


# Acne

**Acne**, also known as **acne vulgaris**, is a long-term skin disease that occurs when hair follicles are clogged with dead skin cells and oil from the skin.<sup>[10]</sup> It is characterized by blackheads or whiteheads, pimples, oily skin, and possible scarring.<sup>[1][2][11]</sup> It primarily affects areas of the skin with a relatively high number of oil glands, including the face, upper part of the chest, and back.<sup>[12]</sup> The resulting appearance can lead to anxiety, reduced self-esteem and, in extreme cases, depression or thoughts of suicide.<sup>[3][4]</sup>

Genetics is thought to be the primary cause of acne in 80% of cases.<sup>[2]</sup> The role of diet and cigarette smoking is unclear, and neither cleanliness nor exposure to sunlight appear to play a part.<sup>[2][13][14]</sup> In both sexes, hormones called androgens appear to be part of the underlying mechanism, by causing increased production of sebum.<sup>[5]</sup> Another frequent factor is excessive growth of the bacterium *Cutibacterium acnes*, which is normally present on the skin.<sup>[15]</sup>

Many treatment options for acne are available, including lifestyle changes, medications, and medical procedures. Eating fewer simple carbohydrates such as sugar may help.<sup>[7]</sup> Treatments applied directly to the affected skin, such as azelaic acid, benzoyl peroxide, and salicylic acid, are commonly used.<sup>[8]</sup> Antibiotics and retinoids are available in formulations that are applied to the skin and taken by mouth for the treatment of acne.<sup>[8]</sup> However, resistance to antibiotics may develop as a result of antibiotic therapy.<sup>[16]</sup> Several types of birth control pills help against acne in women.<sup>[8]</sup> Isotretinoin pills are usually reserved for severe acne due to greater potential side effects.<sup>[8][17]</sup> Early and aggressive treatment of acne is advocated by some in the medical community to decrease the overall long-term impact to individuals.<sup>[4]</sup>

Acne	
Other names	Acne vulgaris
	
Acne vulgaris in an 18-year-old male during puberty	
Specialty	Dermatology
Symptoms	Blackheads, whiteheads, pimples, oily skin, scarring <sup>[1][2]</sup>
Complications	Anxiety, reduced self-esteem, depression, thoughts of suicide <sup>[3][4]</sup>
Usual onset	Puberty <sup>[5]</sup>
Risk factors	Genetics <sup>[2]</sup>
Differential diagnosis	Folliculitis, rosacea, hidradenitis suppurativa, miliaria <sup>[6]</sup>
Treatment	Lifestyle changes, medications, medical procedures <sup>[7][8]</sup>
Medication	Azelaic acid, benzoyl peroxide, salicylic acid, antibiotics, birth control pills, isotretinoin <sup>[8]</sup>
Frequency	633 million affected (2015) <sup>[9]</sup>

In 2015, acne was estimated to affect 633 million people globally, making it the eighth most common disease worldwide.<sup>[9][18]</sup> Acne commonly occurs in adolescence and affects an estimated 80–90% of teenagers in the Western world.<sup>[19][20][21]</sup> Lower rates are reported in some rural societies.<sup>[21][22]</sup> Children and adults may also be affected before and after puberty.<sup>[23]</sup> Although acne becomes less common in adulthood, it persists in nearly half of affected people into their twenties and thirties and a smaller group continue to have difficulties into their forties.<sup>[2]</sup>

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## Classification

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The severity of acne vulgaris (Gr. ἄκμή, "point" + L. vulgaris, "common")<sup>[24]</sup> can be classified as mild, moderate, or severe as this helps to determine an appropriate treatment regimen.<sup>[20]</sup> There is no universally accepted scale for grading acne severity.<sup>[15]</sup> Mild acne is classically defined by the presence of clogged skin follicles (known as comedones) limited to the face with occasional inflammatory lesions.<sup>[20]</sup> Moderate severity acne is said to occur when a higher number of inflammatory papules and pustules occur on the face compared to mild cases of acne and are found on the trunk of the body.<sup>[20]</sup> Severe acne is said to occur when nodules (the painful 'bumps' lying under the skin) are the characteristic facial lesions and involvement of the trunk is extensive.<sup>[20][25]</sup>

Large nodules were previously referred to as cysts, and the term *nodulocystic* has been used in the medical literature to describe severe cases of inflammatory acne.<sup>[25]</sup> True cysts are in fact rare in those with acne and the term *severe nodular acne* is now the preferred terminology.<sup>[25]</sup>

*Acne inversa* (L. invertō, "upside down") and *acne rosacea* (rosa, "rose-colored" + -āceus, "forming") are not true forms of acne and respectively refer to the skin conditions hidradenitis suppurativa (HS) and rosacea.<sup>[26][27][28]</sup> Although HS shares certain common features with acne vulgaris, such as a tendency to clog skin follicles with skin cell debris, the condition otherwise lacks the defining features of acne and is therefore considered a distinct skin disorder.<sup>[26]</sup>

## Signs and symptoms

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Typical features of acne include increased secretion of oily sebum by the skin, microcomedones, comedones, papules, nodules (large papules), pustules, and often results in scarring.<sup>[29][30]</sup> The appearance of acne varies with skin color. It may result in psychological and social problems.<sup>[20]</sup>

## Scars

Acne scars are caused by inflammation within the dermal layer of skin and are estimated to affect 95% of people with acne vulgaris.<sup>[31]</sup> The scar is created by abnormal healing following this dermal inflammation.<sup>[32]</sup> Scarring is most likely to take place with severe acne, but may occur with any form of acne vulgaris.<sup>[31]</sup> Acne scars are classified based on whether the abnormal healing response following dermal inflammation leads to excess collagen deposition or loss at the site of the acne lesion.<sup>[33]</sup>

Atrophic acne scars have lost collagen from the healing response and are the most common type of acne scar (account for approximately 75% of all acne scars).<sup>[32][33]</sup> They may be further classified as ice-pick scars, boxcar scars, and rolling scars.<sup>[31]</sup> Ice-pick scars are narrow (less than 2 mm across), deep scars that extend into the dermis.<sup>[32]</sup> Boxcar scars are round or ovoid indented scars with sharp borders and vary in size from 1.5–4 mm across.<sup>[32]</sup> Rolling scars are wider than icepick and boxcar scars (4–5 mm across) and have a wave-like pattern of depth in the skin.<sup>[32]</sup>

Hypertrophic scars are uncommon, and are characterized by increased collagen content after the abnormal healing response.<sup>[32]</sup> They are described as firm and raised from the skin.<sup>[32][34]</sup> Hypertrophic scars remain within the original margins of the wound, whereas keloid scars can form scar tissue outside of these borders.<sup>[32]</sup> Keloid scars from acne occur more often in men and people with darker skin, and usually occur on the trunk of the body.<sup>[32]</sup>

## Pigmentation

Postinflammatory hyperpigmentation (PIH) is usually the result of nodular acne lesions. These lesions often leave behind an inflamed darkened mark after the original acne lesion has resolved. This inflammation stimulates specialized pigment-producing skin cells (known as melanocytes) to produce more melanin pigment which leads to the skin's darkened appearance.<sup>[35]</sup> People with darker skin color are more frequently affected by this condition.<sup>[36]</sup> Pigmented scar is a common term used for PIH, but is misleading as it suggests the color change is permanent. Often, PIH can be prevented by avoiding any aggravation of the nodule, and can fade with time. However, untreated PIH can last for months, years, or even be permanent if deeper layers of skin are affected.<sup>[37]</sup> Even minimal skin exposure to the sun's ultraviolet rays can sustain hyperpigmentation.<sup>[35]</sup> Daily use of SPF 15 or higher sunscreen can minimize such a risk.<sup>[37]</sup>



A severe case of nodular acne



Nodular acne on the back

## Causes

Risk factors for the development of acne, other than genetics, have not been conclusively identified. Possible secondary contributors include hormones, infections, diet and stress. Studies investigating the impact of smoking on the incidence and severity of acne have been inconclusive.<sup>[2][38][39]</sup> Sunlight and cleanliness are not associated with acne.<sup>[14]</sup>

## Genes

Acne appears to be strongly inherited with 81% of the variation in the population explained by genetics.<sup>[15]</sup> Studies performed in affected twins and first-degree relatives further demonstrate the strongly inherited nature of acne.<sup>[2][15]</sup> Acne susceptibility is likely due to the influence of multiple genes, as the disease does not follow a classic (Mendelian) inheritance pattern. Several gene candidates have been proposed including certain variations in tumor necrosis factor-alpha (TNF-alpha), IL-1 alpha, and CYP1A1 genes, among others.<sup>[19]</sup> The 308 G/A single nucleotide polymorphism variation in the gene for TNF is associated with an increased risk for acne.<sup>[40]</sup> Acne can be a feature of rare genetic disorders such as Apert's syndrome.<sup>[15]</sup> Severe acne may be associated with XXY syndrome.<sup>[41]</sup>

## Hormones

Hormonal activity, such as occurs during menstrual cycles and puberty, may contribute to the formation of acne. During puberty, an increase in sex hormones called androgens causes the skin follicle glands to grow larger and make more oily sebum.<sup>[12]</sup> Several hormones have been linked to acne, including the androgens testosterone, dihydrotestosterone (DHT), and dehydroepiandrosterone (DHEA); high levels of growth hormone (GH) and insulin-like growth factor 1 (IGF-1) have also been associated with worsened acne.<sup>[42]</sup> Both androgens and IGF-1 seem to be essential for acne to occur, as acne does not develop in individuals with complete androgen insensitivity syndrome (CAIS) or Laron syndrome (insensitivity to GH, resulting in very low IGF-1 levels).<sup>[43][44]</sup>

Medical conditions that commonly cause a high-androgen state, such as polycystic ovary syndrome, congenital adrenal hyperplasia, and androgen-secreting tumors, can cause acne in affected individuals.<sup>[45][46]</sup> Conversely, people who lack androgenic hormones or are insensitive to the effects of androgens rarely have acne.<sup>[45]</sup> An increase in androgen and oily sebum synthesis may be seen during pregnancy.<sup>[46][47]</sup> Acne can be a side effect of testosterone replacement therapy or of anabolic steroid use.<sup>[1][48]</sup> Over-the-counter bodybuilding and dietary supplements are commonly found to contain illegally added anabolic steroids.<sup>[1][49]</sup>

## Infections

It is widely suspected that the anaerobic bacterial species *Cutibacterium acnes* (formerly *Propionibacterium acnes*) contributes to the development of acne, but its exact role is not well understood.<sup>[2]</sup> There are specific sub-strains of *C. acnes* associated with normal skin, and moderate or severe inflammatory acne.<sup>[50]</sup> It is unclear whether these undesirable strains evolve on-site or are acquired, or possibly both depending on the person. These strains have the capability of changing, perpetuating, or adapting to the abnormal cycle of inflammation, oil production, and inadequate sloughing of dead skin cells from acne pores. Infection with the parasitic mite *Demodex* is associated with the development of acne.<sup>[30][51]</sup> It is unclear whether eradication of the mite improves acne.<sup>[51]</sup>

## Diet

The relationship between diet and acne is unclear, as there is no high-quality evidence that establishes any definitive link between them.<sup>[52]</sup> High-glycemic-load diets have been found to have different degrees of effect on acne severity.<sup>[7][53][54]</sup> Multiple randomized controlled trials and nonrandomized studies have found a lower-glycemic-load diet to be effective in reducing acne.<sup>[53]</sup> There is weak observational evidence suggesting that dairy milk consumption is positively associated with a higher frequency and severity of acne.<sup>[51][52][53][55][56]</sup> Milk contains whey protein and hormones such as bovine IGF-1 and precursors of dihydrotestosterone.<sup>[53]</sup> These components are hypothesized to promote the effects of insulin and IGF-1 and thereby increase the production of androgen hormones, sebum, and promote the formation of comedones.<sup>[53]</sup> Available evidence does not support a link between eating chocolate or salt and acne severity.<sup>[52][55]</sup> Chocolate does contain varying amounts of sugar, which can lead to a high glycemic load, and it can be made with or without milk. Few studies have examined the relationship between obesity and acne.<sup>[2]</sup> Vitamin B<sub>12</sub> may trigger skin outbreaks similar to acne (acneiform eruptions), or worsen existing acne, when taken in doses exceeding the recommended daily intake.<sup>[57]</sup> Eating greasy foods does not increase acne nor make it worse.<sup>[58][59]</sup>

## Stress

Few high-quality studies have been performed which demonstrate that stress causes or worsens acne.<sup>[60]</sup> While the connection between acne and stress has been debated, some research indicates that increased severity is associated with high stress levels in certain contexts such as hormonal changes seen in premenstrual syndrome.<sup>[61][62]</sup>

## Environmental factors

Mechanical obstruction of skin follicles with helmets or chinstraps can worsen pre-existing acne.<sup>[63]</sup>

## Medications

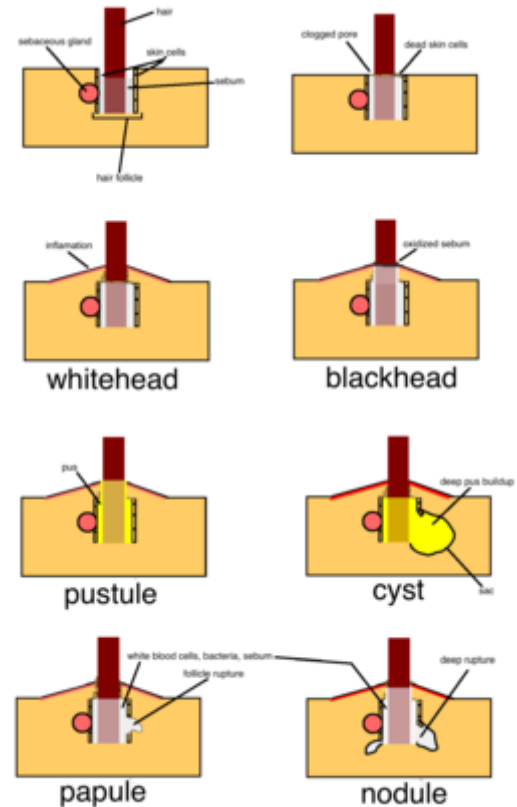
Several medications can worsen pre-existing acne, with examples being lithium, hydantoin, isoniazid, glucocorticoids, iodides, bromides, and testosterone.<sup>[41]</sup>

## Pathophysiology

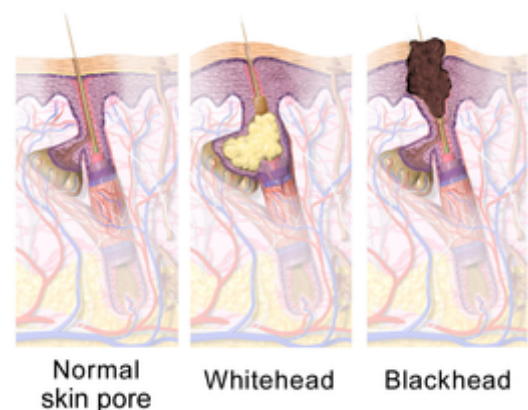
Acne vulgaris is a chronic skin disease of the pilosebaceous unit and develops due to blockages in the skin's hair follicles. These blockages are thought to occur as a result of the following four abnormal processes: a higher than normal amount of oily sebum production (influenced by androgens), excessive deposition of the protein keratin leading to comedo formation, colonization of the follicle by *Cutibacterium acnes* (*C. acnes*) bacteria, and the local release of pro-inflammatory chemicals in the skin.<sup>[50]</sup>

The earliest pathologic change is the formation of a plug (a microcomedone), which is driven primarily by excessive growth, reproduction, and accumulation of skin cells in the hair follicle.<sup>[1]</sup> In normal skin, the skin cells that have died come up to the surface and exit the pore of the hair follicle.<sup>[10]</sup> However, increased production of oily sebum in those with acne causes the dead skin cells to stick together.<sup>[10]</sup> The accumulation of dead skin cell debris and oily sebum blocks the pore of the hair follicle, thus forming the microcomedone.<sup>[10]</sup> This is further exacerbated by the biofilm created by *C. acnes* within the hair follicle.<sup>[45]</sup> If the microcomedone is superficial within the hair follicle, the skin pigment melanin is exposed to air, resulting in its oxidation and dark appearance (known as a blackhead or open comedo).<sup>[1][10][20]</sup> In contrast, if the microcomedone occurs deep within the hair follicle, this causes the formation of a whitehead (known as a closed comedo).<sup>[1][10]</sup>

The main hormonal driver of oily sebum production in the skin is dihydrotestosterone.<sup>[1]</sup> Another androgenic hormone responsible for increased sebaceous gland activity is DHEA-S. Higher amounts of DHEA-S are secreted during adrenarche (a stage of puberty), and this leads to an increase in sebum production. In a sebum-rich skin environment, the naturally occurring and largely commensal skin bacterium *C. acnes* readily grows and can cause inflammation within and around the follicle due to activation of the innate



Simplistic representation of the formation of acne comedones.

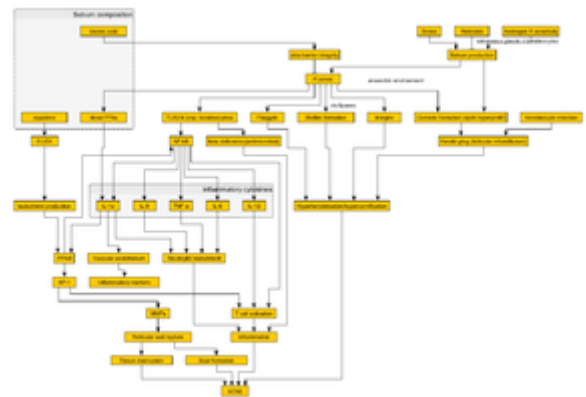


Hair follicle anatomy demonstrating a healthy hair follicle (pictured left), a whitehead or closed comedo (middle picture), and a blackhead or open comedo (pictured right)



immune system.<sup>[10]</sup> *C. acnes* triggers skin inflammation in acne by increasing the production of several pro-inflammatory chemical signals (such as IL-1 $\alpha$ , IL-8, TNF- $\alpha$ , and LTB4); IL-1 $\alpha$  is known to be essential to comedo formation.<sup>[45]</sup>

A major mechanism of acne-related skin inflammation is mediated by *C. acnes*'s ability to bind and activate a class of immune system receptors known as toll-like receptors (TLRs), especially TLR2 and TLR4.<sup>[45][64][65]</sup> Activation of TLR2 and TLR4 by *C. acnes* leads to increased secretion of IL-1 $\alpha$ , IL-8, and TNF- $\alpha$ .<sup>[45]</sup> Release of these inflammatory signals attracts various immune cells to the hair follicle including neutrophils, macrophages, and Th1 cells.<sup>[45]</sup> IL-1 $\alpha$  stimulates increased skin cell activity and reproduction, which in turn fuels comedo development.<sup>[45]</sup> Furthermore, sebaceous gland cells produce more antimicrobial peptides, such as HBD1 and HBD2, in response to binding of TLR2 and TLR4.<sup>[45]</sup>



Flowchart of pathological sequence of events leading to acne

*C. acnes* also provokes skin inflammation by altering the fatty composition of oily sebum.<sup>[45]</sup> Oxidation of the lipid squalene by *C. acnes* is of particular importance. Squalene oxidation activates NF- $\kappa$ B (a protein complex) and consequently increases IL-1 $\alpha$  levels.<sup>[45]</sup> Additionally, squalene oxidation leads to increased activity of the 5-lipoxygenase enzyme responsible for conversion of arachidonic acid to leukotriene B4 (LTB4).<sup>[45]</sup> LTB4 promotes skin inflammation by acting on the peroxisome proliferator-activated receptor alpha (PPAR $\alpha$ ) protein.<sup>[45]</sup> PPAR $\alpha$  increases activity of activator protein 1 (AP-1) and NF- $\kappa$ B, thereby leading to the recruitment of inflammatory T cells.<sup>[45]</sup> The inflammatory properties of *C. acnes* can be further explained by the bacterium's ability to convert sebum triglycerides to pro-inflammatory free fatty acids via secretion of the enzyme lipase.<sup>[45]</sup> These free fatty acids spur production of cathelicidin, HBD1, and HBD2, thus leading to further inflammation.<sup>[45]</sup>

This inflammatory cascade typically leads to the formation of inflammatory acne lesions, including papules, infected pustules, or nodules.<sup>[1]</sup> If the inflammatory reaction is severe, the follicle can break into the deeper layers of the dermis and subcutaneous tissue and cause the formation of deep nodules.<sup>[1][66][67]</sup> Involvement of AP-1 in the aforementioned inflammatory cascade leads to activation of matrix metalloproteinases, which contribute to local tissue destruction and scar formation.<sup>[45]</sup>

## Diagnosis

Acne vulgaris is diagnosed based on a medical professional's clinical judgment.<sup>[15]</sup> The evaluation of a person with suspected acne should include taking a detailed medical history about a family history of acne, a review of medications taken, signs or symptoms of excessive production of androgen hormones, cortisol, and growth hormone.<sup>[15]</sup> Comedones (blackheads and whiteheads) must be present to diagnose acne. In their absence, an appearance similar to that of acne would suggest a different skin disorder.<sup>[28]</sup> Microcomedones (the precursor to blackheads and whiteheads) are not visible to the naked eye when inspecting the skin and can only be seen with a microscope.<sup>[28]</sup> There are many features that may indicate a person's acne vulgaris is sensitive to hormonal influences. Historical and physical clues that may suggest hormone-sensitive acne include onset between ages 20 and 30; worsening the week before a woman's period; acne lesions predominantly over the jawline and chin; and inflammatory/nodular acne lesions.<sup>[1]</sup>

Several scales exist to grade the severity of acne vulgaris, but no single technique has been universally accepted as the diagnostic standard.<sup>[68][69]</sup> Cook's acne grading scale uses photographs to grade severity from 0 to 8 (0 being the least severe and 8 being the most severe). This scale was the first to use a standardized photographic protocol to assess acne severity; since its creation in 1979, the scale has undergone several revisions.<sup>[69]</sup> The Leeds acne grading technique counts acne lesions on the face, back, and chest and categorizes them as inflammatory or non-inflammatory. Leeds scores range from 0 (least severe) to 10 (most severe) though modified scales have a maximum score of 12.<sup>[69][70]</sup> The Pillsbury acne grading scale simply classifies the severity of the acne from grade 1 (least severe) to grade 4 (most severe).<sup>[68][71]</sup>

## Differential diagnosis

Many skin conditions can mimic acne vulgaris, and these are collectively known as acneiform eruptions.<sup>[28]</sup> Such conditions include angiofibromas, epidermal cysts, flat warts, folliculitis, keratosis pilaris, milia, perioral dermatitis, and rosacea, among others.<sup>[20][72]</sup> Age is one factor which may help distinguish between these disorders. Skin disorders such as perioral dermatitis and keratosis pilaris can appear similar to acne but tend to occur more frequently in childhood, whereas rosacea tends to occur more frequently in older adults.<sup>[20]</sup> Facial redness triggered by heat or the consumption of alcohol or spicy food is suggestive of rosacea.<sup>[73]</sup> The presence of comedones helps health professionals differentiate acne from skin disorders that are similar in appearance.<sup>[8]</sup> Chloracne, due to exposure to certain chemicals, may look very similar to acne vulgaris.<sup>[74]</sup>

## Management

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Many different treatments exist for acne. These include alpha hydroxy acid, anti-androgen medications, antibiotics, antiseborrheic medications, azelaic acid, benzoyl peroxide, hormonal treatments, keratolytic soaps, nicotinamide, retinoids, and salicylic acid.<sup>[75]</sup> They are believed to work in at least four different ways, including the following: reducing inflammation, hormonal manipulation, killing *C. acnes*, and normalizing skin cell shedding and sebum production in the pore to prevent blockage.<sup>[15]</sup> Common treatments include topical therapies such as antibiotics, benzoyl peroxide, and retinoids, and systemic therapies including antibiotics, hormonal agents, and oral retinoids.<sup>[20][76]</sup>

Recommended therapies for first-line use in acne vulgaris treatment include topical retinoids, benzoyl peroxide, and topical or oral antibiotics.<sup>[77]</sup> Procedures such as light therapy and laser therapy are not considered to be first-line treatments and typically have an adjunctive role due to their high cost and limited evidence of efficacy.<sup>[76]</sup> Medications for acne work by targeting the early stages of comedo formation and are generally ineffective for visible skin lesions; improvement in the appearance of acne is typically expected between eight and twelve weeks after starting therapy.<sup>[15]</sup>

## Skin care

In general, it is recommended that people with acne do not wash affected skin more than twice daily.<sup>[15]</sup> For people with acne and sensitive skin, a fragrance free moisturizer may be used to reduce irritation. Skin irritation from acne medications typically peaks at two weeks after onset of use and tends to improve with continued use.<sup>[15]</sup> Cosmetic products that specifically say "non-comedogenic", "oil-free", and "won't clog pores" are recommended.<sup>[15]</sup>



## Diet

A diet low in simple sugars is recommended as a method of improving acne.<sup>[53]</sup> As of 2014, evidence is insufficient to recommend milk restriction for this purpose.<sup>[53]</sup>

## Medications

### Benzoyl peroxide

Benzoyl peroxide (BPO) is a first-line treatment for mild and moderate acne due to its effectiveness and mild side-effects (mainly skin irritation). In the skin follicle, benzoyl peroxide kills *C. acnes* by oxidizing its proteins through the formation of oxygen free radicals and benzoic acid. These free radicals are thought to interfere with the bacterium's metabolism and ability to make proteins.<sup>[78][79]</sup> Additionally, benzoyl peroxide is mildly effective at breaking down comedones and inhibiting inflammation.<sup>[77][79]</sup> Benzoyl peroxide may be paired with a topical antibiotic or retinoid such as benzoyl peroxide/clindamycin and benzoyl peroxide/adapalene, respectively.<sup>[36]</sup>



The common acne vulgaris treatment benzoyl peroxide cream

Side effects include increased skin photosensitivity, dryness, redness and occasional peeling.<sup>[80]</sup> Sunscreen use is often advised during treatment, to prevent sunburn. Lower concentrations of benzoyl peroxide are just as effective as higher concentrations in treating acne but are associated with fewer side effects.<sup>[79][81]</sup> Unlike antibiotics, benzoyl peroxide does not appear to generate bacterial antibiotic resistance.<sup>[80]</sup>

### Retinoids

Retinoids are medications which reduce inflammation, normalize the follicle cell life cycle, and reduce sebum production.<sup>[45][82]</sup> They are structurally related to vitamin A.<sup>[82]</sup> Studies show they are underprescribed by primary care doctors and dermatologists.<sup>[15]</sup> The retinoids appear to influence the cell life cycle in the follicle lining. This helps prevent the accumulation of skin cells within the hair follicle that can create a blockage. They are a first-line acne treatment,<sup>[1]</sup> especially for people with dark-colored skin, and are known to lead to faster improvement of postinflammatory hyperpigmentation.<sup>[36]</sup>

Topical retinoids include adapalene, isotretinoin, retinol, tazarotene, trifarotene, and tretinoin.<sup>[47][83]</sup> They often cause an initial flare-up of acne and facial flushing, and can cause significant skin irritation. Generally speaking, retinoids increase the skin's sensitivity to sunlight and are therefore recommended for use at night.<sup>[1]</sup> Tretinoin is the least expensive of the topical retinoids and is the most irritating to the skin, whereas adapalene is the least irritating to the skin but costs significantly more.<sup>[1][84]</sup> Most formulations of tretinoin cannot be applied at the same time as benzoyl peroxide.<sup>[15]</sup> Tazarotene is the most effective and expensive topical retinoid, but is not as well-tolerated.<sup>[1][84]</sup> Retinol is a form of vitamin A that has similar but milder effects, and is used in many over-the-counter moisturizers and other topical products.

Isotretinoin is an oral retinoid that is very effective for severe nodular acne, and moderate acne that is stubborn to other treatments.<sup>[1][20]</sup> One to two months use is typically adequate to see improvement. Acne often resolves completely or is much milder after a 4–6 month course of oral isotretinoin.<sup>[1]</sup> After a single course, about 80% of people report an improvement, with more than 50% reporting complete remission.<sup>[20]</sup> About 20% of patients require a second course.<sup>[20]</sup>

There are concerns that isotretinoin is linked with adverse effects, like depression, suicidality, anemia, although there is no clear evidence to support some of these claims.<sup>[1][20]</sup> Isotretinoin has been found in some studies to be superior to antibiotics or placebo in reducing acne lesions.<sup>[17]</sup> However, a 2018 review comparing inflammatory lesions after treatment with antibiotics versus isotretinoin found no difference.<sup>[85]</sup> The frequency of adverse events was about twice as high with isotretinoin, although these were mostly dryness-related events.<sup>[17]</sup> No increased risk of suicide or depression was conclusively found.<sup>[17]</sup>

Isotretinoin use in women of childbearing age is regulated due to its known harmful effects in pregnancy.<sup>[20]</sup> For such a woman to be considered a candidate for isotretinoin, she must have a confirmed negative pregnancy test and use an effective form of birth control.<sup>[20]</sup> In 2008, the United States started the iPLEDGE program to prevent isotretinoin use during pregnancy.<sup>[86]</sup> iPledge requires the woman under consideration for isotretinoin therapy to have two negative pregnancy tests and mandates the use of two types of birth control for at least one month before therapy begins and one month after therapy is complete.<sup>[86]</sup> The effectiveness of the iPledge program has been questioned due to continued instances of contraception nonadherence.<sup>[86][87]</sup>

## Antibiotics

Antibiotics are frequently applied to the skin or taken orally to treat acne and are thought to work due to their antimicrobial activity against *C. acnes* and their ability to reduce inflammation.<sup>[20][80][88]</sup> With the widespread use of antibiotics for acne and an increased frequency of antibiotic-resistant *C. acnes* worldwide, antibiotics are becoming less effective,<sup>[80]</sup> especially macrolide antibiotics such as topical erythromycin.<sup>[16][88]</sup> Therefore, they are not recommended for use alone but are preferred as part of combination therapy.<sup>[15]</sup> Commonly used antibiotics, either applied to the skin or taken orally, include clindamycin, erythromycin, metronidazole, sulfacetamide, and tetracyclines such as doxycycline and minocycline.<sup>[47]</sup> Doxycycline 40 milligrams daily (low-dose) appears to have similar efficacy to doxycycline 100 milligrams daily and has fewer gastrointestinal side effects.<sup>[15]</sup> When antibiotics are applied to the skin, they are typically used for mild to moderately severe acne.<sup>[20]</sup> Antibiotics taken orally are generally considered to be more effective than topical antibiotics, and produce faster resolution of inflammatory acne lesions than topical applications.<sup>[1]</sup> Topical and oral antibiotics are not recommended for use together.<sup>[88]</sup>

Oral antibiotics are recommended for no longer than three months as antibiotic courses exceeding this duration are associated with the development of antibiotic resistance and show no clear benefit over shorter courses.<sup>[88]</sup> Furthermore, if long-term oral antibiotics beyond three months are thought to be necessary, it is recommended that benzoyl peroxide and/or a retinoid be used at the same time to limit the risk of *C. acnes* developing antibiotic resistance.<sup>[88]</sup>

Dapsone has shown efficacy against inflammatory acne but is generally not a first-line topical antibiotic due to higher cost and lack of clear superiority over other antibiotics.<sup>[1][15]</sup> It is sometimes a preferred therapy in women or for people with sensitive or darker toned skin.<sup>[15]</sup> Topical dapsone is not recommended for use with benzoyl peroxide due to yellow-orange skin discoloration with this

combination.<sup>[10]</sup> While minocycline is shown to be an effective acne treatment, it is no longer recommended as a first-line antibiotic due to a lack of evidence that it is better than other treatments, and concerns of safety compared to other tetracyclines.<sup>[89]</sup>

## Hormonal agents

In women, acne can be improved with the use of any combined birth control pill.<sup>[90]</sup> These medications contain an estrogen and a progestin.<sup>[91]</sup> They work by decreasing the production of androgen hormones by the ovaries and by decreasing the free and hence biologically active fractions of androgens, resulting in lowered skin production of sebum and consequently reduced acne severity.<sup>[10][92]</sup> First-generation progestins such as norethindrone and norgestrel have androgenic properties and can worsen acne.<sup>[15]</sup> Although oral estrogens can decrease IGF-1 levels in some situations and this might be expected to additionally contribute to improvement in acne symptoms,<sup>[93][94]</sup> combined birth control pills appear to have no effect on IGF-1 levels in fertile women.<sup>[91][95]</sup> However, cyproterone acetate-containing birth control pills have been reported to decrease total and free IGF-1 levels.<sup>[96]</sup> Combinations containing third- or fourth-generation progestins including desogestrel, dienogest, drospirenone, or norgestimate, as well as birth control pills containing cyproterone acetate or chlormadinone acetate, are preferred for women with acne due to their stronger antiandrogenic effects.<sup>[97][98][99]</sup> Studies have shown a 40 to 70% reduction in acne lesions with combined birth control pills.<sup>[92]</sup> A 2014 review found that antibiotics by mouth appear to be somewhat more effective than birth control pills at decreasing the number of inflammatory acne lesions at three months.<sup>[100]</sup> However, the two therapies are approximately equal in efficacy at six months for decreasing the number of inflammatory, non-inflammatory, and total acne lesions.<sup>[100]</sup> The authors of the analysis suggested that birth control pills may be a preferred first-line acne treatment, over oral antibiotics, in certain women due to similar efficacy at six months and a lack of associated antibiotic resistance.<sup>[100]</sup>

Antiandrogens such as cyproterone acetate and spironolactone have been used successfully to treat acne, especially in women with signs of excessive androgen production such as increased hairiness or skin production of sebum, or baldness.<sup>[10][47]</sup> Spironolactone is an effective treatment for acne in adult women, but unlike combined birth control pills, is not approved by the United States Food and Drug Administration for this purpose.<sup>[1][36][101]</sup> The medication is primarily used as an aldosterone antagonist and is thought to be a useful acne treatment due to its ability to additionally block the androgen receptor at higher doses.<sup>[36]</sup> Alone or in combination with a birth control pill, spironolactone has shown a 33 to 85% reduction in acne lesions in women.<sup>[92]</sup> The effectiveness of spironolactone for acne appears to be dose-dependent.<sup>[92]</sup> High-dose cyproterone acetate alone has been found to decrease symptoms of acne in women by 75 to 90% within 3 months.<sup>[102]</sup> It is usually combined with an estrogen to avoid menstrual irregularities and estrogen deficiency.<sup>[103]</sup> The medication has also been found to be effective in the treatment of acne in males, with one study finding that a high dosage reduced inflammatory acne lesions by 73%.<sup>[104][105]</sup> However, the side effects of cyproterone acetate in males, such as gynecomastia, sexual dysfunction, and decreased bone mineral density, make its use for acne in this sex impractical in most cases.<sup>[104][105][106]</sup> Hormonal therapies should not be used to treat acne during pregnancy or lactation as they have been associated with birth disorders such as hypospadias, and feminization of the male babies.<sup>[47]</sup> In addition, women who are sexually active and who can or may become pregnant should use an effective method of contraception to prevent pregnancy while taking an antiandrogen.<sup>[107]</sup> Antiandrogens are often combined with birth control pills for this reason, which can result in additive efficacy.<sup>[36][108]</sup>

Flutamide, a pure antagonist of the androgen receptor, is effective in the treatment of acne in women.<sup>[102][109]</sup> It has generally been found to reduce symptoms of acne by 80 or 90% even at low doses, with several studies showing complete acne clearance.<sup>[102][110][111]</sup> In one study, flutamide decreased acne scores by 80% within 3 months, whereas spironolactone decreased symptoms by only 40% in the same time period.<sup>[111][112][113]</sup> In a large long-term study, 97% of women reported satisfaction with the control of their acne with flutamide.<sup>[114]</sup> Although effective, flutamide has a risk of serious liver toxicity, and cases of death in women taking even low doses of the medication to treat androgen-dependent skin and hair conditions have occurred.<sup>[115]</sup> As such, the use of flutamide for acne has become increasingly limited,<sup>[114][116][117]</sup> and it has been argued that continued use of flutamide for such purposes is unethical.<sup>[115]</sup> Bicalutamide, a pure androgen receptor antagonist with the same mechanism as flutamide and with comparable or superior antiandrogenic efficacy but without its risk of liver toxicity, is a potential alternative to flutamide in the treatment of androgen-dependent skin and hair conditions in women.<sup>[107][118][119][120]</sup>

Clascoterone is a topical antiandrogen which has demonstrated effectiveness in the treatment of acne in both males and females and is currently in the late stages of clinical development.<sup>[121][122][123][124]</sup> It has shown no systemic absorption or associated antiandrogenic side effects.<sup>[123][124][125]</sup> In a direct head-to-head comparison, clascoterone showed greater effectiveness than topical isotretinoin.<sup>[123][124][125]</sup> 5 $\alpha$ -Reductase inhibitors such as finasteride and dutasteride may be useful for the treatment of acne in both males and females, but have not been thoroughly evaluated for this purpose.<sup>[1][126][127][128]</sup> In addition, the high risk of birth defects with 5 $\alpha$ -reductase inhibitors limits their use in women.<sup>[1][127]</sup> However, 5 $\alpha$ -reductase inhibitors can be combined with birth control pills to prevent pregnancy, and are frequently used to treat excessive hair in women.<sup>[126]</sup> There is no evidence as of 2010 to support the use of cimetidine or ketoconazole in the treatment of acne.<sup>[129]</sup>

Hormonal treatments for acne such as combined birth control pills and antiandrogens may be considered a first-line therapy for acne under a number of circumstances, including when contraception is desired, when known or suspected hyperandrogenism is present, when acne occurs in adulthood, when acne flares premenstrually, and when symptoms of significant sebum production (seborrhea) are co-present.<sup>[129]</sup> Hormone therapy is effective for acne even in women with normal androgen levels.<sup>[129]</sup>

## **Azelaic acid**

Azelaic acid has been shown to be effective for mild to moderate acne when applied topically at a 20% concentration.<sup>[66][130]</sup> Treatment twice daily for six months is necessary, and is as effective as topical benzoyl peroxide 5%, isotretinoin 0.05%, and erythromycin 2%.<sup>[131]</sup> Azelaic acid is thought to be an effective acne treatment due to its ability to reduce skin cell accumulation in the follicle, and its antibacterial and anti-inflammatory properties.<sup>[66]</sup> It has a slight skin-lightening effect due to its ability to inhibit melanin synthesis, and is therefore useful in treating of individuals with acne who are also affected by post-inflammatory hyperpigmentation.<sup>[1]</sup> Azelaic acid may cause skin irritation but is otherwise very safe.<sup>[132]</sup> It is less effective and more expensive than retinoids.<sup>[1]</sup>

## **Salicylic acid**

Salicylic acid is a topically applied beta-hydroxy acid that stops bacteria from reproducing and has keratolytic properties.<sup>[133][134]</sup> It opens obstructed skin pores and promotes shedding of epithelial skin cells.<sup>[133]</sup> Salicylic acid is known to be less effective than retinoid therapy.<sup>[20]</sup> Dry skin is the most

commonly seen side effect with topical application, though darkening of the skin has been observed in individuals with darker skin types.<sup>[1]</sup>

## Other medications

Topical and oral preparations of nicotinamide (the amide form of vitamin B<sub>3</sub>) have been suggested as alternative medical treatments.<sup>[135]</sup> It is thought to improve acne due to its anti-inflammatory properties, its ability to suppress sebum production, and by promoting wound healing.<sup>[135]</sup> Topical and oral preparations of zinc have similarly been proposed as effective treatments for acne; evidence to support their use for this purpose is limited.<sup>[136]</sup> The purported efficacy of zinc is attributed to its capacity to reduce inflammation and sebum production, and inhibit *C. acnes*.<sup>[136]</sup> Antihistamines may improve symptoms among those already taking isotretinoin due to their anti-inflammatory properties and their ability to suppress sebum production.<sup>[137]</sup>

Hydroquinone lightens the skin when applied topically by inhibiting tyrosinase, the enzyme responsible for converting the amino acid tyrosine to the skin pigment melanin, and is used to treat acne-associated post-inflammatory hyperpigmentation.<sup>[35]</sup> By interfering with new production of melanin in the epidermis, hydroquinone leads to less hyperpigmentation as darkened skin cells are naturally shed over time.<sup>[35]</sup> Improvement in skin hyperpigmentation is typically seen within six months when used twice daily. Hydroquinone is ineffective for hyperpigmentation affecting deeper layers of skin such as the dermis.<sup>[35]</sup> The use of a sunscreen with SPF 15 or higher in the morning with reapplication every two hours is recommended when using hydroquinone.<sup>[35]</sup> Its application only to affected areas lowers the risk of lightening the color of normal skin but can lead to a temporary ring of lightened skin around the hyperpigmented area.<sup>[35]</sup> Hydroquinone is generally well-tolerated; side effects are typically mild (e.g., skin irritation) and occur with use of a higher than the recommended 4% concentration.<sup>[35]</sup> Most preparations contain the preservative sodium metabisulfite, which has been linked to rare cases of allergic reactions including anaphylaxis and severe asthma exacerbations in susceptible people.<sup>[35]</sup> In extremely rare cases, repeated improper topical application of high-dose hydroquinone has been associated with an accumulation of homogentisic acid in connective tissues, a condition known as exogenous ochronosis.<sup>[35]</sup>

## Combination therapy

Combination therapy—using medications of different classes together, each with a different mechanism of action—has been demonstrated to be a more efficacious approach to acne treatment than monotherapy.<sup>[10][47]</sup> The use of topical benzoyl peroxide and antibiotics together has been shown to be more effective than antibiotics alone.<sup>[10]</sup> Similarly, using a topical retinoid with an antibiotic clears acne lesions faster than the use of antibiotics alone.<sup>[10]</sup> Frequently used combinations include the following: antibiotic and benzoyl peroxide, antibiotic and topical retinoid, or topical retinoid and benzoyl peroxide.<sup>[47]</sup> The pairing of benzoyl peroxide with a retinoid is preferred over the combination of a topical antibiotic with a retinoid since both regimens are effective but benzoyl peroxide does not lead to antibiotic resistance.<sup>[10]</sup>

## Pregnancy

Although the late stages of pregnancy are associated with an increase in sebaceous gland activity in the skin, pregnancy has not been reliably associated with worsened acne severity.<sup>[138]</sup> In general, topically applied medications are considered the first-line approach to acne treatment during pregnancy, as they

have little systemic absorption and are therefore unlikely to harm a developing fetus.<sup>[138]</sup> Highly recommended therapies include topically applied benzoyl peroxide (category C) and azelaic acid (category B).<sup>[138]</sup> Salicylic acid carries a category C safety rating due to higher systemic absorption (9–25%), and an association between the use of anti-inflammatory medications in the third trimester and adverse effects to the developing fetus including too little amniotic fluid in the uterus and early closure of the babies' ductus arteriosus blood vessel.<sup>[47][138]</sup> Prolonged use of salicylic acid over significant areas of the skin or under occlusive dressings is not recommended as these methods increase systemic absorption and the potential for fetal harm.<sup>[138]</sup> Tretinoin (category C) and adapalene (category C) are very poorly absorbed, but certain studies have suggested teratogenic effects in the first trimester.<sup>[138]</sup> Due to persistent safety concerns, topical retinoids are not recommended for use during pregnancy.<sup>[139]</sup> In studies examining the effects of topical retinoids during pregnancy, fetal harm has not been seen in the second and third trimesters.<sup>[138]</sup> Retinoids contraindicated for use during pregnancy include the topical retinoid tazarotene, and oral retinoids isotretinoin and acitretin (all category X).<sup>[138]</sup> Spironolactone is relatively contraindicated for use during pregnancy due to its antiandrogen effects.<sup>[1]</sup> Finasteride is not recommended as it is highly teratogenic.<sup>[1]</sup>

Topical antibiotics deemed safe during pregnancy include clindamycin, erythromycin, and metronidazole (all category B), due to negligible systemic absorption.<sup>[47][138]</sup> Nadifloxacin and dapsone (category C) are other topical antibiotics that may be used to treat acne in pregnant women, but have received less study.<sup>[47][138]</sup> No adverse fetal events have been reported from the topical use of dapsone.<sup>[138]</sup> If retinoids are used there is a high risk of abnormalities occurring in the developing fetus; women of childbearing age are therefore required to use effective birth control if retinoids are used to treat acne.<sup>[20]</sup> Oral antibiotics deemed safe for pregnancy (all category B) include azithromycin, cephalosporins, and penicillins.<sup>[138]</sup> Tetracyclines (category D) are contraindicated during pregnancy as they are known to deposit in developing fetal teeth, resulting in yellow discoloration and thinned tooth enamel.<sup>[1][138]</sup> Their use during pregnancy has been associated with development of acute fatty liver of pregnancy and is further avoided for this reason.<sup>[138]</sup>

## Procedures

Comedo extraction is supported by limited evidence but is recommended for comedones that do not improve with standard treatment.<sup>[8][77]</sup> Another procedure for immediate relief is injection of a corticosteroid into an inflamed acne comedo.<sup>[77]</sup> Electrocautery and electrofulguration have also been reported as effective treatments for comedones.<sup>[140]</sup>

Light therapy is a treatment method that involves delivering certain specific wavelengths of light to an area of skin affected by acne. Both regular and laser light have been used. The evidence for light therapy as a treatment for acne is weak and inconclusive.<sup>[8][141]</sup> Various light therapies appear to provide a short-term benefit, but data for long-term outcomes, and for outcomes in those with severe acne, are sparse;<sup>[142]</sup> it may have a role for individuals whose acne has been resistant to topical medications.<sup>[10]</sup> A 2016 meta-analysis was unable to conclude whether light therapies were more beneficial than placebo or no treatment, nor how long potential benefits lasted.<sup>[143]</sup> PDT has the most supporting evidence of all light therapies.<sup>[77]</sup>

When regular light is used immediately following the application of a sensitizing substance to the skin such as aminolevulinic acid or methyl aminolevulinate, the treatment is referred to as photodynamic therapy (PDT).<sup>[10][130]</sup> Many different types of nonablative lasers (i.e., lasers that do not vaporize the top layer of the skin but rather induce a physiologic response in the skin from the light) have been used to

treat acne, including those that use infrared wavelengths of light. Ablative lasers (such as CO<sub>2</sub> and fractional types) have also been used to treat active acne and its scars. When ablative lasers are used, the treatment is often referred to as laser resurfacing because, as mentioned previously, the entire upper layers of the skin are vaporized.<sup>[144]</sup> Ablative lasers are associated with higher rates of adverse effects compared with non-ablative lasers, with examples being post-inflammatory hyperpigmentation, persistent facial redness, and persistent pain.<sup>[8][145][146]</sup> Physiologically, certain wavelengths of light, used with or without accompanying topical chemicals, are thought to kill bacteria and decrease the size and activity of the glands that produce sebum.<sup>[130]</sup> Disadvantages of light therapy can include its cost, the need for multiple visits, time required to complete the procedure(s), and pain associated with some of the treatment modalities.<sup>[10]</sup> Typical side effects include skin peeling, temporary reddening of the skin, swelling, and post-inflammatory hyperpigmentation.<sup>[10]</sup>

Dermabrasion is an effective therapeutic procedure for reducing the appearance of superficial atrophic scars of the boxcar and rolling varieties.<sup>[32]</sup> Ice-pick scars do not respond well to treatment with dermabrasion due to their depth.<sup>[32]</sup> The procedure is painful and has many potential side effects such as skin sensitivity to sunlight, redness, and decreased pigmentation of the skin.<sup>[32]</sup> Dermabrasion has fallen out of favor with the introduction of laser resurfacing.<sup>[32]</sup> Unlike dermabrasion, there is no evidence that microdermabrasion is an effective treatment for acne.<sup>[8]</sup>

Dermal or subcutaneous fillers are substances injected into the skin to improve the appearance of acne scars. Fillers are used to increase natural collagen production in the skin and to increase skin volume and decrease the depth of acne scars.<sup>[147]</sup> Examples of fillers used for this purpose include hyaluronic acid; poly(methyl methacrylate) microspheres with collagen; human and bovine collagen derivatives, and fat harvested from the person's own body (autologous fat transfer).<sup>[147]</sup>

Microneedling is a procedure in which an instrument with multiple rows of tiny needles is rolled over the skin to elicit a wound healing response and stimulate collagen production to reduce the appearance of atrophic acne scars in people with darker skin color.<sup>[144]</sup> Notable adverse effects of microneedling include post-inflammatory hyperpigmentation and tram track scarring (described as discrete slightly raised scars in a linear distribution similar to a tram track). The latter is thought to be primarily attributable to improper technique by the practitioner, including the use of excessive pressure or inappropriately large needles.<sup>[144][148]</sup>

Subcision is useful for treatment of superficial atrophic acne scars and involves the use of a small needle to loosen the fibrotic adhesions that result in the depressed appearance of the scar.<sup>[149][150][151]</sup>

Chemical peels can be used to reduce the appearance of acne scars.<sup>[32]</sup> Mild peels include those using glycolic acid, lactic acid, salicylic acid, Jessner's solution, or a lower concentrations (20%) of trichloroacetic acid. These peels only affect the epidermal layer of the skin and can be useful in the treatment of superficial acne scars as well as skin pigmentation changes from inflammatory acne.<sup>[32]</sup> Higher concentrations of trichloroacetic acid (30–40%) are considered to be medium-strength peels and affect skin as deep as the papillary dermis.<sup>[32]</sup> Formulations of trichloroacetic acid concentrated to 50% or more are considered to be deep chemical peels.<sup>[32]</sup> Medium-strength and deep-strength chemical peels are more effective for deeper atrophic scars, but are more likely to cause side effects such as skin pigmentation changes, infection, and small white superficial cysts known as milia.<sup>[32]</sup>

## Alternative medicine



Complementary therapies have been investigated for treating people with acne.<sup>[152]</sup> Low-quality evidence suggests topical application of tea tree oil or bee venom may reduce the total number of skin lesions in those with acne.<sup>[152]</sup> Tea tree oil is thought to be approximately as effective as benzoyl peroxide or salicylic acid, but has been associated with allergic contact dermatitis.<sup>[1]</sup> Proposed mechanisms for tea tree oil's anti-acne effects include antibacterial action against *C. acnes*, and anti-inflammatory properties.<sup>[65]</sup> Numerous other plant-derived therapies have been observed to have positive effects against acne (e.g., basil oil and oligosaccharides from seaweed); however, few studies have been performed, and most have been of lower methodological quality.<sup>[153]</sup> There is a lack of high-quality evidence for the use of acupuncture, herbal medicine, or cupping therapy for acne.<sup>[152]</sup>

## Self-care

Many over-the-counter treatments in many forms are available, which are often referred to as cosmeceuticals.<sup>[154]</sup> Certain types of makeup may be useful to mask acne.<sup>[155]</sup> In those with oily skin, a water-based product is often preferred.<sup>[155][156]</sup>

## Prognosis

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Acne usually improves around the age of 20, but may persist into adulthood.<sup>[75]</sup> Permanent physical scarring may occur.<sup>[20]</sup> There is good evidence to support the idea that acne and associated scarring negatively affect a person's psychological state, worsen mood, lower self-esteem, and are associated with a higher risk of anxiety disorders, depression, and suicidal thoughts.<sup>[3][31][51]</sup> Another psychological complication of acne vulgaris is acne excoriée, which occurs when a person persistently picks and scratches pimples, irrespective of the severity of their acne.<sup>[61][157]</sup> This can lead to significant scarring, changes in the affected person's skin pigmentation, and a cyclic worsening of the affected person's anxiety about their appearance.<sup>[61]</sup> Rare complications from acne or its treatment include the formation of pyogenic granulomas, osteoma cutis, and solid facial edema.<sup>[158]</sup> Early and aggressive treatment of acne is advocated by some in the medical community to reduce the chances of these poor outcomes.<sup>[4]</sup>

## Epidemiology

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Globally, acne affects approximately 650 million people, or about 9.4% of the population, as of 2010.<sup>[159]</sup> It affects nearly 90% of people in Western societies during their teenage years, but can occur before adolescence and may persist into adulthood.<sup>[19][20][23]</sup> While acne that first develops between the ages of 21 and 25 is uncommon, it affects 54% of women and 40% of men older than 25 years of age,<sup>[47][160]</sup> and has a lifetime prevalence of 85%.<sup>[47]</sup> About 20% of those affected have moderate or severe cases.<sup>[2]</sup> It is slightly more common in females than males (9.8% versus 9.0%).<sup>[159]</sup> In those over 40 years old, 1% of males and 5% of females still have problems.<sup>[20]</sup>

Rates appear to be lower in rural societies.<sup>[22]</sup> While some research has found it affects people of all ethnic groups,<sup>[161]</sup> acne may not occur in the non-Westernized peoples of Papua New Guinea and Paraguay.<sup>[162]</sup>

Acne affects 40–50 million people in the United States (16%) and approximately 3–5 million in Australia (23%).<sup>[100][163]</sup> Severe acne tends to be more common in people of Caucasian or Hispanic descent than in people of African descent.<sup>[21]</sup>

## History

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Pharaohs are recorded as having had acne, which may be the earliest known reference to the disease. Since at least the reign of Cleopatra (69–30 BCE), the application of sulfur to the skin has been recognized as a useful treatment for acne.<sup>[164]</sup> The sixth-century Greek physician Aëtius of Amida is credited with coining the term "ionthos" (ἰονθωξ,) or "acnae", which is believed to have been a reference to facial skin lesions that occur during "the 'acme' of life" (puberty).<sup>[165]</sup>

In the 16th century, the French physician and botanist François Boissier de Sauvages de Lacroix provided one of the earlier descriptions of acne. He used the term "psydracia achne" to describe small, red and hard tubercles that altered a person's facial appearance during adolescence, and were neither itchy nor painful.<sup>[165]</sup>

The recognition and characterization of acne progressed in 1776 when Josef Plenck (an Austrian physician) published a book that proposed the novel concept of classifying skin diseases by their elementary (initial) lesions.<sup>[165]</sup> In 1808 the English dermatologist Robert Willan refined Plenck's work by providing the first detailed descriptions of several skin disorders using a morphologic terminology that remains in use today.<sup>[165]</sup> Thomas Bateman continued and expanded on Robert Willan's work as his student and provided the first descriptions and illustrations of acne accepted as accurate by modern dermatologists.<sup>[165]</sup> Erasmus Wilson, in 1842, was the first to make the distinction between acne vulgaris and rosacea.<sup>[166]</sup> The first professional medical monograph dedicated entirely to acne was written by Lucius Duncan Bulkley and published in New York in 1885.<sup>[167][168]</sup>

Scientists initially hypothesized that acne represented a disease of the skin's hair follicle, and occurred due to blockage of the pore by sebum. During the 1880s, bacteria were observed by microscopy in skin samples affected by acne and were regarded as the causal agents of comedones, sebum production, and ultimately acne.<sup>[165]</sup> During the mid-twentieth century, dermatologists realized that no single hypothesized factor (sebum, bacteria, or excess keratin) could completely explain the disease.<sup>[165]</sup> This led to the current understanding that acne could be explained by a sequence of related events, beginning with blockage of the skin follicle by excessive dead skin cells, followed by bacterial invasion of the hair follicle pore, changes in sebum production, and inflammation.<sup>[165]</sup>

The approach to acne treatment underwent significant changes during the twentieth century. Retinoids were introduced as a medical treatment for acne in 1943.<sup>[82]</sup> Benzoyl peroxide was first proposed as a treatment in 1958 and has been routinely used for this purpose since the 1960s.<sup>[169]</sup> Acne treatment was modified in the 1950s with the introduction of oral tetracycline antibiotics (such as minocycline). These reinforced the idea amongst dermatologists that bacterial growth on the skin plays an important role in causing acne.<sup>[165]</sup> Subsequently, in the 1970s tretinoin (original trade name Retin A) was found to be an effective treatment.<sup>[170]</sup> The development of oral isotretinoin (sold as Accutane and Roaccutane) followed in 1980.<sup>[171]</sup> After its introduction in the United States it was recognized as a medication highly likely to cause birth defects if taken during pregnancy. In the United States, more than 2,000 women became pregnant while taking isotretinoin between 1982 and 2003, with most pregnancies ending in abortion or miscarriage. About 160 babies were born with birth defects.<sup>[172][173]</sup>



Domolene ointment, a mid-1900s medication that was claimed to cure acne

Treatment of acne with topical crushed dry ice (termed "cryoslush") was first described in 1907, but is no longer performed commonly.<sup>[174]</sup> Prior to 1960, the use of X-rays was also a common treatment.<sup>[175][176]</sup>

## Society and culture

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The costs and social impact of acne are substantial. In the United States, acne vulgaris is responsible for more than 5 million doctor visits and costs over US\$2.5 billion each year in direct costs.<sup>[13]</sup> Similarly, acne vulgaris is responsible for 3.5 million doctor visits each year in the United Kingdom.<sup>[20]</sup> Sales for the top ten leading acne treatment brands in the US in 2015, have been reported as amounting to \$352 million.<sup>[177]</sup>

Misperceptions about acne's causative and aggravating factors are common, and those affected by it are often blamed for their condition.<sup>[178]</sup> Such blame can worsen the affected person's sense of self-esteem.<sup>[178]</sup> Until the 20th century, even among dermatologists, the list of causes was believed to include excessive sexual thoughts and masturbation.<sup>[167]</sup> Dermatology's association with sexually transmitted infections, especially syphilis, contributed to the stigma.<sup>[167]</sup>

Acne vulgaris and its resultant scars have been associated with significant social and academic difficulties that can last into adulthood, including difficulties obtaining employment.<sup>[31][179]</sup> Until the 1930s, it was largely seen as a trivial problem among middle-class girls – a trivial problem, because, unlike smallpox and tuberculosis, no one died from it, and a feminine problem, because boys were much less likely to seek medical assistance for it.<sup>[167]</sup> During the Great Depression, dermatologists discovered that young men with acne had difficulty obtaining jobs, and during World War II, some soldiers in tropical climates developed such severe and widespread tropical acne on their bodies that they were declared medically unfit for duty.<sup>[167]</sup>

## Research

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Efforts to better understand the mechanisms of sebum production are underway. The aim of this research is to develop medications that target and interfere with the hormones that are known to increase sebum production (e.g., IGF-1 and alpha-melanocyte-stimulating hormone).<sup>[10]</sup> Additional sebum-lowering medications being researched include topical antiandrogens and peroxisome proliferator-activated receptor modulators.<sup>[10]</sup> Another avenue of early-stage research has focused on how to best use laser and light therapy to selectively destroy sebum-producing glands in the skin's hair follicles in order to reduce sebum production and improve acne appearance.<sup>[10]</sup>

The use of antimicrobial peptides against *C. acnes* is under investigation as a treatment for acne to overcoming antibiotic resistance.<sup>[10]</sup> In 2007, the first genome sequencing of a *C. acnes* bacteriophage (PA6) was reported. The authors proposed applying this research toward development of bacteriophage therapy as an acne treatment in order to overcome the problems associated with long-term antibiotic therapy such as bacterial resistance.<sup>[180]</sup> Oral and topical probiotics are also being evaluated as treatments for acne.<sup>[181]</sup> Probiotics have been hypothesized to have therapeutic effects for those affected by acne due to their ability to decrease skin inflammation and improve skin moisture by increasing the skin's ceramide content.<sup>[181]</sup> As of 2014, studies examining the effects of probiotics on acne in humans were limited.<sup>[181]</sup>

Decreased levels of retinoic acid in the skin may contribute to comedo formation. To address this deficiency, methods to increase the skin's production of retinoid acid are being explored.<sup>[10]</sup> A vaccine against inflammatory acne has shown promising results in mice and humans.<sup>[50][182]</sup> Some have voiced concerns about creating a vaccine designed to neutralize a stable community of normal skin bacteria that is known to protect the skin from colonization by more harmful microorganisms.<sup>[183]</sup>

## Other animals

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Acne can occur on cats,<sup>[184]</sup> dogs,<sup>[185]</sup> and horses.<sup>[186][187]</sup>

## References

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1. Vary JC (November 2015). "Selected Disorders of Skin Appendages--Acne, Alopecia, Hyperhidrosis". *The Medical Clinics of North America* (Review). **99** (6): 1195–211. doi:10.1016/j.mcna.2015.07.003 (<https://doi.org/10.1016%2Fj.mcna.2015.07.003>). PMID 26476248 (<https://pubmed.ncbi.nlm.nih.gov/26476248>).
2. Bhate K, Williams HC (March 2013). "Epidemiology of acne vulgaris". *The British Journal of Dermatology* (Review). **168** (3): 474–85. doi:10.1111/bjd.12149 (<https://doi.org/10.1111%2Fbjd.12149>). PMID 23210645 (<https://pubmed.ncbi.nlm.nih.gov/23210645>).
3. Barnes LE, Levender MM, Fleischer AB, Feldman SR (April 2012). "Quality of life measures for acne patients". *Dermatologic Clinics* (Review). **30** (2): 293–300, ix. doi:10.1016/j.det.2011.11.001 (<https://doi.org/10.1016%2Fj.det.2011.11.001>). PMID 22284143 (<https://pubmed.ncbi.nlm.nih.gov/22284143>).
4. Goodman G (July 2006). "Acne and acne scarring - the case for active and early intervention" (<http://www.racgp.org.au/afp/200607/8194>). *Australian Family Physician* (Review). **35** (7): 503–4. PMID 16820822 (<https://pubmed.ncbi.nlm.nih.gov/16820822>). Archived (<https://web.archive.org/web/20130421103732/http://www.racgp.org.au/afp/200607/8194>) from the original on 21 April 2013.
5. James WD (April 2005). "Clinical practice. Acne". *The New England Journal of Medicine* (Review). **352** (14): 1463–72. doi:10.1056/NEJMcp033487 (<https://doi.org/10.1056%2FNEJMcp033487>). PMID 15814882 (<https://pubmed.ncbi.nlm.nih.gov/15814882>).
6. Kahan, Scott (2008). *In a Page: Medicine* (<https://books.google.com/books?id=46wpAUhUHjMC&pg=PA412>). Lippincott Williams & Wilkins. p. 412. ISBN 9780781770354. Archived (<https://web.archive.org/web/20170906210844/https://books.google.com/books?id=46wpAUhUHjMC&pg=PA412>) from the original on 6 September 2017.
7. Mahmood SN, Bowe WP (April 2014). "Diet and acne update: carbohydrates emerge as the main culprit". *Journal of Drugs in Dermatology* (Review). **13** (4): 428–35. PMID 24719062 (<https://pubmed.ncbi.nlm.nih.gov/24719062>).
8. Titus S, Hodge J (October 2012). "Diagnosis and treatment of acne" (<http://www.aafp.org/afp/2012/1015/p734.html>). *American Family Physician* (Review). **86** (8): 734–40. PMID 23062156 (<https://pubmed.ncbi.nlm.nih.gov/23062156>). Archived (<https://web.archive.org/web/20150218104435/http://www.aafp.org/afp/2012/1015/p734.html>) from the original on 18 February 2015.
9. GBD 2015 Disease Injury Incidence Prevalence Collaborators (October 2016). "Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5055577>). *Lancet*. **388** (10053): 1545–1602. doi:10.1016/S0140-6736(16)31678-6 (<https://doi.org/10.1016%2FS0140-6736%2816%2931678-6>). PMC 5055577 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5055577>). PMID 27733282 (<https://pubmed.ncbi.nlm.nih.gov/27733282>).

10. Aslam I, Fleischer A, Feldman S (March 2015). "Emerging drugs for the treatment of acne". *Expert Opinion on Emerging Drugs* (Review). **20** (1): 91–101. doi:10.1517/14728214.2015.990373 (<https://doi.org/10.1517%2F14728214.2015.990373>). PMID 25474485 (<https://pubmed.ncbi.nlm.nih.gov/25474485>). (subscription required)
11. Tuchayi, Sara Moradi; Makrantonaki, Evgenia; Ganceviciene, Ruta; Dessinioti, Clio; Feldman, Steven R.; Zouboulis, Christos C. (September 2015). "Acne vulgaris". *Nature Reviews. Disease Primers*. **1**: 15033. doi:10.1038/nrdp.2015.33 (<https://doi.org/10.1038%2Fnrdp.2015.33>). PMID 27227877 (<https://pubmed.ncbi.nlm.nih.gov/27227877>).
12. "Frequently Asked Questions: Acne" (<https://web.archive.org/web/20161210141821/https://www.womenshealth.gov/files/assets/docs/fact-sheets/acne.pdf>) (PDF). U.S. Department of Health and Human Services, Office of Public Health and Science, Office on Women's Health. July 2009. Archived from the original (<https://www.womenshealth.gov/files/assets/docs/fact-sheets/acne.pdf>) (PDF) on 10 December 2016. Retrieved 30 July 2009.
13. Knutsen-Larson S, Dawson AL, Dunnick CA, Dellavalle RP (January 2012). "Acne vulgaris: pathogenesis, treatment, and needs assessment". *Dermatologic Clinics* (Review). **30** (1): 99–106, viii–ix. doi:10.1016/j.det.2011.09.001 (<https://doi.org/10.1016%2Fj.det.2011.09.001>). PMID 22117871 (<https://pubmed.ncbi.nlm.nih.gov/22117871>).
14. Schnopp C, Mempel M (August 2011). "Acne vulgaris in children and adolescents". *Minerva Pediatrica* (Review). **63** (4): 293–304. PMID 21909065 (<https://pubmed.ncbi.nlm.nih.gov/21909065>).
15. Zaenglein AL (October 2018). "Acne Vulgaris". *The New England Journal of Medicine* (Review). **379** (14): 1343–1352. doi:10.1056/NEJMcp1702493 (<https://doi.org/10.1056%2FNEJMcp1702493>). PMID 30281982 (<https://pubmed.ncbi.nlm.nih.gov/30281982>).
16. Beylot C, Auffret N, Poli F, Claudel JP, Leccia MT, Del Giudice P, Dreno B (March 2014). "Propionibacterium acnes: an update on its role in the pathogenesis of acne". *Journal of the European Academy of Dermatology and Venereology* (Review). **28** (3): 271–8. doi:10.1111/jdv.12224 (<https://doi.org/10.1111%2Fjdv.12224>). PMID 23905540 (<https://pubmed.ncbi.nlm.nih.gov/23905540>).
17. Vallerand IA, Lewinson RT, Farris MS, Sibley CD, Ramien ML, Bulloch AG, Patten SB (January 2018). "Efficacy and adverse events of oral isotretinoin for acne: a systematic review". *The British Journal of Dermatology*. **178** (1): 76–85. doi:10.1111/bjd.15668 (<https://doi.org/10.1111%2Fbjd.15668>). PMID 28542914 (<https://pubmed.ncbi.nlm.nih.gov/28542914>).
18. Hay RJ, Johns NE, Williams HC, Bolliger IW, Dellavalle RP, Margolis DJ, et al. (June 2014). "The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions". *The Journal of Investigative Dermatology*. **134** (6): 1527–1534. doi:10.1038/jid.2013.446 (<https://doi.org/10.1038%2Fjid.2013.446>). PMID 24166134 (<https://pubmed.ncbi.nlm.nih.gov/24166134>).
19. Taylor M, Gonzalez M, Porter R (May–June 2011). "Pathways to inflammation: acne pathophysiology". *European Journal of Dermatology* (Review). **21** (3): 323–33. doi:10.1684/ejd.2011.1357 (<https://doi.org/10.1684%2Fejd.2011.1357>). PMID 21609898 (<https://pubmed.ncbi.nlm.nih.gov/21609898>).
20. Dawson AL, Dellavalle RP (May 2013). "Acne vulgaris". *BMJ* (Review). **346** (5): 30–33. doi:10.1136/bmj.f2634 (<https://doi.org/10.1136%2Fbmj.f2634>). JSTOR 23494950 (<https://www.jstor.org/stable/23494950>). PMID 23657180 (<https://pubmed.ncbi.nlm.nih.gov/23657180>).
21. Goldberg DJ, Berlin AL (October 2011). *Acne and Rosacea: Epidemiology, Diagnosis and Treatment* (<https://books.google.com/books?id=ZSjauawl1FsC&pg=PA8&dq>). London: Manson Pub. p. 8. ISBN 978-1-84076-150-4. Archived (<https://web.archive.org/web/20160702231501/https://books.google.com/books?id=ZSjauawl1FsC&pg=PA8&dq>) from the original on 2 July 2016.

22. Spencer EH, Ferdowsian HR, Barnard ND (April 2009). "Diet and acne: a review of the evidence". *International Journal of Dermatology* (Review). **48** (4): 339–47. doi:10.1111/j.1365-4632.2009.04002.x (<https://doi.org/10.1111%2Fj.1365-4632.2009.04002.x>). PMID 19335417 (<https://pubmed.ncbi.nlm.nih.gov/19335417>).
23. Admani S, Barrio VR (November 2013). "Evaluation and treatment of acne from infancy to preadolescence". *Dermatologic Therapy* (Review). **26** (6): 462–6. doi:10.1111/dth.12108 (<https://doi.org/10.1111%2Fdth.12108>). PMID 24552409 (<https://pubmed.ncbi.nlm.nih.gov/24552409>).
24. "acne", "vulgar". *Oxford English Dictionary* (CD-ROM) (2nd ed.). Oxford: Oxford University Press. 2009.
25. Zaenglein AL, Graber EM, Thiboutot DM (2012). "Chapter 80 Acne Vulgaris and Acneiform Eruptions". In Goldsmith, Lowell A., Katz, Stephen I., Gilchrest, Barbara A., Paller, Amy S., Lefell, David J., Wolff, Klaus (eds.). *Fitzpatrick's Dermatology in General Medicine* (8th ed.). New York: McGraw-Hill. pp. 897–917. ISBN 978-0-07-171755-7.
26. Dessinioti C, Katsambas A, Antoniou C (May–June 2014). "Hidradenitis suppurativa (acne inversa) as a systemic disease". *Clinics in Dermatology* (Review). **32** (3): 397–408. doi:10.1016/j.clindermatol.2013.11.006 (<https://doi.org/10.1016%2Fj.clindermatol.2013.11.006>). PMID 24767187 (<https://pubmed.ncbi.nlm.nih.gov/24767187>).
27. Moustafa FA, Sandoval LF, Feldman SR (September 2014). "Rosacea: new and emerging treatments". *Drugs* (Review). **74** (13): 1457–65. doi:10.1007/s40265-014-0281-x (<https://doi.org/10.1007%2Fs40265-014-0281-x>). PMID 25154627 (<https://pubmed.ncbi.nlm.nih.gov/25154627>).
28. Dessinioti C, Antoniou C, Katsambas A (January–February 2014). "Acneiform eruptions". *Clinics in Dermatology* (Review). **32** (1): 24–34. doi:10.1016/j.clindermatol.2013.05.023 (<https://doi.org/10.1016%2Fj.clindermatol.2013.05.023>). PMID 24314375 (<https://pubmed.ncbi.nlm.nih.gov/24314375>).
29. Adityan B, Kumari R, Thappa DM (May 2009). "Scoring systems in acne vulgaris" (<https://tspace.library.utoronto.ca/bitstream/1807/48422/1/dv09103.pdf>) (PDF). *Indian Journal of Dermatology, Venereology and Leprology* (Review). **75** (3): 323–6. doi:10.4103/0378-6323.51258 (<https://doi.org/10.4103%2F0378-6323.51258>). PMID 19439902 (<https://pubmed.ncbi.nlm.nih.gov/19439902>).
30. Zhao YE, Hu L, Wu LP, Ma JX (March 2012). "A meta-analysis of association between acne vulgaris and Demodex infestation" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3296070>). *Journal of Zhejiang University. Science. B* (Meta-analysis). **13** (3): 192–202. doi:10.1631/jzus.B1100285 (<https://doi.org/10.1631%2Fjzus.B1100285>). PMC 3296070 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3296070>). PMID 22374611 (<https://pubmed.ncbi.nlm.nih.gov/22374611>).
31. Fife D (April 2016). "Evaluation of Acne Scars: How to Assess Them and What to Tell the Patient". *Dermatologic Clinics* (Review). **34** (2): 207–13. doi:10.1016/j.det.2015.11.009 (<https://doi.org/10.1016%2Fj.det.2015.11.009>). PMID 27015781 (<https://pubmed.ncbi.nlm.nih.gov/27015781>).
32. Levy LL, Zeichner JA (October 2012). "Management of acne scarring, part II: a comparative review of non-laser-based, minimally invasive approaches". *American Journal of Clinical Dermatology* (Review). **13** (5): 331–40. doi:10.2165/11631410-000000000-00000 (<https://doi.org/10.2165%2F11631410-000000000-00000>). PMID 22849351 (<https://pubmed.ncbi.nlm.nih.gov/22849351>).
33. Sánchez Viera M (July 2015). "Management of acne scars: fulfilling our duty of care for patients". *The British Journal of Dermatology* (Review). 172 Suppl 1 (Supplement 1): 47–51. doi:10.1111/bjd.13650 (<https://doi.org/10.1111%2Fbjd.13650>). PMID 25597636 (<https://pubmed.ncbi.nlm.nih.gov/25597636>).

34. Sobanko JF, Alster TS (October 2012). "Management of acne scarring, part I: a comparative review of laser surgical approaches". *American Journal of Clinical Dermatology* (Review). **13** (5): 319–30. doi:10.2165/11598910-000000000-00000 (<https://doi.org/10.2165%2F11598910-000000000-00000>). PMID 22612738 (<https://pubmed.ncbi.nlm.nih.gov/22612738>).
35. Chandra M, Levitt J, Pensabene CA (May 2012). "Hydroquinone therapy for post-inflammatory hyperpigmentation secondary to acne: not just prescribable by dermatologists". *Acta Dermato-Venereologica* (Review). **92** (3): 232–5. doi:10.2340/00015555-1225 (<https://doi.org/10.2340%2F00015555-1225>). PMID 22002814 (<https://pubmed.ncbi.nlm.nih.gov/22002814>).
36. Yin NC, McMichael AJ (February 2014). "Acne in patients with skin of color: practical management". *American Journal of Clinical Dermatology* (Review). **15** (1): 7–16. doi:10.1007/s40257-013-0049-1 (<https://doi.org/10.1007%2Fs40257-013-0049-1>). PMID 24190453 (<https://pubmed.ncbi.nlm.nih.gov/24190453>).
37. Callender VD, St Surin-Lord S, Davis EC, Maclin M (April 2011). "Postinflammatory hyperpigmentation: etiologic and therapeutic considerations". *American Journal of Clinical Dermatology* (Review). **12** (2): 87–99. doi:10.2165/11536930-000000000-00000 (<https://doi.org/10.2165%2F11536930-000000000-00000>). PMID 21348540 (<https://pubmed.ncbi.nlm.nih.gov/21348540>).
38. Rigopoulos E, Korfitis C (2014). "Acne and Smoking". In Zouboulis C, Katsambas A, Kligman AM (eds.). *Pathogenesis and Treatment of Acne and Rosacea*. Berlin: Springer-Verlag. pp. 167–170. ISBN 978-3-540-69374-1.
39. *Acne: Overview* (<https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0072395/>). *PubMed Health*. Cologne: Institute for Quality and Efficiency in Health Care. July 2016. Archived (<https://web.archive.org/web/20170906210844/https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0072395/>) from the original on 6 September 2017. Retrieved 12 March 2017. "It is not clear whether there might be a connection between smoking and acne."
40. Yang JK, Wu WJ, Qi J, He L, Zhang YP (February 2014). "TNF-308 G/A polymorphism and risk of acne vulgaris: a meta-analysis" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3912133>). *PLOS ONE* (Systematic Review & Meta-Analysis). **9** (2): e87806. Bibcode:2014PLoSO...987806Y (<https://ui.adsabs.harvard.edu/abs/2014PLoSO...987806Y>). doi:10.1371/journal.pone.0087806 (<https://doi.org/10.1371%2Fjournal.pone.0087806>). PMC 3912133 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3912133>). PMID 24498378 (<https://pubmed.ncbi.nlm.nih.gov/24498378>).
41. Fitzpatrick, TB (2005). *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology* (5th ed.). New York: McGraw-Hill Medical Pub. Division. p. 2. ISBN 978-0071440196.
42. Hoeger PH, Irvine AD, Yan AC (2011). "Chapter 79: Acne". *Harper's Textbook of Pediatric Dermatology* (3rd ed.). New Jersey: Wiley-Blackwell. ISBN 978-1-4443-4536-0.
43. Shalita AR, Del Rosso JQ, Webster G, eds. (March 2011). *Acne Vulgaris* (<https://books.google.com/books?id=CIPOBQAAQBAJ&pg=PA33>). CRC Press. pp. 33–. ISBN 978-1-61631-009-7. Archived (<https://web.archive.org/web/20161209210819/https://books.google.com/books?id=CIPOBQAAQBAJ&pg=PA33>) from the original on 9 December 2016.
44. Zouboulis CC, Katsambas AD, Kligman AM, eds. (July 2014). *Pathogenesis and Treatment of Acne and Rosacea* (<https://books.google.com/books?id=vnQqBAAQBAJ&pg=PA121>). Springer. pp. 121–122. ISBN 978-3-540-69375-8. Archived (<https://web.archive.org/web/20161210040108/https://books.google.com/books?id=vnQqBAAQBAJ&pg=PA121>) from the original on 10 December 2016.
45. Das S, Reynolds RV (December 2014). "Recent advances in acne pathogenesis: implications for therapy". *American Journal of Clinical Dermatology* (Review). **15** (6): 479–88. doi:10.1007/s40257-014-0099-z (<https://doi.org/10.1007%2Fs40257-014-0099-z>). PMID 25388823 (<https://pubmed.ncbi.nlm.nih.gov/25388823>).



46. Housman E, Reynolds RV (November 2014). "Polycystic ovary syndrome: a review for dermatologists: Part I. Diagnosis and manifestations". *Journal of the American Academy of Dermatology* (Review). **71** (5): 847.e1–847.e10, quiz 857–8. doi:10.1016/j.jaad.2014.05.007 (<https://doi.org/10.1016%2Fj.jaad.2014.05.007>). PMID 25437977 (<https://pubmed.ncbi.nlm.nih.gov/25437977>).
47. Kong YL, Tey HL (June 2013). "Treatment of acne vulgaris during pregnancy and lactation". *Drugs* (Review). **73** (8): 779–87. doi:10.1007/s40265-013-0060-0 (<https://doi.org/10.1007%2Fs40265-013-0060-0>). PMID 23657872 (<https://pubmed.ncbi.nlm.nih.gov/23657872>).
48. Melnik B, Jansen T, Grabbe S (February 2007). "Abuse of anabolic-androgenic steroids and bodybuilding acne: an underestimated health problem". *Journal der Deutschen Dermatologischen Gesellschaft = Journal of the German Society of Dermatology* (Review). **5** (2): 110–7. doi:10.1111/j.1610-0387.2007.06176.x (<https://doi.org/10.1111%2Fj.1610-0387.2007.06176.x>). PMID 17274777 (<https://pubmed.ncbi.nlm.nih.gov/17274777>).
49. Joseph JF, Parr MK (January 2015). "Synthetic androgens as designer supplements" (<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4462045>). *Current Neuropharmacology* (Review). **13** (1): 89–100. doi:10.2174/1570159X13666141210224756 (<https://doi.org/10.2174%2F1570159X13666141210224756>). PMC 4462045 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4462045>). PMID 26074745 (<https://pubmed.ncbi.nlm.nih.gov/26074745>).
50. Simonart T (December 2013). "Immunotherapy for acne vulgaris: current status and future directions". *American Journal of Clinical Dermatology* (Review). **14** (6): 429–35. doi:10.1007/s40257-013-0042-8 (<https://doi.org/10.1007%2Fs40257-013-0042-8>). PMID 24019180 (<https://pubmed.ncbi.nlm.nih.gov/24019180>).
51. Bhate K, Williams HC (April 2014). "What's new in acne? An analysis of systematic reviews published in 2011-2012". *Clinical and Experimental Dermatology* (Review). **39** (3): 273–7, quiz 277–8. doi:10.1111/ced.12270 (<https://doi.org/10.1111%2Fced.12270>). PMID 24635060 (<https://pubmed.ncbi.nlm.nih.gov/24635060>).
52. Davidovici BB, Wolf R (January 2010). "The role of diet in acne: facts and controversies". *Clinics in Dermatology* (Review). **28** (1): 12–6. doi:10.1016/j.clindermatol.2009.03.010 (<https://doi.org/10.1016%2Fj.clindermatol.2009.03.010>). PMID 20082944 (<https://pubmed.ncbi.nlm.nih.gov/20082944>).
53. Bronsnick T, Murzaku EC, Rao BK (December 2014). "Diet in dermatology: Part I. Atopic dermatitis, acne, and nonmelanoma skin cancer". *Journal of the American Academy of Dermatology* (Review). **71** (6): 1039.e1–1039.e12. doi:10.1016/j.jaad.2014.06.015 (<https://doi.org/10.1016%2Fj.jaad.2014.06.015>). PMID 25454036 (<https://pubmed.ncbi.nlm.nih.gov/25454036>).
54. Melnik BC, John SM, Plewig G (November 2013). "Acne: risk indicator for increased body mass index and insulin resistance". *Acta Dermato-Venereologica* (Review). **93** (6): 644–9. doi:10.2340/00015555-1677 (<https://doi.org/10.2340%2F00015555-1677>). PMID 23975508 (<https://pubmed.ncbi.nlm.nih.gov/23975508>).
55. Ferdowsian HR, Levin S (March 2010). "Does diet really affect acne?" (<http://www.skintherapyletter.com/2010/15.3/1.html>). *Skin Therapy Letter* (Review). **15** (3): 1–2, 5. PMID 20361171 (<https://pubmed.ncbi.nlm.nih.gov/20361171>). Archived (<https://web.archive.org/web/20150221185238/http://www.skintherapyletter.com/2010/15.3/1.html>) from the original on 21 February 2015.
56. Melnik, BC (2011). "Evidence for Acne-Promoting Effects of Milk and Other Insulinotropic Dairy Products". *Milk and Milk Products in Human Nutrition. Nestle Nutrition Workshop Series. Paediatric Programme*. Nestlé Nutrition Institute Workshop Series: Pediatric Program. **67**. pp. 131–45. doi:10.1159/000325580 (<https://doi.org/10.1159%2F000325580>). ISBN 978-3-8055-9587-2. PMID 21335995 (<https://pubmed.ncbi.nlm.nih.gov/21335995>).
57. Brescoll J, Daveluy S (February 2015). "A review of vitamin B12 in dermatology". *American Journal of Clinical Dermatology* (Review). **16** (1): 27–33. doi:10.1007/s40257-014-0107-3 (<https://doi.org/10.1007%2Fs40257-014-0107-3>). PMID 25559140 (<https://pubmed.ncbi.nlm.nih.gov/25559140>).

58. "Acne" (<https://www.webmd.com/skin-problems-and-treatments/acne/acne-causes>). WebMD. Retrieved 24 January 2018.
59. Leach O, van Boxel GI (2013). *Crash Course General Medicine – E-Book* ([https://books.google.ca/books?id=vgcXjf\\_15wAC&pg=PA362](https://books.google.ca/books?id=vgcXjf_15wAC&pg=PA362)). Elsevier Health Sciences. p. 362. ISBN 9780723437895.
60. Orion E, Wolf R (November–December 2014). "Psychologic factors in the development of facial dermatoses". *Clinics in Dermatology* (Review). **32** (6): 763–6. doi:10.1016/j.clindermatol.2014.02.015 (<https://doi.org/10.1016%2Fj.clindermatol.2014.02.015>). PMID 25441469 (<https://pubmed.ncbi.nlm.nih.gov/25441469>).
61. Rodriguez-Vallecillo E, Woodbury-Fariña MA (December 2014). "Dermatological manifestations of stress in normal and psychiatric populations". *The Psychiatric Clinics of North America* (Review). **37** (4): 625–51. doi:10.1016/j.psc.2014.08.009 (<https://doi.org/10.1016%2Fj.psc.2014.08.009>). PMID 25455069 (<https://pubmed.ncbi.nlm.nih.gov/25455069>).
62. "Questions and Answers about Acne" ([http://www.niams.nih.gov/Health\\_Info/Acne/default.asp](http://www.niams.nih.gov/Health_Info/Acne/default.asp)). National Institute of Arthritis and Musculoskeletal and Skin Diseases. May 2013. Archived ([https://web.archive.org/web/20150202064933/http://www.niams.nih.gov/health\\_info/acne/default.asp](https://web.archive.org/web/20150202064933/http://www.niams.nih.gov/health_info/acne/default.asp)) from the original on 2 February 2015.
63. Basak SA, Zaenglein AL (November 2013). "Acne and its management". *Pediatrics in Review* (Review). **34** (11): 479–97. doi:10.1542/pir.34-11-479 (<https://doi.org/10.1542%2Fpir.34-11-479>). PMID 24187141 (<https://pubmed.ncbi.nlm.nih.gov/24187141>).
64. Andriessen A, Lynde CW (November 2014). "Antibiotic resistance: shifting the paradigm in topical acne treatment". *Journal of Drugs in Dermatology* (Review). **13** (11): 1358–64. PMID 25607703 (<https://pubmed.ncbi.nlm.nih.gov/25607703>).
65. Hammer KA (February 2015). "Treatment of acne with tea tree oil (melaleuca) products: a review of efficacy, tolerability and potential modes of action". *International Journal of Antimicrobial Agents* (Review). **45** (2): 106–10. doi:10.1016/j.ijantimicag.2014.10.011 (<https://doi.org/10.1016%2Fj.ijantimicag.2014.10.011>). PMID 25465857 (<https://pubmed.ncbi.nlm.nih.gov/25465857>).
66. Sieber MA, Hegel JK (November 2013). "Azelaic acid: Properties and mode of action". *Skin Pharmacology and Physiology* (Review). **27** Suppl 1 (Supplement 1): 9–17. doi:10.1159/000354888 (<https://doi.org/10.1159%2F000354888>). PMID 24280644 (<https://pubmed.ncbi.nlm.nih.gov/24280644>).
67. Simpson NB, Cunliffe WJ (2004). "Disorders of the sebaceous glands". In Burns, Tony, Breathnach, Stephen, Cox, Neil, Griffiths, Christopher (eds.). *Rook's textbook of dermatology* (7th ed.). Malden, Mass.: Blackwell Science. pp. 431–75. ISBN 978-0-632-06429-8.
68. Tan JK, Jones E, Allen E, Pripotnev S, Raza A, Wolfe B (November 2013). "Evaluation of essential clinical components and features of current acne global grading scales". *Journal of the American Academy of Dermatology* (Review). **69** (5): 754–761. doi:10.1016/j.jaad.2013.07.029 (<https://doi.org/10.1016%2Fj.jaad.2013.07.029>). PMID 23972509 (<https://pubmed.ncbi.nlm.nih.gov/23972509>).
69. Chiang A, Hafeez F, Maibach HI (April 2014). "Skin lesion metrics: role of photography in acne". *The Journal of Dermatological Treatment* (Review). **25** (2): 100–5. doi:10.3109/09546634.2013.813010 (<https://doi.org/10.3109%2F09546634.2013.813010>). PMID 23758271 (<https://pubmed.ncbi.nlm.nih.gov/23758271>).
70. O' Brien SC, Lewis JB, Cunliffe WJ. "The Leeds Revised Acne Grading System" ([https://web.archive.org/web/20151125021231/http://carepathways4gp.org.uk/Acne\\_Care\\_Pathway/LEEDS\\_score\\_files/Acne%20Grading%20System.pdf](https://web.archive.org/web/20151125021231/http://carepathways4gp.org.uk/Acne_Care_Pathway/LEEDS_score_files/Acne%20Grading%20System.pdf)) (PDF). The Leeds Teaching Hospitals. Archived from the original ([http://carepathways4gp.org.uk/Acne\\_Care\\_Pathway/LEEDS\\_score\\_files/Acne%20Grading%20System.pdf](http://carepathways4gp.org.uk/Acne_Care_Pathway/LEEDS_score_files/Acne%20Grading%20System.pdf)) (PDF) on 25 November 2015. Retrieved 23 November 2015.

71. Purdy S, Deberker D (May 2008). "Acne vulgaris" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2907987>). *BMJ Clinical Evidence* (Review). **2008**: 1714. PMC 2907987 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2907987>). PMID 19450306 (<https://pubmed.ncbi.nlm.nih.gov/19450306>).
72. Del Rosso JQ, Silverberg N, Zeichner JA (April 2016). "When Acne is Not Acne" ([https://touroroscholar.touro.edu/tuncom\\_pubs/13](https://touroroscholar.touro.edu/tuncom_pubs/13)). *Dermatologic Clinics* (Review). **34** (2): 225–8. doi:10.1016/j.det.2015.12.002 (<https://doi.org/10.1016%2Fj.det.2015.12.002>). PMID 27015783 (<https://pubmed.ncbi.nlm.nih.gov/27015783>).
73. Archer CB, Cohen SN, Baron SE (May 2012). "Guidance on the diagnosis and clinical management of acne". *Clinical and Experimental Dermatology* (Review). **37** Suppl 1 (Supplement 1): 1–6. doi:10.1111/j.1365-2230.2012.04335.x (<https://doi.org/10.1111%2Fj.1365-2230.2012.04335.x>). PMID 22486762 (<https://pubmed.ncbi.nlm.nih.gov/22486762>).
74. Kanerva L, Elsner P, Wahlberg JH, Maibach HI, eds. (2013). *Handbook of Occupational Dermatology* (<https://books.google.com/books?id=0DzvCAAQBAJ&pg=PA231>). Springer Science & Business Media. p. 231. ISBN 978-3-662-07677-4. Archived (<https://web.archive.org/web/20170906210844/https://books.google.com/books?id=0DzvCAAQBAJ&pg=PA231>) from the original on 6 September 2017.
75. Ramos-e-Silva M, Carneiro SC (March 2009). "Acne vulgaris: review and guidelines". *Dermatology Nursing* (Review). **21** (2): 63–8, quiz 69. PMID 19507372 (<https://pubmed.ncbi.nlm.nih.gov/19507372>).
76. Simonart T (December 2012). "Newer approaches to the treatment of acne vulgaris". *American Journal of Clinical Dermatology* (Review). **13** (6): 357–64. doi:10.2165/11632500-000000000-00000 (<https://doi.org/10.2165%2F11632500-000000000-00000>). PMID 22920095 (<https://pubmed.ncbi.nlm.nih.gov/22920095>).
77. Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, Baldwin HE, Berson DS, et al. (May 2016). "Guidelines of care for the management of acne vulgaris". *Journal of the American Academy of Dermatology* (Review). **74** (5): 945–73.e33. doi:10.1016/j.jaad.2015.12.037 (<https://doi.org/10.1016%2Fj.jaad.2015.12.037>). PMID 26897386 (<https://pubmed.ncbi.nlm.nih.gov/26897386>).
78. Leccia MT, Auffret N, Poli F, Claudel JP, Corvec S, Dreno B (August 2015). "Topical acne treatments in Europe and the issue of antimicrobial resistance". *Journal of the European Academy of Dermatology and Venereology* (Review). **29** (8): 1485–92. doi:10.1111/jdv.12989 (<https://doi.org/10.1111%2Fjdv.12989>). PMID 25677763 (<https://pubmed.ncbi.nlm.nih.gov/25677763>).
79. Gamble R, Dunn J, Dawson A, Petersen B, McLaughlin L, Small A, et al. (June 2012). "Topical antimicrobial treatment of acne vulgaris: an evidence-based review". *American Journal of Clinical Dermatology* (Review). **13** (3): 141–52. doi:10.2165/11597880-000000000-00000 (<https://doi.org/10.2165%2F11597880-000000000-00000>). PMID 22268388 (<https://pubmed.ncbi.nlm.nih.gov/22268388>).
80. Sagransky M, Yentzer BA, Feldman SR (October 2009). "Benzoyl peroxide: a review of its current use in the treatment of acne vulgaris". *Expert Opinion on Pharmacotherapy* (Review). **10** (15): 2555–62. doi:10.1517/14656560903277228 (<https://doi.org/10.1517%2F14656560903277228>). PMID 19761357 (<https://pubmed.ncbi.nlm.nih.gov/19761357>).
81. Brandstetter AJ, Maibach HI (August 2013). "Topical dose justification: benzoyl peroxide concentrations". *The Journal of Dermatological Treatment* (Review). **24** (4): 275–7. doi:10.3109/09546634.2011.641937 (<https://doi.org/10.3109%2F09546634.2011.641937>). PMID 22103743 (<https://pubmed.ncbi.nlm.nih.gov/22103743>).
82. Riahi RR, Bush AE, Cohen PR (June 2016). "Topical Retinoids: Therapeutic Mechanisms in the Treatment of Photodamaged Skin". *American Journal of Clinical Dermatology* (Review). **17** (3): 265–76. doi:10.1007/s40257-016-0185-5 (<https://doi.org/10.1007%2Fs40257-016-0185-5>). PMID 26969582 (<https://pubmed.ncbi.nlm.nih.gov/26969582>).

83. "Drug Trials Snapshots: Akliel" (<https://www.fda.gov/drugs/resources-information-approved-drugs/drug-trials-snapshots-akliel>). *U.S. Food and Drug Administration (FDA)*. 11 October 2019. Archived (<https://web.archive.org/web/20191119042107/https://www.fda.gov/drugs/resources-information-approved-drugs/drug-trials-snapshots-akliel>) from the original on 19 November 2019. Retrieved 18 November 2019.  This article incorporates text from this source, which is in the *public domain*.
84. Foti C, Romita P, Borghi A, Angelini G, Bonamonte D, Corazza M (September 2015). "Contact dermatitis to topical acne drugs: a review of the literature". *Dermatologic Therapy* (Review). **28** (5): 323–9. doi:10.1111/dth.12282 (<https://doi.org/10.1111%2Fdth.12282>). PMID 26302055 (<https://pubmed.ncbi.nlm.nih.gov/26302055>).
85. Costa CS, Bagatin E, Martimbianco AL, da Silva EM, Lúcio MM, Magin P, Riera R (November 2018). "Oral isotretinoin for acne" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6383843>). *The Cochrane Database of Systematic Reviews*. **11**: CD009435. doi:10.1002/14651858.cd009435.pub2 (<https://doi.org/10.1002%2F14651858.cd009435.pub2>). PMC 6383843 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6383843>). PMID 30484286 (<https://pubmed.ncbi.nlm.nih.gov/30484286>).
86. Tan J, Boyal S, Desai K, Knezevic S (April 2016). "Oral Isotretinoin: New Developments Relevant to Clinical Practice". *Dermatologic Clinics* (Review). **34** (2): 175–84. doi:10.1016/j.det.2015.11.002 (<https://doi.org/10.1016%2Fj.det.2015.11.002>). PMID 27015777 (<https://pubmed.ncbi.nlm.nih.gov/27015777>).
87. Prevost N, English JC (October 2013). "Isotretinoin: update on controversial issues". *Journal of Pediatric and Adolescent Gynecology* (Review). **26** (5): 290–3. doi:10.1016/j.jpag.2013.05.007 (<https://doi.org/10.1016%2Fj.jpag.2013.05.007>). PMID 24147278 (<https://pubmed.ncbi.nlm.nih.gov/24147278>).
88. Walsh TR, Efthimiou J, Dréno B (March 2016). "Systematic review of antibiotic resistance in acne: an increasing topical and oral threat" (<http://orca.cf.ac.uk/102767/1/acne.pdf>) (PDF). *The Lancet. Infectious Diseases* (Systematic Review). **16** (3): e23–33. doi:10.1016/S1473-3099(15)00527-7 (<https://doi.org/10.1016%2FS1473-3099%2815%2900527-7>). PMID 26852728 (<https://pubmed.ncbi.nlm.nih.gov/26852728>).
89. Garner SE, Eady A, Bennett C, Newton JN, Thomas K, Popescu CM (August 2012). "Minocycline for acne vulgaris: efficacy and safety" ([http://www.cochrane.org/CD002086/SKIN\\_minocycline-for-acne-vulgaris-efficacy-and-safety](http://www.cochrane.org/CD002086/SKIN_minocycline-for-acne-vulgaris-efficacy-and-safety)). *The Cochrane Database of Systematic Reviews* (8): CD002086. doi:10.1002/14651858.CD002086.pub2 (<https://doi.org/10.1002%2F14651858.CD002086.pub2>). PMID 22895927 (<https://pubmed.ncbi.nlm.nih.gov/22895927>).
90. Arowojolu AO, Gallo MF, Lopez LM, Grimes DA (July 2012). "Combined oral contraceptive pills for treatment of acne". *The Cochrane Database of Systematic Reviews* (Systematic Review & Meta-Analysis). **7** (7): CD004425. doi:10.1002/14651858.CD004425.pub6 (<https://doi.org/10.1002%2F14651858.CD004425.pub6>). PMID 22786490 (<https://pubmed.ncbi.nlm.nih.gov/22786490>).
91. Kuhl, H. (1999). "Hormonal Contraception". *Estrogens and Antiestrogens II*. Handbook of Experimental Pharmacology. 135 / 2. pp. 363–407. doi:10.1007/978-3-642-60107-1\_18 ([https://doi.org/10.1007%2F978-3-642-60107-1\\_18](https://doi.org/10.1007%2F978-3-642-60107-1_18)). ISBN 978-3-642-64261-6. ISSN 0171-2004 (<https://www.worldcat.org/issn/0171-2004>).
92. Kamangar F, Shinkai K (October 2012). "Acne in the adult female patient: a practical approach". *International Journal of Dermatology*. **51** (10): 1162–74. doi:10.1111/j.1365-4632.2012.05519.x (<https://doi.org/10.1111%2Fj.1365-4632.2012.05519.x>). PMID 22994662 (<https://pubmed.ncbi.nlm.nih.gov/22994662>).
93. Kuhl H (August 2005). "Pharmacology of estrogens and progestogens: influence of different routes of administration" ([http://hormonebalance.org/images/documents/Kuhl%2005%20%20Pharm%20Estro%20Progest%20Climacteric\\_1313155660.pdf](http://hormonebalance.org/images/documents/Kuhl%2005%20%20Pharm%20Estro%20Progest%20Climacteric_1313155660.pdf)) (PDF). *Climacteric*. **8** Suppl 1: 3–63. doi:10.1080/13697130500148875 (<https://doi.org/10.1080%2F13697130500148875>). PMID 16112947 (<https://pubmed.ncbi.nlm.nih.gov/16112947>).

94. Duarte FH, Jallad RS, Bronstein MD (November 2016). "Estrogens and selective estrogen receptor modulators in acromegaly". *Endocrine*. **54** (2): 306–314. doi:10.1007/s12020-016-1118-z (<https://doi.org/10.1007/s12020-016-1118-z>). PMID 27704479 (<https://pubmed.ncbi.nlm.nih.gov/27704479>).
95. Kuhl, H. (1997). "Metabolische Effekte der Östrogene und Gestagene" [Metabolic effects of estrogens and progestogens]. *Der Gynäkologe* (in German). **30** (4): 357–369. doi:10.1007/PL00003042 (<https://doi.org/10.1007/PL00003042>). ISSN 0017-5994 (<http://www.worldcat.org/issn/0017-5994>).
96. Wiegratz I, Kuhl H (2002). "Managing cutaneous manifestations of hyperandrogenic disorders: the role of oral contraceptives". *Treatments in Endocrinology*. **1** (6): 372–86. doi:10.2165/00024677-200201060-00003 (<https://doi.org/10.2165/00024677-200201060-00003>). PMID 15832490 (<https://pubmed.ncbi.nlm.nih.gov/15832490>).
97. Arowojolu AO, Gallo MF, Lopez LM, Grimes DA (July 2012). "Combined oral contraceptive pills for treatment of acne". *The Cochrane Database of Systematic Reviews* (7): CD004425. doi:10.1002/14651858.CD004425.pub6 (<https://doi.org/10.1002/14651858.CD004425.pub6>). PMID 22786490 (<https://pubmed.ncbi.nlm.nih.gov/22786490>).
98. Powell A (April 2017). "Choosing the Right Oral Contraceptive Pill for Teens". *Pediatric Clinics of North America* (Review). **64** (2): 343–358. doi:10.1016/j.pcl.2016.11.005 (<https://doi.org/10.1016/j.pcl.2016.11.005>). PMID 28292450 (<https://pubmed.ncbi.nlm.nih.gov/28292450>).
99. Słopień R, Milewska E, Rynio P, Męczekalski B (March 2018). "Use of oral contraceptives for management of acne vulgaris and hirsutism in women of reproductive and late reproductive age" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5925193>). *Przegląd Menopauzalny = Menopause Review*. **17** (1): 1–4. doi:10.5114/pm.2018.74895 (<https://doi.org/10.5114/pm.2018.74895>). PMC 5925193 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5925193>). PMID 29725277 (<https://pubmed.ncbi.nlm.nih.gov/29725277>).
100. Koo EB, Petersen TD, Kimball AB (September 2014). "Meta-analysis comparing efficacy of antibiotics versus oral contraceptives in acne vulgaris". *Journal of the American Academy of Dermatology* (Systematic Review & Meta-Analysis). **71** (3): 450–9. doi:10.1016/j.jaad.2014.03.051 (<https://doi.org/10.1016/j.jaad.2014.03.051>). PMID 24880665 (<https://pubmed.ncbi.nlm.nih.gov/24880665>).
101. Layton AM, Eady EA, Whitehouse H, Del Rosso JQ, Fedorowicz Z, van Zuuren EJ (April 2017). "Oral Spironolactone for Acne Vulgaris in Adult Females: A Hybrid Systematic Review" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360829>). *American Journal of Clinical Dermatology*. **18** (2): 169–191. doi:10.1007/s40257-016-0245-x (<https://doi.org/10.1007/s40257-016-0245-x>). PMC 5360829 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360829>). PMID 28155090 (<https://pubmed.ncbi.nlm.nih.gov/28155090>).
102. Bettoli V, Zauli S, Virgili A (July 2015). "Is hormonal treatment still an option in acne today?". *The British Journal of Dermatology*. 172 Suppl 1: 37–46. doi:10.1111/bjd.13681 (<https://doi.org/10.1111/bjd.13681>). PMID 25627824 (<https://pubmed.ncbi.nlm.nih.gov/25627824>).
103. Diamanti-Kandarakis E (October 1998). "How actual is the treatment with antiandrogen alone in patients with polycystic ovary syndrome?". *Journal of Endocrinological Investigation*. **21** (9): 623–9. doi:10.1007/BF03350788 (<https://doi.org/10.1007/BF03350788>). PMID 9856417 (<https://pubmed.ncbi.nlm.nih.gov/9856417>).
104. Ward A, Brogden RN, Heel RC, Speight TM, Avery GS (July 1984). "Isotretinoin. A review of its pharmacological properties and therapeutic efficacy in acne and other skin disorders". *Drugs*. **28** (1): 6–37. doi:10.2165/00003495-198428010-00002 (<https://doi.org/10.2165/00003495-198428010-00002>). PMID 6235105 (<https://pubmed.ncbi.nlm.nih.gov/6235105>).
105. Rasmusson, Gary H. (1986). *Chemical Control of Androgen Action*. Annual Reports in Medicinal Chemistry. **21**. pp. 179–188. doi:10.1016/S0065-7743(08)61128-8 ([https://doi.org/10.1016/S0065-7743\(08\)61128-8](https://doi.org/10.1016/S0065-7743(08)61128-8)). ISBN 9780120405213. ISSN 0065-7743 (<http://www.worldcat.org/issn/0065-7743>).

106. Giltay EJ, Gooren LJ (2009). "Potential side effects of androgen deprivation treatment in sex offenders". *The Journal of the American Academy of Psychiatry and the Law*. **37** (1): 53–8. PMID 19297634 (<https://pubmed.ncbi.nlm.nih.gov/19297634>).
107. Azarchi S, Bienenfeld A, Lo Sicco K, Marchbein S, Shapiro J, Nagler AR (June 2019). "Androgens in women: Hormone-modulating therapies for skin disease". *Journal of the American Academy of Dermatology*. **80** (6): 1509–1521. doi:10.1016/j.jaad.2018.08.061 (<https://doi.org/10.1016%2Fj.jaad.2018.08.061>). PMID 30312645 (<https://pubmed.ncbi.nlm.nih.gov/30312645>).
108. Oudenhoven MD, Kinney MA, McShane DB, Burkhart CN, Morrell DS (August 2015). "Adverse effects of acne medications: recognition and management". *American Journal of Clinical Dermatology*. **16** (4): 231–242. doi:10.1007/s40257-015-0127-7 (<https://doi.org/10.1007%2Fs40257-015-0127-7>). PMID 25896771 (<https://pubmed.ncbi.nlm.nih.gov/25896771>).
109. Husein-ElAhmed H (2015). "Management of acne vulgaris with hormonal therapies in adult female patients". *Dermatologic Therapy*. **28** (3): 166–72. doi:10.1111/dth.12231 (<https://doi.org/10.1111%2Fdth.12231>). PMID 25845307 (<https://pubmed.ncbi.nlm.nih.gov/25845307>).
110. Nguyen HL, Tollefson MM (August 2017). "Endocrine disorders and hormonal therapy for adolescent acne". *Current Opinion in Pediatrics*. **29** (4): 455–465. doi:10.1097/MOP.0000000000000515 (<https://doi.org/10.1097%2FMOP.0000000000000515>). PMID 28562419 (<https://pubmed.ncbi.nlm.nih.gov/28562419>).
111. Diamanti-Kandarakis E (September 1999). "Current aspects of antiandrogen therapy in women" (<https://books.google.com/books?id=9rfNZL6oEO0C&pg=PA707>). *Current Pharmaceutical Design*. **5** (9): 707–23. PMID 10495361 (<https://pubmed.ncbi.nlm.nih.gov/10495361>).
112. Shelley WB, Shelley ED (2001). *Advanced Dermatologic Therapy II* (<https://books.google.com/books?id=vuJsAAAAMAAJ>). W. B. Saunders. ISBN 978-0-7216-8258-7.
113. Balen A, Franks S, Homburg R, Kehoe S (October 2010). *Current Management of Polycystic Ovary Syndrome* (<https://books.google.com/books?id=0rtUBAAQBAJ&pg=PA132>). Cambridge University Press. pp. 132–. ISBN 978-1-906985-41-7.
114. Trivedi MK, Shinkai K, Murase JE (March 2017). "A Review of hormone-based therapies to treat adult acne vulgaris in women" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5419026>). *International Journal of Women's Dermatology*. **3** (1): 44–52. doi:10.1016/j.ijwd.2017.02.018 (<https://doi.org/10.1016%2Fj.ijwd.2017.02.018>). PMC 5419026 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5419026>). PMID 28492054 (<https://pubmed.ncbi.nlm.nih.gov/28492054>).
115. Giorgetti R, di Muzio M, Giorgetti A, Girolami D, Borgia L, Tagliabracci A (March 2017). "Flutamide-induced hepatotoxicity: ethical and scientific issues". *European Review for Medical and Pharmacological Sciences*. **21** (1 Suppl): 69–77. PMID 28379593 (<https://pubmed.ncbi.nlm.nih.gov/28379593>).
116. Yasa C, Dural Ö, Bastu E, Uğurlucan FG (2016). "Hirsutism, Acne, and Hair Loss: Management of Hyperandrogenic Cutaneous Manifestations of Polycystic Ovary Syndrome". *Gynecology Obstetrics & Reproductive Medicine*: 1. doi:10.21613/GORM.2016.613 (<https://doi.org/10.21613%2FGORM.2016.613>). ISSN 1300-4751 (<https://www.worldcat.org/issn/1300-4751>).
117. Barros B, Thiboutot D (2017). "Hormonal therapies for acne". *Clinics in Dermatology*. **35** (2): 168–172. doi:10.1016/j.clindermatol.2016.10.009 (<https://doi.org/10.1016%2Fj.clindermatol.2016.10.009>). PMID 28274354 (<https://pubmed.ncbi.nlm.nih.gov/28274354>).
118. Blackledge GR (1996). "Clinical progress with a new antiandrogen, Casodex (bicalutamide)". *European Urology*. 29 Suppl 2 (2): 96–104. doi:10.1159/000473847 (<https://doi.org/10.1159%2F000473847>). PMID 8717470 (<https://pubmed.ncbi.nlm.nih.gov/8717470>).

119. Fradet Y (February 2004). "Bicalutamide (Casodex) in the treatment of prostate cancer". *Expert Review of Anticancer Therapy*. **4** (1): 37–48. doi:[10.1586/14737140.4.1.37](https://doi.org/10.1586/14737140.4.1.37) (<https://doi.org/10.1586/14737140.4.1.37>). PMID [14748655](https://pubmed.ncbi.nlm.nih.gov/14748655) (<https://pubmed.ncbi.nlm.nih.gov/14748655>).
120. Hassoun LA, Chahal DS, Sivamani RK, Larsen LN (June 2016). "The use of hormonal agents in the treatment of acne". *Seminars in Cutaneous Medicine and Surgery*. **35** (2): 68–73. doi:[10.12788/j.sder.2016.027](https://doi.org/10.12788/j.sder.2016.027) (<https://doi.org/10.12788/j.sder.2016.027>). PMID [27416311](https://pubmed.ncbi.nlm.nih.gov/27416311) (<https://pubmed.ncbi.nlm.nih.gov/27416311>).
121. Marson JW, Baldwin HE (January 2019). "New Concepts, Concerns, and Creations in Acne". *Dermatologic Clinics* (Review). **37** (1): 1–9. doi:[10.1016/j.det.2018.07.002](https://doi.org/10.1016/j.det.2018.07.002) (<https://doi.org/10.1016/j.det.2018.07.002>). PMID [30466681](https://pubmed.ncbi.nlm.nih.gov/30466681) (<https://pubmed.ncbi.nlm.nih.gov/30466681>).
122. Timmins, Peter (2018). "Industry update: the latest developments in the field of therapeutic delivery, July 2018". *Therapeutic Delivery* (Review). **9** (11): 797–809. doi:[10.4155/tde-2018-0055](https://doi.org/10.4155/tde-2018-0055) (<https://doi.org/10.4155/tde-2018-0055>).
123. Trivedi MK, Bosanac SS, Sivamani RK, Larsen LN (August 2018). "Emerging Therapies for Acne Vulgaris". *American Journal of Clinical Dermatology* (Review). **19** (4): 505–516. doi:[10.1007/s40257-018-0345-x](https://doi.org/10.1007/s40257-018-0345-x) (<https://doi.org/10.1007/s40257-018-0345-x>). PMID [29594974](https://pubmed.ncbi.nlm.nih.gov/29594974) (<https://pubmed.ncbi.nlm.nih.gov/29594974>).
124. Tan AU, Schlosser BJ, Paller AS (June 2018). "A review of diagnosis and treatment of acne in adult female patients" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5986265>). *International Journal of Women's Dermatology* (Review). **4** (2): 56–71. doi:[10.1016/j.ijwd.2017.10.006](https://doi.org/10.1016/j.ijwd.2017.10.006) (<https://doi.org/10.1016/j.ijwd.2017.10.006>). PMC [5986265](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5986265) (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5986265>). PMID [29872679](https://pubmed.ncbi.nlm.nih.gov/29872679) (<https://pubmed.ncbi.nlm.nih.gov/29872679>).
125. Aslam I, Fleischer A, Feldman S (March 2015). "Emerging drugs for the treatment of acne". *Expert Opinion on Emerging Drugs*. **20** (1): 91–101. doi:[10.1517/14728214.2015.990373](https://doi.org/10.1517/14728214.2015.990373) (<https://doi.org/10.1517/14728214.2015.990373>). PMID [25474485](https://pubmed.ncbi.nlm.nih.gov/25474485) (<https://pubmed.ncbi.nlm.nih.gov/25474485>).
126. Azzouni F, Zeitouni N, Mohler J (February 2013). "Role of 5 $\alpha$ -reductase inhibitors in androgen-stimulated skin disorders". *Journal of Drugs in Dermatology*. **12** (2): e30-5. PMID [23377402](https://pubmed.ncbi.nlm.nih.gov/23377402) (<https://pubmed.ncbi.nlm.nih.gov/23377402>).
127. Danby FW (27 January 2015). *Acne: Causes and Practical Management* (<https://books.google.com/books?id=Z1yFBQAAQBAJ&pg=PA147>). John Wiley & Sons. pp. 147–. ISBN [978-1-118-23277-4](https://books.google.com/books?id=Z1yFBQAAQBAJ&pg=PA147).
128. Marchetti PM, Barth JH (March 2013). "Clinical biochemistry of dihydrotestosterone". *Annals of Clinical Biochemistry*. **50** (Pt 2): 95–107. doi:[10.1258/acb.2012.012159](https://doi.org/10.1258/acb.2012.012159) (<https://doi.org/10.1258/acb.2012.012159>). PMID [23431485](https://pubmed.ncbi.nlm.nih.gov/23431485) (<https://pubmed.ncbi.nlm.nih.gov/23431485>).
129. Katsambas AD, Dessinioti C (2010). "Hormonal therapy for acne: why not as first line therapy? facts and controversies". *Clinics in Dermatology*. **28** (1): 17–23. doi:[10.1016/j.clindermatol.2009.03.006](https://doi.org/10.1016/j.clindermatol.2009.03.006) (<https://doi.org/10.1016/j.clindermatol.2009.03.006>). PMID [20082945](https://pubmed.ncbi.nlm.nih.gov/20082945) (<https://pubmed.ncbi.nlm.nih.gov/20082945>).
130. Pugashetti R, Shinkai K (July 2013). "Treatment of acne vulgaris in pregnant patients". *Dermatologic Therapy* (Review). **26** (4): 302–11. doi:[10.1111/dth.12077](https://doi.org/10.1111/dth.12077) (<https://doi.org/10.1111/dth.12077>). PMID [23914887](https://pubmed.ncbi.nlm.nih.gov/23914887) (<https://pubmed.ncbi.nlm.nih.gov/23914887>).
131. Morelli V, Calmet E, Jhingade V (June 2010). "Alternative therapies for common dermatologic disorders, part 2". *Primary Care* (Review). **37** (2): 285–96. doi:[10.1016/j.pop.2010.02.005](https://doi.org/10.1016/j.pop.2010.02.005) (<https://doi.org/10.1016/j.pop.2010.02.005>). PMID [20493337](https://pubmed.ncbi.nlm.nih.gov/20493337) (<https://pubmed.ncbi.nlm.nih.gov/20493337>).



132. "Azelaic Acid Topical" (<https://www.nlm.nih.gov/medlineplus/druginfo/meds/a603020.html>). National Institutes of Health. Archived (<https://web.archive.org/web/20130913064712/http://www.nlm.nih.gov/medlineplus/druginfo/meds/a603020.html>) from the original on 13 September 2013. Retrieved 9 September 2013.
133. Madan RK, Levitt J (April 2014). "A review of toxicity from topical salicylic acid preparations". *Journal of the American Academy of Dermatology* (Review). **70** (4): 788–792. doi:10.1016/j.jaad.2013.12.005 (<https://doi.org/10.1016%2Fj.jaad.2013.12.005>). PMID 24472429 (<https://pubmed.ncbi.nlm.nih.gov/24472429>).
134. Well D (October 2013). "Acne vulgaris: A review of causes and treatment options". *The Nurse Practitioner* (Review). **38** (10): 22–31, quiz 32. doi:10.1097/01.NPR.0000434089.88606.70 (<https://doi.org/10.1097%2F01.NPR.0000434089.88606.70>). PMID 24048347 (<https://pubmed.ncbi.nlm.nih.gov/24048347>).
135. Rolfe HM (December 2014). "A review of nicotinamide: treatment of skin diseases and potential side effects". *Journal of Cosmetic Dermatology* (Review). **13** (4): 324–8. doi:10.1111/jocd.12119 (<https://doi.org/10.1111%2Fjocd.12119>). PMID 25399625 (<https://pubmed.ncbi.nlm.nih.gov/25399625>).
136. Brandt S (May 2013). "The clinical effects of zinc as a topical or oral agent on the clinical response and pathophysiologic mechanisms of acne: a systematic review of the literature". *Journal of Drugs in Dermatology* (Review). **12** (5): 542–5. PMID 23652948 (<https://pubmed.ncbi.nlm.nih.gov/23652948>).
137. Layton AM (April 2016). "Top Ten List of Clinical Pearls in the Treatment of Acne Vulgaris". *Dermatologic Clinics* (Review). **34** (2): 147–57. doi:10.1016/j.det.2015.11.008 (<https://doi.org/10.1016%2Fj.det.2015.11.008>). PMID 27015774 (<https://pubmed.ncbi.nlm.nih.gov/27015774>).
138. Tyler KH (March 2015). "Dermatologic therapy in pregnancy". *Clinical Obstetrics and Gynecology* (Review). **58** (1): 112–8. doi:10.1097/GRF.0000000000000089 (<https://doi.org/10.1097%2FGRF.0000000000000089>). PMID 25517754 (<https://pubmed.ncbi.nlm.nih.gov/25517754>).
139. Meredith FM, Ormerod AD (October 2013). "The management of acne vulgaris in pregnancy". *American Journal of Clinical Dermatology* (Review). **14** (5): 351–8. doi:10.1007/s40257-013-0041-9 (<https://doi.org/10.1007%2Fs40257-013-0041-9>). PMID 23996075 (<https://pubmed.ncbi.nlm.nih.gov/23996075>).
140. Bologna JL, Jorizzo JL (2012). *Dermatology* (3rd ed.). St. Louis, Mo.: Mosby Elsevier. p. 558. ISBN 9780702051821.
141. Posadzki P, Car J (May 2018). "Light Therapies for Acne". *JAMA Dermatology*. **154** (5): 597–598. doi:10.1001/jamadermatol.2018.0110 (<https://doi.org/10.1001%2Fjamadermatol.2018.0110>). PMID 29541753 (<https://pubmed.ncbi.nlm.nih.gov/29541753>).
142. Hamilton FL, Car J, Lyons C, Car M, Layton A, Majeed A (June 2009). "Laser and other light therapies for the treatment of acne vulgaris: systematic review". *The British Journal of Dermatology* (Systematic Review & Meta-Analysis). **160** (6): 1273–85. doi:10.1111/j.1365-2133.2009.09047.x (<https://doi.org/10.1111%2Fj.1365-2133.2009.09047.x>). PMID 19239470 (<https://pubmed.ncbi.nlm.nih.gov/19239470>).
143. Barbaric J, Abbott R, Posadzki P, Car M, Gunn LH, Layton AM, et al. (September 2016). "Light therapies for acne" ([http://www.cochrane.org/CD007917/SKIN\\_use-light-therapy-acne](http://www.cochrane.org/CD007917/SKIN_use-light-therapy-acne)). *The Cochrane Database of Systematic Reviews*. **9**: CD007917. doi:10.1002/14651858.CD007917.pub2 (<https://doi.org/10.1002%2F14651858.CD007917.pub2>). PMC 6457763 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6457763>). PMID 27670126 (<https://pubmed.ncbi.nlm.nih.gov/27670126>).
144. Cohen BE, Elbuluk N (February 2016). "Microneedling in skin of color: A review of uses and efficacy". *Journal of the American Academy of Dermatology* (Review). **74** (2): 348–55. doi:10.1016/j.jaad.2015.09.024 (<https://doi.org/10.1016%2Fj.jaad.2015.09.024>). PMID 26549251 (<https://pubmed.ncbi.nlm.nih.gov/26549251>).

145. Ong MW, Bashir SJ (June 2012). "Fractional laser resurfacing for acne scars: a review". *The British Journal of Dermatology* (Review). **166** (6): 1160–9. doi:10.1111/j.1365-2133.2012.10870.x (<https://doi.org/10.1111%2Fj.1365-2133.2012.10870.x>). PMID 22296284 (<https://pubmed.ncbi.nlm.nih.gov/22296284>).
146. Abdel Hay R, Shalaby K, Zaher H, Hafez V, Chi CC, Dimitri S, et al. (April 2016). "Interventions for acne scars". *The Cochrane Database of Systematic Reviews* (Systematic Review & Meta-Analysis). **4**: CD011946. doi:10.1002/14651858.CD011946.pub2 (<https://doi.org/10.1002%2F14651858.CD011946.pub2>). PMID 27038134 (<https://pubmed.ncbi.nlm.nih.gov/27038134>).
147. Soliman YS, Horowitz R, Hashim PW, Nia JK, Farberg AS, Goldenberg G (July 2018). "Update on acne scar treatment" (<https://www.mdedge.com/cutis/article/169785/acne/update-acne-scar-treatment>). *Cutis* (Review). **102** (1): 21, 25, 47, 48. PMID 30138491 (<https://pubmed.ncbi.nlm.nih.gov/30138491>).
148. Pahwa M, Pahwa P, Zaheer A (July 2012). " "Tram track effect" after treatment of acne scars using a microneedling device". *Dermatologic Surgery* (Case Report & Literature Review). **38** (7 Pt 1): 1107–8. doi:10.1111/j.1524-4725.2012.02441.x (<https://doi.org/10.1111%2Fj.1524-4725.2012.02441.x>). PMID 22587597 (<https://pubmed.ncbi.nlm.nih.gov/22587597>).
149. Lanoue J, Goldenberg G (May 2015). "Acne scarring: a review of cosmetic therapies". *Cutis* (Review). **95** (5): 276–81. PMID 26057505 (<https://pubmed.ncbi.nlm.nih.gov/26057505>).
150. Kroepfl L, Emer JJ (November 2016). "Combination Therapy for Acne Scarring: Personal Experience and Clinical Suggestions". *Journal of Drugs in Dermatology* (Review). **15** (11): 1413–1419. PMID 28095556 (<https://pubmed.ncbi.nlm.nih.gov/28095556>).
151. Zaleski-Larsen LA, Fabi SG, McGraw T, Taylor M (May 2016). "Acne Scar Treatment: A Multimodality Approach Tailored to Scar Type". *Dermatologic Surgery* (Review). **42** Suppl 2 (Supplement 2): S139-49. doi:10.1097/DSS.0000000000000746 (<https://doi.org/10.1097%2FDSS.0000000000000746>). PMID 27128240 (<https://pubmed.ncbi.nlm.nih.gov/27128240>).
152. Cao H, Yang G, Wang Y, Liu JP, Smith CA, Luo H, Liu Y (January 2015). "Complementary therapies for acne vulgaris" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4486007>). *The Cochrane Database of Systematic Reviews* (Systematic Review & Meta-Analysis). **1**: CD009436. doi:10.1002/14651858.CD009436.pub2 (<https://doi.org/10.1002%2F14651858.CD009436.pub2>). PMC 4486007 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4486007>). PMID 25597924 (<https://pubmed.ncbi.nlm.nih.gov/25597924>).
153. Fisk WA, Lev-Tov HA, Sivamani RK (August 2014). "Botanical and phytochemical therapy of acne: a systematic review". *Phytotherapy Research* (Systematic Review). **28** (8): 1137–52. doi:10.1002/ptr.5125 (<https://doi.org/10.1002%2Fptr.5125>). PMID 25098271 (<https://pubmed.ncbi.nlm.nih.gov/25098271>).
154. Decker A, Graber EM (May 2012). "Over-the-counter Acne Treatments: A Review" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3366450>). *The Journal of Clinical and Aesthetic Dermatology* (Review). **5** (5): 32–40. PMC 3366450 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3366450>). PMID 22808307 (<https://pubmed.ncbi.nlm.nih.gov/22808307>).
155. Goodman G (2009). "Cleansing and moisturizing in acne patients". *American Journal of Clinical Dermatology* (Review). **10** Suppl 1 (Suppl 1): 1–6. doi:10.2165/0128071-200910001-00001 (<https://doi.org/10.2165%2F0128071-200910001-00001>). PMID 19209947 (<https://pubmed.ncbi.nlm.nih.gov/19209947>).
156. Bajaj L, Berman S (2011). *Berman's Pediatric Decision Making* ([https://books.google.com/books?id=NPhnHrDQ1\\_kC&pg=PA572](https://books.google.com/books?id=NPhnHrDQ1_kC&pg=PA572)). Elsevier Health Sciences. p. 572. ISBN 978-0323054058. Archived ([https://web.archive.org/web/20170906210844/https://books.google.com/books?id=NPhnHrDQ1\\_kC&pg=PA572](https://web.archive.org/web/20170906210844/https://books.google.com/books?id=NPhnHrDQ1_kC&pg=PA572)) from the original on 6 September 2017.

157. Bope ET, Kellerman RD (2014). *Conn's Current Therapy 2015: Expert Consult — Online* (<https://books.google.com/books?id=Hv8fBQAAQBAJ&pg=PT335>). p. 299. ISBN 978-0-323-31956-0. Archived (<https://web.archive.org/web/20170906210844/https://books.google.com/books?id=Hv8fBQAAQBAJ&pg=PT335>) from the original on 6 September 2017.
158. Berger, William D. James, Dirk M. Elston, Timothy G. (2011). *Andrews' Diseases of the skin : clinical dermatology* (11th ed.). [London]: Saunders/ Elsevier. p. 234. ISBN 9781437703146.
159. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. (December 2012). "Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6350784>). *Lancet*. **380** (9859): 2163–96. doi:10.1016/S0140-6736(12)61729-2 (<https://doi.org/10.1016%2FS0140-6736%2812%2961729-2>). PMC 6350784 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6350784>). PMID 23245607 (<https://pubmed.ncbi.nlm.nih.gov/23245607>).
160. Holzmänn R, Shakery K (November 2013). "Postadolescent acne in females". *Skin Pharmacology and Physiology* (Review). 27 Suppl 1 (Supplement 1): 3–8. doi:10.1159/000354887 (<https://doi.org/10.1159%2F000354887>). PMID 24280643 (<https://pubmed.ncbi.nlm.nih.gov/24280643>).
161. Shah SK, Alexis AF (May 2010). "Acne in skin of color: practical approaches to treatment". *The Journal of Dermatological Treatment* (Review). **21** (3): 206–11. doi:10.3109/09546630903401496 (<https://doi.org/10.3109%2F09546630903401496>). PMID 20132053 (<https://pubmed.ncbi.nlm.nih.gov/20132053>).
162. Tan JK, Bhate K (July 2015). "A global perspective on the epidemiology of acne". *The British Journal of Dermatology* (Review). 172 Suppl 1 (Supplement 1): 3–12. doi:10.1111/bjd.13462 (<https://doi.org/10.1111%2Fbjd.13462>). PMID 25597339 (<https://pubmed.ncbi.nlm.nih.gov/25597339>).
163. White GM (August 1998). "Recent findings in the epidemiologic evidence, classification, and subtypes of acne vulgaris". *Journal of the American Academy of Dermatology* (Review). **39** (2 Pt 3): S34–7. doi:10.1016/S0190-9622(98)70442-6 (<https://doi.org/10.1016%2FS0190-9622%2898%2970442-6>). PMID 9703121 (<https://pubmed.ncbi.nlm.nih.gov/9703121>).
164. Keri J, Shiman M (June 2009). "An update on the management of acne vulgaris" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3047935>). *Clinical, Cosmetic and Investigational Dermatology* (Review). **2**: 105–10. PMC 3047935 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3047935>). PMID 21436973 (<https://pubmed.ncbi.nlm.nih.gov/21436973>).
165. Tilles G (September 2014). "Acne pathogenesis: history of concepts". *Dermatology* (Review). **229** (1): 1–46. doi:10.1159/000364860 (<https://doi.org/10.1159%2F000364860>). PMID 25228295 (<https://pubmed.ncbi.nlm.nih.gov/25228295>).
166. Bologna JL, Jorizzo JL (2012). *Dermatology* (3rd ed.). St. Louis, Mo.: Mosby Elsevier. p. 545. ISBN 9780702051821.
167. Brumberg JJ (9 June 2010). "Perfect Skin" (<https://books.google.com/books?id=S-rNTj6lIIVAC>). *The Body Project: An Intimate History of American Girls*. Knopf Doubleday Publishing Group. pp. 57–94. ISBN 9780307755742. Archived (<https://web.archive.org/web/20170312063855/https://books.google.com/books?id=S-rNTj6lIIVAC>) from the original on 12 March 2017.
168. Bulkley LD (1885). *Acne; Its Etiology, Pathology and Treatment* ([https://books.google.com/books?id=k081g\\_YSZfwC](https://books.google.com/books?id=k081g_YSZfwC)). New York: G.P. Putnam's Sons. Archived ([https://web.archive.org/web/20170312051633/https://books.google.com/books?id=k081g\\_YSZfwC](https://web.archive.org/web/20170312051633/https://books.google.com/books?id=k081g_YSZfwC)) from the original on 12 March 2017.

169. Dutil M (November–December 2010). "Benzoyl peroxide: enhancing antibiotic efficacy in acne management" (<http://www.skintherapyletter.com/2010/15.10/2.html>). *Skin Therapy Letter* (Review). **15** (10): 5–7. PMID 21076800 (<https://pubmed.ncbi.nlm.nih.gov/21076800>). Archived (<https://web.archive.org/web/20170227150410/http://www.skintherapyletter.com/2010/15.10/2.html>) from the original on 27 February 2017.
170. "Tretinoin (retinoic acid) in acne". *The Medical Letter on Drugs and Therapeutics*. **15** (1): 3. January 1973. PMID 4265099 (<https://pubmed.ncbi.nlm.nih.gov/4265099>).
171. Jones H, Blanc D, Cunliffe WJ (November 1980). "13-cis retinoic acid and acne". *Lancet*. **2** (8203): 1048–9. doi:10.1016/S0140-6736(80)92273-4 (<https://doi.org/10.1016%2FS0140-6736%2880%2992273-4>). PMID 6107678 (<https://pubmed.ncbi.nlm.nih.gov/6107678>).
172. Bérard A, Azoulay L, Koren G, Blais L, Perreault S, Oraichi D (February 2007). "Isotretinoin, pregnancies, abortions and birth defects: a population-based perspective" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1859978>). *British Journal of Clinical Pharmacology*. **63** (2): 196–205. doi:10.1111/j.1365-2125.2006.02837.x (<https://doi.org/10.1111%2Fj.1365-2125.2006.02837.x>). PMC 1859978 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1859978>). PMID 17214828 (<https://pubmed.ncbi.nlm.nih.gov/17214828>).
173. Holmes SC, Bankowska U, Mackie RM (March 1998). "The prescription of isotretinoin to women: is every precaution taken?". *The British Journal of Dermatology*. **138** (3): 450–5. doi:10.1046/j.1365-2133.1998.02123.x (<https://doi.org/10.1046%2Fj.1365-2133.1998.02123.x>). PMID 9580798 (<https://pubmed.ncbi.nlm.nih.gov/9580798>).
174. Green RG (May 1968). "No soap and dry ice or a treatment for acne" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2281078>). *Canadian Family Physician*. **14** (5): 21–2. PMC 2281078 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2281078>). PMID 20468218 (<https://pubmed.ncbi.nlm.nih.gov/20468218>).
175. Semon HC (May 1920). "The X-Ray Treatment of Acne Vulgaris" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2337520>). *British Medical Journal* (Review). **1** (3099): 700–2. doi:10.1136/bmj.1.3099.700 (<https://doi.org/10.1136%2Fbmj.1.3099.700>). PMC 2337520 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2337520>). PMID 20769902 (<https://pubmed.ncbi.nlm.nih.gov/20769902>).
176. "Acne Vulgaris and X-Ray Treatment". *New England Journal of Medicine*. **219** (24): 971. December 1938. doi:10.1056/NEJM193812152192414 (<https://doi.org/10.1056%2FNEJM193812152192414>).
177. "Sales of the leading acne brands in the United States in 2015 (in million U.S. dollars)" (<https://www.statista.com/statistics/448473/leading-us-acne-brands/>). *statista: The Statistics Portal*. Statista Inc. Archived (<https://web.archive.org/web/20170312195114/https://www.statista.com/statistics/448473/leading-us-acne-brands/>) from the original on 12 March 2017. Retrieved 12 March 2017.
178. Goodman G (August 2006). "Acne--natural history, facts and myths" (<http://www.racgp.org.au/afpbackissues/2006/200608/20060805goodman.pdf>) (PDF). *Australian Family Physician* (Review). **35** (8): 613–6. PMID 16894437 (<https://pubmed.ncbi.nlm.nih.gov/16894437>). Archived (<https://web.archive.org/web/20150211105957/http://www.racgp.org.au/afpbackissues/2006/200608/20060805goodman.pdf>) (PDF) from the original on 11 February 2015.
179. Brown MM, Chamlin SL, Smidt AC (April 2013). "Quality of life in pediatric dermatology". *Dermatologic Clinics* (Review). **31** (2): 211–21. doi:10.1016/j.det.2012.12.010 (<https://doi.org/10.1016%2Fj.det.2012.12.010>). PMID 23557650 (<https://pubmed.ncbi.nlm.nih.gov/23557650>).
180. Farrar MD, Howson KM, Bojar RA, West D, Towler JC, Parry J, et al. (June 2007). "Genome sequence and analysis of a *Propionibacterium acnes* bacteriophage" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1913406>). *Journal of Bacteriology*. **189** (11): 4161–7. doi:10.1128/JB.00106-07 (<https://doi.org/10.1128%2FJB.00106-07>). PMC 1913406 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1913406>). PMID 17400737 (<https://pubmed.ncbi.nlm.nih.gov/17400737>).

181. Baquerizo Nole KL, Yim E, Keri JE (October 2014). "Probiotics and prebiotics in dermatology". *Journal of the American Academy of Dermatology* (Review). **71** (4): 814–21. doi:10.1016/j.jaad.2014.04.050 (<https://doi.org/10.1016%2Fj.jaad.2014.04.050>). PMID 24906613 (<https://pubmed.ncbi.nlm.nih.gov/24906613>).
182. Liu PF, Hsieh YD, Lin YC, Two A, Shu CW, Huang CM (2015). "Propionibacterium acnes in the pathogenesis and immunotherapy of acne vulgaris". *Current Drug Metabolism* (Review). **16** (4): 245–54. doi:10.2174/1389200216666150812124801 (<https://doi.org/10.2174%2F1389200216666150812124801>). PMID 26264195 (<https://pubmed.ncbi.nlm.nih.gov/26264195>).
183. MacKenzie, D. "In development: a vaccine for acne" (<https://www.newscientist.com/article/dn20958-in-development-a-vaccine-for-acne.html#VRoBMbqL6QY>). *New Scientist*. Archived (<https://web.archive.org/web/20150402105716/http://www.newscientist.com/article/dn20958-in-development-a-vaccine-for-acne.html#VRoBMbqL6QY>) from the original on 2 April 2015. Retrieved 30 March 2015.
184. White SD, Bordeau PB, Blumstein P, Ibisch C, Guaguère E, Denerolle P, Carlotti DN, Scott KV (1 September 1997). "Feline acne and results of treatment with mupirocin in an open clinical trial: 25 cases (1994–96)". *Veterinary Dermatology*. **8** (3): 157–164. doi:10.1046/j.1365-3164.1997.d01-16.x (<https://doi.org/10.1046%2Fj.1365-3164.1997.d01-16.x>). ISSN 1365-3164 (<https://www.worldcat.org/issn/1365-3164>).
185. *Veterinary Medicine* (<https://books.google.com/books?id=GvciAQAAIAAJ&lpg=PA824>). 1914. Archived (<https://web.archive.org/web/20170312122829/https://books.google.com/books?id=GvciAQAAIAAJ&lpg=PA824>) from the original on 12 March 2017.
186. Radostits OM, Gay CC, Hinchcliff KW, Constable PD (28 December 2006). *Veterinary Medicine: A textbook of the diseases of cattle, horses, sheep, pigs and goats* (<https://books.google.com/books?id=JP7TBQAAQBAJ&lpg=PT3539>). Elsevier Health Sciences. ISBN 9780702039911. Archived (<https://web.archive.org/web/20170312124704/https://books.google.com/books?id=JP7TBQAAQBAJ&lpg=PT3539>) from the original on 12 March 2017.
187. White DS (1917). *A Text-book of the Principles and Practice of Veterinary Medicine* (<https://books.google.com/books?id=fOXbAAAAMAAJ&lpg=PA258>). Lea & Febiger. Archived (<https://web.archive.org/web/20170312130702/https://books.google.com/books?id=fOXbAAAAMAAJ&lpg=PA258>) from the original on 12 March 2017.

## Further reading

- Paller AS, Mancini AJ (2015). *Hurwitz's Clinical Pediatric Dermatology: A Textbook of Skin Disorders of Childhood And Adolescence*. Elsevier. ISBN 978-0323244756.
- Cordain L, Lindeberg S, Hurtado M, Hill K, Eaton SB, Brand-Miller J (December 2002). "Acne vulgaris: a disease of Western civilization". *Archives of Dermatology*. **138** (12): 1584–90. doi:10.1001/archderm.138.12.1584 (<https://doi.org/10.1001%2Farchderm.138.12.1584>). PMID 12472346 (<https://pubmed.ncbi.nlm.nih.gov/12472346>).
- Del Rosso JQ (December 2013). "The role of skin care as an integral component in the management of acne vulgaris: part 1: the importance of cleanser and moisturizer ingredients, design, and product selection" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3997205>). *The Journal of Clinical and Aesthetic Dermatology*. **6** (12): 19–27. PMC 3997205 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3997205>). PMID 24765221 (<https://pubmed.ncbi.nlm.nih.gov/24765221>).

## External links

-  Media related to Acne at Wikimedia Commons

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- Questions and Answers about Acne ([https://www.niams.nih.gov/Health\\_Info/Acne/default.asp](https://www.niams.nih.gov/Health_Info/Acne/default.asp)) - US National Institute of Arthritis and Musculoskeletal and Skin Diseases

[p://apps.who.int/classifications/icd10/browse/2016/en#/L70.0](https://apps.who.int/classifications/icd10/browse/2016/en#/L70.0)) • **ICD-9-CM:** 706.1 (<http://www.icd9data.com/getICD9Code.ashx?icd9=706.1>) • **MeSH:** D000152 ([https://www.nlm.nih.gov/cgi/mesh/2015/MB\\_cgi?field=uid&term=D000152](https://www.nlm.nih.gov/cgi/mesh/2015/MB_cgi?field=uid&term=D000152)) • **DiseasesDB:** 10765 (<http://www.diseasesdatabase.com/ddb10765.htm>)

**External resources**

**MedlinePlus:** 000873 (<https://www.nlm.nih.gov/medlineplus/ency/article/000873.htm>) • **eMedicine:** [derm/2 \(https://emedicine.medscape.com/derm/2-overview\)](https://emedicine.medscape.com/derm/2-overview) • **Patient UK:** [Acne \(https://patient.info/doctor/acne-vulgari\)](https://patient.info/doctor/acne-vulgari)

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