Türk Pediatri Arşivi
Turkish Archives of Pediatrics

Invited Review

Acne vulgaris

Ertuğrul H. Aydemir

Department of Dermatology, İstanbul University Cerrahpaşa Faculty of Medicine, İstanbul, Turkey

Abstract

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit and it is observed equally in both sexes and nearly all races. It generally begins at puberty, but the healing period is variable. There is no known etiological factor, except genetic tendency. Androgens play a very limited role in some female patients. The effects of cosmetics, foods and drinks are also discussible and too limited.

There are four factors in acne pathogenesis:

a) Increase of the sebum excretion
b) Keratinization of infrainfundibulum
c) Bacterial colonization of the follicle
d) Inflammation

It is mainly observed on the face and back, shoulders and chest. Initial lesions are comedons. Papules, pustules and cysts of severe types follow it. The most important factor in treatment is a very good patient-physician communication. Topical or systemic treatment or both can be used depending on the severity of acne. Benzoyl peroxyde, azelaic acid, AHA's antibiotics, retinoic acid and derivatives are the topical choices. For systemic treatment antibiotics are the most commonly used medicines, but isotretinoine has a very spesific place with the possibility of permanent healing. All kind of treatments need approximately six months for a good result.

Key words: Acne vulgaris, etiology, treatment

"Acne vulgaris" (adolescent acne) is one of the dermatoses which is discussed and interpreted most commonly. It is a chronic inflammatory disease of the pilocebaceous unit and observed equally in both genders (1-3). It usually starts in the adolescence, but its time of ending is variable. Its age of onset may be 18-20 years or it may be delayed until 25-30 years. Sometimes it may start at more advanced ages (1-4). "Acne vulgaris" which does not affect the general health status, which has no vital danger and which appears to be a simple disease may constitute a big and important problem just with its appearance in the present social life in which human communication has reached a top level, because our skin and especially our face is the number one organ for this communication and is very important in terms of body perception. In addition, the adolescence during which acne is observed with the highest rate is an age period in which body perception is at the highest level and appearance can sometimes be everything. At these ages, the severity of present lesion may be perceived as 10-fold, 100-fold or more and may lead to very severe psychological problems including mainly depression. In addition, acne which may lead to persistent scars in the long term is much more important compared to its function and its objective problems and should absolutely be treated.

Although acne is a disease of pilosebaceous unit, it develops in the middle part of the sebaceous follicle channel and not in the sebaceous glands. There are multiple sebaceous glands in the face and scalp, chest and back. In adults, most of the hair follicles in the face cause to predisposition to acne together with sebaceous glands (1-8).

No special gene has been found in acne which is considered a multifactorial and multi-gene disease. Inheritance affects the activity and size of the sebaceous glands. If there is acne scar in both parents, the risk of development in the child increases very much (1-5).

Address for Correspondence: Ertuğrul H. Aydemir, Department of Dermatology, İstanbul University Cerrahpaşa Faculty of Medicine, İstanbul, Turkey.
E-mail: ehaydemir2003@yahoo.com

Received: 21.03.2013 **Accepted:** 28.03.2013

DOI:10.5152/tpa.2014.1943

It is observed less commonly in Asia and in black people and it may reach up to 70-95% in adolescence in Western populations (general frequency 15-90%). Since it is observed very rarely in local populations far from western life style, it is thought that western life style is also considerably effective together with genetic, familial and ethnic factors (1, 4, 6, 8-12).

There is no known serious trigerring factor in the etiology except for partial effects of androgenic hormones which are effective in a limited portion of female patients (especially in accompaniment of polycystic ovary syndrome). No significant change could be found in the blood levels. It is thought that the effect is related with increased receptor sensitivity in acne patients compared to normal individuals and the main triggerring factor is assumed to be this increased sensitivity. In the pre-adolescence period, early acnes which especially begin before the age of 9 years may be a simple sign of adolescence or an indicator of a hormonal problem; one should be careful (1-3, 6, 8, 10-12).

Although the effect of food and stress have been discussed intensively, definite evidence about this could not be demonstrated. The relation between foods and acne has been discussed intensively in the last 50 years. Although the beliefs of patients in this direction are very strong and there were periods during which this theory was important, scientific bases are very weak. 20-25 years after 1950 were the years of food limitations and written diet list years for acne. Fried food, cola, dried fruits, fatty foods were the main culprits. Subsequently, diet was disfavoured for a long time, but in the last 3-4 years, it has come to the forefront in a more procedural way and for limited products. However, there is ultimately no definite evidence and the place of diet is very controversial. Currently, it seems that diet has no place at all (1, 6, 8-12).

Among external factors, cosmetics as trigerring factors have been always blamed. When fat based cosmetics are used frequently and for a long time, they may lead to development of acne or exacerbate present acnes. They are observed mostly on the cheeks and chin (1-5).

In the pathogenesis of acne, four main components have always been mentioned:

a) Increased sebum
b) Keratinization of the middle part of the infindibulum (Infrainfundibulum)
c) Bacterial colonization of the follicle
d) Inflammation of the follicle and its surroundings (1, 3-5, 7-9).

Sebum is like fuel of the inflammation in acne. It is accepted to be involved in the whole pathogenesis of the disease and acne is not observed in its absence. In addition to increase in the amount of sebum, the structure of sebum also shows changes and the main pathology of acne or the prerequisite is increase in sebum. Increase in sebum provides an appropriate setting for growth of bacteriae and indirectly contributes to the inflammatory phase. There is also a change in the production and adherences of the keratinized cells in the follicles and blackheads are formed as a result of combination of these adhered cells and sebum. In time, sebaceous glands become atrophic and undifferentiated epithelial cells replace them (1, 5-9).

The main microorganism which is localized in the follicle and involved in the pathogenesis of acne is *Propionibacterium Acnes*. It grows well at anearobic conditions and uses sebum as food. *Staf. Aureus, P. Orbiculare* and rarely *Demodex Follicularum* are present, but they do not affect the process of inflammation. Inflammation which occurs against growing *P.Acnes* constitutes the inflammatory elements of acne including papule and pustule (2, 3, 5, 13-15).

Acne is localized in regions where sebaceous glands are found intensively including mainly the face, back, chest and shoulders. The initial lesions are blackheads. On the blackheads which are typical and easily recognized, the follicular mouths are open and their tips appear black. Although big and open blackheads look ugly, inflammation does not develop in these spots, but it develops in big blackheads with open or closed tips. Papules with erythema are the first signs of inflammation and pustules follow these. Rarely, cystic acne types in which the sebaceous glands become very large and lead to subcutaneous nodules are observed. These look ugly and are resistant to treatment (1-7).

The most improtant point in treatment of acne is to establish a very good physican-patient collaboration, to listen to the patient with interest, to elucidate the patient, to give adequate information about the disease and to provide maximal treatment compliance by establishing realistic expectations. Again, the erroneous information of the patient including "some foods increase acne and hepatic disorder causes to acne" should be corrected. Make-up should not be limited except avoiding fatty products and it should be kept in mind that make-up may have very positive psychological contributions in women. Treatment has a slow development. The patient should be given a target period of 6 months. It should be emphasized that 80-90% improvement will occur at the end of this period, but it may recur when treatment is discontinued and therefore continuity of a low level treatment is necessary (4, 6, 16-20).

The most important part of treatment is topical treatment. Topical treatment may be used alone or in combination with systemic treatment. In addition, it is also sufficient alone in maintenence treatment. Topical treatment agents include antibiotics, antiseptics, comedolytics and keratinolytics. Non-inflammatory acnes with only comedon or acnes with mild and moderate inflammation may be in this group (5-8). Regular washing may decrease development of acne to a certain extent. Avoiding irritant products or irritation by excessively frequent washing and rubbing and preferring soft cleaners are beneficial. Since antiseptic soaps and solutions can not enter into the follicles, they are not effective on *P.Acnes* and increase the risk of gram negative folliculitis. In topical treatment, the main principle of application independent of the quality of the product used is application of the drugs on the whole face preserving the surroundings of the eyes and the corners of the mouth and nostrils, because all areas where acnes are present or where acne may develop should be

under treatment. The most commonly used treatment agents include benzoyl peroxide, retinoic asids, antibiotics and azelaic asid (3, 4, 6, 8, 9, 16-19).

Topical antibiotics prevent development of inflammation by inhibiting growth of *P. acnes*. They are used alternately with other antibiotics or antiseptics, since resistance to antibiotics may occur. In addition, they also have direct anti-inflammatory effects. They have weak effects on old lesions. The most commonly used ones among these include erythromycine, clindamycine, nadifloxacin and tetracycline (1-2 times a day) (3, 4, 6-9, 16-19).

Topical antiseptics also act in the same way. Resistance to these agenst does not develop and it has been reported that they have similar effects as antibiotics (they generally have slower and weaker action). The most commonly used antiseptics include benzoyl peroxide (the most widely used one), azelaic acid and sodium sulfacetamide. They also have mild comedolytic action. Their use in combination with antibiotics increases both the action and decreases the risk of resistance (3, 4, 6-9, 16-19).

Retinoids are one of the most commonly used drugs in acne. They have very good keratolytic and comedolytic effects. No drug is better than retinoids in treatment of comedon (up to 70% reduction in the number of blackheads in 2 months). They have a very strong action on open and closed blackheads; they provide removal of the old ones and prevent production of new ones. An indirect antibacterial action occurs for *P. acnes* with decrease in stasis and anaerobic setting. They also decrease the number of inflammatory lesions. Growth of *P.Acnes* stops indirectly and inflammation is inhibited. Their use in combination with antibiotics and antiseptics gives a very good result. They cause to irritation in the first 20-30 days, but later the skin develops tolerance and irritation decreases. This period should be explained very well to the patient and discontinuation of treatment with fear of the picture should be prevented. The most commonly used agents in this group include tretinoin and adapalen (3, 8, 17-19).

Alpha hydroxy acids (5-10%) may also be used as supportive products in treatment.
Among classical keratolytics, salicylic acid (2-5%) and resorcin are used with a low rate at the present time (3%). In pregnant women, all topical products including mainly retionids should be discontinued. Only azelaic acid is allowed (3-9, 16-19).

Systemic treatment in acne is indicated only in moderate and severe types of acne (above the mild acne class which remains in the limit of comedonal disease or less than 20 papules) in which topical treatment can not be efficient. Systemic treatment consists of antibiotics, hormones, isoretinoine and very rarely corticosteroids. Principally, the priority of antibiotic and their character of being the most commonly used drug (92%) have not changed currently, but the rates might have changed a little with wide and more encouraged use of especially isoretinoine (3-9, 17-20).

The actual action of systemic antibiotics is inhibition of growth of *P. acnes*. They also indirectly prevent inflammation caused by *P. acnes*. however, they also have direct anti-inflammatory action. 20% improvement may be expected in 2 months, 60% improvement may be expected in 4 months and 80% improvement may be expected in 6 months.

Among systemic antibiotics, tetracyclines are the most commonly preferred ones because of their efficiency and few side effects. Recently, doxycycline has come to the fore. Other commonly used and efficient antibiotics include trimetoprime and erythromycine. Many others have been tried with different success rates. While systemic antibiotic treatment could be continued for 3-6 months until recently, it is thought that systemic treatment sould not be used longer than 1-2 months in recent years. It is reccomended that topical antibiotics should not be used when a systemic antibiotic is used to prevent development of resistance and antibiotics should not be used alone in treatment (3-9, 17-22).

Hormonal therapies decrease androgen levels in the circulation and tissues. The cells of the pilosebaceous unit which metabolize androgen including follicular keratinocytes and sebocytes and the androgenic effects on them are inhibited and a decrease of 12.5-65% occurs in sebum secretion. Antiandrogens are an option only for female patients and their use is limited. They may be preferred when hyperandrogenism (polycystic ovary) is present or when there is no response to classical treatment (3-10, 23-25).

Retinoids (isotretinoine) is the only drug which acts on the four main factors in acne and is considered a revolution in treatment of acne. While is used commonly especially in problematic types like classical acnes, it may also be currently used in persistent moderate classical acnes which lead to psychological problems. They decrease production of sebum, inactivate sebaceous glands with active inflammation and reduce them. They change the structure of lipids. They indirectly reduce the number of bacteriae by decreasing the amount of sebum. In addition, they prevent development of comedon in two ways by regulating keratinization. If they are used at an appropriate dose and for an appropriate time, they provide permanent action with a rate of 80-90% without recurrence. On the other hand, they may increase liver enzymes, triglyceride and cholesterol levels. In addition to other rare side effects including tendency to depression and problems in the bones, their most important side effect is teratogenic action when used during pregnancy. Therefore, one should be very careful in female patients. Both retinoids and antiandrogens should be definetly prescribed by dermatologists (3-10, 18-20, 26, 27).

Conclusively, acne is an important disease which can be treated with meticulous approach and in close collaboration with the patient.

Peer-review: This manuscript was prepared by the invitation of the Editorial Board and its scientific evaluation was carried out by the Editorial Board.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The author declared that this text has received no financial support.

References

1. Aydemir EH. Akne vulgaris etyopatojenez ve patolojisi. Çukurova Tıp Günleri. Adana, 2002.
2. Gülekon A. Akne etyopatojenezi. II. Vakıf Gureba Tıp Kongresi. İstanbul, 1995.
3. James WD, Berger T, Elston DM. Çev ed: Aydemir EH. Andrew's deri hastalıkları. İstanbul: Nobel Tıp Kitabevi 2008: 231-50.
4. Simpson NB, Cunliff WJ. Disorders of the sebaceous glands. In: Burns T (ed). Textbook of dermatology. 7. Baskı. Oxford: Blackwell Science 2004; 3: 43-1.
5. Plewig G, Wolff HH. Braun Falco's Dermatology. Berlin: Springer 2000: 1053-82.
6. Thiboutot DM. Acne. An overview of clinical research findings. Dermatol Clin 1997; 15: 97-109.
7. Thiboutot DM. Acne and rosacea. New and emerging therapies. Dermatol Clin 2000; 18: 63-71.
8. Smith EV, Grindlay DJC, Williams HC. What's new in acne? An analysis of systematic reviews published in 2009-2010. Clin Exp Dermatol 2011; 36: 119-23.
9. Kurokawa IF, Danby W, Ju Q, et al. New developments in our understanding of acne pathogenesis and treatment. Exp Dermatol 2009; 18: 821-32.
10. Arora MK, Yadav A, Saini V. Role of hormones in acne vulgaris. Clin Biochem 2011; 44: 1035-40.
11. Danby FW. Nutrition and acne. Clin Dermatol 2010; 28: 598-604.
12. Davidovici BB, Wolf R. The role of diet in acne: facts and controversies. Clin Dermatol 2010; 28: 12-6.
13. Shaheen B, Gonzalez M. A microbial aetiology of acne: what is the evidence? BJD 2011; 165: 474-85.
14. Kalaycıyan A, Bahar H, Oğuz O, Torun MM, Aydemir EH. Akne vulgarisin şiddeti üzerine bakterilerin etkisi. T Klin J Dermatol 2001; 11: 146-9.
15. Polat E, Aygün G, Ergin R, ve ark. Akne vulgaris patolojisinde demodex folliculorum ve P.acnes'in rolü. Türkiye Parazitoloji Dergisi 2003; 27: 148-51.
16. Sykes N, Webster GF. Acne. Drugs 1994; 48: 59-70.
17. Ditre CM, WhitneyKM. Management strategies for acne vulgaris. Clin Cosmet Investig Dermatol 2011; 4: 41-53.
18. Cunliffe W. Acne vulgaris. In: Lebwohl M, Heymann WR. Treatment of Skin Disease'de Yaz. London 2002: 6-14.
19. Cunliff W, Seukeran. Acne. In: Katsambas AD, Lotti TM. European handbook of dermatologic treatments. Berlin: Springer 1999: 3-10.
20. Aydemir EH. Aknede sistemik tedavi yaklaşımları. Ankara: 16. Prof. Dr. A.Lütfü Tat Simpozyumu, 2003.
21. Karaduman A. Aknede sistemik antibiyotikler ve bakteriyel direnç. Adana: II. Çukurova Dermatoloji Günleri 1998: 37-43.
22. Leyden JL. Current issues in antimicrobial therapy for the treatment of acne. JEADV 2001: 51-5.
23. Show JC. Hormonal therapy in dermatology. Dermatol Clin 2001; 19: 169-78.
24. Thiboutot DM. Endocrinological evaluation and hormonal therapy for women with difficult acne. JEADV 2001: 57-61.
25. Tunalı Ş, Bülbül E. Aknede antiandrojen tedavi. II.Çukurova Dermatoloji Günleri. Adana, 1998: 61-7.
26. Giovanna JD. Systemic retinoid therapy. Dermatol Clin 2001; 19: 161-7.
27. Katsambas A. Oral isotretinoin in acne, only in severe cases? Regional meeting medical education in dermatology. Rhodes 2001.