

# 2005 CE Series - Lesson Eight

## Acne Vulgaris and Its Treatment

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### Goals and Objectives

**Goals:** To provide the pharmacist with information regarding acne vulgaris and its treatment.

**Objectives:** After completing this article, the pharmacist should be able to:

1. Discuss the epidemiology of acne vulgaris
2. Describe the major clinical features of acne vulgaris
3. Discuss the main products involved in the topical treatment of acne vulgaris
4. Discuss the drugs used systemically to treat acne vulgaris
5. Counsel patients regarding all aspects of acne vulgaris therapy

Acne is an inflammatory disease of the skin with the formation of an eruption of papules or pustules. The most common form is acne vulgaris, which is chronic acne that usually occurs during adolescence with comedones, nodules, papules and pustules on the face, neck and upper part of the trunk.

Acne vulgaris is the most common skin disorder of the second and third decades of life, affecting more than 75 percent of individuals between 12 and 25 years of age. It is not life-threatening, but its victims suffer psychological problems and physical problems which usually require some form of therapeutic intervention.

### Epidemiology

Despite its prevalence, there is not much information available concerning acne vulgaris based on scientific inquiry. Numerous myths and unsubstantiated theories concerning foods, cleansing techniques, and treatments persisted for many years. Factual information concerning acne vulgaris has only been gathered for 50 years.

The exact physiological mechanism that initiates the various changes involved with the onset of puberty is unknown, but it appears to be associated with the release of gonadotropic hormone from the anterior pituitary which results in androgens and estrogen production and/or secretion. These hormones are responsible for the secondary sex characteristics and many of the cutaneous disorders associated with adolescence and the onset of puberty.

Acne may be present at birth, but is most commonly associated with puberty. In males, where it occurs the same as in females, its peak occurs between the ages of 17 and 19, while in females, the greatest time is between 15 and 17 years of age. Although the severity of acne usually declines during the early years of the second decade, it may be very active in some patients during their 30's and 40's. Females tend to develop acne vulgaris at an earlier age and to have the disorder longer than males. Males appear to have a more complex form of acne vulgaris. Genetic factors may play a role in the more complex form of the disease.

It is possible that stress, lack of sleep, and menses in the female result in increased sebum (mixture of triglycerides, wax esters, and sterol esters) formation, which eventually causes the inflammatory process. Each of these events can alter hormone secretion which could result in the initiation of the processes associated with acne vulgaris.

Finally, ingestion of certain foods and drugs can cause acneiform eruptions. Halogens, especially an excess of iodide in seafood, salt, and health foods, can worsen acne. Chocolate has not been found to have a significant effect. High-dose corticosteroids can cause a pustular, monotonous form of acne, especially on the trunk. Acne is more common in depressed patients who are on lithium therapy, as well as that seen in epileptics who are taking phenytoin or phenobarbital.

### **Pathogenesis**

The formation of lesions associated with acne vulgaris is related to the secretion of androgen. Androgens appear to cause hypertrophy of the sebaceous gland and an increased production of sebum associated with this disorder.

The process of keratinization is also altered which results in an obstruction in the normal flow of sebum onto the skin surface. Comedones are formed and may be either open comedones (blackheads) or closed comedones (whiteheads). The blackheads cause few problems, but the whiteheads continue the previously described process. Eventually, sebum spills onto the surrounding dermis and the inflammatory process is initiated. This occurs primarily with the presence of trapped bacteria. The bacteria, *Propionibacterium acnes*, is a primary culprit in acne vulgaris and produces substances which contribute to the inflammatory process. Immune response may also be involved as individuals with acne vulgaris have a much higher antibody titer against *P. acnes*.

### **Clinical Features**

Typically, acne vulgaris is recognized by the comedones which occur. In the mild form, it is limited to blackheads and whiteheads. As the disease becomes more complex, papules, nodules and pustules may develop. The predominate sites of acne are the face, chest, back and shoulders. The disease is often more severe in the winter and less active during the warm months. As the lesions resolve, they are often considered to be permanent scars, but usually gradually subside as the overall condition is controlled.

In severe pustular forms of acne, the scars may appear as punched out pits and remain permanently after the disease is under control.

### **General Treatment**

The treatment of acne vulgaris can often be difficult because it is a chronic condition that requires individualized therapy to achieve any meaningful results. In the last two decades, there have been

advances in treatment that have been beneficial. For many years, the use of ineffective treatment regimens, a lack of concern for the psychological and physical trauma encountered with severe forms of the disease, and the many myths surrounding its etiology and therapy impeded the development of new and beneficial treatment programs.

Acne vulgaris is a treatable disease. The patient must comply and understand the entire treatment program. Most of the therapy is prophylactic. Therefore, results may not be achieved for several months. Once control is achieved, then a maintenance plan must be adhered to as long as the tendency to acne vulgaris persists.

General skin care is also important. Appropriately cleansing the skin with soap and water can remove excess oil. However, there is no evidence that excessive cleansing offers therapeutic benefit and, in some instances, may cause problems. Astringents are of limited value, but are easy to use and, with their alcohol base, make the face feel cool. Cosmetic use should be limited, but, if used, should be removed with soap and water.

### **Topical Drug Therapy**

Appropriate topical therapy is very important to the successful management of acne vulgaris. For many years, salicylic acid, sulfur and resorcinol were the primary topical substances used to treat acne vulgaris. Although these dry and exfoliating agents cause peeling and drying, remove oils from the skin surface and suppress lesions to a limited degree, they do not prevent new lesions. These agents may be somewhat useful in mild acne vulgaris, but are not the topical agents of choice.

The agent most often used for topical therapy is benzoyl peroxide. It is safe and effective for acne vulgaris and the agent found in most nonprescription products. It is an organic peroxide which is easily incorporated into vehicles used for base formulas that are used in acne vulgaris therapy.

The primary action of benzoyl peroxide is to reduce the follicular microflora, especially *P. acnes*.

Benzoyl peroxide is active against a wide variety of organisms. It is particularly effective in reducing inflammatory lesions, free fatty acids, and *P. acnes* in patients with acne vulgaris.

Although its exact mechanism of action is not known, benzoyl peroxide slowly releases free oxygen which interacts with sulfhydryl compounds and is a strong bactericidal agent. Benzoyl peroxide appears to enhance blood flow to the skin, increases the sebum excretion rate, and is comedolytic. All of these factors enhance its usefulness as a treatment for acne vulgaris.

Benzoyl peroxide can cause transient irritation when applied to the skin which is not abnormal in the initial stages of using the agent. However, in some individuals, significant irritation, contact dermatitis, and/or allergic eczema can occur. Although these are not common, it often warrants a reevaluation of the therapeutic program. Benzoyl peroxide is absorbed by the skin, converted to benzoic acid and excreted. Complete hematologic and urinalysis evaluations have shown no evidence of systemic effects.

Vitamin A was administered orally for many years for the treatment of acne vulgaris.

Unfortunately, the dose required to reduce hyperkeratosis was often in the toxic range. However, during the past decade, topical vitamin A has been used with excellent results. It causes decreased formation of comedones, an expulsion of existent comedones, a reduction of inflammatory lesions, and an increased ease of penetration for benzoyl peroxide. Unfortunately, it is potentially

irritating and should be used properly in the available 0.025% - 0.1% concentrations and dosage forms. A conservative approach to therapy (i.e., alternate day) should be used in the beginning.

The combination of benzoyl peroxide and vitamin A has been used with success and usually results in an increased therapeutic effect and a reduction of side effects.

Tazarotene and adapalene are retinoid compounds that are similar to vitamin A. These compounds are used topically to treat acne. Their exact mechanism of action is not completely understood, but these drugs appear to bind to specific retinoic acid receptors in the nucleus of the acne lesions. Adverse effects include skin irritations (e.g., itching, redness, burning).

Topical antibiotics are used for inflammatory acne. These drugs do not destroy comedones. Antibiotics exert their effects primarily by their antibacterial activity against *P. acnes*. Topical antibiotics are usually applied twice a day to skin after washing with soap and water. A response to topical antibiotics may be more rapid than with other therapies. Improvement may be seen within 2 to 3 weeks, but maximum results often are not seen for several months. Erythema and stinging are the most common adverse effects. This is usually associated with the vehicle used. Antibiotics used include clindamycin, erythromycin, and some tetracyclines.

In the past, topical therapy with ultraviolet light was used. However, this peeling technique is no longer advised, since carcinogenesis is associated with ultraviolet light exposure. Cryotherapy is useful to produce peeling and reduce inflammation. Another mechanism is to use intralesional steroid injections, but this technique should only be performed by someone who is skilled.

### **Antibiotic Therapy**

Antibiotics are used both systemically and topically in the treatment of acne vulgaris. They suppress *P. acnes* and inhibit bacterial lipases which result in a reduction in the concentration of free fatty acids. Broad spectrum antibiotics, such as tetracycline and its derivatives, have been valuable in the treatment of the inflammatory pustules and nodules of acne vulgaris.

Tetracycline is most frequently prescribed and is effective, inexpensive, and, generally, free of side effects. The initial dose is usually 1,000 milligrams daily for a month. Then, the dosage is gradually reduced to 250 milligrams daily or every other day. A minimum of one month of therapy is required before any beneficial effects can be detected because many weeks of therapy are required to achieve an effective level of tetracycline in the skin.

Tetracycline is incompletely absorbed from the GI tract and absorption is impaired by food as well as aluminum hydroxide gel, iron supplements, milk and other sources of bi- and trivalent cations. Therefore, patients should be counseled to take this medication on an empty stomach (i.e., one hour before or two hours after meals). Low dosage tetracycline therapy can be continued for months without many side effects. This major problem encountered is vaginal moniliasis in female patients. GI tract symptoms, such as nausea or diarrhea, occur infrequently.

Patients should be cautioned not to take outdated tetracycline products that are remaining or retained after therapy because they may cause serious side effects.

Minocycline is a tetracycline derivative which has the advantage of requiring fewer doses and a higher affinity for sebaceous areas. However, it is more expensive than tetracycline.

Erythromycin is inexpensive and has been effective and safe in the treatment of acne vulgaris. As with tetracycline, low doses of erythromycin, such as 250 milligrams twice daily are usually used.

Clindamycin and sulfamethoxazole/trimethoprim have also been used, but each has limitations (e.g., adverse effects) that result in more limited use.

Although few side effects occur, complete baseline blood counts as well as hepatic and renal function screening studies should be done at least every year, when using long-term antibiotic therapy.

### **Isotretinoin**

Oral isotretinoin, a vitamin A derivative, is now a treatment of choice for severe, recalcitrant, nodulocystic acne vulgaris. It is the only acne drug that works against all components of acne genesis. It is not only active against *P. acnes*, but it impedes comedogenesis and significantly inhibits sebum production. Remarkable, this drug is able to prevent scarring and also to improve existing scars. It produces lasting remissions. A dosage of 0.5 to 1 mg/kg/day (1 kilogram = 2.2 pounds) for 16 weeks improves response and often makes a second treatment course unnecessary. Less aggressive dosages usually yield less-than-optimal results.

Isotretinoin is not without side effects. The most formidable is its teratogenicity. Pregnancy must be excluded before initiation of treatment. All women of childbearing potential who use the drug must use an adequate birth control method (i.e., oral contraceptive products). Since there can be severe CNS defects seen in offspring of women who have taken the drug during pregnancy, abortion is strongly recommended should pregnancy occur during treatment.

Elevated triglyceride and liver enzyme levels are often seen in patients taking isotretinoin. Pretreatment multichannel biochemical analysis and lipid profile are needed to screen patients with preexisting laboratory abnormalities. Patients who complain of headaches require fundoscopic examination to rule out pseudo-tumor cerebri. As this can occur with tetracycline therapy as well, it is best not to give both drugs simultaneously.

Almost all patients on isotretinoin therapy have dry mucous membranes that can cause problems such as chapped lips, blepharitis, nosebleed, vaginal dryness and urethritis. Local care with petrolatum and lubricants allows most patients to continue therapy.

In general, isotretinoin should be reserved for patients with stubborn, severe acne vulgaris that does not respond to routine therapy.

### **Other Drug Therapy**

A variety of other drugs have been used to treat acne vulgaris. In some instances, severe acne vulgaris requires brief treatment with systemic corticosteroid therapy. Paradoxically, dexamethasone and prednisone, drugs that clearly can aggravate acne when used in moderate doses, can benefit acne when used briefly in low doses. They aid treatment in both men and women by reducing the inflammatory component.

In many women, stubborn acne vulgaris may reflect endocrine dysfunction. Excess androgens stimulate the sebaceous gland, whereas estrogens do just the reverse. The prescribing of oral contraceptives is often an easy first step. However, in general, high-estrogen/low progesterone agents are required to show any benefit. Since side effects are greater with high-estrogen products, this therapy is not ideal. Some patients even have flare-ups because of the progesterone component of birth control pills.

### **Conclusions**

Untreated acne vulgaris will often persist throughout adulthood and may result in scarring. The many new and effective treatment programs available often provide beneficial results, especially if the patient complies with the program and is properly counseled regarding the appropriate use of the drugs employed and the overall benefits of the entire treatment program.

The pharmacist is frequently the health professional who provides the counseling and support for treatment and must play an active role.

**Table 1**  
**Examples of Medications Used to Treat Acne Vulgaris**

<b>Medication</b>	<b>Major Ingredient</b>
Clearasil	Benzoyl Peroxide
Oxy	Benzoyl Peroxide
Acnotex	Sulfur
Acnomel	Sulfur
Komed	Salicylic Acid
RA Lotion	Resorcinol
Minocin	Minocycline
Cleocin	Clindamycin
Sumycin	Tetracycline
E.E.S.	Erythromycin
Decadron	Dexamethasone
Orasone	Prednisone
Accutane	Isotretinoin
Avage	Tazarotene
Differin	Adaptene

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