishmaniosis) with damage of the palate and nose cartilage. Persons who had dermal leishmaniosis retain lifelong immunity to the Leishmania strain, which had caused the disease.

Classification. According to epidemiological features, dermal leishmaniosis is divided into:

Old World leishmaniosis (anthroponotic and zoonotic subtypes), which is found in countries of the Eastern Hemisphere (carrying agents – mosquitoes of *Phlebotomus* class);

New World leishmaniosis (American dermal leishmaniosis) which is found in countries of the Western Hemisphere (carrying agents – mosquitoes of *Lutzomyia* class).

Depending on the biological characteristics of the pathogen, epidemiology and clinical presentation are two types of dermal leishmaniosis:

1) **urban**, or late-ulcerous (chronic) anthroponotic type;

2) **rural**, or acute necrotising (zoonotic, desert) type.

The pathogen's reservoir in the urban type is a sick person from which mosquitoes become infected, while in the rural type these are rodents with dermal leishmaniosis (squirrels, gerbils).

Clinical picture of Old World dermal leishmaniosis. The clinical picture and course of dermal leishmaniosis largely depend on its type. Each type has certain regularities, which is reflected in the length of the incubation period, the rate of development process, peculiarities of the clinical course and duration of the disease.

Anthroponotic, first type of dermal leishmaniosis (synonyms: Ashgabat ulcers, Kokand disease, salek, yearling, dry or chronic leishmaniosis). This type of the disease is also called *anthropophilic*, because the pathogen's reservoir *(L. tropica minor)* is a human, contrary to the 2nd type – zoonotic, whose pathogen's reservoir *(L. tropica major)* is wild rodents.

The incubation period of the first type varies between 2-4 months to 1-2 years. The pathological process starts with appearance of a 2-3 mm bump. The bump is flat, slightly raised above the surrounding healthy skin, without inflammation. The bump is brownish, frequently with a small central hole filled with dry scale in the middle. As the bump increases, it gradually rises above the skin level, is often round in shape, sometimes with slight protrusions at any edge.

The bump grows slowly and 2-3 months later becomes reddish. The bump's surface in the first two months is smooth, later thin scales appear. 3-6 months later,

dense brown lamellar flaky crusts develop. Scraping reveals shiny erosive surface. Once formed, the ulcer gradually increases as the granuloma grows, but the ulcer's growth is slower than the increase in the infiltrate. Light squeezing of the ulcer's sides exposes very scarce serous secretion, sometimes with small purulent lumps on the surface. As the ulcer develops, slow formation of scars begins.

Zoonotic, or second type of dermal leishmaniosis. *Synonyms: desert-rural type of dermal leishmaniosis, Murhab ulcer, Pendin ulcer.* Due to the fact that the pathogen's reservoir in this type is wild rodents, it is also called zoonotic. This type of the disease (pathogen – *L. tropica major*) is found in Africa, mostly in Sahara deserts, the Arabian Peninsula and the Central Asian countries. Here, large infestation of rodents is recorded, and often outbreaks of disease affecting large numbers of people are observed.

The incubation period in the acute necrotizing form is shorter, it is from 1 week to 1-2.5 months (usually 10-20 days).

This disease begins with formation of a compacted bump (5-10 mm in diameter) or node (10 to 20 mm in diameter), most often around the extremities (especially the lower).The second type of dermal leishmaniosis differs from the first type by sudden onset, presence of swelling around the bump or node with rapid growth of rash elements. In a number of cases the process may begin with a formation resembling a furuncle with its typical acute inflammatory phenomena, but differing from it by softer consistency and lesser sensitivity. Then, 1-2 weeks later, necrosis occurs in the center of the node. The resulting exudate forms a dense crust, exposing a small ulcer after removal. The bottom of the ulcer is uneven, covered with necrotic plaque. At palpation, pastiness is found in the ulcer bottom.

round the primary ulcer there are sometimes new secondary smaller leishmanioms (satellite Leishmania), which undergo the same cycle of development and turn into ulcers and gradually merge with the primary ulcer.

Tuberculoid type of dermal leishmaniosis (synonyms: metaleishmaniosis, lupous leishmaniosis, papulose leishmaniosis). From a pathogenic point of view, bumps in this type of leishmaniosis are rudimentary immature leishmanioms converted to protracted form as a result of already developed, but unstable immunity. The disease is more common in childhood and adolescence. The main element of rash in the tuberculoid form is a small yellow-brown bump. Usually bumps surround a healed ulcer with a ring or semicircle.

Diagnosis. Dermal leishmaniosis is diagnosed on the basis of clinical symptoms, taking into account climatic and epidemiological factors and laboratory detection of Borovsky's corpuscles. This requires correct sampling of the examination material. In closed leishmanioms (bumps, nodes) it is necessary to make a puncture using a sharp scalpel and obtain tissue for smear from the depth of the node. If there are ulcers, material is sampled around them, along the edge of infiltration using tweezers.

Material is applied on the glass and stained by Romanovsky-Giemsa. Borovsky's corpuscles are found in macrophages and around them.

Pathomorphology. In the initial stages, when mass reproduction of the pathogen occurs, the process begins with an inflammatory reaction. Only later granulomatous infiltrate consisting mainly of histiocytes, plasma cells and a small number of neutrophils is formed. Acanthosis is observed in the epidermis before formation of ulcers.

Differential diagnosis. Dermal leishmaniosis with syphilis, skin tuberculosis, abrasions are differentiated. An ulcer formed instead of granuloma may be easily confused with syphilitic ecthyma, tuberculous ulcer, chronic ulcerative pyoderma and some deep dermatomycoses.

Such ulcer differs from common streptococcal ecthyma by the presence of a potent iliac roll infiltrate at the edge. A similar infiltrate also surrounds syphilitic ecthyma, but near the ulcer it is more express.

Prognosis. The prognosis is favorable. The disease ends in recovery without treatment, after a development cycle from bump to ulcers and scar. Long-term immunity remains after recovery.

Treatment. Treatment of dermal leishmaniosis should be comprehensive, specific, and performed using both topical and systemic agents.

Systemic treatment should be performed using preparations of pentavalent antimony mitefosine, pentamidine salts (as a first-line therapy), amphotericin B, metaciclinus, rifampicin, dapsone are also prescribed.

In the presence of a single early small bump and without inflammation; such bump can be removed surgically (diathermocoagulation).

In the presence of acute inflammation, lotions with different disinfectants, anti-inflammatory and antiseptic creams, ointments are prescribed.

Prevention. Prevention of dermal leishmaniosis should be performed in several directions and include measures both with respect to the source of infection (human – in case of anthroponotic type, rodents – in case of zoonotic) and carrier (mosquitoes). Of special significance is the earliest possible identification of patients and their treatment, measures of personal prophylaxis are also necessary.

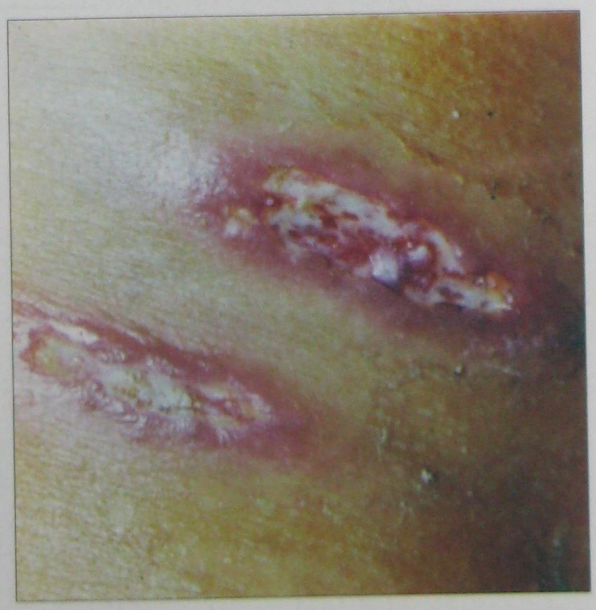

Рис. 15.1. Dermal leishmaniosis (zoonotic type).

It is very important to destroy rodents, processing facilities (both residential and commercial) in endemic areas using various insecticides and to use repellents

Individual prophylaxis of persons staying in endemic areas for a long time, vaccinations with live culture of zoonotic Borovsky's corpuscles are performed, which provides rapid development of immunity to both types of leishmaniosis.

1. Leishmaniosis is:

A. Systemic autoimmune diseases
B. Infectious disease of the nervous system
C. Sexually transmitted disease
D. Protozoan transmissible disease
E. Parasitic disease

2. Carriers of leishmaniosis are:

A. Flies
B. Pets
C. Fish
D. Mosquitoes
E. All of the above is true

3. Main clinical types of leishmaniosis are:

A. Urban
B. Tuberculoid
C. Desert-rural
D. Metaleishmaniosis
E. All of the above is true

4. Pathogen's reservoir of acute necrotizing leishmaniosis is:

A. Cattle
B. Horses
C. Cats
D. Wild rodents
E. All of the above is true, except wild rodents

5. The primary element of rash in leishmaniosis is:

A. Blister
B. Node
C. Bump
D. Roseola
E. All of the above is false

6. The primary acute necrotizing form of leishmaniosis occurs:

A. Predominantly in winter
B. During the autumn-winter period
C. In summer
D. During the summer-autumn period
E. Independent of the period

7. Materials to search for Borovsky's corpuscles should be stained with:

A. Methylene blue
B. By Gram
C. Brilliant green
D. By Ziehl-Nielsen
E. By Romanovsky-Giemsa

8. The following drugs are prescribed in leishmaniosis:

A. Metacycline
B. Mitephosine
C. Amphotericin B
D. Solusurminum
E. All of the above

9. The following occurs in tuberculoid form of leishmaniosis:

A. Bumps
B. Nodes
C. Ulcers
D. Scars
E. All of the above is true

10. Dermal leishmaniosis should be differentiated with:

A. Folliculitis
B. Lupus
C. Syphilophyma
D. Epithelioma
E. All of the above

Task 1. A 30-year-old patient developed an infiltration in the chin area 10 days ago, and later an ulcer formed. According to past history, 20 days ago the patient returned from Turkmenistan. Examination of the chin showed a doughy 3.5-4 cm node, with an irregular ulcer in the center with sharp edges, rough grainy, sometimes ocher deposits. Along the edge of the ulcers there was an inflammatory infiltrated aureola.

a) Set a provisional diagnosis:
- **A.** Borovsky's disease
- **B.** Lupus
- **C.** Hofmann's disease
- **D.** Scrofuloderma
- **E.** Beck's sarcoid

b) Which groups of drugs are used to treat this disease?

Task 2. Two months after returning from Uzbekistan a 12-year-old girl developed on the skin of the left lower leg an inflammatory node up to 1.5 cm in diameter, and a ulcer with sharp edges appeared later in the center. After some time small bumps developed around the ulcer, which underwent similar changes and merged with the main ulcer.

a) Which disease is this:
- **A.** Tuberculous chancre
- **B.** Lupus
- **C.** Leishmaniosis
- **D.** Scrofuloderma
- **E.** Tuberculoid lepra

b) What diseases should be excluded in differential diagnosis?

Task 3. Two months ago a 13-year-old boy developed a brownish non-inflammatory bump up to 2 mm in diameter on the cheek appeared, filled with a barely visible dry scales in the center. After 4 months the bump became red, and dark brown crust developed in the center. According to past history, in summer the boy stayed in southern European countries with his parents.

a) What is the most likely diagnosis:
- **A.** Tuberculous chancre
- **B.** Lupus
- **C.** Tuberculoid lepra
- **D.** Scrofuloderma
- **E.** Borovsky's disease

b) Identify ways to clarify the diagnosis.

Task 4. After examining the patient the dermatologist assumed that he had leishmaniosis. A scraping to detect Borovsky's corpuscles was made from the affected site.

a) What method should be selected to stain the drug:
- **A.** Staining with methylene blue
- **B.** By Gram
- **C.** By Romanovsky-Giemsa
- **D.** By Ziehl-Nielsen
- **E.** Argentation

b) What is the essence of prevention of dermal leishmaniosis?

Answers to the questions of the first level of complexity
1 – D; **2** – D; **3** – E; **4** – D; **5** – C; **6** – D; **7** – E; **8** – E; **9** – E; **10** – E
Answers to the questions of the second and third levels of complexity
1a – A; **2a** – C; **3a** – E; **4a** – C

16 TOPIC

Cheilites

Cheilites (*cheilitis*) is a group of diseases in which inflammation is localized only on the lips (on the red border, mucous membrane), as well as some diseases, whose course is characterized by predominant lesion of the red border of the lips.

TRAINING AND EDUCATIONAL OBJECTIVES

- To summarize the modern concept of the etiopathogenesis of cheilites
- To distinguish routes and possible conditions of the body's sensitization
- To identify factors influencing the course of cheilites
- To summarize characteristics of the clinical course of cheilites
- To determine general principles of differential diagnosis, treatment and prevention of cheilites To identify therapeutic tactics for patients with cheilitis

TO KNOW:

- etiopathogenic characteristics of cheilites;
- peculiarities of classification and clinical manifestations of independent (weather, exfoliative, glandular, contact and actinic) and symptomatic (atopic, of eczematous cheilitis, plasma cell, macrochilia etc.) cheilites;
- comparative description of independent and symptomatic cheilites;
- principles of treatment and prevention of independent and symptomatic cheilites.

TO BE ABLE TO:

- correctly collect past history of patients with cheilitis;
- set a diagnosis based on clinical presentation,
- determine diagnostic tests to confirm the diagnosis,
- perform differential diagnosis of patients with diseases having similar clinical picture;
- prescribe individual pathogenetic treatment.

The term «*cheilitis*» denotes not the cause of the disease, characteristics of its course and morphological changes, but only on the localization of the pathological process. The red border, the mucous membrane of the lips may be involved in this process in many dermatoses, characterized in most cases by diffuse inflammation. Lesion of the lips may be a manifestation of allergic, infectious diseases, cancer, and various other states. There is still no generally accepted classification of cheilites, and this makes it difficult to diagnose and leads to prescription of non-rational therapy.

Classification. Cheilites is divided into two groups: independent and symptomatic.

The group *of independent cheilites* includes meteorological, exfoliative, glandular, contact and actinic cheilites.

The group *of symptomatic cheilites* include atopic, of eczematous cheilitis (lip eczema), plasma cell, macrocheilitis (Rossolimo-Melkersson-Rosenthal's syndrome), cheilitis on the background of ichthyosis and caused by vitamin deficiency.

Meteorological cheilitis

Meteorological or simple cheilitis (*cheilitis meteorological)* is an inflammatory disease of the mouth caused by physical effects of various meteorological factors on the red border.

Etiopathogenesis. The factors that cause development of meteorological cheilitis may be moisture, dryness, wind, heat, cold, dust. Often the disease develops in people who work outdoors, especially in adverse weather conditions.

Clinical picture. In meteorological cheilitis, the red border of the lips is affected, usually the lower one, along its entire length. The lip becomes slightly erythematous, dry, often covered with small scales, patients suffer from dry or tight sensation, many lick their lips, which leads to increased dryness, peeling, and then the red border infiltration. When scales are removed, painful erosion is exposed and may bleed. The skin and mucous lips are unchanged.

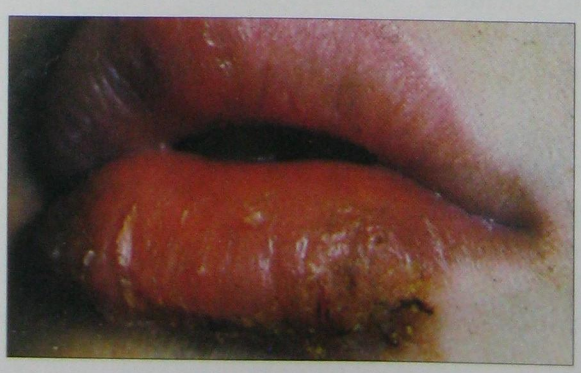

Fig. 16.1. Meteorological cheilitis.

Diagnosis. The diagnosis is set based on past history and physical examination. Laboratory tests are not advisable.

Differential diagnosis. It is necessary to differentiate meteorological cheilitis with allergic, actinic, atopic with cheilitis and dry form of exfoliative cheilitis.

Treatment. To treat meteorological cheilitis, it is necessary to exclude or

diminish the impact of meteorological factors. Recommendation: topical barrier creams, vitamin therapy (B_2, B_6, B_{12}, PP, C).

Prognosis is favorable.

Exfoliative cheilitis

Exfoliative cheilitis *(cheilitis exfoliativa),* ***synonym: Mikulicz-Кьmmel's disease*** is a chronic disease that affects only the vermilion border. The skin and mucous membrane are never involved in the pathological process.

Etiopathogenesis is not fully studied. The disease can be caused by neurogenic mechanisms and thyroid dysfunction.

Clinical picture. There are two forms of the disease: dry and exudative, both are different phases of the same disease and can easily be transformed into each other.

The exudative form of exfoliative cheilitis is characterized by appearance of grayish-yellow scales, crusts on the red border of the lips, which cover the red border with a layer from corner to corner of the mouth, beginning from the transition zone of the oral mucosa, *Klein's line,* till the middle of the vermilion border. Sometimes the crust is rather large and hangs from the lips like an apron. The disease is accompanied by severe burning and soreness, especially when the lips are closed, when eating and talking. Such patients almost always keep their mouth half open.

The dry form of exfoliative cheilitis, just as exudative, characterized by localized lesions only on the red border of one or both lips. The lesion is in the form of a ribbon extending from the mouth corner to corner and from Klein's line to the middle of the red border of the lips. Commissure of the mouth remains free from lesions. Part of the red border belonging to the skin always remains unaffected. Gray or grayish-brown flakes are tightly attached to the red border in the center and a little behind on the edges. Patient suffers from burning and dryness. After 5-7 days flakes easily exfoliate, exposing bare shiny red surface with no erosion.

Diagnosis. Diagnosis of exfoliative cheilitis is divided into:

- *clinical* (based on past history and physical examination);
- *laboratory* (thyroid function tests);
- *instrumental* (histopathological study if necessary, if acanthosis, parakeratosis, hyperkeratosis is observed).

Differential diagnosis. The exudative form must be differentiated from exudative form of actinic cheilitis, pemphigus vulgaris, erosive and ulcerative form of lupus, other types of cheilites.

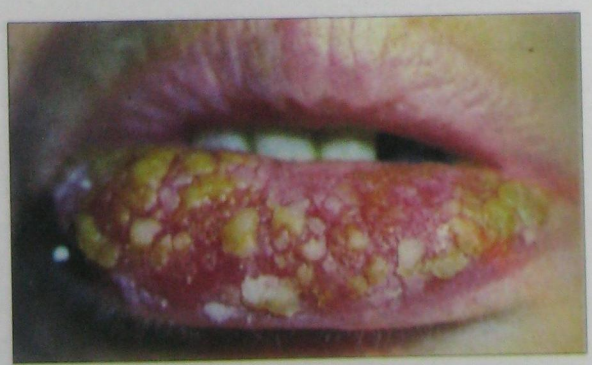

Fig. 16.2. Exfoliative cheilitis (exudative form).

Treatment. Treatment of patients with exfoliative cheilitis is a difficult task and implies correction of concomitant neurological and endocrine pathology. Local therapy should include sanation of the oral cavity, use of keratoplasty means (oil solution of vitamin A and E, kartolin). Local corticosteroids are used in the exudative form.

Prognosis is favorable. Subject to correction of endocrine and psychopathological disorders, quite stable remission is achieved.

Glandular cheilitis

Glandular cheilitis *(cheilitis glandularis)* is a disease that develops as a result of hyperplasia, hyperthyroidism, and often heterotypic form of the salivary glands in the vermilion border and the transition zone.

Etiopathogenesis. The cause of glandular cheilitis can be a congenital anomaly in which a large number of small salivary mucous glands are located in the transition zone (Klein's zone) and red border, or the glads may have normal location, and their ducts are moved to the surface of the red border. Under the influence of stimulation the glands become hypertrophied and produce discharge intensively.

Clinical picture. There are primary and secondary glandular cheilitis.

Primary glandular cheilitis is manifested mainly after puberty. In the area of the mucous membrane transition in the vermillion border of the lips, and sometimes on the red border there are prominent dilated entries of salivary glands in the form of red dots, excreting droplets of saliva. 5-10 seconds after the lips are dried, salivation from entries of the salivary glands become clearly visible, and saliva covers the lip like dew drops.

Development *of secondary glandular cheilitis* is obviously due to the fact that the inflammatory infiltrate, characteristic of the underlying disease, irritates the salivary glands, causing their hyperplasia and hyperactivity. In this case, against the background of the main manifestations of the disease, more frequently on lip mucosa in the transition zone area there are enlarged entries of salivary glands excreting droplets of saliva.

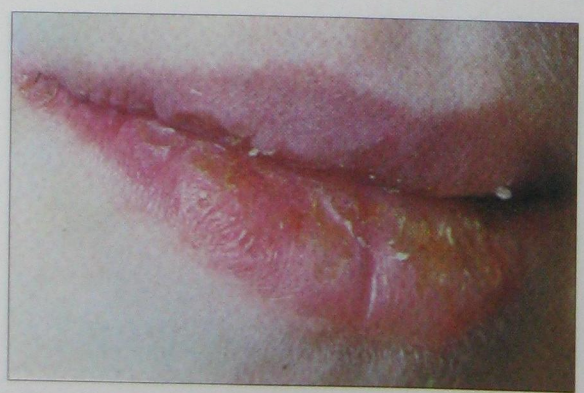

Fig. 16.3. Exfoliative cheilitis (dry form).

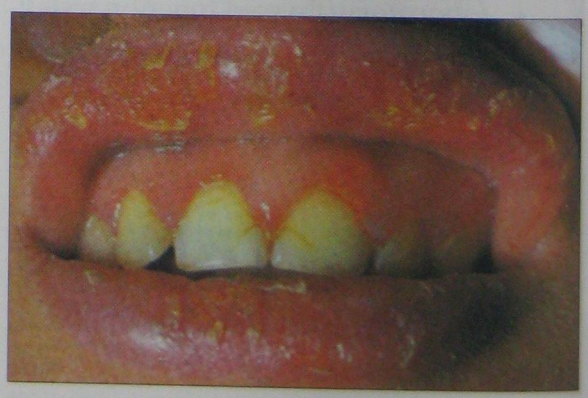

Fig. 16.4. Exfoliative cheilitis (dry form).

Frequent wetting of the red border with saliva in glandular cheilitis contributes to dryness, maceration and leads to chronic fissures. Later on, the mucosa and the red border may gradually coarsen.

Diagnosis. Diagnosis of the disease based on past history and physical examination is not difficult.

Differential diagnosis. Differential diagnosis of glandular cheilitis is easy due to clear clinical signs and presence of enlarged ducts of glands.

Treatment. Anti-inflammatory corticosteroid ointments, punctate electrocoagulation of hypertrophied glands or cryodestruction are used to treat glandular cheilitis.

If a patient with glandular cheilitis has a great number of abnormal glands, their surgical excision is performed. In secondary glandular cheilitis it is necessary to treat the underlying disease.

Prognosis is favorable. At superficial electrocoagulation or cryodestruction clogging of ducts of salivary glands and formation of cysts may be observed.

Contact allergic cheilitis

Contact allergic cheilitis *(cheilitis alergica contactis)* is a disease, developing due to sensitization of the vermilion border or, less frequently – mucosa, to chemicals and occurs when lip mucosa direct contacts the allergen.

Etiopathogenesis. Contact allergic cheilitis is a clinical manifestation of delayed-type hypersensitivity. Most often it is a reaction to chemicals used in lipstick, toothpaste and other cosmetic products, in particular fluorescent substances and eosin, rhodamine, etc. This disease mostly affects women.

Clinical picture. In clinical terms, contact allergic cheilitis is manifested through severe burning and itching. Usually the process is localized on the red border of the lips, sometimes it extends slightly to the skin of the lips. At the point of contact with the allergen there occurs a rather well-defined erythema and slight peeling. In long-term course of the disease the red border of the lips become dry and has small transverse grooves and cracks.

Diagnosis. Contact allergic cheilitis is diagnosed based on clinical examination findings and, where appropriate, allergy tests.

Differential diagnosis. This disease is differentiated with dry forms of exfoliative cheilitis, actinic and atopic cheilitis.

Treatment. In treatment of allergic contact cheilitis first of all it is necessary to eliminate a causative factor of the disease. If the clinical picture of the disease is mildly expressed, it is possible to prescribe only local treatment – corticosteroid ointments to be applied 5-6 times a day. In more severe cases, desensitizing therapy should be used.

Prognosis is favorable subject to maximum elimination of the allergen.

Actinic cheilitis

Actinic cheilitis *(cheilitis actinica)* is a chronic disease caused by hypersensitivity of the red border of the lips to sunlight.

Etiopathogenesis. the main causes of this cheilitis are delayed reaction to ultraviolet rays, i.e. actinic cheilitis develops in people with sensitization of the red border of the lips to solar radiation. The dry form of actinic cheilitis is considered to be elective precancer.

Classification. There are exudative and xeronous (dry) forms of actinic cheilitis.

Clinical picture. The *exudative form of actinic cheilitis* is often found in individuals with hypersensitivity to sun exposure, so the clinical picture is consistent with evidence of acute allergic contact dermatitis.

In spring the red border of the lower lip *in the xeronous (dry) form of actinic cheilitis* turns bright red, covered with small dry silvery-white scales. The lesion covers the entire surface of the red border. A number of patients develop keratinization areas on the red border; sometimes verrucous mass occur.

Diagnosis. Actinic cheilitis is diagnosed on the basis of medical history and physical examination. If necessary, a smear mark to exclude cellular atypia, and dermal biopsy is recommended.

Differential diagnosis. There is actinic cheilitis with dry forms of exfoliative cheilitis, atopic and meteorological cheilitis. A characteristic diagnostic feature is the process exacerbation under the influence of insolation.

Treatment. First of all, it is necessary to recommend that the patient avoids sun exposure and changes an occupation, if it is associated with prolonged stay in the open air. Hyposensitization drugs, nicotinic acid are prescribed. Topical steroids are used locally inactinic cheilitis.

Prognosis is favorable, however in long-term keratosis is necessary to exclude malignancy.

Symptomatic cheilites

Symptomatic cheilites is a group of cheilites, which are one of the main clinical manifestations of the underlying disease. There are atopic cheilitis, eczematous cheilitis, plasma cell cheilitis, Miescher's granulomatous macrocheilitis, Meiji's trophoderm, and Rossolimo-Melkersson-Rosenthal's syndrome.

Atopic cheilitis *(cheilitis atopica)* is one of the symptoms of atopic dermatitis, which is often the only manifestation of this disease at its certain stages.

Etiopathogenesis. Atopic cheilitis is a genetically caused disease accompanied by disorders of the central and autonomic nervous system. It is more common in girls and boys aged 4 to 17 years old.

Clinical picture. In clinical terms, atopic cheilitis affects the red border of the lips and always the skin, and the process is more intensive in the corner of the mouth. The part of the red border, adjacent to the oral mucosa and the oral mucosa remain unaffected.

The disease manifests itself through itching, erythema and lip lichenification.

Diagnosis and differential diagnosis. In exfoliative cheilitis, unlike atopic, a part of the vermilion border is always affected in the form of a strip from the Klein's line to the middle of the red border; a part of the vermilion border adjacent to the skin is intact; the process never affects the skin of the lips and does not cover the corners of the mouth; there is no erythema and lip lichenification; the course of the disease characterized by monotony and lack of remission. Past history of patients with actinic cheilitis shows a clear dependence of exacerbations on insolation; there is no frank lesion of the mouth corners characteristic of atopic cheilitis. In allergic contact cheilitis lichenification is only observed during prolonged course of the disease; there are no sores at the corners of the mouth; the course depends on direct contact with the allergen. In some cases, differential diagnosis of atopic cheilitis with symmetrical streptococcal or candida bridoes can be quite difficult. In bridoes, localization of the lesion is limited only to the mouth corners; as a rule, lichenification is not observed.

Treatment. Treatment includes prescription of antihistamines and sedatives, vitamins.

Eczematous cheilitis *(cheilitis eczematosa).* All types of eczematous cheilitis are grouped together according to similarity of clinical manifestations, but they occur for different reasons. There are eczematous cheilites:

1) caused by seborrheic eczema;
2) microbial eczematous cheilitis;

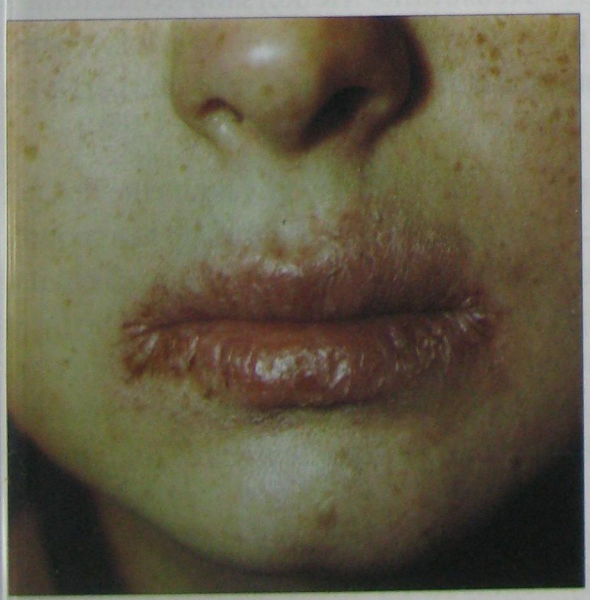

Fig. 16.5. Cheilitis of eczematous cheilitis.

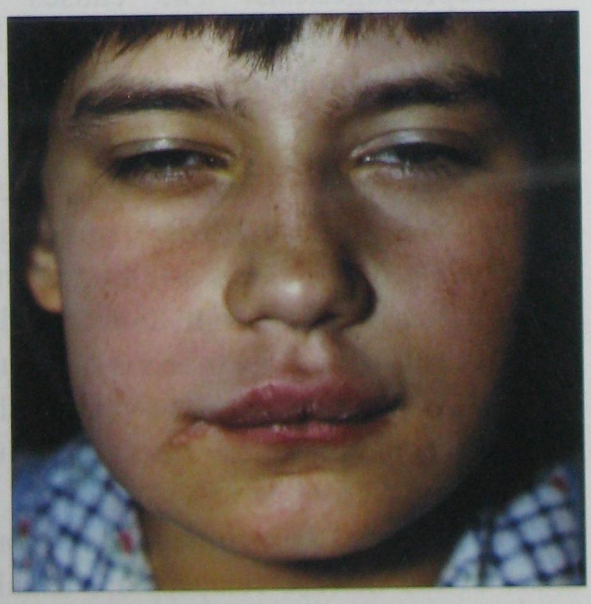

Fig. 16.6. Macrocheilitis (Rossolimo-Melkersson-Rosenthal's syndrome).

3) contact eczematous cheilitis.

Cheilitis in seborrheic eczema. Cheilitis is one of the symptoms of seborrheic eczema, but only the lips may be affected. In clinical terms, it manifests through hyperemia of the red border of the lips, occurrence of easily separated flakes, bubbles. Skin of the lips and the red border is dry, cracks and flakes appear.

Microbial eczematous cheilitis cheilitis. Re-develops against seborrheic eczema due pyococcal infection (mainly streptococcal) at the site of formation. Clinical manifestations correspond to microbial eczema.

Contact eczematous cheilitis cheilitis. Develops due to an allergic reaction to a variety of chemicals (in the lipstick, toothpaste, etc.). The clinical picture is consistent with acute or chronic eczema and is quite varied: swelling of the lips, bright hyperemia, blisters with subsequent formation of crusts. Elimination of allergen leads to rapid resolution of cheilitis.

Treatment. In eczematous cheilitis treatment is similar to that of eczema. Topical steroids and antibiotics are used.

***Macrocheilitis** (macrocheiliti).* This is the name for Rossolimo-Melkersson-Rosenthal's syndrome Meiji's trophoderm, Miescher's granulomatous macrocheilitis, characterized by persistent lip swelling. At this time it is known that granulomatous Miescher's cheilitis is not an independent nosological form of the disease and is a variant of Rossolimo-Melkersson-Rosenthal's syndrome with development of granulomatous infiltrate in the affected tissue. Meiji's trophoderm refers to angiotrophoneurosis. Rossolimo-Melkersson-Rosenthal's syndrome combines a triad of symptoms: macrocheilia (persistent increase in the lip), neuritis of the facial nerve, folded tongue, and a chronic disease with a tendency to recur. The disease occurs both in men and in women at any age, but most often between 16 and 35 years old.

Etiopathogenesis. The causes of Rossolimo-Melkersson-Rosenthal's syndrome are not fully clear. Neurological manifestations of Rossolimo-Melkersson-Rosenthal's syndrome often may include neuritis or facial nerve paresis and paralysis of the facial muscles.

Clinical picture. The onset of the disease is sudden. During few hours the lips get swollen. Swelling lasts 3-6 days, seldom less, sometimes longer, even up to a month. At the same time there is swelling of the mucous membranes of the oral cavity. Examination reveals deformation of the lips, the increase in their volume. The lip is dense at palpation. The mucous membrane of the mouth may be edematous, its surface becomes uneven, with a white cushion along the line of the teeth compression. There develops quite clear coarsening of the mucosa, various degrees of folding and lobulation of the tongue.

The course of Rossolimo-Melkersson-Rosenthal's syndrome is chronic. At the onset of the disease relapses are usually replaced by more or less prolonged remissions, during which all symptoms of the disease resolve. Later, macrocheilia and paralysis of the facial nerve become stable.

Diagnosis. Some patients with Rossolimo-Melkersson-Rosenthal's syndrome may lack both the folding of the tongue and paralysis of the facial nerve. The only symptom of the disease in this case is macrocheilitis.

The impairment of the facial nerve manifests through the face distortion to the healthy side, smoothing of the nasolabial fold. There are signs of the cranial nerve impairment (trigeminal, auditory, etc.).

Along with a thorough dental examination of the patient, identification of odontogenic, tonsillogenic and other sites of infection it is necessary to determine sensitivity to bacterial allergens with leukolysis reaction, as well as the neurological status.

Differential diagnosis. It is performed with angioedema, lymphangioma, hemangioma, collateral edema of the lips in periostitis of the upper or lower jaw.

Treatment. Treatment of Rossolimo-Melkersson-Rosenthal's syndrome is performed in two directions: surgical and conservative. In surgical treatment, which is performed for cosmetic purposes, a part of lip tissue is excised. However, surgical treatment does not prevent recurrences of the disease. Conservative treatment includes corticosteroids, broad-spectrum antibiotics and synthetic anti-malarial drugs.

1. What is the predominant localization of lesions in cheilites:

A. Corners of the mouth
B. Lip mucosa
C. Klein's zone only
D. All surface of the red border of the lips
E. All of the above

2. The group of independent cheilites comprises:

A. Meteorological
B. Exfoliative
C. Glandular
D. Actinic
E. All of the above

3. There are the following types of symptomatic cheilites:

A. Atopic cheilitis
B. Macrocheilitis
C. Meiji's trophoderm
D. Rossolimo-Melkersson-Rosenthal's syndrome
E. All of the above

4. Exfoliative cheilitis has two forms:

A. Dry and exudative
B. Seborrheal and genuine
C. Verrucous and intertrigo
D. Vegetative and pustular
E. None of the above

5. The following is observed in the serous form of glandular cheilitis:

A. Bloody dew symptom
B. Dew symptom
C. Apple jelly symptom
D. Stearic spot symptom
E. Probe symptom

6. Actinic cheilitis is a chronic disease caused by:

A. Hyperplasia, hyperactivity and often heterotypia of salivary glands around the red border of the lips
B. Effect of various meteorological factors on the red border of the lips
C. Solar hypersensitivity the red border of the lips
D. Sensitization of the red border of the lips to chemicals
E. Clinical manifestations of the underlying disease

7. There are the following types of eczematous cheilitis:

A. Caused by seborrheic eczema
B. Caused by microbial eczema
C. Contact eczematous cheilitis
D. None of the above
E. All of the above

8. Rossolimo-Melkersson-Rosenthal's syndrome unites a triad of symptom:

A. Macrocheilia, face angioneurosis, hoarse voice
B. Macrocheilia, sinusitis, vestibulitis
C. Macrocheilia, mitral insufficiency, optic neuritis
D. Macrocheilia, facial nerve neuritis, folded tongue
E. None of the above

9. Differential diagnosis of Rossolimo-Melkersson-Rosenthal's syndrome is performed with:

A. Quincke's edema
B. Lymphangioma
C. Hemangioma
D. Collateral edema of lips in periostitis of the upper or lower jaw
E. All of the above

Task 1. A 46 year-old patient complains of dryness, itching, peeling of the red border of the lips. The disease occurs in cold windy weather.

a) Set a provisional diagnosis:
- **A.** Atopic cheilitis
- **B.** Meteorological cheilitis
- **C.** Glandular cheilitis
- **D.** Actinic cheilitis
- **E.** Exfoliative cheilitis

b) Specify preventive measures and prognosis.

Task 2. A 34-year-old woman contacted a dermatologist complaining of oral mucosa lesions. According to past history, symptoms in the form oferythema of the red border, minor swelling, peeling, itching repeatedly occurred in this patient after using certain types of lipsticks.

a) Which is the most probable diagnosis:
- **A.** Contact allergic dermatitis
- **B.** Common contact dermatitis
- **C.** genuine lip eczema
- **D.** Contact allergic cheilitis
- **E.** Actinic cheilitis

b) Determine a treatment tactics.

Task 3. A 32-year-old woman contacted a dermatologist complaining of spontaneous increase of the red border, painful sensations in that area. *Objectively*: lip swelling and congestive hyperemia. Clearly visualized enlarged ducts of the salivary glands excreting transparent viscous secret in the form of droplets (dew symptom). Around the ducts entries there is inflammatory infiltration.

a) Which disease can be assumed:
- **A.** Urticaria fever
- **B.** Contact allergic cheilitis
- **C.** Serous glandular cheilitis
- **D.** Common contact dermatitis
- **E.** Purulent glandular cheilitis

b) Perform differential diagnosis of this disease.

Task 4. A 16-year-old contacted a dermatologist complaining of rash on the lip mucosa, surrounding skin and sensation of dryness and tightness in these areas. *Clinically*: the red border of the lips and the surrounding skin are hyperemic, with cracks and easily detaching scales on the surface.

a) What is the possible provisional diagnosis:
- **A.** Cheilitis caused by seborrheic eczema
- **B.** Cheilitis caused by microbial eczema
- **C.** Contact eczematous cheilitis cheilitis
- **D.** Rossolimo-Melkersson-Rosenthal's syndrome
- **E.** None of the above

b) Specify therapeutic and preventive recommendations.

Task 5. A woman contacted a dermatologist complaining of deformation of the upper lip, increase in its volume and itching. According to past history, the disease onset was sudden. The upper lip got swollen within a few hours. *Objectively*: there is amorphous swelling of the upper lip, its edge is twisted in the form of a proboscis and it detached from the teeth. The upper lip is bluish, dense at palpation. Swelling of the oral mucous membranes is observed.

a) Set a provisional diagnosis:
- **A.** Atopic cheilitis
- **B.** Macrocheilitis
- **C.** Purulent glandular cheilitis
- **D.** Rossolimo-Melkersson-Rosenthal's syndrome
- **E.** Urticaria fever

b) What is the necessary pre-hospitalization assistance?

Answers to the questions of the first level of complexity
1 – E; 2 – E; 3 – E; 4 – A; 5 – B; 6 – C; 7– E; 8 – D; 9 – E
Answers to the questions of the second and third levels of complexity
1a – B; 2a – D; 3a – C; 4a – A; 5a – B

17 TOPIC Erythema multiforme

TRAINING AND EDUCATIONAL GOALS

- Publicize modern representations of erythema multiforme aetiopathogenesis
- Determine factors influenced on course of erythema multiforme
- Separate particularities of clinical progression of disease
- Determine general principles of differential diagnostics, curing and preventive treatment of erythema multiforme

TO KNOW:

- ethiopathogenetic particularities of rosacea and its pathomorphology;
- particularities of classification and clinical implications of these diseases;
- principles of diagnostics and differential diagnostics
- principles of curing and preventive measures.

TO BE ABLE TO:

- interview the patient with erythema multiforme correctly;
- represent the diagnosis on the basis of clinical presentation;
- carry out the diagnostic tests for confirmation the diagnosis, if necessary;
- carry out the differential diagnostics with diseases having similar clinical presentation;
- assign a curing.

Erythema multiforme

Erythema multiforme *(Erythema exsudativum multiforme)* – disease of skin based on damage of dermis vesicles, abruptly progressed and characterized by polymorphism of rash, cyclic anticipated course in form of strongly expressed target-typed exanthema with specific badge-typed papules, often damage of oral mucosa and genital organs in form of bulla and painful anabrosis. Disease has a tendency for self-resolving. Systematic damage occurs rarely.

Causation of erythema multiforme is pluricasual. The most possible is virus causation. The promoting agents could be a medicamental allergy, gastrointestinal disorders, endocrine and visceral diseases.

Pathogenic mechanism. The pathogenic mechanism of disease is not studied but in general it is deemed that erythema multiforme is a syndrome of hypersensitivity.

Discovering of antigens of catarrhal fever's virus and DNA in skin locus of some patients with erythema multiforme supports the theory of a fact that pathogenic mechanism could be a cellular immune response directed to destroying of keratinocytes which serves for expression of catarrhal fever's virus antigens.

Classification. There are two main forms of erythema multiforme - idiopathic and toxicoallergic.

Idiopathic form of erythema multiforme has infectoallergic genesis. Most cases provoked by virus of catarrhal fever. The erythema multiforme is also associated with contact irritants (dinitrochlorbenzene, poison ivy, tropic sorts of wood) as well as systematic diseases (autoimmune progesterone dermatosis, sarcoidosis, polyarteritis nodosa, Wegner's granulomatosis, lymphadenoma, cancer and leukaemia).

Toxicoallergic form of erythema multiforme has allergic genesis. Disease concerned with progression of immune-complex response for different antibiotics, sulfanilamides, barbiturates, serosities and vaccines on area of dermis upper seam vesicles. For the long time toxicoallergic form of erythema multiforme and Stevens-Johnson's syndrome were considered as one disease. Recently the tendency have appeared according to which the heavy and light form are considered to be a parts of spectrum of the same disease (as a rule, resulting of virus infections) while the Stevens-Johnson's syndrome and toxic epidermal necrolysis are considered as separate nosological entities, connected mostly with medicamental hypersensitivity.

Clinical findings. The disease mostly occurs resulting in suffered acute respiratory viral infections. Before appearance of rashes the general weakness and painful joints could be observed.

For erythema multiforme the typical is polymorphism of rashes. Most often rashes localized on extensor surfaces of forearms, anticnemions, hips, back side of hands. The palms and feet are also affected as well as oral mucosa, and skin of genital organs. Rash is characterized by appearance of bright-pink edematous maculas and exudative

papules of up to 20 mm and more in size having red with cyanochroic tone color. Papules are surrounded by cyanosed scyphus, have a tendency for peripheral growth, fallen in center. At first papules arranged in focus but resulting in peripheral growth they interlocked between each other. The vesicles and bulla could appear in center of papules. They resolved with formation of anabrosis or crust. So, for erythema multiforme the target-typed rashes are typical each of which has not less than three different areas:

- *central disk of dark erythema or purpura* which could become necrotic or transform into solid vesicle;
- *ring of pale edematous area* which is felt;
- *outer ring of erythema.*

Rashes are accompanied by heat esthesia, rarely weak pruritus. Disease continues for 3-4 weeks after which the remission occurs with often backsets (up to 4-5 times per year).

The Stevens-Johnson's syndrome is a heavy form of erythema multiforme. The disease begins spontaneously with rapid high raising of body's temperature, the rushes have bullous nature. Most often the oral mucosa coats, soft and hard palate, genital organs, conjunctive and cornea of the eyes are affected. The men gets the progression of urethritis, and women gets the progression of vulvovaginitis and the erythematous, papular and bulla rashes are appear on the skin of face, body and extremities. Resulting in bulla evolution the solid bleeding anabrosis and necrotic ulcers embarrasses the meal are left. The general weakness and intoxication appear. The disease often ends mortally.

Pathomorphological mechanism. Histologically the epidermis hydrops is observed and especially of all layers of dermis. The perivascular infiltration from neutrophils, lymphocytes, histiocytes and small amount of eosinocytes progresses in

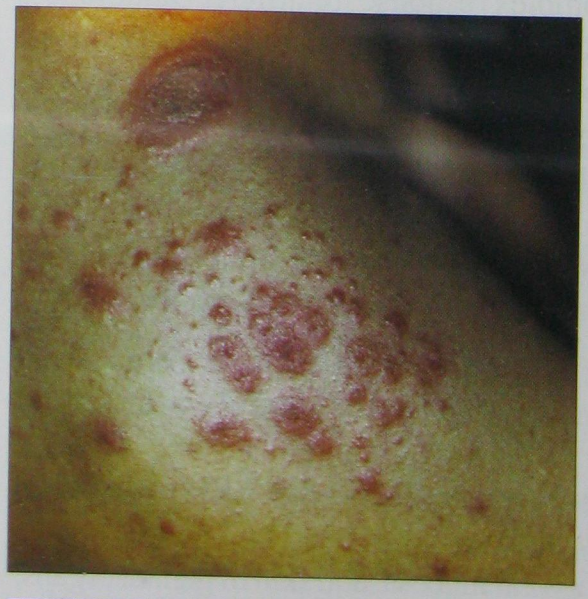

Fig. 17.1. Erythema multiforme.

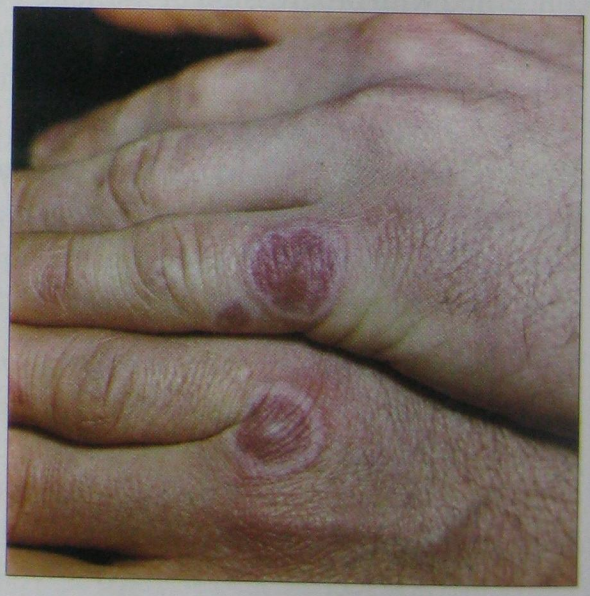

Fig. 17.2. Erythema multiforme.

papillary and reticular dermis, the swelling of vesicles walls and their endothelium occur, the picrinofilty of separate collagen fibers appears. In central part of locus the rapid necrobiosis of elastic fibers and small bleedings occur, and the spongiosis in epidermis.

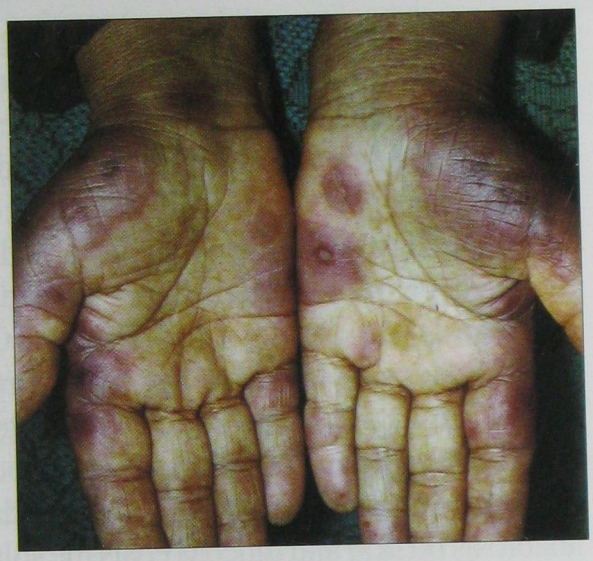

Fig. 17.3. Erythema multiforme.

Diagnostics. Determination of diagnosis for erythema multiforme is based on the following data:

- *clinical examination* (clinical presentation of erythema multiforme on skin is characterized by polymorphism of rash, presence of rash in form of badges, typical location on distal areas of extremities);
- *laboratory examination* (complete blood cell count – deviations occur rarely, decreasing of ESR and intermediate leukocytosis is observed at heavy form of disease);
- *instrumental examination* (inadvisable because of low informational content).

Differential diagnostics. In contradistinction from erythema multiforme at:

- *urticarial vasculitis* there are no target-typed locus;
- *medicamental rashes* there are no target-typed locus, the rashes are generalized;
- *Duhring disease* the pruritus, heat, herpetiform polymorphism of rash (papules – bulla), positive test with potassium iodide, eosinophilia, and typical pathognomia are observed;
- *acantholytic pemphigus* there are monomorphic rash of bubbles observed of different size and any location, progressive course, positive Nikolsky's sign, presence of Tsank cells in impression smears;
- *secondary papular lues* – the papular rash of cyanochroic-red color and dense consistence with furfur in central part of papule and formation of peripheral Biett's collar, general impressions are absent, serological responses on lues are positive;
- *erythema annulare* there are more individual locus of different location, long-term course, absence of locus on mucosa coats typical;
- *Kawasaki's disease* there are such signs appear as red lips, strawberry tongue, water retention of palms and lymphadenopathy;
- *herpetic gingivostomatitis* there are no locus of skin affections.

Curing. In most cases especially at light form of erythema multiforme the disease resolved independently and requires for symptomatic measures only for relief of pruritus and weakness. For curing of erythema multiforme at first instance the salicylates (salicylic natrium, pyramidon or anodynine), sulfanilamide drugs (sulfadimine, norsulfazole up to 2-4 g per day) antibiotics (erythromycin by 0.3 g 4-5 times per day and others) are assigned. There are antihistaminic medicaments assigned (cetirizine, citrine Suprastin and others), large doses of cevitamic acid (not less than 1.5-2 g per day), folic acid (by 0.03 g three times per day).

At Stevens-Johnson's symptom the corticosteroid therapy is assigned (prednisolone by 45-60 mg daily) with gradual lowering to the maintenance doses.

The symptomatic therapy is used locally (neutral dusts, magmas, pastes) for protection of affected areas from secondary infection. After paracentesis of bulla, anabrosis on skin and mucosa coats the solutions of antiseptics are drawn. AT absence of exudation it is possible to assign corticosteroid unctures or

At curing of lesions on mucosa coats the care is extremely important thing. The care of oral cavity is carried out with implementation of antiseptic solutions (chlorhexidine, 3% of hydrogen dioxide) and local corticosteroid medical agents.

Long-term systematic use of acyclovir or valacyclovir is indicated at backsets of erythema multiforme concerned with herpes.

Preventive measures and prognostication. In case of affection of oral cavity the diet is indicated with exclusion of spicy food, the food in liquid form only is desirable. The sanitation of body, discovering of focal infection's locus, especially in maxillofacial area, and cold water treatment are indicated. The elimination of provoking factors is necessary (herpetic and mycotic infection).

The prognosis of disease is favorable as a rule.

1. Determine right name of pathogenetic theory for erythema multiforme:

A. Infection-allergic
B. Toxic
C. Metabolic
D. Genetic
E. Neurogenic

2. Call clinical forms of erythema multiforme depending on its pathogenetic mechanism:

A. Localized and generalized
B. Symptomatic and true
C. Idiopathic and toxicoallergic
D. Erythematosus and bullous
E. Erythematosus and pustular

3. What primary components are not encountered at erythema multiforme:

A. Papule
B. Macule
C. Bulla
D. Tubercle
E. All of above mentioned is correct

4. Call heavy form of erythema multiforme:

A. Layel's syndrome
B. Stevens-Johnson's syndrome
C. Kazabach-Merrit's syndrome
D. Martorella's syndrome
E. Gujero-Blume's syndrome

Task 1. The female patient refers to the dermatologist with complains for rashes on skin of lower extremities which appeared after intake of sulfanilamide medications. *Unbiased*: the rashes located on extensor surfaces of anticnemions and hips in form of bright-pink edematous spots and papules of up to 3 cm in size. Papules surrounded by cyanochroic nimbus, have a tendency for peripheral growth and felt in center. In some places papules interlocked between each other forming rings on the background of red-cyanochroic erythema.

a) Determine the provisional diagnosis:
- **A.** Annular centrifugal Daria's erythema
- **B.** erythema multiforme
- **C.** Nodular erythema
- **D.** Fixed erythema
- **E.** Erythema migrans

b) Give therapeutic and prevention recommendations.

Task 2. The male patient of 45 years old went to institutional treatment in dermatological department. He complains for suddenly rapid rise of body's temperature accompanied by pain in joints, throat, headaches, occurrence of rash. *Unbiased*: There are anabrosis covered by bleeding crusts on the oral mucosa, extremities, and conjunctiva and in area of genital organs on the background of slightly infiltrated erythema.

a) Determine the provisional diagnosis:
- **A.** Stevens-Johnson's syndrome
- **B.** Layel's syndrome
- **C.** Kazabach-Merrit's syndrome
- **D.** Martorella's syndrome
- **E.** Gujero-Blume's syndrome

b) Make a plan for examination and curing of the patient.

Answers for first level self-control questions
1 – A; 2 – C; 3 – D; 4 – B
Answers for second and third level self-control questions
1a – B; 2a – A

18 TOPIC

Systemic diseases of connective tissue – collagenoses

Collagenoses (diffuse diseases of connective tissue) are characterized by mucoid and fibrinoid degeneration of connective tissue, often damage of joints, serous coats, skin, internal organs, and nervous system. The basis of mechanism of progression of collagen diseases is mostly autoimmune process with affection of different morphofunctional systems. The most often in practice of dermatologist the scleroderma, lupus erythematosus and acute disseminated myositis are encountered regarding to collagenoses group.

TRAINING AND EDUCATIONAL GOALS

- Determine possible conditions and trigger factors of occurrence of scleroderma, lupus erythematosus and acute disseminated myositis
- Learn the classification and particularities of different forms of scleroderma, lupus erythematosus and acute disseminated myositis
- Determine general course and clinical implications of causation of mentioned diseases' different forms.
- Determine typical evidences of scleroderma, lupus erythematosus and acute disseminated myositis
- Determine principles of therapy of scleroderma, lupus erythematosus and acute disseminated myositis

18.1 Scleroderma

Scleroderma *(Sclerodermia)* – idiopathic disease characterized by sclerotic affection of skin of locus or diffuse nature with foregoing occurrence of fibrosis.

TO KNOW:

- modern conceptions of aetiopathogenesis of scleroderma;
- factors precipitating the progression of this disease;
- classification of scleroderma;
- pathomorphological changes in skin at scleroderma;
- clinical profile of different forms of this disease;
- its laboratory diagnostic criteria;
- principles and approaches of curing measures and periodic health examination at scleroderma.

TO BE ABLE TO:

- interview and make a diagnosis for the patient with scleroderma correctly;
- carry out the differential diagnostics with dermatosis having similar clinical presentation;
- assign corresponding laboratory examinations for confirmation of diagnosis;
- assign balanced curing for the patient with scleroderma.

Aetiopathogenesis. The causation and pathogenetic mechanism of scleroderma are studied not enough. It's progression could be concerned with suffered inflectional diseases as well as after introduction of serosities, vaccines, medicamental drugs, after physical and psychical trauma or burns.

Scleroderma belongs to multifactor diseases with polygenetic inheritance. The significant role in its progression the immune (including autoimmune) and metabolic disorders are play. Major pathophysiological processes are in three systems – vascular, immune and fibroblasts.

Classification. There are following types of scleroderma:

1. Isolated scleroderma (not more than two lesion focuses observed):
   - Circumscribed;
   - linear;
   - white-spot disease;
   - morphea;
   - Pazzini-Pierini's idiopathic atrophoderma (superficial isolated scleroderma).
2. Diffuse progressive or systematic scleroderma.

Clinical findings. Isolated and systemic scleroderma is the types of one pathological process. Isolated scleroderma could transform into systemic. There are three stages of general course of sclerotic pathological process – *swelling, induration and atrophy*.

Isolated scleroderma (*Sclerodermia circumscripta*). There are morphea guttata, linear, white-spot disease and morphea forms of isolated scleroderma by clinical course.

Morphea guttata is evidenced by pink-red spots of rounded shape with lilac peripheral collar. Then in area of spot the induration progresses which could be superficial or penetrates deeply in dermis. In area of locus skin has primrose painting reminding the

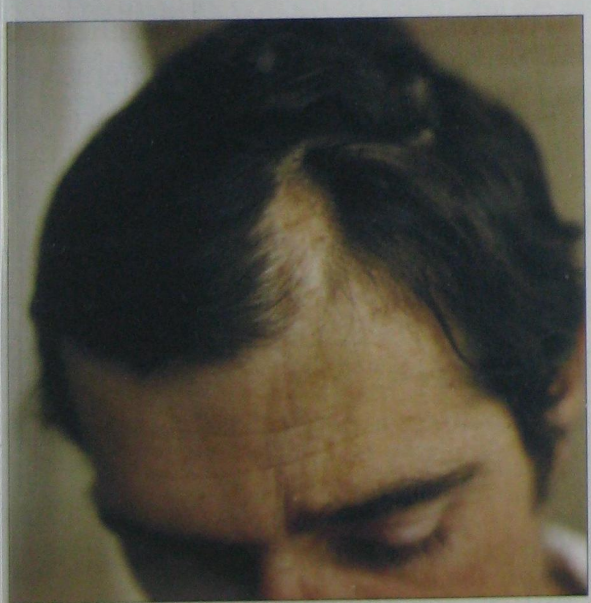

Fig. 18.1. Morphea guttata.

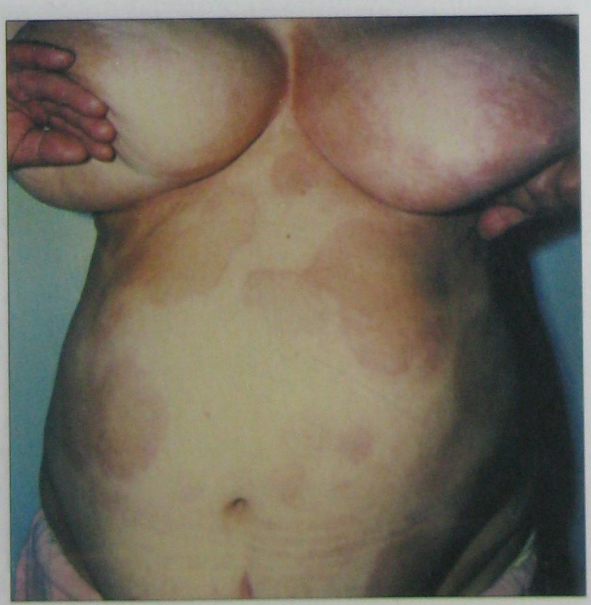

Fig. 18.2. Morphea guttata.

color of ivory. There is no hair on skin, no hidrosis and sebaceous excretions, the sensitivity is weak. There are light paresthesias observed. Process located on the body, extremities, and face. Further evolution of scleroderma locus is in disappearance of lilac ring, gradual resorption of induration and appearance of atrophy.

Linear scleroderma or scleroderma striata (sclerodermia linearis) is an original form of localized scleroderma which often occurs in children age. The affection is usually begins on hairy part of head then goes to sin of metope, dorslim of nose reminding the cicatricial tissue after strike by sabre (*un coup de sabre*). The lesion focuses at linear scleroderma are located on upper or more often on lower extremities. The patients with linear scleroderma are noticed the progression of atrophy and disorder of extremities bones growth, presence of *spina bifida*, and micro sclerosis. The lesion focuses at linear scleroderma could be also located along the vesicles, nerves, transfer from skin to the mucosa coat.

The course of linear scleroderma is the same as morphea guttata.

White-spot disease (sclerodermia guttata) more often located on skin of neck, sternum and alvus. This disease is usually typical for women. The glance depigment atrophic spots of pea size appear at this disease around the hair follicles with tendency for interlocking and with erythematous peripheral collar.

In rare cases the *morphea* is observed (*sclerodermia anularis*)

Pazzini-Pierini's idiopathic atrophoderma (superficial isolated scleroderma) is evidenced by slightly pigmented cyanotic rashes of round and oval shape on body, arms, hips with weak atrophy.

Localized variant is associated with CREST-syndrome called by first letters of containing symptoms (*calcinosis, Rayneud's disease, esophageal dysmotility, sclerodactyly, teleangiectasia*).

Systemic or diffuse scleroderma (*sclerodermia diffusa progressiva*). Systemic scleroderma is a systemic disease which is evidenced by affection of connective tissue and vesicles of degenerative-necrotic nature. There are prodromes observed in form of general weakness, pain in joints, and fever.

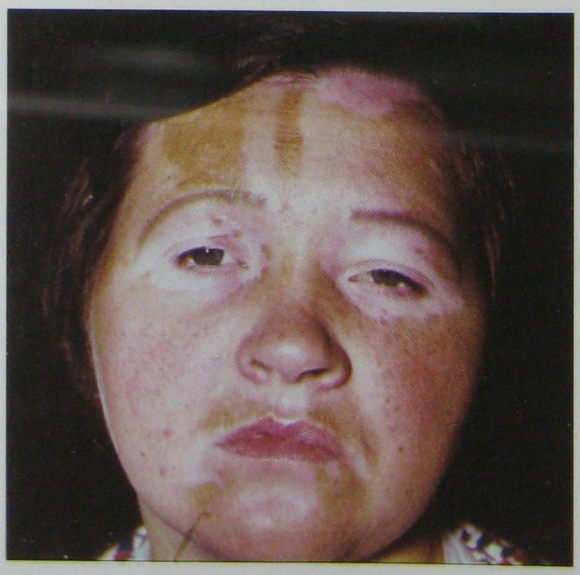

Fig. 18.3. Linear scleroderma in area of metope in association with white spot disease.

Systemic scleroderma includes *skin* (sclerodactylia, acrosclerosis, Tnibierge-Weissenbach syndrome) and *non-skin* (muscular-joint, gastrointestinal, pulmonic, cardiovascular, hepatic, and neurological) *syndromes*.

The affection of skin begins from extremities and face (*acrosclerosis*). At diffuse scleroderma the process could spread to the body. There are numerous

telangiectasis appear on skin of face and sternum, the change of ingius and defluxion are observed. In the beginning of disease the skin is diffusion and edematous, cold, not folded. For incipience of systemic scleroderma there are Reynaud's syndrome, arthralgia, polycardia, often infections of respiratory infections typical. Then skin symptomatic progresses with occurrence of induration, especially on opisthenar and dorsum of feet. Face becomes masklike, the telangiectasis appear, areas of hyper and depigmentation.

At final stage the sclerotic process is spread to subcutaneous fat and muscles bearing against bones. The movements become harder, the mimic is absent, the mucosal coats of mouth and esophagus are affected, the oral fissure is narrowed. Fingers of hands becomes thin and are in semiflexed position, its movement is limited (sclerodactylia). These sclerodermia changes can lead to the mutilation on the hands and feet. The skin over joints is hard and tensioned; the movements in joints are hindered. Most of patients are observed the fibrous changes of muscles progressed primary or after scleroderma changes of skin. Some patients with scleroderma, usually at acrosclerosis, the deposit of calcium is evidenced in subcutaneous fat (*Thibierge-Weissenbach's syndrome*), usually on hips, buttock, hands, around the joints. These deposits could burst resulting in occurrence of fistula from which the friable calcareous mass is discharged.

Pathomorphological mechanism. At histological examination in the beginning of progression of morphea process the swelling of derma is being discovered, the infiltrate consisting of lymphocytes is between fascicles of collagen fibers. The elastic tissue is dead in these locations. Infiltrate could appear also in subcutaneous fat. The thinning of spinous layer and vacuolization of cells of basal layer occurs in epidermis. During induration stage the sclerosis of collagen fibers, luminal occlusion, lymphoid infiltrate absence of hair, atrophy of oil and sudoriferous glands, sclerosis of hypoderm, thinning of epidermis and intumescence of horny layer are observed.

Diagnostics. Preventive diagnosis is hard to determine. Antinuclear antibodies are found in 97% of cases with implementation of HEp 2 cells as a substrate. Antibodies for centromeres are found in 50-70% of cases of isolated disease (CREST-syndrome), antibodies for antitopoisomerase (ScI-70) found approximately in 36% of cases at diffuse form of disease. Levels of Я-halactosidase and N-terminal procollagen III peptide is raised and it is a sign of enhancement of collagen's metabolism because of activation of fibroblasts.

Pathomorphological presentation at systemic scleroderma is mostly the same as for localized but fibrosis-degenerative changes in collagen fibers and vesicles are expressed more fully.

At diffuse scleroderma the inner organs are often affected – esophagus, lungs, heart, rarely kidney, gastrointestinal tract, bones, and often several organs at the same time. Sometimes the diseases of inner organs are progress without changes on skin. At damages of esophagus the fibrotic changes of muscle tissue, exulcerations and diverticula appear. In lungs the signs of pulmonary fibrosis are discovered radiologically.

At affection of cardiovascular system the intumescence of myocardium, endocardium and intima of aorta are observed and the fibrinoid degeneration of intima in vesicles.

At acrosclerosis the atrophy of finger bones and osteoporosis could progress. At kidney's affection the sclerodermic nephropathy is observed evidenced in form of oliguria, azotemia, uremia and being ended fatally. At histological examination the fibrinoid degeneration of arteriols, glomerulus and bleedings in cortical substance are discovered.

At diffuse scleroderma ambilateral cataract could appear which occurs in young age and sometimes before skin affections. The dry keratocnjunctivitis could progress. The telangiectasis and angioma could occur on nasal mucosa which is accompanied by nasal bleedings.

Differential diagnostics. The *localized scleroderma* should be differed from white spot disease, indeterminate leprosy, pseudoleukoderma, facial hemiatrophy, morphea-like basalioma, kraurosis vulvae, and lymphangioma.

At indeterminate leprosy the changes on skin are characterized by spotty rushes of different tone (from pink to cyanochroic). In area of spots the pain, tactile and temperature sensitivity is decreased.

Pseudoleukoderma appears of patients on place of previous locus of chromophytosis and psoriasis as well as of persons influenced to excessive solar or ultraviolet irradiation. These spots have no induration and disappear after weakening of san-tan.

It is harder to differentiate the linear scleroderma with linearly oriented keloid-typed nevus. It's typical signs could be a manifestation in first months of life and long-lasting existence of nevus without expressed changes during many years.

Diffuse scleroderma is differentiated with Raynaud's disease, acute disseminated myositis, pseudo scleroderma, Bushke's scleroderma, Arndt-Jaffe scleropoikidermia, sclerema and newborn's scleroderma, and systemic lupus erythematosus.

Curing. There is no efficient curing of scleroderma. In certain cases the prednisolone and methotrexate is advised systematically.

Preventive measures. The primary preventive measures of localized scleroderma are in sanitation of locus of chronic infection and timely curing of neuroendocrine diseases.

During secondary prevention it is necessary to remember that patients with scleroderma are counter-indicative for working in cold premises, as well as at work connected with damaging of skin and vibration.

Dermatologist examines persons with circumscribed scleroderma twice per year. Laboratory examinations (clinical and biochemical analysis of blood and urine) are carried our one or two times per year, the radiology of lungs and esophagus is carried out yearly. The duration of observance is three years if there are no backsets.

Prognosis. Course of progressive systematic sclerosis is changeable and unpredictable. The result of disease depends on damage of kidney (uremia, accelerated hypertension), heart and lungs (pulmonary fibrosis, pneumonia).

18.2 Lupus erythematosus

Lupus erythematosus is a disease characterized by fibrinoid degeneration of connective tissue with incompletely known causation and complicated pathogenetic mechanism which include participation of immune, genetic, metabolic neuroendocrine and outer causes.

TO KNOW:

- modern conceptions of aetiopathogenesis of lupus erythematosus;
- factors precipitating the progression of this disease;
- classification of lupus erythematosus;
- pathomorphological changes in skin at lupus erythematosus;
- clinical profile of different forms of this disease;
- its laboratory diagnostic criteria;
- principles and approaches of curing measures and periodic health examination at this disease.

TO BE ABLE TO:

- interview and make a full diagnosis correctly;
- carry out the differential diagnostics with diseases having similar clinical presentation;
- assign corresponding laboratory examinations for confirmation of diagnosis;
- assign balanced curing for the patient with lupus erythematosus; determine the preventive measures.

Aetiopathogenesis. The leading theory of progression of lupus erythematosus for the now is an autoimmune theory. Precipitating factors could be different B-cellular activators including infections; As a result the range of antibodies is produced against cellular antigens like DNA, RNA and RNA-protein complexes. Resulting in influence of antibodies on cells' nucleus (leukocytes) the patient gets the LE-cells. The appearance of LE-phenomena in peripheral blood and bone marrow (some nucleophagocytosis) is conditioned by unique «antinuclear factor". LE-factor is an immunoglobulin G which is antibody for nucleoprotein.

The progression of mucoid degeneration is typical and expressed depolymerization of main substance of connective tissue with following deposit of fibrinoid in affected tissues. Interaction of antibodies with antigens of connective tissue leads to liberation of mucopolysaccharides and glucoproteins (haptens). On newly formed antigens the immune competent lymphocytes produce corresponding antibodies. The patients with lupus erythematosus are discovered the malfunction of genital and other endocrine glands as well as disorder of protein, carbohydrate and adipose metabolism and others. The presence of acroasphyxia, Reynaud's disease, and perniosis leads to progression of lupus erythematosus on affected areas of skin.

Epidemiology. The incidence of lupus erythematosus is 0.25-1% among all dermatological diseases. This disease appears mostly of persons from 20 to 40 years old. The disease is widespread in countries with wet cold sea climate. Despite of good isolation the lupus erythematosus occurs rarely in tropical countries which is possible to be connected with more expressed protection of pigmented (dark) skin from influence of solar beams. Women suffers more often than men.

Classification. There are following types of lupus erythematosus:

1. Chronic lupus erythematosus
   - Discoides;
   - Disseminatus;
   - Erythema centrifugum Biett
   - Kaposi-Irgang's heavy form
2. Lupus erythematodes systemicus
   - Acute;
   - Subacute.

Clinical findings. The clinical performance of lupus erythematosus depends on form of disease.

Lupus erythematosus discoides. At lupus erythematosus discoides the process begins from occurrence (on the face as usual) of pink-red edematous spot which is sclerosed and covered by fine greyish crusts closely fitted to openings of hair follicles. On the bottom surface of crust at its removal the fine acicula are visible – these are corneal plugs tightly entered into the openings of hair follicles. At attempting of their removal the patient feels pain (Besnier's symptom). After removal of crusts the surface

of locus reminds lemon peel. Square of locus increases, the new similar locuses appear. The infiltration, keratosis, hyperemia, and swelling are intensified on the periphery of locus. There is an ulerythema gradually appears in center, the skin is thinned and easily folded. The major typical signs of lupus erythematosus discoides are erythema, infiltration, hyperkeratosis, and atrophy. In addition to this, the teleangiectasia and hyperpigmentation could be observed.

The size of locuses of lupus erythematosus (diameter from 0.5 to 5 cm and more) and quantity varies from one to a number. The typical location is nose and cheeks. The locuses of lupus erythematosus discoides are gradually spreads by periphery and have a form of butterfly which back is on the nose and wings are on the cheeks.

Subjective feelings are expressed in weak pruritus and tingling. There are weakly expressed general evidences could be observed such as anemia, increasing of ESR, decreasing of quantity of albumins and increasing of content of globulins, especially of gamma-globulins, appearance of S-reactive protein and cryoglobulins. The patients with lupus erythematosus discoides and lupus erythematosus disseminatus the dystrophic changes of connective tissues are discovered not only in lesion focuses but also on an externally healthy skin.

Lupus erythematosus disseminatus. Lupus erythematosus disseminatus is evidenced by numerous dispersed lesion focuses on the skin of face, sternum, hands, feet and other areas. This form occurs of 12.5-22% of patients with lupus erythematosus.

The locuses of lupus erythematosus disseminatus have erythematous-edematous nature or the form of disks which are typical for lupus erythematosus discoides. The infiltration and hyperkeratosis are nod observed in erythematous-edematous locuses of cyanochroic color. The lupus erythematosus disseminatus could be transformed into discoides or systematic form.

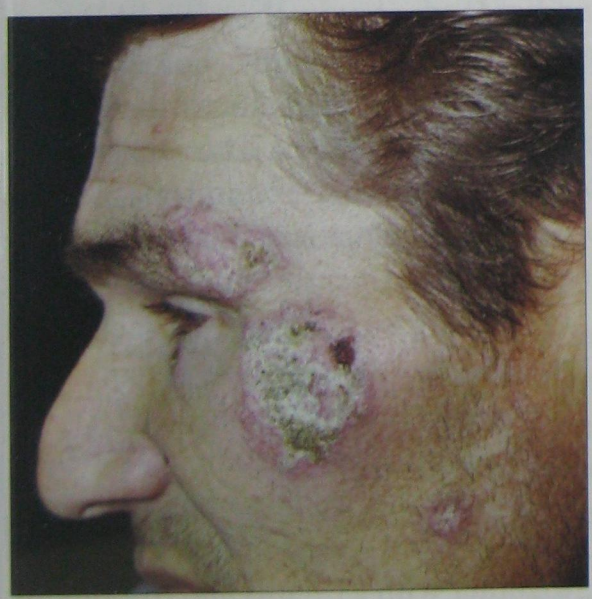

Fig. 18.4. Lupus erythematosus discoides.

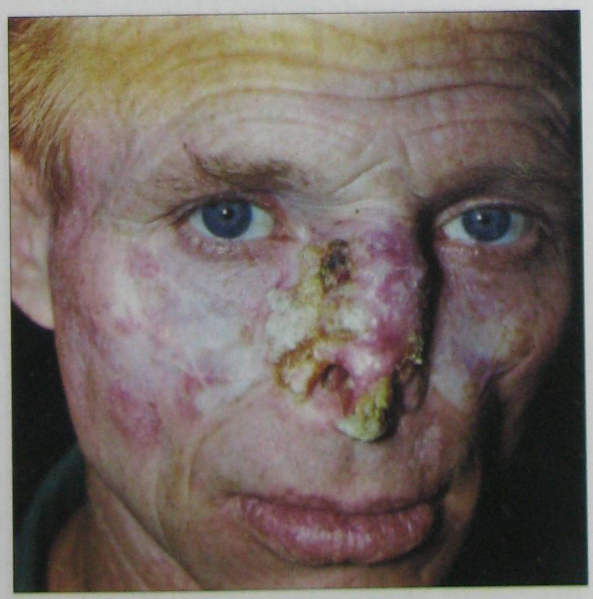

Fig. 18.5. Verrucous form of lupus erythematosus discoides complicated by carcinoma.

Erythema centrifugum Biett. By its clinical findings the erythema centrifugum Biett is significantly differs from lupus erythematosus discoides by absence of infiltration, hyperkeratosis and atrophy in the locus.

Erythema centrifugum by course is different than lupus erythematosus discoides as it fast answers the medical treatment but has often backsets because of which it sometimes called migrant. Among patients with lupus erythematosus the patients with erythema centrifugum is 5-11%. ***Lupus erythematodes profundus Kaposi-Irgang.*** At lupus erythematodes profundus Kaposi-Irgang together with typical discoides locuses or independently in subcutaneous fat one or several sclerotic and movable nodular components appears. The color of skin above them at first is not changed but then it gets cyanochroic-red tone, the peeling is not evidenced.

Lupus erythematodes systemicus is a serious general disease which more often occurs of young women. Its course could be acute, subacute and chronic. The disease progresses suddenly or rarely from chronic form of lupus erythematosus discoides or lupus erythematosus disseminatus.

The most typical is an affection of skin of face in form of diffuse edematous erythema with strict borders reminding cellulitis. Erythema could be spread to the neck and upper part of sternum. Erythema and light atrophy often appear on the palms and feet. The nodes often have hemorrhagic painting.

There is also affection of many organs and systems typical for lupus erythematodes systemicus: the pain in joints and muscles, pneumonia, pleurisy, affection of liver, kidney, lien, leukopenia, anemia, trombocytopenia and others are observed.

Diagnostics. During lupus erythematosus diagnostics except data of clinical examination it is important to discover the cells of lupus erythematosus (LE-cells) which are neutrophilous leukocytes containing phagocytosed nucleoids. There are also so called rosettes could be found which are the assemblies of leukocytes around homogenized nucleus of sphacelous leukocytes containing DNA. The leukocytes containing in rosette could phagocytize the homogeneous mass and be transformed into cell of lupus erythematosus. Except LE-cells and rosettes there are Gross's hematoxylin bodies discovered in blood of patient with lupus erythematosus. These bodies are the residues of lysed but still not phagocytized nucleus which together with LE-cells and rosettes are the result of nucleolysis.

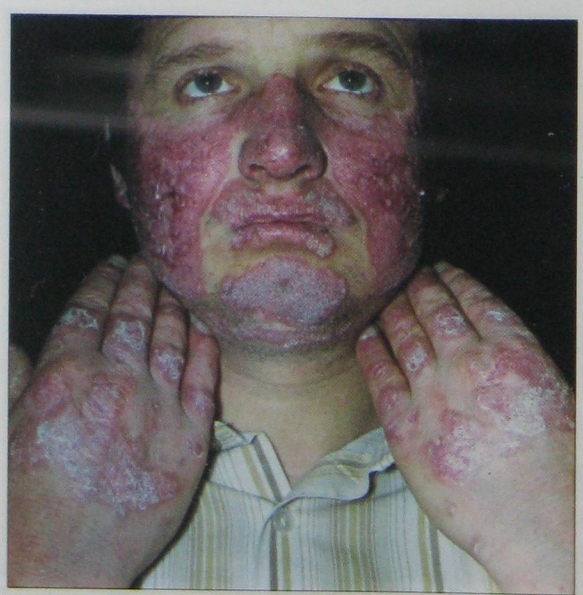

Fig. 18.6. Lupus erythematosus disseminatus.

In dry blood of patients suffered from lupus erythematodes systemicus the LE-factor is discovered concerned with function of gamma-globulins of blood plasma which comes into contact with nucleus of leukocytes and causes its destruction. The antibodies for La (SS-B) nucleus antigen coexisted with antibodies for Ro (anti-SS-A) nucleus antigen and usually absent as single antibodies.

Pathomorphological mechanism. The lesion focuses at lupus erythematodes have specific histopathology which is hydropic (vacuolar) degeneration of basal layer of epidermis with locus atrophy of epidermis; sclerotic mononuclear cellular infiltrate in upper layers of dermis, around the appendages of skin and vesicles which runs to the deep layers of dermis; subepidermal deposits of immunoglobulin in locuses (test for presence of lupus strip).

Differential diagnostics. *Lupus erythematosus discoides* and its disseminatus form could be discovered without any problems. At incipience the disease is distinguished with psoriasis, seborrheic dermatitis, Hutchinson's syndrome, pseudopelade, black-dot ringworm, favus, acne erythematosa, and lupus.

It is possible to distinguish the lupus erythematosus from psoriasis on the basis of location of rashes: at lupus erythematosus it is on face and at psoriasis it is on hairy part of head, body and extremities.

The signs on the basis of which the lupus erythematosus could be differed from seborrheic dermatitis are location of seborrheal rashes in skin folds, unclear borders of locuses covered by fat crusts, pruritus, and enhancement of course of process in summer.

At black-dot ringworm and favus the peeling and cicatrization on hairy part of the head could appear in connection with which they remind the lupus erythematosus.

Distinguish the *lupus erythematodes systemicus* from other diseases is harder than its' discoides form, especially at incipience with acute course.

At cellulitis reddening on the face the assumption could appear about presence of sacred fire. However, the hyperemia is not so bright, has bluish tone, and distinguished by torpenty of course at acute lupus erythematodes. It is necessary to distinguish the lupus erythematodes from diffuse scleroderma. At last one usually the serious general eyesores, fever, and numerous affections of inner organs are present.

The rashes at lupus erythematodes systemicus could remind the evidences of acute disseminated myositis, however, at last one they have more congestive nature.

Curing. For curing of lupus erythematodes there are system steroids (prednisolone, dexamethasone), immunosuppressive agents, aromatic retinoids (tigasone), and non-steroidal anti-inflammatory medicamental drugs used. Light-exposed areas of the skin should be protected by sun-screens with high sun protection factor. For curing of lupus erythematodes discoides the fluorinated topical steroids and injections of triamcinolone (intralesional) are used. Light-exposed areas of the skin should be protected by sun-screens with high sun protection factor.

Preventive measures and prognosis. The ultra violet irradiation (exposure to light), UHV-therapy, abuse of some medicamental drugs (antibiotics – penicillin, tetracycline; sulfanilamides; isoniazid, hydralazine, phenothiazine, vaccines) are counter-indicative.

The prognosis of lupus erythematodes discoides regarding to life and working ability is favorable, but its transformation into lupus erythematodes systemicus is possible. The prognosis regarding recuperation is doubtful as disease have tendency to the backsets.

18.3 Dermatomyositis

Dermatomyositis is a serious chronic idiopathic inflammatory myopathy characterized by bilateral affection of proximal muscles and typical locuses on skin.

TO KNOW:

- modern conceptions of aetiopathogenesis of dermatomyositis;
- factors precipitating the progression of this disease;
- classification of dermatomyositis (primary, secondary and juvenile);
- pathomorphological changes in skin at this disease;
- clinical profile of primary, secondary and juvenile dermatomyositis;
- its laboratory diagnostic criteria;
- principles and approaches of curing measures and periodic health examination of patients at dermatomyositis.

TO BE ABLE TO:

- interview and make a full diagnosis correctly for patient with dermatomyositis;
- carry out the differential diagnostics with diseases having similar clinical presentation;
- assign corresponding laboratory examinations for confirmation of diagnosis;
- assign balanced curing for the patient with dermatomyositis;
- determine the preventive measures for dermatomyositis.

Aetiopathogenesis. Dermatomyositis is an autoimmune disease of connective tissue with unknown causation. Disease appears often after infection damages of upper air passages, recrudescence of tonsillitis, pharyngitis as well as result of epidemic roseola, influenza, streptococcosis, and rheumatism. The process involves both cellular and antibody-mediated immune responses. Approximately in 15-20% of cases of clinical dermatomyositis of adults and children the specific for myositis Mi-2 antibodies are found. Some patients have the antibodies for (Jo-1) transport RNA-synthetase as immunologic marker. Nonmalignant form of dermatomyositis is associated with Mi-2 antibodies having immunogenic markers DR-7, DRw-53 and DQ-2 while the pseudotrichiniasis associated with other myositis antibodies is characterized by very increased frequency of alleles HLA-DRB1*0301 and DQA1*0501. The deposit of membrane attack complex of complement in intramuscular vesicles and fixed expression of interleukine-1 as well as molecules of cell-cell adhesion-1 and molecules of adhesion of vascular cage-1 in endothelial cell of capillary tubes are possible responsible for damage of vesicles especially expressed at juvenile form of disease. Cellular immune mechanism also plays significant role which is confirmed by presence of activated T-lymphocytes in inflammatory infiltrates.

This pathology is observed rarely, usually in age of from 20 to 50 years. The children of from 1.5 to 15 years old suffer too which is about 20% of patients with dermatomyositis. The women affected more often.

The significant association with malignant swellings is established of patients who are older than 50 years. Such patients should be examined for presence of oncologic pathology.

Classification. There are *primary* (idiopathic), *secondary* (symptomatic, paraneoplastic) and *juvenile* (more often women suffer) dermatomyositis distinguished.

Clinical findings. The disease often begins in acute form. The temperature of body is rising suddenly, the general condition is affected. Typical erythema is around the eyes, on cheeks, palpebrae, extensor surfaces of upper and lower extremities, in area of joints. The erythema is especially typical on superior eyelids and around them in form of eyeglasses. It could goes to the nose and in such cases reminds erythema in form of butterfly at lupus erythematosus. Erythema on the neck and on extremities, in area of face could be accompanied by water retention; it is often located around the joints in area of elbows, knees, ankles, on the body of hands. At spreading the erythema from neck to arms, dorsum and sternum the affection has form of pelerine. Sometimes the lichenoid rashes, bullous components, and hemorogic spots are observed in area of erythema. The bullous components could exulcerate in future. Often on the background of erythema the telangiectasis are appear which causes to more intensive coloration of skin. It is necessary to notice the affection of mostly opened areas of skin exposed to often influence of solar irradiation.

Further according to regress of rashes the peeling appears together with white-ceramic colored spots surrounded by telangiectasis. The pruritus of skin is strong

rarely. At long-lasting course of disease the changes of skin could be observed reminding the changes at poikiloderma in form of depigment or hyper pigment areas, atrophy, and telangiectasis. The changes of skin are earliest and typical sign of dermatomyositis and could be the only symptom for the long time.

Another typical symptom of dermatomyositis is an affection of muscles which is often discovered at beginning of disease. The patients complain for suddenly appeared pains or pains appeared while moving or at examination of muscles by touch. Morbidity rate is extremely expressed at extension of extremities. The affection of muscles of extremities and of rotator cuffs is progressed more often. Sometimes the difficulties occur at swallowing. The changes in muscles are evidenced in its enlargement, water retention and tenderness. At long-lasting course of disease there are contractures and atrophy of muscles progressed.

Many patients with dermatomyositis have a progress of affection of mucosal coats. Diseases of inner organs at dermatomyositis are expressed by malfunction of myocardium, endocardium, and respiratory organs. Last-mentioned is conditioned by affection of intercostal muscles and diaphragm. That's why ventilation of lungs is not sufficient which could cause to pneumonia. More often the affections of gastrointestinal tract are evidenced. Except dysphagia there are disorders of chewing process, abdominal migraine, and enterocolitis observed; almost half of patients have their kidney and lien enlarged, many of them have all lymphatic nodes enlarged.

The significant role plays relatively often evidence of malignant swelling at dermatomyositis, mostly the stomach cancer is observed.

The course of dermatomyositis is acute as usual. Thanking to curing the remissions could occur, sometimes positive, but then the recrudescences occur again with more severe course.

Pathomorphological mechanism. The most changes occur in dermis, where the delayering of collagen fibers discovered as well as their thickening and further sclerosis. In subcutaneous fat the locuses of lymphoid infiltration, fibrous tissue, and sometimes calcium tophus appear.

There are inflammatory and degenerative evidences observed in muscles.

Differential diagnostics. Dermatomyositis at incipience is distinguished with *acute lupus erythematosus*. At further course of dermatomyositis the some semblance with incipience of scleroderma systematics and myxedema could occur.

Usually the crucial significance for diagnostics the results of histological examination of muscles have as well as enzyme multiplied immunoassay.

Curing. If dermatomyositis is associated with neoplastic transformation the removal of mass lesion in most cases leads to improvement of dermatomyositis course and even to recuperation. The main curing is in assigning of oral steroids starting from loading doses (1 mg/kg of body mass for prednisolone) which then titrated to the maintenance ones (10-20 mg per day). Gradually the azathioprine is added as well as cytostatics (azathioprine 3-4 mg/kg, metatrexate, and cyclophosphamide). At remission stage the remedial gymnastics and massage are connected.

Preventive measures and prognosis. There is no primary preventive measures, and secondary provides avoiding of recrudescences. It is not recommended to abuse the antibiotics, sulfanilamides, and hormonal contraceptives. It is also should avoid the frigorism, exposure to light, and use sun-protective measures. The mortality in case of absence of curing is up to 70%, the disability is possible.

1. What of the following dermatosis are not belong to diseases of connective tissue:

A. Epidermophytosis
B. Lupus erythematosus
C. Dermatomyositis
D. Psoriasis
E. Scleroderma

2. There are following types of localized scleroderma:

A. Circumscribed
B. Linear
C. White spot disease
D. Morphea
E. All of mentioned above

3. There are three stages of course of sclerotic pathological process:

A. Induration, lichenification and sclerotherapy
B. Swelling, induration and atrophy
C. Infiltration, exulcerations and cicatrization
D. Erythematous, infiltrative stages and resorption
E. Swelling, erythematous stage and resorption

4. LE-factor is:

A. Immunoglobulin G, which is antibody for cell's cytoplasm
B. Immunoglobulin A, which is antibody for nucleoprotein
C. Immunoglobulin G, which is antibody for RNA
D. Immunoglobulin G, which is antibody for nucleoprotein
E. Immunoglobulin M, which is antibody for nucleoprotein

5. What of following forms is not belonging to chronic lupus erythematosus:

A. Bazin's disease
B. Discoides
C. Disseminatus
D. Erythema centrifugum Biett
E. Lupus erythematodes profundus Kaposi-Irgang

6. For clinical symptomatology of lupus erythematosus is not typical:

A. Infiltrated spots
B. Hyperkeratosis follicularis
C. Presence of pruritus
D. Ulerythema
E. Absence of pruritus

7. The following is not a form of lupus erythematosus discoides:

A. Lupus erythematodes gypseus
B. Lupus erythematodes papilomatosus et verrucosus
C. Lupus erythematodes tumidus
D. Lupus erythematodes dissiminatus
E. All answers are incorrect

8. The following is not a typical clinical-diagnostic criterion of dermatomyositis:

A. Affection of skin in form of swelling and erythema in form of "glasses"
B. Myositis, myodania, ceratinuria
C. Damage of digestive tract
D. Hyperkeratosis follicularis
E. Rapid reduction of weight

9. Secondary preventive of dermatomyositis provides avoiding of:

A. Abuse of antibiotics and sulfanilamides
B. Exposure to light
C. Frigorism
D. Hormonal contraceptives
E. All of above mentioned

Task 1. The female patient visit a dermatologist with complains for rash on skin and upper extremities and some numbness. According to the words of patient, pathological process began two months ago from occurrence of pink-red spot of round shape with lilac collar on periphery. Later in the area of spot the superficial induration of ivory color progressed. The patient had no curing. *Unbiased*: the infiltrated locus of primrose color is observed on the skin of arm. It could be taken into fold with hard. There is no hair on skin in area of rushes, no diaphoresis and sebaceous excretions, the sensitivity id weak.

a) What disease such symptoms are most typical for:
- **A.** Circumscribed scleroderma
- **B.** Strumoderma
- **C.** Bazin's disease
- **D.** Elephantiasis graecorum
- **E.** Dermatomyositis

b) What additional examinations should be carried out for determination of final diagnosis?

Task 2. At histological examination the swelling of dermis is discovered, the infiltrate containing of lymphocytes is between fascicle of halogen fibers. The streaming of spinous layer and vacuolization of cells of basal layer are observed in epidermis. The sclerosis of collagen fibers, lymphoid infiltrate, luminal occlusion, and absence of hair, atrophy of oil and perspiratory glands, sclerosis of hypoderm, thinning of epidermis and thickening of corneal layer are discovered.

a) What disease such symptoms are most typical for:
- **A.** Dermatomyositis
- **B.** Lupus erythematosus systemicus
- **C.** Bazin's disease
- **D.** Elephantiasis graecorum
- **E.** Scleroderma

b) Determine the patient surveillance.

Task 3. The female patient visit a dermatologist with complains for presence of rash on the right cheek appeared after excessive exposure to light. It is known from anamnesis that process began from appearance of pink-red infiltrated spot of up to 3 cm in size and covered by tightly fitted fine greyish crusts on skin of face. On the bottom surface of crusts at their removal the fine spinelets are visible. At attempting of removal the crusts the pain is filled. After removal of crusts the surface of locus reminds lemon peel.

a) Determine the provisional diagnosis:
- **A.** Bazin's disease
- **B.** Lupus erythematosus discoides
- **C.** Circumscribed scleroderma
- **D.** Erythema centrifugum Biett
- **E.** Lupus erythematodes profundus Kaposi-Irgang

b) What nosologies this disease is most often distinguished with?

Task 4. The female patient visit a dermatologist with complains for rise of body's temperature, presence of pain in muscles, joints, headache, faintness, and skin rash around the eyes. The disease began in acute form after influenza being suffered. *Unbiased*: the erythema of cyanochroic-red color in form of glasses is observed on skin around the eyes and the telangiectasis on its background which condition the more intensive coloring of the skin.

a) What diagnosis should be though for:
- **A.** Strumoderma
- **B.** Lupus erythematosus
- **C.** Dermatomyositis
- **D.** Bazin's disease
- **E.** Scleroderma

b) Carry out the differential diagnostics.

Answers for first level self-control questions
1 – A; **2** – E; **3** – B; **4** – D; **5** – A; **6** – C; **7** – D; **8** – D; **9** – E
Answers for second and third level self-control questions
1a – A; **2a** – E; **3a** – B; **4a** – C

19 TOPIC

Genodermatosis – genetic disorders of the skin

TRAINING AND EDUCATIONAL GOALS

- Discover the applicability of the problem and make a presentation of major moments of aetiopathogenesis of genodermatosis
- Determine the main groups of genetic pathological processes in skin and cutaneous appendages
- Interpret general course and clinical presentation of different genodermatosis
- Determine clinical findings of typical evidences of bullous genodermatosis
- Learn the diagnostic criteria of ichthyosis
- Determine principles of therapy and prognosis of course of genodermatosis

TO KNOW:

- classification of genodermatosis;
- etiology and pathogenetic mechanism of genodermatosis;
- clinical particularities of modern curing of bullous genodermatosis;
- diagnostic criteria for determination of different forms of ichthyosis;
- principles of curing and preventive measures being implemented regarding patients with genodermatosis.

TO BE ABLE TO:

- interview the patient with genodermatosis;
- analyze the clinical presentation and results of laboratory examinations;
- carry out differential diagnostics with diseases having similar clinical presentation;
- assign balanced curing for the patient with genodermatosis;
- carry out the psychodiagnosis and psychocorrection.

Epidemiology. According to data of WHO, about one third of all genetic diseases are the dermatosis, the genetic nature of which is proven. The crucial role of genetic factor is determined for approximately 200 of skin diseases. In other words, the genetic diseases accounts for 10% of all known dermatosis for the now. The number of genodermatosis is all the time increased year after year because of development of knowledge about reasons and pathogenesis of these diseases of skin.

Pathogenesis. The great majority of genetic diseases of skin are conditioned by drop gene-mutations which are failed to be found.

The basis of modern genetic classifications is a type of transferring of mutant gene in generations and particularities of its allocation in autosomes or in gonosomes. The penetrance (possibility of associated trait of gene depending on influence of environment) and expressivity (degree of manifestation) of gene are also taken into consideration.

The sebaceous adenoma, Hopf's disease, partial albinism, atopic dermatitis, congenital dermal aplasia, Hailey- Hailey disease, Darier's disease, keratoma of palms and feet, neurofibromatosis, porphyria cutanea tarda, ichthyosis vulgaris, psoriasis, Mibelli's disease, simple epidermolysis bullosa and others are passed by autosomal-dominant inheritance.

The dystrophic epidermolysis bullosa, acrodermatitis enteropathica, xerodermia pigmentosum, epidermodysplasia verruciformis, lamellar exfoliation of the newborn, Urbach-Wiethe disease, congenital erythropoietic porphyria, native polykeratosis of Turen, and wide range of syndrome diseases (Grenbland-Strandberg, Rothmund, Blum, Verner etc.) are passed by autosomal-recessive inheritance.

Sex-controlled (X chromosome) dominant inheritance is observed at follicular atrophic keratosis, Bloch-Sulzberger syndrome.

Sex-controlled recessive inheritance (X chromosome) is observed at anhidrotic ectodermal dysplasia, dystrophic form of epidermolysis bullosa, diffuse angiokeratoma, and ichthyosis vulgaris.

Genetic diseases of skin with dominant type of inheritance are more numerous than diseases with recessive type. This is mostly conditioned by a fact that it is difficult to trace the recessive gene of human. It is necessary to mention that genetic diseases could be evidenced either straight after born or in different periods of life (in childhood, youthful and even in adult age). The same genodermatosis could be passed by different ways either dominantly or recessively which in some degree makes impact on particularities of clinical symptomatology, course and prognosis of these dermatoses.

Classification. There was a variety of attempts for creation of clinical classification of genetic diseases of skin. For the now there are following groups of genetic pathological processes in skin and cutaneous appendages:

- *physiological anomalies* (heterochronia and hair poliosis, sunspots, lentigo etc.);
- *metabolic defects* (albinism, pigmentation of xerodermia, porphyria, xanthomatosis etc.);

- *elastic tissue developmental disabilities* (epidermolysis bullosa, Ehlers-Danlos syndrome and others);
- *dyskeratosis* (ichthyosis, keratoderma, Devergi's disease and so on);
- *ectodermal dysplasia* (alopecia adnata, anonychia, hypertrichosis) and other anomalies.

It is considered to be regular from the clinical point of view the division of genetic diseases on three main groups:

1. Skin diseases, in occurrence of which the crucial role is played by genetic factors (group of ichthyosis: ichthyosis vulgaris, lamellar exfoliation of the newborn and genetous ichtyosiform erythemas; bullous hemodermatosis, genetous dysplastic diseases, phacomatosis and others).

2. Dermatosis which genetic occurrence is also practically assured but type of inherent pass determined indistinctly and in a great measure is conditioned by environmental effect (weeping dermatitis, psoriasis, acne vulgaris, and atopic dermatitis). These diseases often called as diseases of genetic disposition.

3. Some dermatosis at which, as a rule, similar diseases are not observed among near relatives, but the hereditary transmission is registered in separate groups of patients (lichen acuminatus, seborrheic dermatitis, white spot disease).

Bullous genodermatosis

The diseases of this group are characterized by occurrence of different by size bullae on skin and in separate cases – on mucosal coats too. The bullae appear as a response for even insignificant pressure. The group of genetous bullous dermatosis includes epidermolysis bullosa, Hailey-Hailey disease, porphyry, Bloch-Sulzberger syndrome, and ichthyosiform affections.

Epidermolysis bullosa (*epidermolysis bullosa hereditaria*). As issue of certain diagnosis decided not only chronically but also with obligatory attraction of morphological examination, the meaning of simple or dystrophic forms of epidermolysis bullosa hereditaria is important for the practician physician.

Epidermolysis bullosa hereditaria was firstly described by *J. Hutchinson* (1875) and *T. Fox* (1879). *H. Kebner* (1886) name this disease the epidermolysis bullosa and *L. Broc* (1902) – the traumatic pemphigus. Epidermolysis bullosa is discovered as heterogenic group of genetically conditioned diseases of skin among which either dominantly and recessively inherited forms. They are divided by three groups in accordance with results of morphological researches. There are 24 clinical types of this disease. Accordingly to this the groups of usual, boundary and dystrophic epidermolysis bullosa are distinguished.

Aetiology and pathogenetic mechanism. Aetiology of all forms of epidermolysis bullosa is determined by numerous genetic mutations in different chromosomes. Its pathogenetic mechanism is discovered not enough. At all forms

there are genetically conditioned structural failures at level of basal membrane. At variety of clinical forms the enzymatic failures are discovered in epidermis.

Clinical findings. The common for all clinical forms of epidermolysis bullosa is an early appearance of disease, more often in childbirth or in first days after birth of child. The appearance of bullae and anabrosis on skin and mucosal coats as result of weak mechanical injury or hyperthermia is typical. Presence or absence of cicatricial tissues after regenerative process is a basis for division of clinical forms of epidermolysis bullosa by dystrophic and usual ones.

Usual generalized epidermolysis bullosa

The disease begins of child from birth or in first month of life. At first bullae appear on feet, then on hands, further – in places of friction by clothes and nappies. In 20-30 min after shear stress of skin the tin-walled bullae appear on it. After breaking the bulla's tegmentum the regenerative process occurs during several days. The cicatricial tissues are not discovered. General condition of patients is not broken, the course of disease is mild, the intellect is not suffer, the legs are not damaged, the Nikolsky's sing is negative. At adulthood the spontaneous recovery is possible.

Delayed or localized epidermolysis bullosa (synonyms: the Weber-Coccain's syndrome, summer epidermolysis bullosa of feet and hands). The disease begins in ephebic or of adults as usual in summer. The allocation of bullae is limited by palms and plantae.

Group of dystrophic bullous epidermolysis

Dystrophic bullous epidermolysis is represented by non-regular group of genetically conditioned inheritable bullous diseases, part of which is passed by autosomal-dominant and the other part is by autosomal-recessive way.

Pathogenically at autosomal-dominant forms the incompleteness of constitution of anchor fibrillas, i.e. structures connecting the basal membrane with dermis. Histopathology at all clinical forms of dystrophic bullous epidermolysis is similar. The bullae allocated under basal membrane which is away with dermis together with epidermis and is a part of bulla's tegmentum («dermolythic» bulla). The expressed swelling and homogenization of collagen fibers are observed under bulla in dermis. Elastic fibers bloat, in some places they are disorganized either in area of bulla and at well-looking areas of skin.

There are following clinical forms are distinguished in group of dystrophic bullous epidermolysis:

- hyperplastic form of habitual dystrophic bullous epidermolysis of dominant type;
- albopapuloid form;
- atrophied form;
- autosomal-recessive bullous epidermolysis in one's turn is divided for:

– polydysplatic;
– generalized;
– localized.

Hyperplastic type of dominant habitual dystrophic bullous epidermolysis. The disease begins from moment of birth or first months of life when on injured areas of skin as well as on mucosal coats the bullae appear. The spontaneous rash is rarely observed. On places of bullae regression the hypertrophic and keloid cicatrixes and verruciformis hyperkeratosis appear. The mucosal coats are affected often and seriously. The appearance of bullae on mucosal coats leads to formation of secondary ciactrical stenosis of fauces, gorge, and esophagus, and corneal opacity. Hair and teeth has no changed. The mend occurs at periods, gravidism and, as a rule, during adolescence. The duration of life of patients with bullous epidermolysis is not decreased significantly.

Albopapuloid form of dominant dystrophic bullous epidermolysis. The disease begins from two-year age and proceeds by a type of hyperplastic epidermolysis bullosa. With coming of adolescence (even earlier for some children) the occurrence of bullae in area of extremities is stopped and fine indurated white papules appear on skin, mostly on body. These components become larger and interlock gradually, their surface becomes of ivory color. General condition of the patients is satisfactory. The miliums appear on the places of bullae and the cicatricial tissues occur. The Nikolsky's

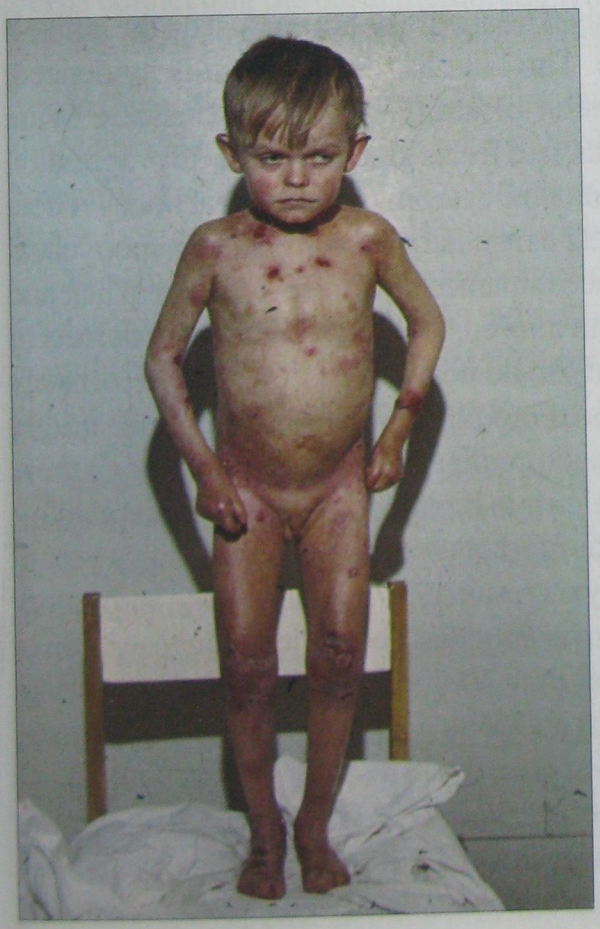

Fig. 19.1. Bullous dystrophic epidermolysis.

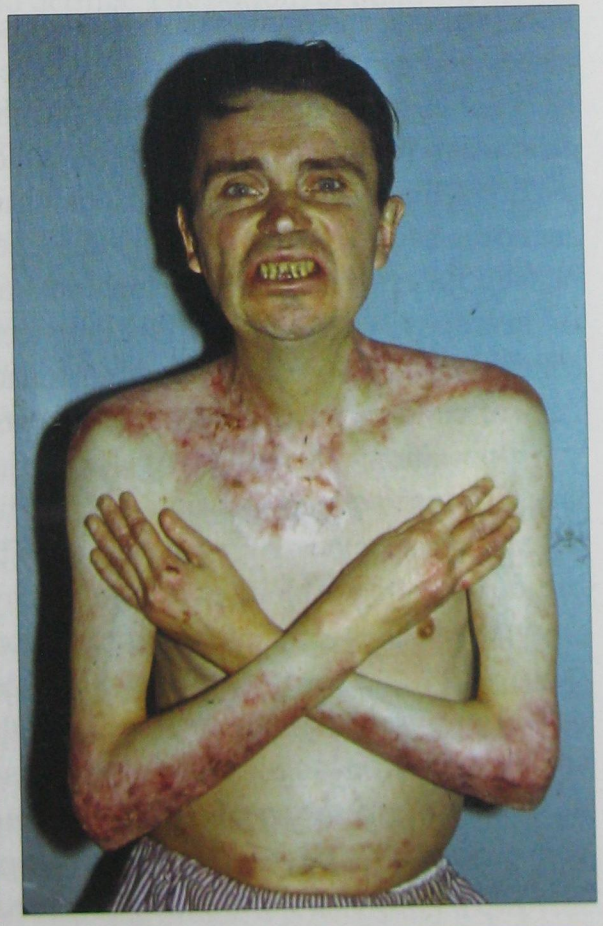

Fig. 19.2. Bullous dystrophic epidermolysis.

sign is rarely could be positive. The prognosis for life is favorable. It is considered that this form is a milder variant of hyperplastic form of epidermolysis bullosa.

Atrophic form of dominant dystrophic bullous epidermolysis. The disease begins from moment of birth. The generalized injury of skin progresses in first days of life already. The bullae appear on most injured areas of skin such as hands, feet, elbows, neck, and lumbus. The mucosal coats are not injured. Bodies of nails are burned-out of all of patients. Physical development could be postponed, and the intellectual is not suffered. With age, the bullae appear rarely, and the presence of disease of adult patients could be evidenced by dystrophy of nails and atrophic cicatricial tissues on elbows, knees and anticnemions only.

Recessive bullous epidermolysis

This group of diseases is characterized by severest course. The following is distinguished: dystrophic polydysplastic bullous epidermolysis (non-generalized and generalized) and dystrophic inverse localized.

Polydysplastic dystrophic bullous epidermolysis. The disease begins from moment of birth and could cause death at an early age. It is evidenced since first minutes of child's life and in moment of birth the bullae and anabrosis could appear on the large areas of baby's skin. In first days of life the bullae appear either as result of mild injury of skin, pressure, and friction or spontaneously. The anabrosis appear fast on the bullae's places and process gets a spread nature. The Nikolsky's symptom is evidenced. Regeneration occurs slowly with formation of atrophic cicatricial tissues. Wide cicatrization of skin in area of elbows, hands, and feet is gradually leads to progression of contractures, symphasodyctylias, and autoamputations of phalangeal bones. There are no nails from birth or gradually disappear as a result of occurrence of hyponycheal bullae. Ulerythema of hairy part of head is accompanied by diffuse rarefying of hair and its dystrophy. All of patients have their teeth injured. The caries, numerous defects of dental enamel, compromised dentitions, and paradontosis are observed. Approximately 20% of children have their mucosal coats of mouth cavity, esophagus and straight intestine injured. The bullae with hemorrhagic content are also could appear on these areas. The process of cicatrization on mouth leads to limitation of tongue displaceability, atrophy of mamelons, and mycrostomia. The most often causes of death on first year of life are dermatogen blood poisoning, asphyxia resulted by ingression into respiratory passages of bullae tegmentum and aspiration pneumonia. The ability for regeneration of injuries of skin is decreased in age of older than 30 years. The traumatisms are not healed on some areas during several months and could vegetare. The dermoid cancer could progress on long-lastly opened areas of skin.

Generalized dystrophic bullous non-mutilans epidermolysis. It is similar with clinical form described above but proceeds more mildly and differs by absence of injury of mucosal coats and by less severe course of disease in adult age (rare and more and more mild backsets). The cicatrization does not lead to autoamputations.

Localized dystrophic bullous epidermolysis. AT this form the beginning of disease is in first days of life and characterized by appearance of bullae with serosanguineous content which are located in places of maximal pressure and friction (feet, knees, elbows, and hands). The atrophy progresses in area of bullae, the milim-typed encapsulations occur, but these changes are less evidenced than at generalized form. The dystrophy of nails is evidenced on palms and feet. The injury of oral mucosa proceeds mildly. The dystrophy of nails is often encountered.

Pathomorphological mechanism. Histopathological examinations carried out by the means of submicroscopy became the basis for division of all forms of bullous epidermolysis by regular, boundary and dystrophic bullous epidermolysis.

At *regular forms* the appearance of bullae in epidermis occurs due to cytolysis of basal epidermal cells and this is reflected on electron diffraction patterns in view of full-blown swelling of their cytoplasm with abruption of cell envelopes. The bulla's tegmentum is all rafted epidermis and the bottom is an undamaged basal membrane.

The bullae at *boundary forms* appear on level of light plate of basal membrane. It is conditioned by inheritable incompleteness by desmos of basal epithelian cells and fixing tonofilaments. The bottom of bulla is made of plate of basal membrane.

At *dystrophic forms* the appearance of bullae is on the border of basal membrane and dermis which is concerned with genetically conditioned incompleteness of fixing fibrils connecting the basal membrane with dermis. The bottom of bulla is a dermis and this leads to formation of cicatricial tissues.

Differential diagnostics. The inheritable bullous epidermolysis of children should be distinguished from inheritable bullous ichthyosiform erythrodermatitis, epidemic and syphilous pemphigus, acrodermatitis enteropathica, inheritable erythropoietic porphyria, and Bloch-Sulzberger syndrome.

The inheritable bullous epidermolysis of adults should be distinguished from non-heritable bullous epidermolysis, bullous variant of multiform exudative erythema, pemphigus vulgaris, pemphigoid, Duhring disease, delayed skin porphyry, toxic epidermal necrolysis, and bullous form of mast cell disease.

Curing. From first days of life of child it is necessary to create a regime of minimal injury of skin for him (soft nappies and clothes with scarring outside). The skin should be lubricated and hydrated to make it soft, elastic and more resistant against influence of mechanical irritants.

On account of a fact that at autosomal-recessive bullous epidermolysis the excess of structurally-changed collagenase is produced the *pathogenetic therapy* is provide the abuse of drugs inhibiting of its production and activity (large doses of vitamin E, retinoids).

Symptomatic therapy is a basis of curing of patients with bullous epidermolysis. It includes the abuse of pluripotential antibiotics at secondary contamination, antihistamines at well-marked pruritus, and anabolic drugs. It is necessary to provide a due care for oral cavity (antiseptics). It is undesirable to implement systemic and