ACNE

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PREVALENCE
About 17 million Americans have acne. It is the most common skin disease treated by physicians. Acne can appear at any age, although there are peaks of incidence in adolescence and again for females near the time of menopause. Acne and adolescence are so closely associated that 80–90% of all teenagers have at least some lesions at any given time.

In adolescence, acne affects both males and females. Boys tend to have more lesions and more severe disease than do girls. This is probably due to the causal association with androgen (testosterone) levels. In adulthood, acne is more common in women, particularly the week or 2 before menses and at the onset of menopause. In menstruating females, the occurrence of lesions prior to menses is related to the increase in progesterone levels after ovulation and just before menses. Progesterone has androgenic effects and therefore causes these increases in acne lesions. The occurrence in menopausal females is also related to relative androgen predominance in the face of declining estrogen levels seen with menopause. Neonates (just-born babies) can present with acne because of the intra-uterine hormonal stimulation from maternal hormones.

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ESTIMATING SEVERITY OF DISEASE
Unfortunately, the severity of acne is often overlooked or minimized by physicians. Conversely, severity is often overestimated by patients, especially adolescents, due to the severe social stigma that can develop as the result of even a few mild or moderate lesions. Since acne most commonly involves the face, lesions are readily obvious in social settings. Individuals with deep inflammatory nodules and cysts may be scarred for life in more than one way. Studies have shown that persons who have moderate to severe acne in youth frequently fail to realize their full potential in finding jobs or choosing careers suitable to their actual abilities.

The most common measurement tool for acne is a grading system which classifies according to the severity of lesions in grades 1 through 4, as follows:

Grade 1: mild acne, comedones present, minimal to no inflammation;
Grade 2: moderate acne, some inflammation present, some papules and pustules present;
Grade 3: moderately severe acne, larger nodules and pustules with inflammation;
Grade 4: severe acne, large nodules and cysts, scarring.

This system considers the progression of severity from slightly visible comedones to inflammatory lesions to multiple severe pustular and cystic lesions.

Another system for grading acne divides the face into regions and then counts the number of lesions. The lesion count can further be divided by type into comedones, inflammatory lesions, and nodular and cystic lesions. This is quite time-consuming and probably more useful in research studies than in a clinical setting.
Mild or comedonal acne consists of comedones (blackheads and whiteheads) only and is non-inflammatory. Inflammatory acne consists of both comedones and a substantial number of inflammatory lesions (pustules and papules). Inflammatory lesions can leave permanent scars. A mixture of both inflammatory and non-inflammatory acne exhibits all types of lesions including severe inflammatory lesions (markedly reddened pustules) and possibly cystic lesions (lesions more than 0.5 cm in diameter with a soft top that are losing their inflammation). It is most common to have a mixture of lesions at any one time. Treatment is chosen based on severity of disease, so this estimation is important.

**ACNE CAUSATION AND PROGRESSION**

**The Pilosebaceous Unit**

The basic skin structure most commonly affected by acne is the pilosebaceous unit, comprising the sebaceous gland, vellus hair, and pore (duct).

The function of the sebaceous gland is to produce sebum, an oily or lipid-based substance. It was once thought that sebum had no particular function; however, recent research has shown that sebum transports the antioxidant vitamin E to the skin’s surface. The pore is the opening that carries sebum to the epidermal surface and is lined with epidermal cells.

The number of pilosebaceous units that appear on the face, upper neck, and chest is 9 times the number found elsewhere on the body. The pilosebaceous unit is under stimulation at birth from maternal hormones, atrophies (becomes smaller and less active) during childhood, and then re-emerges during adolescence, again due to hormonal stimulation. Hormonal stimulation can occur also during menopause.

**Causation**

The primary cause of acne is obstruction of the pilosebaceous unit. Hormones, sebum, abnormal keratinization, and bacteria contribute to the obstruction of the pilosebaceous unit in the following ways:

- Higher androgen levels cause the overproduction of sebum, which can occur during direct elevation of androgens (during both male and female puberty) or relatively higher androgen levels compared to estrogen levels (during the premenstrual period, during female menopause).

- Increased sebum production and desquamation (flaking) of epithelial-lining cells contribute to obstruction of the pore and lead to formation of the microcomedone. The microcomedone is very small and cannot be seen. Alterations in sebum lipids interfere with normal sebocyte differentiation, thus affecting sebum production. Ratios of saturated to unsaturated fatty acids change. Squalene is one of the most common lipids produced by the skin. During an inflammatory process, such as acne, squalene can be oxidized by free radicals and form squalene peroxide, which is particularly pro-inflammatory.

- The bacterial organism involved in the pathogenesis (cause) of acne is P. acnes (Propionibacterium acnes). P. acnes is a normal inhabitant of skin. However, the increased amount of sebum and obstruction of the pore provide an environment conducive to proliferation of P. acnes. As P. acnes increases in number, it uses sebum as a nutritive source, causing sebum conversion to free fatty acids, which are very irritating. The immune system is activated by both the free fatty acids and the large amounts of P. acnes, and inflammation thus ensues.

- Abnormal keratinization causes overcornification of skin, further contributing to pore obstruction and inflammation.

**Progression**

Microcomedones increase in size to form comedones. The comedone, which may be open or closed, is the essential focus lesion in acne. Open comedones (blackheads), have an enlarged pore due to the
material within, are open to the surface, and have a black color due to melanin pigment in the cells that were shed and decomposed. Closed comedones (whiteheads) have a layer of epithelial cells that covers the pore and a tiny, microscopic opening to the skin surface, which is the pore of the pilosebaceous unit.

In the closed microcomedone or comedone, the epithelial duct wall ruptures and the acne lesion progresses from comedone to pustule or papule. The term “cyst” is a misnomer and refers to what actually is a large, inflamed, pus-filled nodule greater than 0.5 cm in diameter in which the cell wall is comprised of inflammatory cells and scar tissue.

A substantial number of severely inflamed pustules or papules leading to “cyst” development can be termed nodular cystic acne. The body will repair severe inflammation with scarring. Scars are permanent, and will persist throughout life.

Hormonal influences are very important in acne development and progression. Acne actually begins to develop at age 8 or 9, when adrenarche occurs. Adrenarche is the activation of the adrenal gland, occurring before puberty and associated with increased DHEA levels. DHEA is one of the hormones produced by the adrenal gland. Some of the DHEA is converted to androgens by a metabolic pathway, leading to microcomedone development. With puberty in the female, DHEA is the primary source of androgens, since some of it is converted to androgens. With female puberty, both estrogen and progesterone increase as menarche (the beginning of menses) occurs and the ovaries begin to produce female hormones. Some of this ovarian estrogen is converted to androgens as a byproduct.

Progestrone itself has androgenic effects. The increased severity of acne in male adolescents is due to their higher androgen secretion compared to females. As puberty passes, hormonal levels decrease and acne resolves. However, in adult women progestrone increases in the 2 weeks before menses, causing effects that are more androgenic and leading to the spike in acne lesions during this time. With female menopause, estrogen and progesterone levels decrease as the ovaries fail (stop hormone production). At this point, without the overriding effect of high estrogen and progesterone levels, DHEA from the adrenals again becomes important. The DHEA, which is androgenic because of its conversion to testosterone, causes the increase in acne seen with female menopause.

OTHER CAUSES OF ACNE

Birth Control

For adult females taking oral contraceptives (birth control pills) can cause acne. The choice of which type of birth control medicine to take is most important in determining its effect on acne. Most oral contraceptives contain both estrogens and progestins (synthetic progesterone). Those containing progestins that are more androgenic can contribute to acne. Pills containing relatively more estrogen and a progestin that is less androgenic do not contribute to acne development and are sometimes used to treat acne. The “progesterone only” method of birth control, either by pill or by injection, can contribute to acne progression via androgenic effects.

Other Medications

Other medicines that can be related to the development of acne include lithium, cortisone-type medicines, and anabolic (testosterone-type or androgenic) steroids. Some medicines used to treat cancer, such as epidermal growth factor receptor inhibitors, can cause an acniform (acne-like) rash. Although the rash looks like typical acne, closer inspection reveals the signature lesion of acne, the comedone, is absent.

Endocrine Disorders

Another rare but possible cause of acne is endocrine disorders of various types, which lead to overproduction of androgenic substances.

Environmental Factors

Environmental factors occasionally play a role in acne.
Young people employed in places where they come into contact with grease, such as auto repair shops or fast-food restaurants, may experience a worsening of acne.

Stress
At the present time, we are unsure if stress can exacerbate acne or if the acne itself causes the increased stress. An increase in lesion number has been noted and may relate to relative increases in cortisol, which is androgenic, with stress.

PATIENT EDUCATION FACTS AND MYTHS
There are many public misconceptions about acne. Some important facts for general patient education are listed here:

- Acne is not caused by dirty skin. Washing the skin more, or more vigorously, is not warranted and will not be helpful, and injury induced by vigorous washing may cause more inflammation and induce progression of lesions. The visible black part of the blackhead is not dirt—it is melanin and oxidized material, and cannot be removed by washing.

- Dietary factors sometimes may relate to acne. The Western diet, which encourages insulin resistance and tends toward obesity, is high in sugars and simple carbohydrates. This type of diet predisposes to acne development and worsens existing acne. Insulin resistance stimulates androgen receptors which then become more sensitive to androgens, thus contributing to acne development.

- Therapy succeeds by preventing the formation of new acne lesions. Therefore, it is important to treat all acne-prone skin, and not just single acne lesions, with topical agents.

- Any practice that further traumatizes (injures) acne lesions contributes to more inflammation and progression of disease. This includes picking at lesions and wearing athletic gear over lesions.

- Use of pomade on hair may plug the pilosebaceous unit if pomade comes into contact with the skin, leading to acne development. This can be prevented by being careful to avoid facial skin when placing these products on the hair.

- Cosmetics, including makeup and moisturizers, that contain large amounts of oil can worsen acne.

- Acne is related to hormonal factors, as explained above. Young women may experience flare-ups just prior to menses. Because of the hormonal influences occurring during adolescence, it is an acne-prone period for both young men and women. The perimenopausal period is another acne-prone time for women.

- The treatment of acne requires some time. It will not go away overnight but requires persistence and consistent, effective treatment. Usually, weeks are required with any treatment before improvement is seen. When treatment is stopped prematurely, the acne returns.

- Deep scars are permanent. The object of continuing treatment and being consistent with treatment is to avoid progression to severe lesions and scarring. Scar treatment has become multimodal and now includes chemical peels, dermabrasion, ablative and non-ablative laser resurfacing, dermal fillers, and excision. These techniques also may be combined with treatment of the aging face.

TREATMENT
Treatments for acne include counteracting androgens, decreasing inflammation, decreasing sebum production, preventing follicular plugging, and reducing P. acnes proliferation.

Non-inflammatory Acne
Non-inflammatory acne and comedones may be treated with a single agent applied topically. Topical therapy refers to putting a treatment on top of the skin. There are a variety of single agents available, which may have
A variety of effects that include antibacterial activity, mild anti-inflammatory activity, lipid-dissolving cleansing action to remove lipid plugs from pores, and desquamative activity to remove dead epithelial cells on the skin and pore surfaces, and encourage epithelial cell turnover.

Two or more agents may be required for non-inflammatory acne that is not responsive to a single agent, or for inflammatory acne. If two or more different agents are chosen, they should have different mechanisms of action, so as to potentiate each other.

Common topical therapies include benzoyl peroxide, topical antibiotics (clindamycin topical or erythromycin topical), topical retinoids (tretinoin, adapalene, or tazarotene), azelaic acid, salicylic acid, milk and fruit acids (also called alpha hydroxy acids, or AHAs, which include glycolic acid, lactic acid, malic acid, citric acid, and mixed fruit acids), and products decreasing inflammation.

Sometimes the extraction (removal) of comedones with a small instrument, called a comedone extractor, may be done in the doctor’s office. Some medical literature terms this surgery, although it is not surgery in the traditional sense and cannot be used to treat scarring. Removal of comedone contents with a comedone extractor in the doctor's office is acceptable and helpful. It differs greatly from “picking at” lesions at home, which causes more inflammation and is harmful.

Severe Inflammatory Acne

Topical treatment alone will not be effective in treating severe inflammatory acne, because it cannot penetrate deeply enough through the skin's surface to treat the most severely inflamed nodules and cysts. Severe acne requires systemic treatment (medicine taken orally). Systemic therapies cause distribution of the drug throughout the entire body. Common systemic therapies include oral antibiotics (erythromycin and the tetracyclines, including tetracycline, minocycline, and doxycycline) and hormonal therapy (oral contraceptives). Cystic lesions also may be injected with steroids to control inflammation, while severe nodular cystic acne usually requires Accutane (isotretinoin, or 13-cis-retinoic acid). Accutane is a pill with significant potential side effects, usually reserved for the most severe acne cases. It causes drying of the skin, eyes, mouth, and mucus membranes in all people, as well as desquamation of skin. Because Accutane is teratogenic (tumor-causing) and will cause malformations in 60% of exposed fetuses, doctors will never place a female patient on Accutane unless there is reliable protection against pregnancy. Accutane also requires blood-test monitoring.

Hormonal therapy with non-androgenic oral contraceptives may be used to combat severe inflammatory acne. If not effective, treatment with spironolactone, an anti-androgen, may be tried.

Scarring

Scars are often thought to be permanent, persist into adulthood, and be treatable only with a procedure. However, superficial scarring can be improved with topical products that have resurfacing activity.

Each of these therapies, whether topical or systemic, has a list of advantages, disadvantages, potential toxicities, and contraindications depending upon its own unique properties. Most of them may be used in combination, although Accutane is used alone as monotherapy. The topical agents may be used singly for comedonal non-inflammatory acne, but if this type of acne is highly inflammatory or non-responsive to therapy with a single topical agent, then therapy with more than one agent is usually required.

PRODUCT RECOMMENDATIONS

iS CLINICAL® products helpful in treating acne include:

ACTIVE SERUM™, PRO-HEAL® SERUM ADVANCE®, HYDRA-COOL® SERUM, CLEANSING COMPLEX, WHITE LIGHTENING™ SERUM, WHITE LIGHTENING™ COMPLEX.

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iS products helpful in treating acne include: EXTREME PROTECT SPF 30, ECLIPSE SPF 50+, EXFOLIATING ENZYME TREATMENT.

REFERENCES


