



## 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, it 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, it is more common in women particularly the week or two 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 (testosterone) effects and causes the increase in acne lesions during this time. The occurrence in menopausal females is also related to relative androgen (testosterone) predominance in the face of declining estrogen levels seen with menopause. Neonates (just-born babies) can present with acne as because of the intra-uterine hormonal stimulation from maternal hormones.

People with acne, especially teenagers, tend to self-medicate. Each year in the US over \$100 million is spent on over-the-counter products to treat acne.

## Estimating Severity of Disease

Unfortunately, the severity of acne is often overlooked or minimized by physicians. Conversely, severity is often over-estimated by patients, especially adolescents, due to the severe social stigmata that can developed 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 had moderate to severe acne in youth frequently fail to realize their full potential in finding jobs or choosing careers suitable to their actual potential.

One 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 is probably more useful in research studies than in the clinical setting.

In clinical settings, it is probably more useful to classify the severity of acne according to the general severity of lesions. This system must consider the progression of lesions from slightly visible comedone, to inflammatory lesions, to multiple severe pustular and cystic lesions.

As a matter of definition, mild or comedonal acne would involve comedones (blackheads and whiteheads) only and be non-inflammatory. Inflammatory acne has both comedones and a substantial number of inflammatory lesions of pustules and papules. Inflammatory lesions can leave permanent scars. A mixture of both inflammatory and non-inflammatory acne has all types of lesions including severe inflammatory lesions (markedly reddened pustules) and possibly cystic lesions (lesions over 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, which is comprised of the sebaceous gland, vellus hair, and 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 duct (or pore) is the opening that carries the sebum to the epidermal surface and is lined with epidermal cells. Vellus hairs are rudimentary hairs found on all parts of the body except the palms and soles.

The number of pilosebaceous units that appear on the face, upper neck and chest, is nine 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.

*Causation* – The primary cause of acne is obstruction of the pilosebaceous unit. The triad of hormones, sebum, and bacteria contributes to the obstruction of the pilosebaceous unit in the following ways:

- Higher androgen (male hormone or testosterone) levels cause the over-production 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 pre-menstrual period, during female menopause).
- The two factors of increased sebum production and desquamation of epithelial lining cells contribute to obstruction of the duct and lead to formation of the microcomedone. The microcomedone is very small and cannot be seen.
- The bacterial organism involved in the pathogenesis (cause) of acne is *Propionibacterium acnes* (*P. acnes*). *Propionibacterium acnes* is a normal inhabitant of skin. However, the increased amount of sebum and obstruction of the duct 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.

*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 the duct, 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 duct 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 actually a misnomer and refers to large inflammatory pus-filled nodules greater than 0.5 cm in diameter in which the cell wall is composed 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, can be deep or superficial, and will persist throughout life.

Hormonal influences are very important in acne development and progression. Acne actually begins to develop at age eight or nine when the 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 (testosterone) since some of it is converted to androgens. With female puberty, both estrogen and progesterone increase as menarche (beginning of menses) occurs and the ovaries begin to produce female hormones. Some of this ovarian estrogen is converted to androgens as a byproduct. Progesterone 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 progesterone 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). Now without the over-riding 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* – Some medicines can cause acne. In adult females taking birth control pills (oral contraceptives), the choice of which type of birth control medicine 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 (like testosterone) will 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.

*Endocrine Disorders* – Another rare but possible cause of acne is endocrine disorders of various types which lead to over-production of androgenic substances.

*Environmental Factors* – Environmental factors occasionally play a role in acne. Young people employed in places where they come in 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 at exam time. This 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, will not be helpful, and injury induced by vigorous washing may cause more inflammation and induce progression of lesions. The black visible part of the blackhead is not dirt—it is melanin and oxidized material and cannot be removed by washing.
- Diet has no effect on acne. Many studies have been done regarding this and no foods have been shown to contribute to acne progression or development. Consequently, dietary modification will not help this disease. There is one exception to this regarding the individual patient. If an individual notices the idiosyncratic relationship of a particular food to acne, they should avoid that food.

However, the association of a food substance with acne in one particular person cannot be generalized to the entire patient population with acne.

- Therapy succeeds by preventing the formation of new acne lesions. Therefore, it is important to treat all acne-prone skin with topical agents and not just single acne lesions.
- 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 gland if it comes into contact with the skin, leading to acne development. This can be avoided 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, this entire period is an acne-prone time for the individual.
- 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.
- Scarring is permanent. The object of continuing treatment and being consistent with treatment is to avoid progression to severe lesions and scarring. Scars can only be removed or lessened via surgical procedures.

## Treatment

*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, which include antibacterial activity, mild anti-inflammatory activity, a lipid-dissolving cleansing action to remove lipid plugs from pores, and desquamative activity to remove dead epithelial cells on the skin and pore surface and encourage epithelial cell turnover.

Two agents are required for non-inflammatory acne not responsive to a single agent or to inflammatory acne. If two different agents are chosen, they should have different mechanisms of action so as not to be redundant.

Common topical therapies include benzoyl peroxide, topical antibiotics (clindamycin topical marketed as Cleocin-T or erythromycin topical), topical retinoids (Retin-A, Renova, adapalene or Differin, tazarotene or Tazorac), azelaic acid (Azelex), salicylic acid, milk and fruit acids (also called AHAs, including glycolic acid, lactic acid, malic acid, citric acid, 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 at treating severe inflammatory acne because it cannot penetrate deep enough through the skin's surface to treat the severely inflamed nodules and cysts. Severe acne requires systemic treatment (medicine taken orally). Systemic therapies cause distribution of the drug throughout the entire organism. Common systemic therapies include oral antibiotics (erythromycin and the tetracyclines including tetracycline, minocycline, and doxycycline), hormonal therapy (oral contraceptives), and Accutane (isotretinoin, 13-cis-retinoic acid).

Severe nodular cystic acne usually requires Accutane (13-cis-retinoic acid or isotretinoin), a pill with significant potential side effects usually reserved for the most severe acne cases. It causes drying of the skin, eyes, mouth, mucus membranes in all people as well as desquamation (flaking) 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 pregnancy protection.

*Scarring* – Scars are permanent, persist into adulthood, and can only be treated surgically.

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, reserved for the most severe acne cases, is used alone as monotherapy. The topical agents may be used singly for comedonal non-inflammatory acne but if this type of acne is non-responsive to therapy with a single topical agent or is inflammatory, then therapy with more than one agent is required.

## Product Recommendations

iS CLINICAL® products helpful in treating acne include: ACTIVE SERUM™, PRO-HEAL™ SERUM ADVANCE+, HYDRA-COOL™ SERUM, CLEANSING COMPLEX, SPF 25 TREATMENT SUNSCREEN, and SPF 20 POWDER SUNSCREEN.

## References

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