

Acne vulgaris

Acne vulgaris is a chronic inflammatory disease of sebaceous glands and hair follicles (so-called pilosebaceous units). It mainly affects young people in puberty. It is a non-infectious multifactorial disease. It mainly affects areas of the skin rich in sebaceous gland follicles - the face, the upper half of the back and the upper half of the torso.

Chronic inflammation of the pilosebaceous unit is caused by blockage of the outlet of the sebaceous follicle and continues with the development of non-inflammatory (microcomedones and comedones) and inflammatory lesions (papules, pustules, cysts). The inflammation is not of an infectious nature, but a reaction to foreign material in the follicle. In its pathogenesis, excessive production of sebum, retention of horn at the mouth of the follicles and colonization by the anaerobic bacteria *Propionibacterium acnes* are important.^{[1][2]}

Etiopathogenesis

Genetic influences

Family occurrence of acne is frequent, probably based on polygenic inheritance. The size and function of sebaceous glands, keratin production and hormonal conditions are genetically influenced.^[1]

Hormonal influences

The quantity and quality of sebum production is subject to hormonal regulation, it rises significantly during puberty. Increased sebum production directly correlates with the degree of acne involvement. Sebum secretion is stimulated by androgens (of testicular, ovarian and adrenal origin). They increase sebum production by accelerating the multiplication of sebaceous gland cells (holocrine type of secretion). During puberty, there is a relative increase in the level of androgens even in girls due to the imbalanced secretion of gonadal hormones. Another risk factor is the increased sensitivity of androgen receptors of the sebaceous glands at normal androgen levels. The sensitivity of the sebaceous glands to androgens is genetically determined. Sebum secretion is inhibited by estrogens. They have a direct suppressive effect on the sebaceous glands and reduce the action of androgens by feedback via gonadotropins. Acne (and seborrhea) improves in the estrogenic phase of the cycle, during ovulation, pregnancy, lactation and worsens in the luteal phase of the cycle and at the beginning of pregnancy. The function of the sebaceous glands is further influenced by the hormones of the pituitary gland, thyroid glands, adrenal glucocorticoids and the action of the CNS.^[1]

Keratinization disorder

Retention hyperkeratosis at the mouth of hair follicles is significant in the pathogenesis of acne. Increased production of horn cells in the upper part of the follicular duct with a decrease in their elimination from the follicle as a result of greater intercellular cohesion leads to the accumulation of sebaceous masses. This highlights the primary manifestation of acne - the comedone or blackhead. More pronounced keratinization is supported by:

- irritation by lipids or free fatty acids when sebum penetrates the outlet of hair follicles,
- genetic influences,
- the effect of androgens,
- increased hydration of the cornea at the mouth of the follicles (premenstrual seepage, increased sweating in heat and stuffiness),
- exposure to UV radiation,
- mechanical friction.^[1]

Bacterial flora

Propionibacterium acnes and to a lesser extent *Propionibacterium granulosum* indirectly influence the pathogenesis of acne. They are anaerobic organisms that multiply in the ducts of sebaceous gland follicles. They produce a number of biologically active substances (lipases – break down the triglycerides of sebum into free fatty acids; proteases – enable the penetration of the follicle contents through the follicular wall; hyaluronidase – enable its spread in the dermis). Acts antigenically. They produce a low-molecular substance that stimulates the chemotaxis of polymorphonuclear leukocytes and monocytes. People with acne have higher numbers of these bacteria. However, neither the severity of acne nor the degree of secondary inflammatory changes is proportional to the amount of bacteria.^[1]

Immune factors and the formation of inflammation

Inflammation around the pilosebaceous unit is a reaction to foreign material in the follicle - applies:

- irritation by free fatty acids,
- antigenic stimulation by the bacterial wall of propionibacteria,
- chemotactic action of propionibacteria on polymorphonuclear cells and monocytes,
- a substance with prostaglandin characteristics produced by propionibacteria.

In more severe forms of acne (especially in acne conglobata and acne fulminans), a disorder of cellular immunity, hypoalbuminemia and an increase in immunoglobulins are demonstrated.^[1]

Spontaneous resolution of acne with increasing age

With age, the impermeability of the horn cell barrier at the mouth of hair follicles increases and better protects the epithelium of the sebaceous gland against comedogenic substances. The sensitivity of sebaceous gland receptors to androgens gradually decreases.^[1]

Clinical manifestations

The first manifestations of acne usually appear in the early period of puberty, the maximum incidence is in girls between the ages of 16 and 17. a year, for boys between 18 and 19 a year. Up to 90% of young people are affected, and the manifestations are often only discrete. Acne usually disappears by the age of 20-25, rarely lasting longer. In adulthood, approximately 5% of women and 1% of men are affected.^[1]

Acne affects the so-called seborrheic predilection localization - face, back and chest, sometimes also shoulders and arms.

The primary manifestation of acne is a comedone – a closed white pimple, then an open black comedone is formed. The black coloring is caused by melanin. Both types are functionally closed. Comedones are gradually transformed by inflammation, papules and pustules are formed, and in more severe cases, infiltrates, abscesses and sebaceous or corn cysts.



Acne vulgaris papulosa

According to the predominant type of efflorescence, acne is clinically divided into:

- *acne comedonica*,
- *acne papulosa*,
- *acne pustulosa*,
- *acne cystica a nodulocystica*,
- *acne indurata et abscedens*,
- *acne conglobata* – when expressions merge.

Papules and pustules heal within 10 days, usually without scarring. Larger inflammatory processes can leave a scar (often sunken, sometimes keloidally raised).^[1]

Clinical variants

Acne premenstrualis

Sudden onset of painful inflammatory bumps on the chin, in the nasolabial folds and on the sides of the cheeks a few days before menses.

Acne of adult women – acne postpubertalis

It only appears in adulthood, usually after 18, sometimes after 25 years of age, regardless of the appearance of acne during puberty. Premenstrual exacerbation is typical. The cause is an increased sensitivity of the sebaceous glands to androgenic hormones. Comedones are usually absent, because the keratinization of the epithelium of the follicle of the sebaceous glands is not disturbed, and seborrhea is often absent.

Acne androgenica (virilizing syndromes)

It occurs in women as a result of overproduction of ovarian or adrenal androgens, e.g. in ovarian tumors, polycystic ovary syndrome, luteoma and adrenal tumors. Androgens can also be produced by peripheral conversion from estrogens. Other manifestations of virilization (hirsutism, male pattern hair loss, androgenic defluvium) are often present.

Acne neonatorum

It appears in the first week of life, spontaneously disappears after two months. Minor inflammatory manifestations on the forehead and cheeks. Conditioned by transplacental stimulation of the adrenal glands with an increase in the production of steroids and adrenal androgens after delivery.

Acne infantum

It appears in boys at 3 months of age and usually resolves by 7 months of age. It develops as a result of a rapid decrease in estrogen after childbirth and a subsequent increase in the secretion of gonadotropins and an increase in the production of testosterone in the testes (by negative feedback).

Acne excoriata

It is created by scratching and squeezing the often inconspicuous manifestations of acne. The subsequent inflammatory reaction is often more pronounced, healing is lengthy, excoriations, hemorrhagic crusts occur, and often heal with hyperpigmentation or a scar.

Acne conglobata

A severe form of acne that occurs more often in men. Large confluent inflammatory bumps and abscesses appear, fistulas and necrosis stand out, extensive atrophic and hypertrophic scars are formed. These manifestations are mainly on the chest, back, shoulders, sometimes also on the arms and buttocks; the face is less affected.

Acne inversa

A severe variant of acne conglobata with confluent abscesses with hemorrhagic-purulent contents and fistulas affecting the intertriginous areas. Impairment of the apocrine glands occurs secondarily, the primary being the occlusion of the ducts of the pilosebaceous unit as in acne and the formation of comedones. Hypalbuminemia, cellular immunity disorder, decreased serum iron level, etc. are often present.

Acne fulminans

A life-threatening, acutely occurring form of acne of the acne conglobata character with the formation of necrosis, exulceration of manifestations and with general toxic symptomatology (fever, joint and muscle pain, anorexia, weight loss, general nausea), increased sedimentation and leukocytosis. It requires hospitalization, administration of total corticoids and antibiotics, followed by oral isotretinoin.

Acne tropicalis

It develops in tropical climates in men with a history of acne. It has the character of acne conglobata.

SAPHO syndrome

Acne conglobata and/or Pustulosis palmoplantaris, Hyperostosis and Osteitis – most often on the sternoclavicular joint.^[1]

Differential diagnosis

Acne venenata

It is caused by the external action of chemical substances with a comedogenic effect - petroleum derivatives (vaseline, mineral oils), tar, chlorine compounds (they act simultaneously hepato- and nephrotoxic).

- Acne cosmetica – it is caused by excessive use of cosmetic creams, lotions, but also some soaps and detergents.

Acne from physical causes

It occurs in places of friction (*acne mechanica*) – on the neck of violinists, under headbands, etc.

- Mallorca acne (*acne aestivalis*) - a stuffy environment, UV radiation, unsuitable sun creams and oils contribute to its development.

Acneiform eruption, acne medicamentosa

The cause is usually steroids used internally, or anabolics; antiepileptic drugs, sedatives, especially lithium, barbiturates, some oral contraceptives, vitamin B6 and B12, preparations with iodine and bromine, nifedipine, antibiotics, cyclosporin A, photochemotherapy (PUVA) etc.

Gram-negative folliculitis

It occurs during long-term treatment with broad-spectrum antibiotics, when the reduction of propionibacteria and other skin saprophytes leads to an overgrowth of gram-negative bacteria (*Klebsiella*, *Enterobacteriaceae*, *E. coli*, *Proteus*).

Rosacea

 For more information see Rosacea.

It appears after the age of 40 on the forehead and cheeks. Erythemas and telangiectasias predominate.

Demodicidosis

Overgrowth of *Demodex folliculorum* as a result of a violation of the microclimate of the skin (poor hygiene and excessive use of cosmetic creams). Follicular bound pustules on the face.

Dermatitis perioralis

It mostly affects women, most often around 30 years of age. Papules to papulopustules with slight scaling in the nasolabial folds, on the chin and around the eyes.

Folliculitis eczematosa barbae

Follicular bound papulopustules, eczematization and scaling in the beard on the upper lip and chin.

Acne necrotica, acne varioliformis

Pyoderma with papules with central necrosis.

Virilizing syndromes.^[1]

Treatment

Acne treatment should begin at the moment of the appearance of the first symptoms (comedones), this is the only way to prevent the development of more severe forms and eventual scarring. Due to the chronicity of the disease, the effect of the treatment is usually apparent after a month at the earliest. The choice of therapy is determined by the severity of the clinical picture, i.e. the number and nature of skin efflorescences, the extent of skin involvement, the duration of the disease and the method of healing. Combinations of local medicinal preparations are preferred - one starts with one preparation and, after adaptation and good tolerance, another is gradually added. Treatment is long-term, maintenance treatment in the remission phase is important. Active cooperation of the patient is essential.^{[1][3][4]}

Principles of treatment

Comedogenic acne

Topical retinoids are the drug of first choice, with azelaic acid or benzoyl peroxide as an alternative.

Papulopustular acne (mild to moderate forms)

The drug of first choice is a combination of benzoyl peroxide with adapalene or clindamycin, an alternative is monotherapy with azelaic acid, benzoyl peroxide or a topical retinoid, or combination of topical erythromycin with isotretinoin or tretinoin.^{[4][5]}

Another recommendation

- regular mechanical cleaning of the skin (approx. 2x a week, after steaming) - removal of comedones to prevent the development of inflammatory lesions;
- do not squeeze, do not scratch;
- do not use products leading to excessive degreasing (soap, washing gel);
- avoid risk factors from the external environment and unsuitable cosmetic products - use non-comedogenic cosmetic products;
- adequate psychotherapeutic approach^{[1][4]}
- a low glycemic index diet and reduced intake of cow's milk^{[6][7][8][9][10][11]}

Local treatment

Retinoids

- tretinoin, adapalene, isotretinoin
- has a keratolytic and comedolytic effect
- they reduce cell adhesion, thereby canceling retention hyperkeratosis
- stimulate the mitotic activity of keratinocytes, due to which closed comedones change into open ones and they are then released
- they dampen keratin production and lead to a thinning of the stratum corneum
- they stimulate the formation of new blood capillaries, thereby improving blood circulation
- they increase transepidermal penetration and thus increase the effectiveness of other substances, for example benzoyl peroxide
- suitable for acne with a more prominent presence of comedones
- the effect usually starts at the end of the 1st month of therapy
- in the 2nd-3rd week of treatment, a temporary worsening may occur due to the acceleration of the inflammatory transformation of existing comedones ("rebound phenomenon")
- they help maintain disease remission
- after adaptation of the skin, it is advisable to potentiate the effect by combining with other external agents -

for example, erythromycin in combination with anti-inflammatory zinc salts

Benzoyl peroxide

- it is mainly antimicrobial, but also keratolytic and comedolytic
- oxygenates the deeper sections of the pilosebaceous unit and thereby reduces the number of anaerobic propionibacteria in the follicle
- does not induce bacterial resistance
- suitable as an initial therapy in the case of significant predominance of inflammatory lesions
- the effect often starts within 2 weeks
- can be combined with local antibiotics or adapalene (tretinoin inactivates it by oxidation)

Antibiotics

- erythromycin, clindamycin
- to reduce propionibacteria
- especially suitable for acne papulopustulosa
- always in the form of breathable vehicles, never in the form of ointments
- the risk of developing resistance with long-term use

Azelaic acid

- comedolytic, antibacterial and anti-inflammatory effect
- normalizes disturbed keratinization in the follicles
- suppresses the growth of bacteria, especially *P. acnes*
- reduces inflammation
- it does not cause bacterial resistance, so it can be used long-term^{[1][3]}

Overall treatment

Antibiotics

- Tetracyclines (doxycycline) and erythromycin
- The disadvantage of tetracyclines is the risk of phototoxic or photoallergic reactions, it is not advisable to apply them during the period of solar exposure

Isotretinoin

- the most effective overall drug
- indicated mainly for acne conglobata, or for milder forms with resistance to other general therapy
- strong sebostatic effect, regulation of keratinization of the follicular mouth, immunomodulating effects
- teratogenic, long elimination half-life
- necessary monitoring of triglycerides, cholesterol and liver tests (before and after treatment)
- side effects - manifestations of hypervitaminosis A (dry skin and mucous membranes, epistaxis, ...)
- cannot be combined with tetracyclines due to the risk of intracranial hypertension

Antiandrogens and hormonal therapy

- can only be used in girls (at least 2 years after menarche) and in women
- for example cyproterone acetate in combination with ethinyl estradiol (contraceptive preparation Diane-35); drospirenone (Yadin), dienogest (Jeanine), chlormadinone acetate (Belara)
 - an adverse effect is an increased risk of thromboembolism
- glucocorticoids to suppress the evening peak of glucocorticoid secretion
- spironolactone - with the necessity of monitoring sodium and potassium levels^[1]

Corrective dermatological and other treatment options

Links

External links

Nevoralová Z.: Nové přístupy v léčbě akné (2013) (<https://www.pediatricpropraxi.cz/pdfs/ped/2013/06/02.pdf>)

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