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SKINCARE

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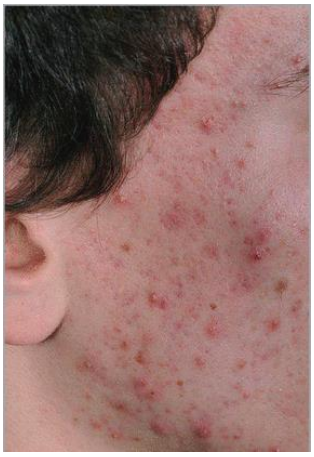
Contents

ACNE

What is acne?

Acne vulgaris is defined as a chronic disorder that affects the skin, causing irregular skin with zits, pimples and/or redness.



Example of moderate acne vulgaris (by clinical standards).

4 Major factors contribute to the pathogenesis of acne.

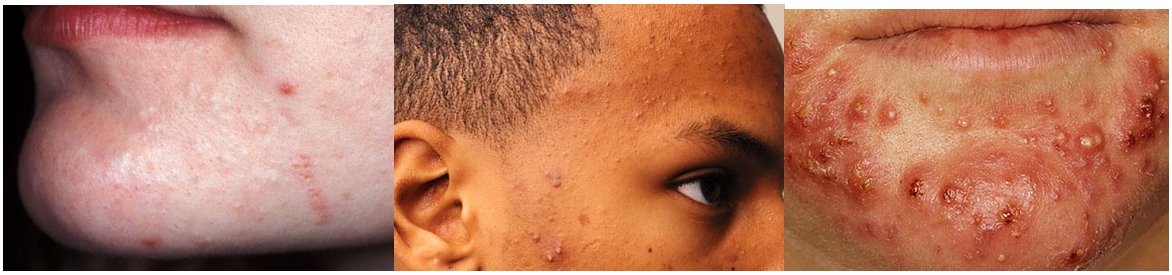
1) A higher than normal amount of sebum production, an oily substance produced by certain glands in the skin. Androgens like testosterone increase sebum production.
2) Excess of the protein keratin leading to the formation of a clogged follicle/pore (comedo).
3) Bacterial colonization (*Propionibacterium acnes)* in the follicle/pore.
4) Inflammation by a hyperactive immune response of the skin (either innate or adaptive/learnt).

Genetics play a major role in the time of onset and in the severity of acne [1, 2]. A Chinese study found heritability estimates of 78% in first-degree relatives.

In the U.S. acne affects 85% of 12-24 year olds. While more commonly found in adolescents, a survey in a large sample showed that 73% of 20+ year olds reported having acne. Acne is more common in women than in men, in part due to differences in skin structure.

When people hear of acne, pimples are commonly the first thing that pops in their mind (no pun intended). However, pimples, more formally *pustules*, are only one form of acne lesion. Moreover, acne is commonly confused with folliculitis and post-inflammatory hyperpigmentation. While somewhat similar in appearance, these are actually very different skin disorders that require different treatments. As such, the first step in the treatment of acne is a differential diagnosis to see if you have acne and if so, which type you have, which can further influence the best treatment option. Below are the most common types of acne lesions.

Clinicians generally divide between mild, moderate and several severe forms acne (left to right pictures below), all characterized by different amounts/severity of acne lesions.



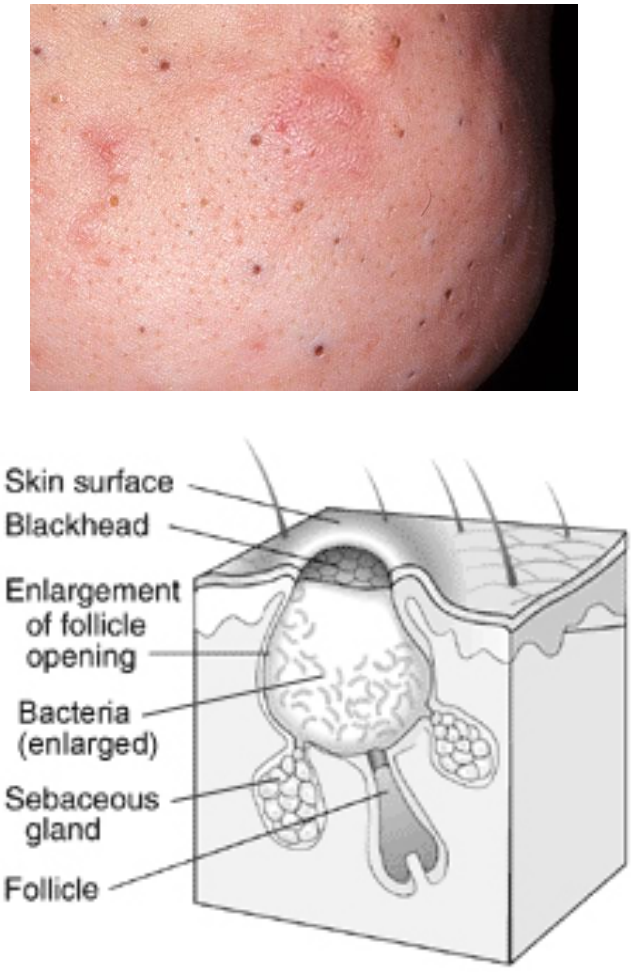
There are also multiple forms of acne lesions.

Comedones: blackheads and whiteheads

Comedones are typically classified as a non-inflammatory acne lesion. They form when a hair follicle becomes clogged with sebum (oil) and dead skin cells.

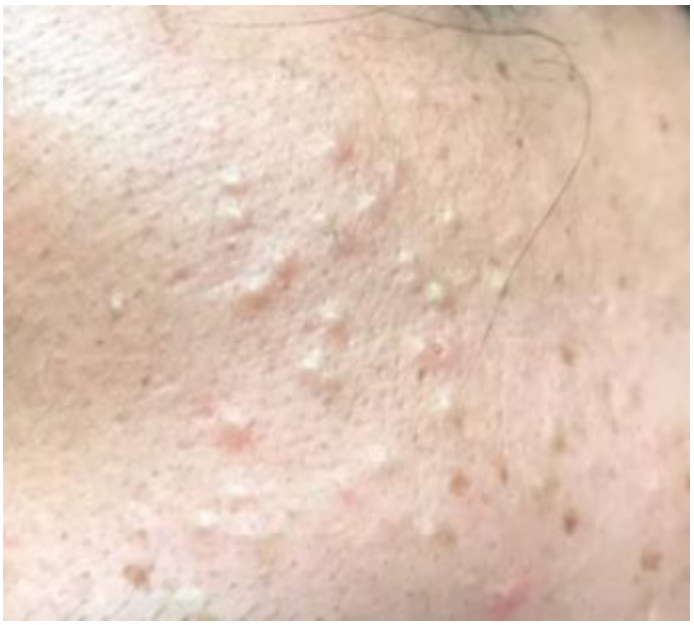
There are two different types of comedones (singular: comedo), named for their appearance: blackheads and whiteheads.

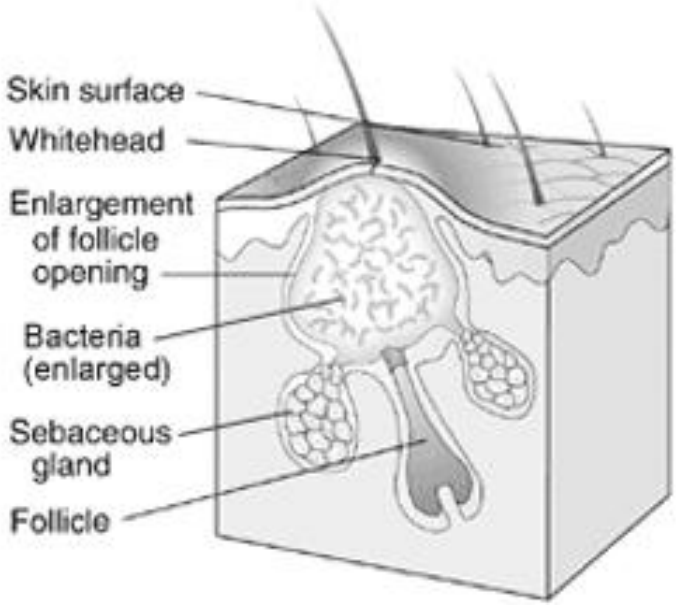
In the case of blackheads, sebum is being blocked and bacteria start to build up. They appear black, because the sebum is oxidized when exposed to the air.



Blackheads.

A whitehead on the other hand is a closed pore that swells under the skin.



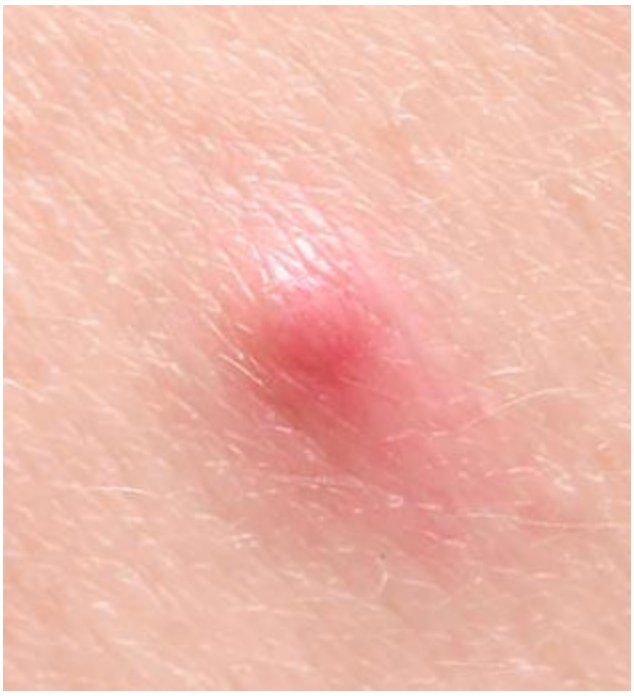


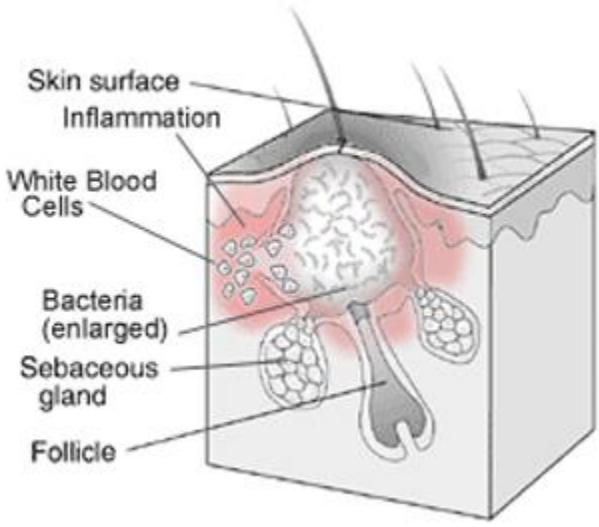
Whiteheads.

Other acne lesions are typically inflammatory.

Papules

These are essentially inflamed comedones. They look like red/pink small bumps in the skin, usually don't contain any fluids and are very sensitive to touch.

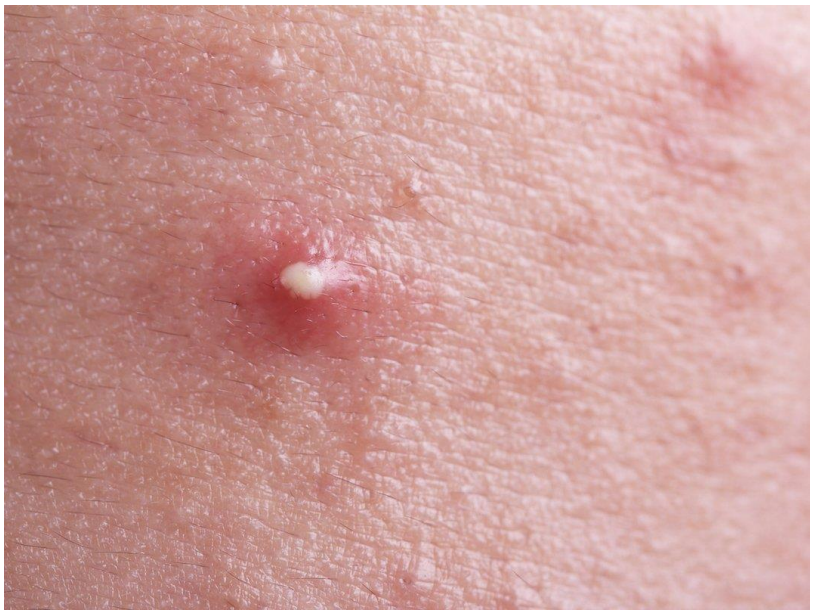


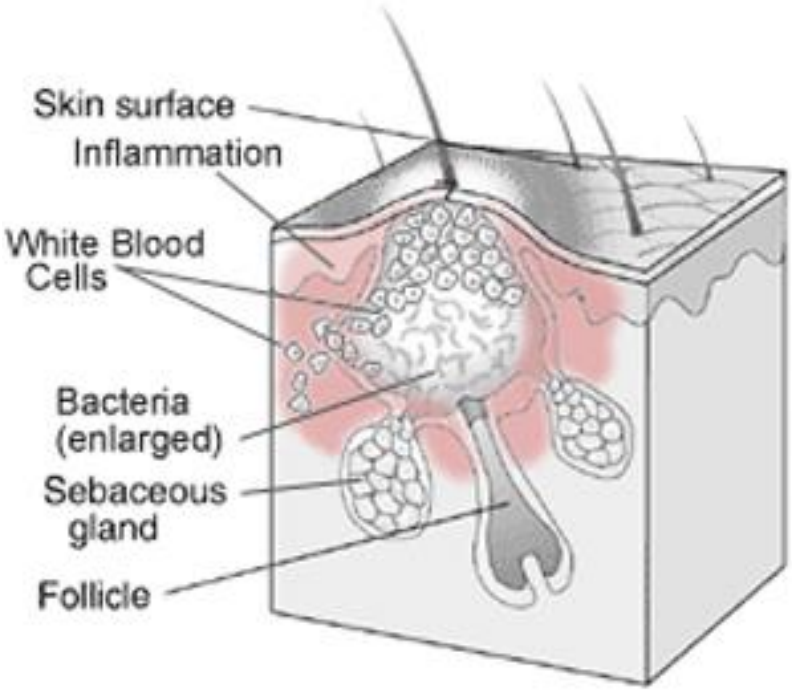


Papules.

Pustules

Pustules look similar to inflamed whiteheads (mini-pustules). They are filled with pus and have a red ring around them. The pus, usually white or yellow, is a mixture of bacteria, white blood cells and dead skin cells.



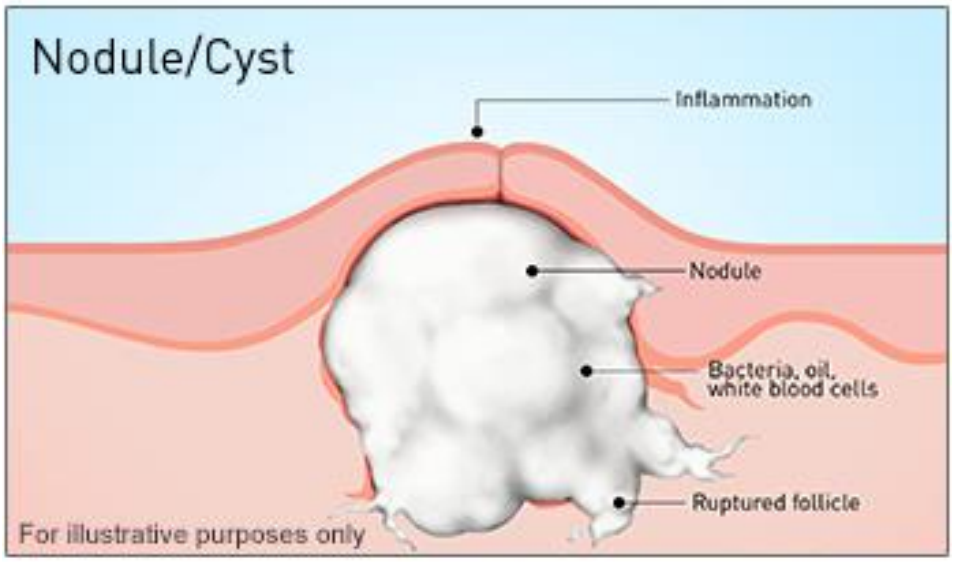


Pustules

Are you grossed out yet? If not, here comes the good stuff.

Nodules and cysts

These are the most painful form of acne. They are large, inflamed, extend to deeper layers of your skin and can even do permanent tissue damage, which can result in scars. The images below show examples of nodules (left) and cysts (right).



In sum:

- Acne vulgaris is a disorder of the skin characterized by excess sebum (oily substance) production, excess keratin (protein in skin), bacterial colonization and an overly aggressive immune response.

- Acne exists in a non-inflammatory (comedones) and inflammatory form. Non-inflammatory acne includes whiteheads and blackheads, while the inflammatory type includes papules, pustules, nodules and cysts.

Now let's discuss how to get rid of these lesions.

Treatment

The treatment of acne always needs to be individualized and monitored, as some people don't tolerate certain medications well. Your options also depend on what you can legally obtain over the counter without a prescription. First-line treatment should generally center on lifestyle changes and safe topicals. Only when these fail, should the more dangerous oral medications be considered.

Washing

While washing is often recommended to reduce acne, a systematic review found washing frequency is not correlated with facial acne. So the idea that people with acne must have poor hygiene is unjustified.

Exercise induced sweat and truncal acne also do not seem to be related.

In fact, regular soap is ineffective at reducing acne and may even make acne worse by irritating the skin.

Overall, while certain types of foam wash or moisturizer have shown promise for certain types of acne, especially if poor hygiene or dry skin contributed to the onset of acne, most commonly available soaps, washes and other facial products have not been shown to reduce acne.

Light therapy

Research on light therapy to reduce acne is promising. Anecdotal reports are quite consistent in the acne reducing effect of sunlight, as long as you don't get sunburned. Research findings are also overall positive but less consistent, in part because much research is done on people using retinoids, which make the skin more susceptible to damage from UV radiation. Light therapy seems to be similarly effective as oral antibiotics and without the side-effects to boot.

For individuals using retinoid medication or wanting to avoid skin damage from UV radiation, UV-free blue light therapy has been shown to be effective in acne (1) as well as phototherapy with blue-red mixed light. This form of light therapy requires a special light box or lamp (high intensity, narrow band 405–420 nm light) that you keep close to your face for a certain period of the day, usually at least 20 minutes.

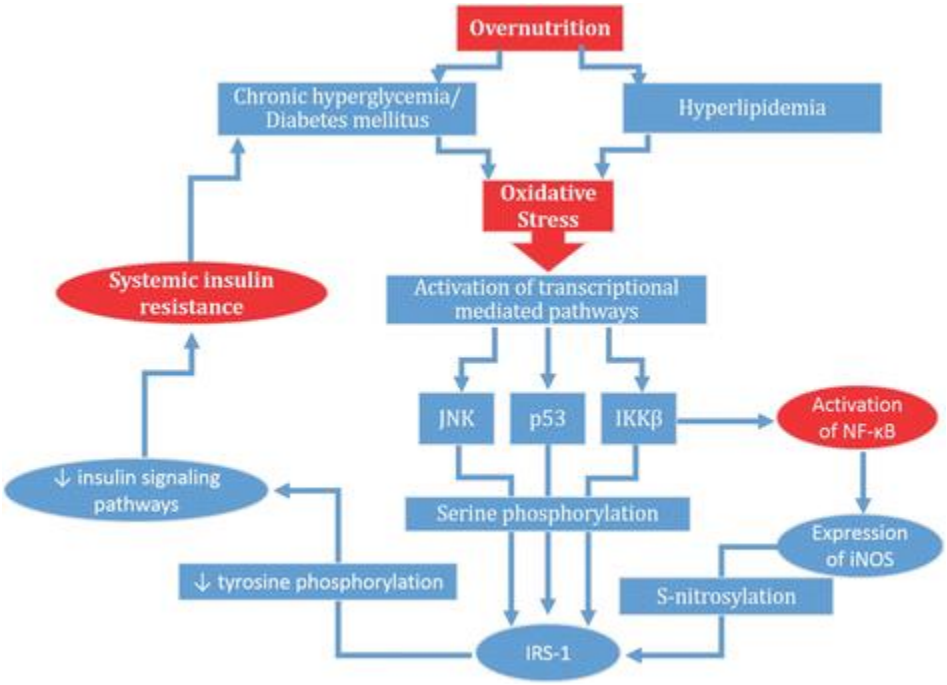
See the section on tanning for how to get a healthy level of sunlight exposure.

Diet

Researchers have long been skeptical of the role of our diets in the formation of acne, in spite of many anecdotal reports finding what seem to be clear effects of dietary changes on acne severity. Indeed, in spite of many early studies having difficulty finding a relation, it is now quite well accepted in the scientific community that an inflammatory diet can exacerbate acne. Insulin appears to be a key culprit with a very direct relation with acne formation [2]. Insulin mediated insulin-like growth factor-1 (IGF-1) signalling activates all major causes of acne directly in your genes:

- Increased follicular inflammation
- Comedogenesis
- Increased proliferation of keratinocytes
- Increased subaceous lipogenesis
- Increased sebum production

Insulin, inflammation and blood sugar are inherently related to each other, as you learned earlier: see the figure below for a recap.



The relation between diet quality, inflammation and insulin resistance. High blood sugar and certain fatty acid levels stimulate reactive oxygen species (ROS) production, causing inflammation. Inflammation in turn causes insulin resistance by i.a. metabolic stress on the pancreas. Insulin resistance exacerbates the rise in blood sugar levels, which causes a reinforcing effect on the whole cycle. Source

Most highly processed (junk) foods are inflammatory. They have a high glycemic and insulin index with few anti-oxidants to compensate for this. Several anti-oxidants can reduce inflammation in the body, thereby plausibly reducing acne. The intake of vitamins A, B, C, D, E and K in particular has been linked to skin health in multiple studies. For acne, an increased intake of zinc [2] has been found to help, especially for the more inflammatory lesions.

Supplementation of these specific anti-oxidants is not needed if you're already getting them from your diet. They are only a small part of the overall effect of your diet. Several

studies, not to mention countless of anecdotal reports, have found that overall diet quality is significantly related to acne. Specifically, a high intake of seafood, fuit and vegetables and a low intake of processed foods, especially sugar and fast food, is associated with reduced acne [1, 2, 3, 4, 5, 6].

Fish oil has also been found to reduce acne severity, presumably by reducing inflammation, especially in individuals with moderate to severe acne.

In line with its detrimental effects of insulin and glucose levels, irregular meal timing is also associated with increased acne. Eating at similar times every day can improve glucose and insulin regulation and thereby reduce inflammation and acne.

A healthy gut microbiome may also help. One study found that the use of probiotics, in this case added to a general antibiotics treatment, may improved acne. Again there is no need to supplement probiotics if your diet maintains a healthy gut microbiome: see the course module on health science.

In contrast, most whole foods should not cause problematic levels of inflammation in people with normal carb tolerance with one likely exception: dairy.

Dairy

A multitude of studies have linked dairy consumption to acne. For example:

- Evidence from a huge observational study (*n* = 47355) found that dairy products, specifically skim milk, are associated with acne.
- The same researchers conducted 2 prospective follow-up studies confirming the relation between dairy and acne. Specifically, in girls, acne was associated with total milk intake, whole milk, low-fat milk, and skim milk. In boys, acne was associated with the intake of skim milk but not whole milk.
- A prospective study in students found a high intake (≥ 2 glasses per day) of full-fat dairy products was associated with moderate to severe acne. In contrast to

the other studies, they found no significant relation between acne and intake of semi-skimmed or skimmed dairy products.

- Another study in Malaysian 18-30 year olds found that the frequency of milk and ice cream consumption was significantly higher in people with acne compared to controls.
- A study in Italian 10-24 year olds found an increased risk of acne with milk consumption, especially skimmed milk.

In two of the studies above there were no associations between acne and cheese or yogurt, so overall, skimmed dairy with milk in particular is most strongly related to acne. This is consistent with insulin, not any specific substance in dairy, being the problem. Milk is highly insulinogenic, but milk fat can decrease the insulin spike, reducing the problem. Anti-inflammatory foods or substances may also reduce the problem. Adding lactoferrin, a strong anti-inflammatory, to milk can reduce acne.

However, some research suggests that dairy is inherently acne promoting even independent of its insulinogenic effect. Some of the micro-RNA from cows ends up in their milk and can survive pasteurization, thereby interacting with the human genome. The result may be reduced expression of certain guardian proteins that help reduce acne.

You know what other skimmed dairy product is incredibly insulinogenic? Whey protein. Indeed, whey protein supplementation has also been linked to acne in many studies, including in bodybuilders, and several researchers have cautioned against the supplementation of whey in people prone to acne [1, 2, 3, 4]. However, a 6-month long RCT in young Thai adults found no significant effect of 30 g daily whey protein supplementation on acne severity.

Another commonly reported cause of acne is chocolate.

Chocolate

As many people have experienced, several controlled studies have found that eating chocolate, even 99% dark chocolate, can increase acne. The effect is quite acute, manifesting in several days or even overnight. Why chocolate can cause acne is still unclear, as chocolate is rich in anti-inflammatory flavonoids that you would expect to be beneficial. The oleic acid fatty acid may be the culprit, but other foods rich in mono-unsaturated fat do not seem to cause acne, so this is a questionable hypothesis.

All in all, the ideal anti-acne diet seems to boil down to the paleo diet: a diet built on whole foods without dairy, chocolate or highly processed foods. Indeed, native non-westernized people living in Papua New Guinea and Paraguay show no signs of acne.

Body composition

As per the health science topic, being lean and muscular improves insulin sensitivity to the extent that type II diabetes is basically unheard of in lean and muscular strength trainees. Increased insulin sensitivity reduces chronic inflammation levels considerably. Anecdotally, even androgenic-anabolic steroid using bodybuilders riddled with acne often experience almost complete remission of acne when they diet down to contest shape.

Research in the general population is less consistent, but the trend is that being overweight increases acne.

- A study of 3000 patients of 6-11 year olds found the BMI of patients with acne to be slightly higher than in individuals without acne (19.5 vs. 18.2 respectively), especially when looking at inflammatory lesions.
- A large study (*n* = 4744) showed that overweight and obesity was associated with more acne in girls but not in boys (18-19 years old).
- Older research in 2720 british soldiers found no difference in weight between soldiers, aged 15–19, with or without acne. Soldiers aged 20–40 with acne,

however, were significantly heavier (5.6 kg) than soldiers aged 20–40 without acne.

- This study in women found being heavier was related to acne. This study in women too found BMI to be related to acne, though another found no relation between BMI and acne severity.
- An Italian study found a reduced risk of acne in people (10-24 years) with lower BMI, especially in males.

Body fat distribution likely also plays a role. An android (male) body fat distribution with a centralized fat storage pattern (apple shape) is associated with insulin resistance, inflammation and a poor blood lipid profile, which in turn is associated with acne.

Benzoyl peroxide

Of all the anti-acne products you can purchase over the counter these days in most first-world countries, there is only one ingredient with very strong scientific support: benzoyl peroxide creme. Topical benzoyl peroxide (BPO) is the gold standard treatment for mild and moderate acne. It reduces the size of sebaceous glands, oxidizes bacterial proteins and reduces the amount of oil on the skin.

Formulations are available at concentrations of 2.5, 5, 10 and 20%. Depending on severity, a higher concentration around 10% is recommended. Usually, 5% is sufficient to control mild acne.

BPO is also safe for use even in pregnant and lactating women.

Formulations that combine BPO with the antibiotic clindamycin can be extra effective, especially for papulopustular acne.

BPO is not entirely free from side-effects, however. Like most effective anti-acne agents, it dries out the skin. The effect varies from mild desquamation to scaliness and possibly even skin cracking. As such, BPO should only be used every other night at first before moving up to daily use to reduce skin irritation.

Secondly, benzoyl peroxide makes some people more sensitive to the sun (specifically UVB waves), so beware of sunburn (see the section on tanning).

Another big consideration for use is that BPO has strong oxidative potential, so strong that it acts as a bleach. In other forms, it can be used to bleach your teeth, for example (but don't try this with the anti-acne formulation!) Unfortunately, this means BPO can bleach and stain your colored clothing and bedding, even your hair sometimes in large amounts. So be careful when you apply it. If you apply it on your face, make sure you wash it off thoroughly before you come into contact with any surfaces you don't want to bleach. If you apply it to your body, it's generally best to apply it before you go to bed and sleep under 100% white bed sheets and linen. White clothing should not stain from bleaching, but make sure you wash it separately from anything that's not also 100% white. Any colored fabrics will quickly be covered with orange stains if they come into contact with BPO, even indirectly. Wash your hands thoroughly after applying it anywhere on yourself.

Salicylic acid

Salicylic acid works as a keratolytic, bacteriocide and comedolytic agent by causing the cells of the epidermis (top skin layer) to shed more readily, opening clogged pores and

neutralizing bacteria within, preventing pores from clogging up again by constricting pore diameter, and allowing room for new cell growth.

Topical 0.5% and 2% solutions are effective to reduce acne. While not as well established as BPO, in the research we have it seems to be even more effective.

Side effects include only mild skin irritation in a small number of white skinned people. Dark skinned people, however, should be very careful with salicyclic acid, as it can increase the risk of post-inflammatory hyperpigmentation (discussed below). Azelaic acid, discussed below, is preferable for dark skinned individuals.

Salicylic acid is available in many forms, including cremes, but salicylic pads are most commonly used for acne treatment. Adults can usually apply pads 1-3 times per day. As with BPO, you have to assess how your skin reacts and adjust your dosage accordingly to minimize side-effects.

For slightly more aggressive use, a salicyclic acid facial peel can improve inflammatory as well as non-inflammatory acne.

Azelaic acid

Azelaic acid reduces acne via several mechanisms: it kills many acne-causing bacteria, it reduces keratin production and it's anti-inflammatory. It can be specifically useful in patients with very sensitive skin types who cannot tolerate other topicals, because it has almost no serious side effects. Multiple research reviews [1, 2, 3, 4] support that 20% azelaic acid applied twice a day to the skin is effective to reduce mild to moderate acne, especially comedonal acne, with effects comparable to BPO, salicyclic acid and topical retinoids like tretinoin.

For severe acne, azelaic acid can be used in combination with other compounds, such as tetracyclines (antibiotics) or anti-androgens.

Azelaic acid has a mild potential as a bleaching agent. However, azelaic acid is typically too weak of a bleach to stain your clothing.

Prescription medication (retinoids)

When over the counter topicals are insufficient to control acne, retinoids should be considered.

Retinoids are chemically related to vitamin-A. Retinoids target microcomedones, are comedolytic and anti-comedogenic (meaning they break down and prevent formation of comedones), they increase skin turn-over and they have anti-inflammatory effects.

Topical use is the first choice of treatment, because of the side-effects of oral use (discussed below).

Importantly, benzoyl peroxide inactivates retinoids. For this reason, usually one is applied at bedtime, the other in the morning.

Retinoic acid / Tretinoin

Tretinoin is the acid form of vitamin A and is also known as “all-trans retinoic acid” (ATRA). It reduces sebum production and is the most commonly used prescription drug for acne and aging skin. Evidence shows it to be very effective for facial acne. It is available as a cream or gel (brand names Aberela, Airol, Renova, Atralin, Retin-A, Avita, or Stieva-A).

There are strong diminishing returns of dosage. For example, this study found similar benefits of 0.1% and 0.025% topical tretinoin in a long term study. More importantly, despite similar benefits, irritation rates were significantly greater with the higher dosage.

Tretinoin, or any retinoid for that matter, should not be used by pregnant women, as it is absorbed by the skin (and body) and may impair development of the child or even cause birth defects [2, 3].

Adapalene

Adapalene is a third generation retinoid most effective in treating comedones, and chemically more stable than tretinoin. It is also available in combination with benzoyl peroxide. While being less potent than the other retinoids it's also less irritating. You can get it as 0.1% or 0.3% gel, solution, or cream. This makes adapalene suitable for those who are intolerant to the other retinoid topicals.

Isotretinoin (oral)

If acne is very severe and other forms of topical treatment don't show any improvement, then a systemic (meaning: affecting the whole body, not just the skin) retinoid (derivative of vitamin A) like isotretinoin may be warranted. Oral isotretinoin is the only agent addressing all four pathogenic mechanisms.

The catch with oral isotretinoin is its toxicity. It is a potent teratogen, meaning it can disturb physiological development (which can also cause birth defects in pregnant women) and cause mental retardation.

Moreover, it can increase serum triglycerides and provoke pancreatitis and pseudotumour cerebri. Side effects may even be worse in exercising individuals. Isotretinoin use also has potential links with mental disorders.

Nonetheless, isotretinoin is extremely effective and leads to complete remission of acne lesions in 85% of patients within the first 4 months.

If you decide to use isotretinoin, be wary of the dosage. A higher dose of isotretinoin has been shown to lead to a flare of acne after 3-6 weeks of treatment. This is most likely related to the degree of sebaceous cell apoptosis (cell death of the sebum producing cells). This can be avoided by using doses below 0.2 mg/kg per day.

While it depends on the person (tolerance, side effects, etc.), research shows 0.1 mg/kg per day generally is effective (i.e. 5–10 mg/day) and increasing the dosage does not

result in a better clearance of acne. The length of treatment should be tailored to the individual's response as well. For permanent benefits related to cell death of sebum secreting cells, treatment should be continued for 2-4 months after complete clearance of acne [1, 2, 3].

Isotretinoin should be consumed with meals to improve bioavailability.

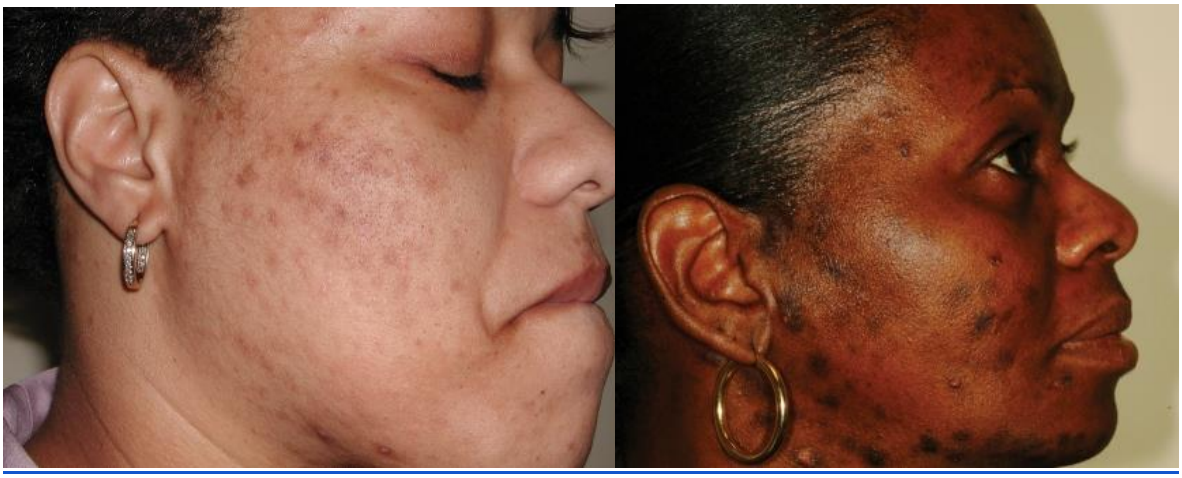
Before considering isotretinoin therapy, read this review.

In sum:

- Retinoids are related to vitamin-A and help multiple of the underlying factors of acne formation.
- You can only get retinoids with a prescription, in the forms of a topical gel/cream/solution (retinoic acid or adapalene) or capsules to be taken orally (isotretinoin).
- The topical forms are generally very effective at treating acne. The oral form (isotretinoin) is much more aggressive (with serious side-effects, such as disturbance of physiological development and potential psychiatric effects) and should only be taken if all other treatments haven't helped. It's normally only prescribed for very severe acne. Make sure to use the lowest effective dosage to reduce the chances of serious side-effects: 0.1 mg/kg (5-10 mg) per day is generally recommended.
- Pregnant women should never use retinoids in any form, as it can cause birth defects.

Acne-induced post-inflammatory hyperpigmentation (PIH)

Post-inflammatory hyperpigmentation (PIH) refers to a local excess of dark pigment (melanin) following acne inflammation. It can arise in all skin types but is far more common in darker skin types. The dark spots aren't true scars as they disappear with time and don't involve changes to the collagen of the skin. The color of the hyperpigmentation (red, purple, brown or even bluish) can vary depending on skin tone and location in the skin,



Post-inflammatory hyperpigmentation.

Treatment

The daily use of a broad-spectrum sunscreen (sun protection factor 15 or greater) is considered an essential part of any therapeutic regimen for PIH, as sunburn greatly exacerbates the risk of PIH.

There are multiple ways to treat PIH like the use of chemical peeling and laser therapy, but you should always start with topical therapy. The two other forms of therapy hold some promise but are less researched and may cause more serious side effects.

The (topical) depigmenting treatment usually targets different steps in the production of melanin, but they most commonly they inhibit tyrosinase, an enzyme involved in melanin production. Here's a list.

Hydroquinone

The first line gold standard treatment in PIH is generally hydroquinone 2%. It is the most widely used skin-lightening agent and is usually available over the counter. It should be used immediately after the acne is gone. Usually, you can see the depigmenting effects after 4-6 week of therapy. The most common side effects associated with hydroquinone are skin irritation (sometimes after contact), which can be treated with topical steroids.

Mequinol

This is a derivative and alternative to hydroquinone and available by prescription. Research shows it is less irritating to the skin. One study found it to work at least as well as 4 % hydroquinone in patients with mild-to-moderate facial PIH.

Azelaic acid

While generally used for acne, azelaic acid is also used for PIH. A cream of 20% azelaic acid has been found to be superior to 2% hydroquinone in the treatment of melasma [2], a condition of excessive skin pigmentation, to whiten the skin by reducing melanocyte activity. Its primary mechanism of action is blocking tyrosinase. Azelaic acid should be applied twice daily and can be combined with retinoids for optimal results.

Retinoids

As mentioned in the section on acne vulgaris, retinoids are related to vitamin A. A 40-week study in 54 black patients with PIH was conducted with 0.1% tretinoin. While it was effective in treating PIH lesions, 50% of patients developed retinoid dermatitis (irritation by contact of the skin). In practice, many available products combine hydroquinone and retinoids.

Adapalene (0.1-0.3) and tazarotene (0.05% and 0.1%) creams or gels are effective in the treatment of PIH and generally have few side effects.

Glycolic acid (GA) peels

GA induces epidermolysis, disperses basal layer melanin, and increases dermal collagen synthesis. It is available in concentrations of 20-70%. One study in 16 black individuals had both the control and experimental group take 2% hydroquinone/10% glycolic acid gel twice daily and 0.05% tretinoin cream at night. The experimental group added 6 chemical peels with GA (68% maximum concentration) on top of that. The peel group showed a trend for more rapid and greater improvement compared to the control group.

Salicylic acid (SA) peels

Salicylic acid induces keratolysis by breaking lipid linkages between epithelioid cells in the skin. It is generally used in concentrations from 20-30%. A study in asian individuals showed SA to be an effective form of treatment and it can be a safe and efficacious option for black skinned individuals too.

The above treatment options are relatively well established. When those are not available or effective, the following treatment options hold promise.

Arbutin

Arbutin is another derivative of Hydroquinone, but without the melanotoxic effects. A clinical study showed 3% deoxyarbutin to be effective in the treatment of solar lentigines in light-skinned patients, but there was no significant clinical response in the subset of dark-skinned patients.

Ascorbic acid (AA) or vitamin C

Ascorbic acid is typically used in 5-10% concentrations and can be combined with other agents like hydroquinone. It is generally well tolerated and its derivatives have shown some efficacy. However, most studies looked at the treatment of melasma and did not include PIH [1, 2].

Niacinamide (derivative of niacin)

Niacinamide is not very effective, but at least it's harmless, so it may be worth trying. Topical 2 to 5 % niacinamide has shown to help PIH alone and in conjunction with N-acetyl glucosamine (see below). It can be use as an adjunct for severe PIH or as monotherapy for very mild PIH if you can't get anything else.

N-acetyl glucosamine (NAG)

N-acetyl glucosamine is an amino sugar that is a precursor to hyaluronic acid. It is very tolerable and typically used in 2 % concentrations alone or in conjunction with niacinamide (mentioned above).

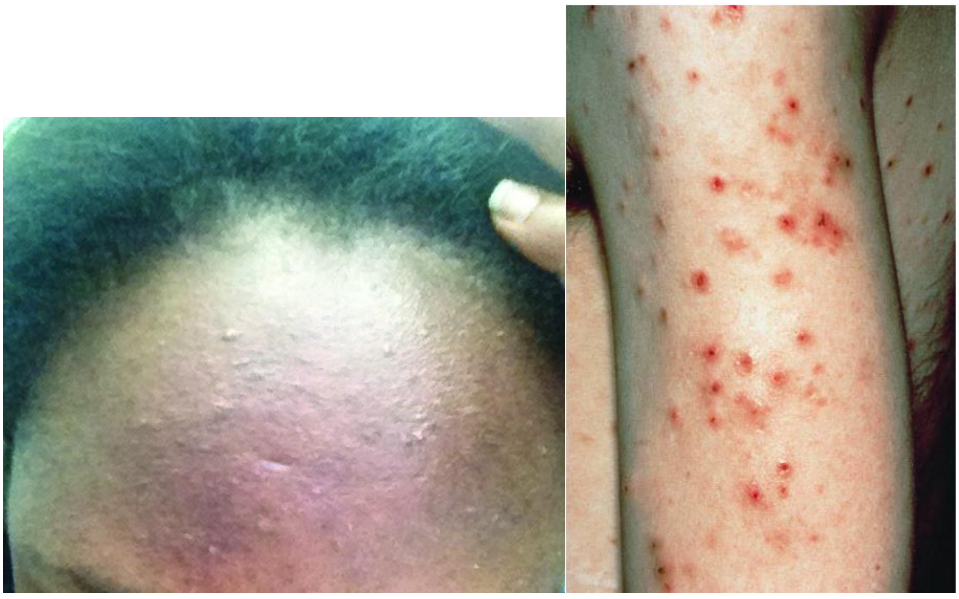
In sum:

- Post-inflammatory hyperpigmentation is a long-term discoloring of the skin after an acne lesion.
- PIH is more common in darker-skinned people, and can be treated with topicals (hydroquinone, azalaic acid, and retinoids). Some products are available that combine them. For fewer side-effects, adapalene and tazarotene are recommended.
- Chemical peels, such as glycolic acid and salicylic acid have been shown to more rapidly improve PIH.
- Other than commonly-used topicals or chemical peels, arbutin, ascorbic acid, niacinamide, or N-acetyl glucosamine can be used, specifically in milder cases of PIH.

Folliculitis

Folliculitis is a more general term referring to the inflammation of hair follicles and it is not to be confused with acne vulgaris. Often people have a combination of folliculitis and acne.

One condition for example is Malassezia Folliculitis (also known as Pityrosporum folliculitis). This is caused by yeasts (fungi) and can look very similar to acne. Notably, there are also bacterial forms of folliculitis.



Folliculitis.

Folliculitis can remain very mild for a long time and then flare up with humid weather or in the summer months. It also generally flares up and calms down more frequently than acne..

Other causes of folliculitis can be the extended use of antibiotics, the use of steroids, oily skin, occlusive (tight) clothing, heavy moisturizers and the usage of hot tubs/spas.

In many cases, medical treatment of folliculitis is not necessary. For example, in the case of folliculitis caused by Pseudomonas aeruginosa (a disease-causing bacterium) (usually in hot tubs/spas), symptoms peak at around 2-4 days after infection and improve spontaneously after 7-10 days. In this specific case, treatment might even prolong the infection.

In sum:

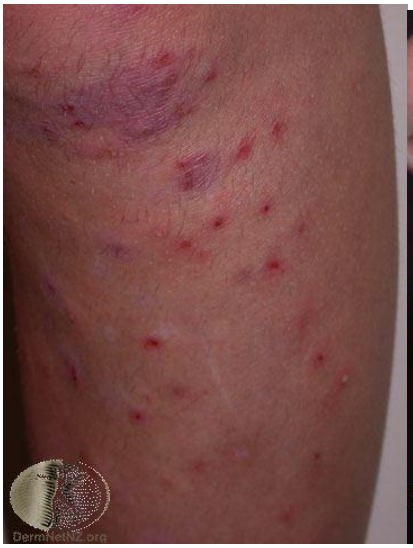
- Folliculitis is an infection of hair follicles and should not be confused with acne.
- Folliculitis often comes and goes, influenced by humid/warm weather, antibiotics use, occlusive clothing, and usage of hot tubs/spas.
- In some cases, folliculitis is caused by bacteria, and in general, it doesn't require further treatment.

Differential diagnosis of acne, folliculitis and PIH

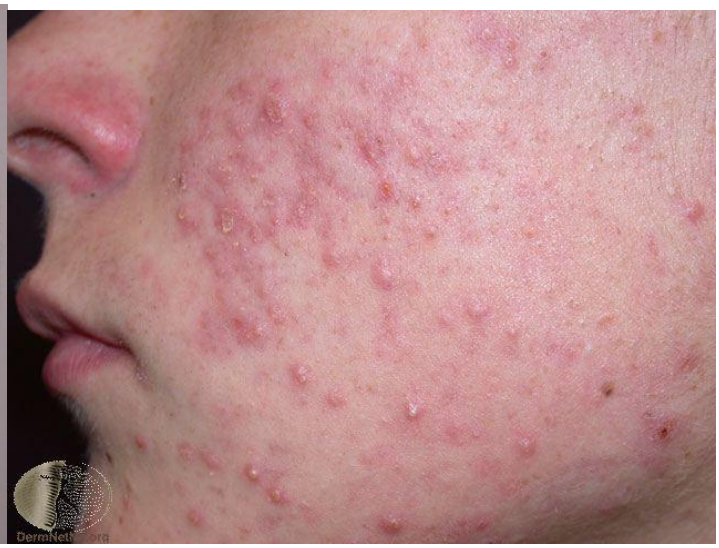
Since many forms of folliculitis and acne look virtually identical, it is sometimes hard to differentiate as the symptoms even overlap sometimes.

Notably, folliculitis is a lot more common in places of rubbing or irritation and usually gets worse with sweating and humid weather. If it is indeed folliculitis, how you treat it will depend on whether it was caused by bacteria or yeast.

A typical indication that you have folliculitis is also that you don't respond to therapies used for acne.

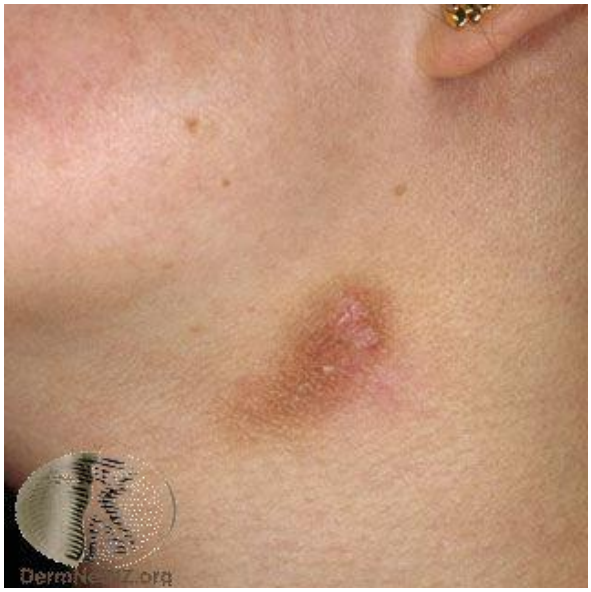


Folliculitis.



Acne vulgaris.

As implied in the name, postinflammatory hyperpigmention is a patch left on the skin after the original lesion has healed. It is diagnosed by taking a careful history and examining the skin. Dermal melanosis generally gives a characteristic hue to the skin colour (grey-purple-brown) and is a lot more common in darker skinned individuals.



Postinflammatory hyperpigmentation from violin playing friction.

Summary on acne et al.

- Acne vulgaris is a disorder of the skin, characterized by:
    - increased sebum (oily skin lubricant) production
    - excess keratin production (important structural skin protein)
    - an accumulation of bacteria
    - an overly aggressive immune response
- We can categorize acne into a non-inflammatory (no red lesions: whiteheads and blackheads) and inflammatory (red lesions: papules, pustules, and nodules/cysts) acne.
- The best treatment encompasses several aspects.
    1. Evaluate your lifestyle and diet. Washing your face excessively may just irritate the skin. Eating more fish and vegetables and cutting out dairy, especially skim milk, and processed foods, especially high-GI carbs and trans-fats, may help. Additionally, make sure your gut health is in order and your diet is rich in micronutrients and anti-oxidants. A healthy amount of sun exposure or UV-free light therapy may also help.
    2. If none of those improve the acne, start looking at non-prescription treatments, such as the combination of benzoyl peroxide and clindamycin. Beware of side-effects such as skin irritation, which increase with the strength of the treatment. A combination of topical and systemic therapies with oral antibiotics is recommended for moderately severe inflammatory acne as standard therapy. It should only be used for milder inflammatory acne that fails to respond to topical therapy.
    3. If you experience no satisfactory reduction in acne with the above treatment, then you can consider retinoid treatments. Beware that these have more severe side-effects, and can therefore often only be legally obtained with a prescription from your doctor. The topical forms are generally very effective at treating acne. As a last-option treatment, you may consider the oral retinoid isotretinoin, which is much more aggressive with serious side-effects, such as disturbance of physiological development and possible psychiatric effects.

Pregnant women should never use retinoids in any form, as they can cause birth defects.

- Post-inflammatory hyperpigmentation (PIH) is a long-term discoloration of the skin after an acne lesions has healed. They are more common in darked-skinned people and can be treated with topicals (hydroquinone, azalaic acid, and retinoids) and chemical peels, among other options. These have differing side-effects (see the section on PIH).
- Folliculitis, an infection of the hair follicles, is often confused with acne, because they look-a-like. It often flares up and calms down, depending on different things, like climate, clothing, and hot tub/spa use.

CELLULITE

What is cellulite?

Cellulite is a common skin phenomenon most seen in post-adolescent women. 85% to 98% of women over 20 years old have it to some degree [2]. Since the majority of women have it, cellulite has been called 'an invented disease'. Cellulite is characterized by orange-peel or cottage cheese-like skin, typically affecting the upper legs and buttocks of women most strongly.

Cellulite is graded into different categories of severity with grade 0 being no cellulite and grade 4 being strong orange-peel texture with deep raised and depressed areas. See the illustration below (warning: NSFW).

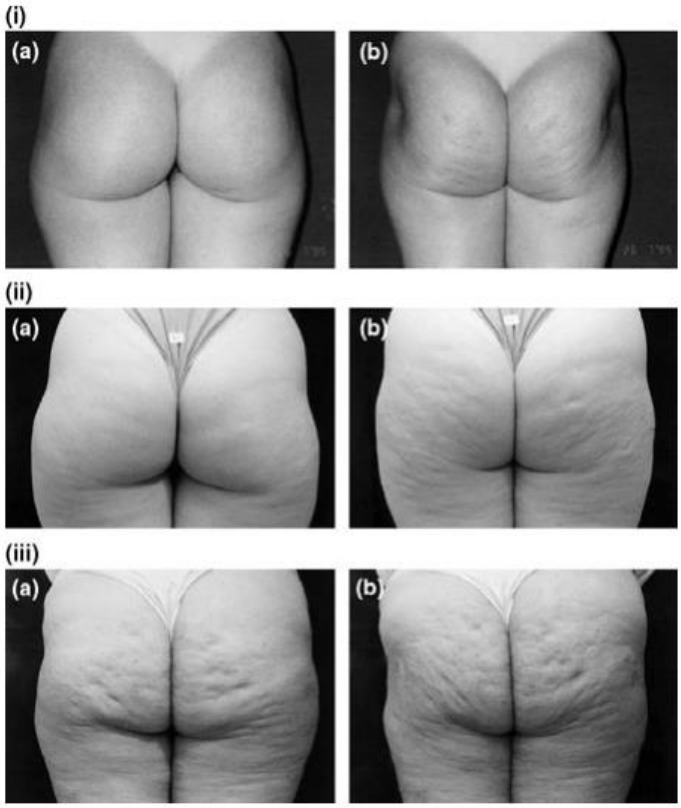


Figure 1 Cellulite grade at grade II (i), grade III (ii) and grade 4 (iii) at rest (a) and after gluteal contraction (b). From Rossi and Vergnanini [5].

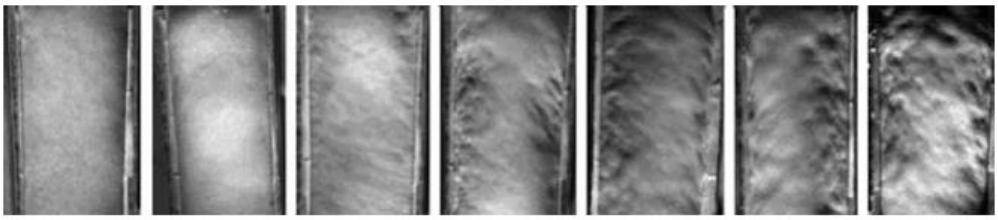
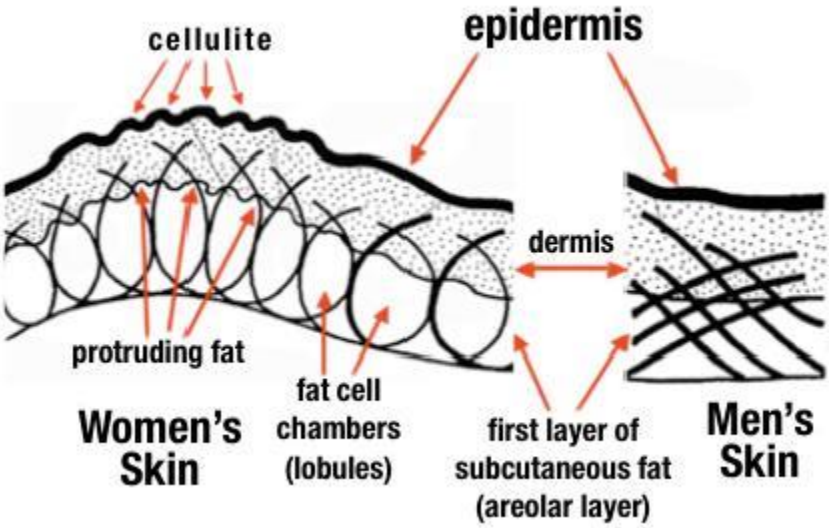


Figure 2 Photonumerical scale representative of the different grades of cellulite on compressed thighs: from no cellulite (left) to very severe signs of cellulite (right). From Perin *et al.* [6].

Causes

Cellulite is the result of fat deposits protruding through the skin [2]. This is why it occurs mainly in areas with large amounts of fat storage, notably over the hamstrings and glutes in women. Even given a similar level of fat storage though, cellulite is dramatically more common in women than men because women have a different skin structure. The upper part of the subcutaneous tissue is thicker and the fat cell chambers are larger and more radial, causing them to protrude through the crisscrossing

connective tissue and skin. The protrusion causes the skin to form pits like a water mattress lying on a field of rocks.



Source: Adapted from Nurnberger & Muller 1978 and Angehrn, Kuhn & Voss 2007.

Treatment

There's an enormous market for anti-cellulite treatments and a correspondingly large literature on the topic. Unfortunately, much of the research is industry sponsored and lacks randomization, proper control groups, double blinding and controlled outcome measures. Nevertheless, when we review the literature on the efficacy of available cellulite treatments, the conclusion from independent, high-quality, randomized, controlled trials is clear [1, 2, 3, 4, 5]. As Zerini et al. (2015): "no treatment is completely successful as none is more than mildly and temporarily effective." In other words, all those creams, fancy laser/radio/shockwave treatments and even surgical interventions do not cure cellulite. At best, they mildly disguise or reduce the appearance of the cellulite for a short period. If you're willing to undergo serious procedures to temporarily reduce cellulite, the evidence is currently strongest for subcision and collagenase injections [2, 3], both of which are FDA-approved for the treatment of cellulite. Both rely on temporarily breaking up the collagen structure of the skin, either by injecting enzymes that break down collagen or by mechanically breaking up the collagen with needles (subcision), and both obviously cause skin irritation. Subcision can cause bruising and pigmentation changes that last for months.

Fortunately, there is one major exception, arguably the most obvious 'treatment' of all: fat loss. Rather than try to modify the structure of the skin with fancy treatments, you just get rid of the fat that makes the skin bumpy. The severity of cellulite correlates with body fat level [2] and fat loss reduces the appearance of cellulite [2]. Other treatments of cellulite that show success partially do so because they result in fat loss [2, 3], not because they change the skin structure. Anecdotally, it's quite clear in female physique competitors that the visibility of cellulite comes and goes along with body fat. Some women will always retain some cellulite, but many women have no visible cellulite anymore in most lighting conditions below 20% body fat.

While fat loss typically reduces cellulite immediately, it sometimes first worsens, especially in leaner women. This is probably related to increased skin compliance when

the fat underneath the skin disappears and the skin becomes looser. The cellulite should become less visible once the skin tightens up and, anecdotally, this tends to be the case.

Muscle growth should increase the positive effect of fat loss, as growth in any body part's circumference increases skin tightness and reduces the relative thickness of the subcutaneous fat layer. There is no direct research on this, but various researchers and anecdotal evidence agree exercise helps reduce the appearance of cellulite.

Conclusion on cellulite

Cellulite is a physiological phenomenon of the skin caused by protruding fat cells. It affects most women to some degree. There is no cure and it's not harmful. The best way to reduce its appearance is to lose fat, build muscle and be in overall good health so that the skin can tighten up along with the fat loss. Any other treatments are at best moderately and temporarily effective. Medically speaking, no treatment is needed, because cellulite is not a medical pathology. It's a normal feature of human skin, especially for women.

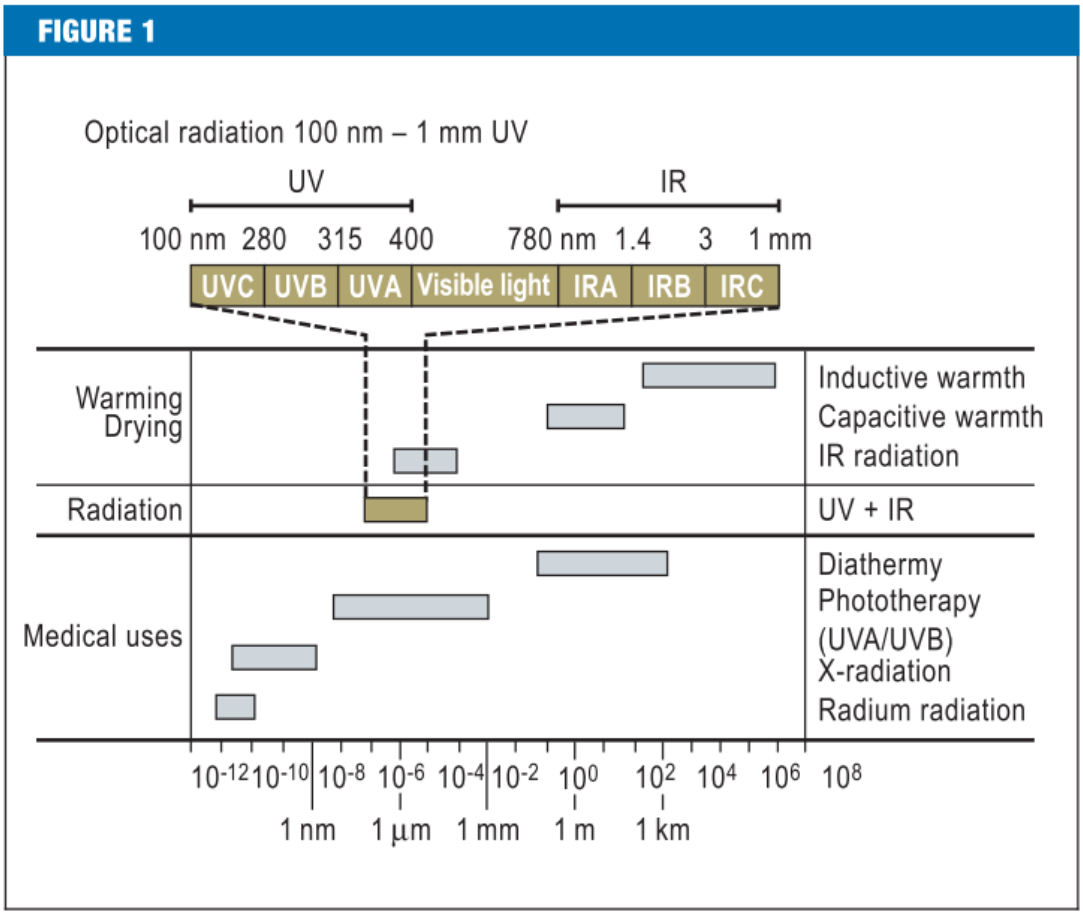
TANNING

Sun bathing

Sun bathing is a common practice to get more tanned. The tan is the result of melanin pigment accumulation in the skin. Melanin is produced by melanocytes to protect the skin from ultraviolet (UV) radiation in sunlight (or a tanning booth). Ultraviolet radiation is a form of high-energy optical radiation with a wavelength shorter than visible light, somewhere in the range of 100-400 nm (see image below). UV radiation accounts for about 10% of the sun's total energy output. It can be classified based on its wavelength.

- UVC is the shortest, meaning it is highest in energy.
- UVA is the longest.
- UVB is in the middle.

Fortunately, thanks to filtration by the ozone layer, only UVA and UVB reach the earth's surface. Earth would be a pretty dry place if UVC ever reached the ground.



Spectrum of electromagnetic radiation; UV, ultraviolet; IR, infrared

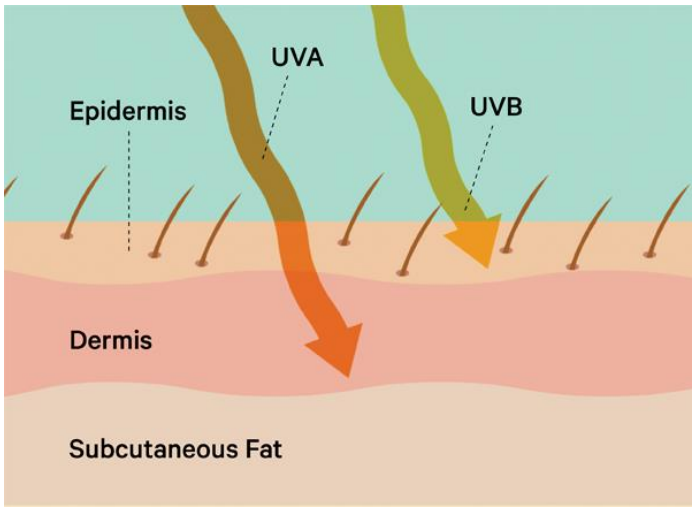
Source

Dangers of the sun

Anyone who's ever fallen asleep on the beach can attest to the fact that while UVA and UVB can give you that 'sexy bronzed look', they can also cause skin damage. In fact, excess UVB waves are carcinogenic, meaning they can potentially give you cancer.

UVA waves are not as directly carcinogenic, but they can penetrate the deeper layers of the skin, which can cause dermal (deep skin layer) changes in addition to epidermal (upper skin layer) ones. Specifically, these waves suppress the immune system and

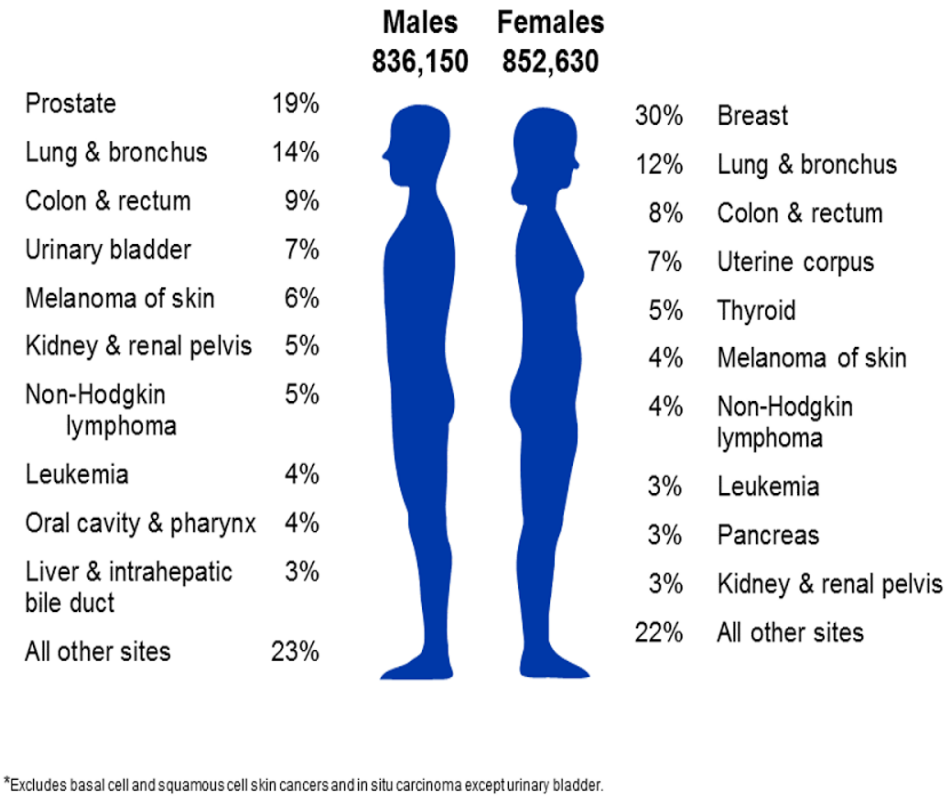
form reactive oxygen species (ROS), which damage DNA, cell membranes and enzymes.



Source

In short, UVA radiation enhances the carcinogenic effect of UVB. Not exactly an ideal one-two punch.

The risk of cancer is particularly large in the skin. Skin cancer is not a trivial concern. Non-melanoma skin cancer is one of the most common type of cancer in areas of the world with a light-skinned population. Over the US population as a whole though, the risk is not as high as for things like prostate or breast cancer: see the image below.



Source: Cancer Statistics 2017, American Cancer Society

Other risks of excess UV radiation include the promotion of skin aging, such as formation of wrinkles and pigmentary changes.

The figure below shows a brief overview of the mechanisms behind UV-induced skin aging.

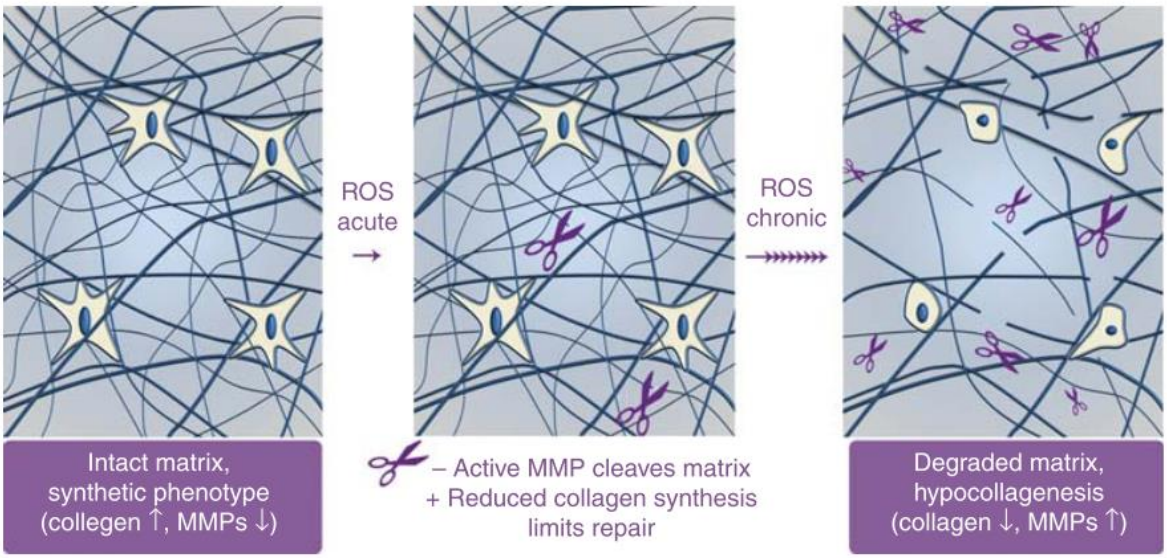


Figure 3. Accumulation of fragmented collagen in the dermal extracellular matrix leads to sustained reduction of collagen production in chronologically aged and photoaged human skin. (*Left* panel) In young skin, intact collagen within the dermal extracellular matrix provides attachment sites and mechanical resistance for fibroblasts. Fibroblasts are able to stretch and, under relatively high mechanical tension, show normal collagen homeostasis (collagen production is high, MMP production is low). (*Middle* panel) On exposure to UV irradiation (photoaging) or oxidative stress (chronological aging), elevated ROS activate signaling cascades that promote reduced collagen synthesis and increased MMP production. Active MMPs cleave the collagenous extracellular matrix, whereas reduced procollagen production limits repair. (*Right* panel) Accumulation of collagen fragments, which occurs with chronic UV exposure and the passage of time, impairs the mechanical and functional properties of the dermal extracellular matrix. Fibroblasts respond to this degraded dermal extracellular microenvironment by up-regulating MMP expression and down-regulating collagen production, thereby creating a self-sustaining phenotype that promotes skin fragility and age-related diseases.

Terms used in figure

***Extracellular matrix**: A collection of molecules that are produced by the skin cell and secreted into the space outside the cell. These molecules have structural and biochemical functions.*

***Fibroblasts**: Cells that produce this extracellular matrix and collagen (important structural protein found in bones, skin, muscles and tendons).*

***MMP**: Matrix metalloproteinases are enzymes break down most extracellular matrix proteins.*

In other words, there's a web (matrix of collagen and other structural molecules) holding multiple skin cells together to form the skin (extracellular matrix). When UV waves penetrate the skin, scissor-enzymes (MMP) start cutting this web down, while

simultaneously preventing repair of the web (collagen synthesis ↓). After a longer time in the sun, the collagen fragments accumulate, which prevents the web from functioning properly. Fibroblasts react by producing even more scissor-enzymes and producing less collagen, causing a downward spiral that leads to fragile skin and age-related diseases.

In conclusion, UV radiation's effect on the skin is similar to aging: the skin becomes more brittle and inelastic. Combined with the increased risk of cancer, excess sun exposure forms a health risk.

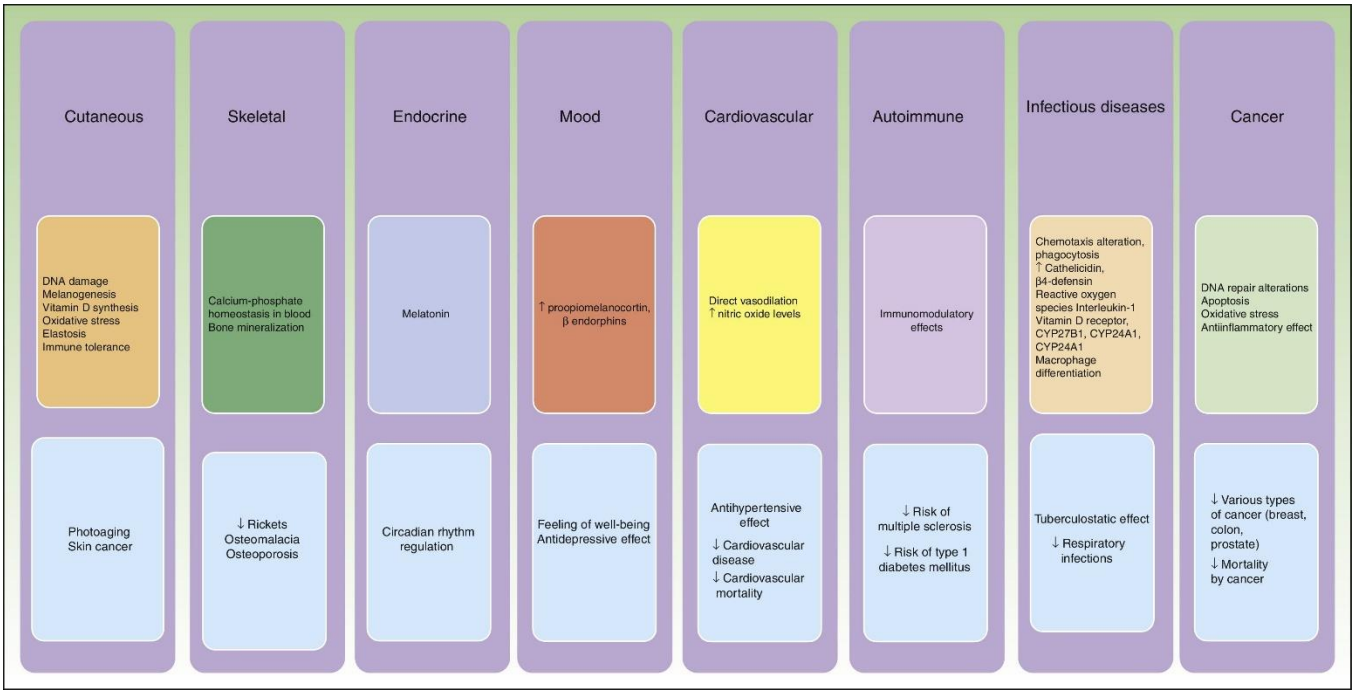
However, this doesn't mean you should spend your entire life lurking in the shadows. As with almost everything, the dose makes the poison.

Health benefits of sun exposure

A moderate level of sun exposure is good for your health. In low doses, sunlight has anti-inflammatory effects, it is a key zeitgeber to synchronize your biorhythm and it improves subjective wellbeing quite significantly. Low dose sun exposure has been found to be protective against cancer, not just skin cancer but also other cancers.

Therefore, going full vampire and avoiding all sun exposure is a risk factor for all-cause mortality in and of itself. *(Ed: Mortality is technically not a concern for vampires.)*

See the image below for an overview of the health effects of sunlight.



View full-screen source image

Many of sunlight's health benefits are mediated by vitamin D. UVB radiation is required for vitamin D production. Some forms of this vitamin can be regarded as hormones, which interact with over 2000 genes in the human body. If you cut out all sun exposure, you may even develop UV radiation deficiency, which has been linked to multiple negative outcomes [2], such as:

- cardiovascular diseases
- autoimmune diseases
- skeletal diseases
- diabetes
- increased cancer risk, including breast, colon, lung, lymphoma, pancreatic, ovarian and prostate cancer.

Certain estimates based on a Norwegian population can shed light (no pun intended) on the cost-benefit ratio of proper sun exposure. Here, the negative effects of sun overexposure were estimated to result in 200–300 more cutaneous malignant melanoma (a type of skin cancer) deaths per year. However, it would also increase the

population's vitamin D production by about 25 nmol/l, which could translate to roughly 4000 fewer instances of internal cancers and about 3000 fewer cancer deaths overall. So the sun is potentially promoting one rarer type of cancer (cutaneous malignant melanoma), while preventing a more common one.

Depending on where you live and the season, it can be easy or difficult to get enough vitamin D production from sunlight. During the summer, as little as 3-30 minutes can be enough when the sun is at its peak (usually between 10 AM and 4 PM) and at least 40% of your skin is exposed (e.g. when sunbathing or on the beach). The darker your skin color (pigmentation), the longer it will take. Caucasians, especially redheads, can stick to the lower end of the time range while black skinned individuals (no, not 'African Americans': we are literally talking about skin type here) should aim for the top end.

As a rule of thumb, for enough natural vitamin D production it's necessary to get 50% of the sun exposure needed to cause a mild sunburn. When considering the figure in the previous section, this would mean that 7 minutes of sun exposure for individuals with a pale skin would be sufficient, if at least 20% of the body is exposed. The 'rule of nine' helps to estimate the amount of exposure: "The face accounts for 9% of the body surface, each arm for 9%, each leg for 18%, and the abdomen and the back for 18% each."

Sun exposure is incredibly effective to replenish vitamin D stores compared to vitamin D supplementation. Moreover, unlike with supplementation, there's no risk of toxicity, as vitamin D production automatically decreases when serum levels are sufficiently high. See the image below for a comparison of vitamin D replenishment of sun exposure vs. low dose vitamin D supplementation.

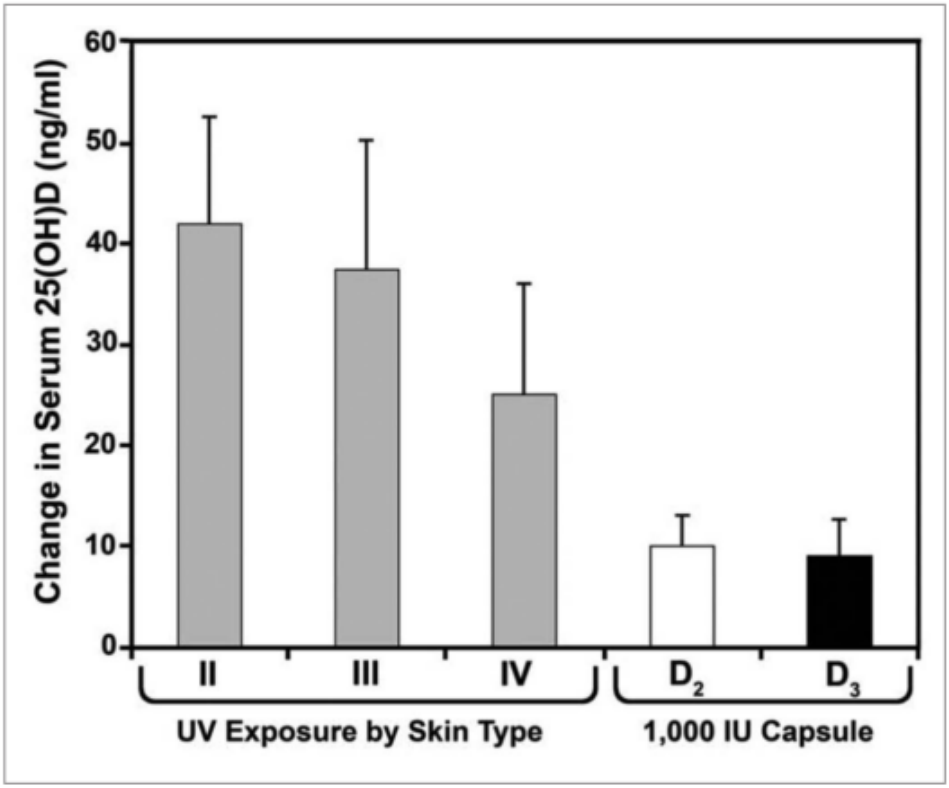
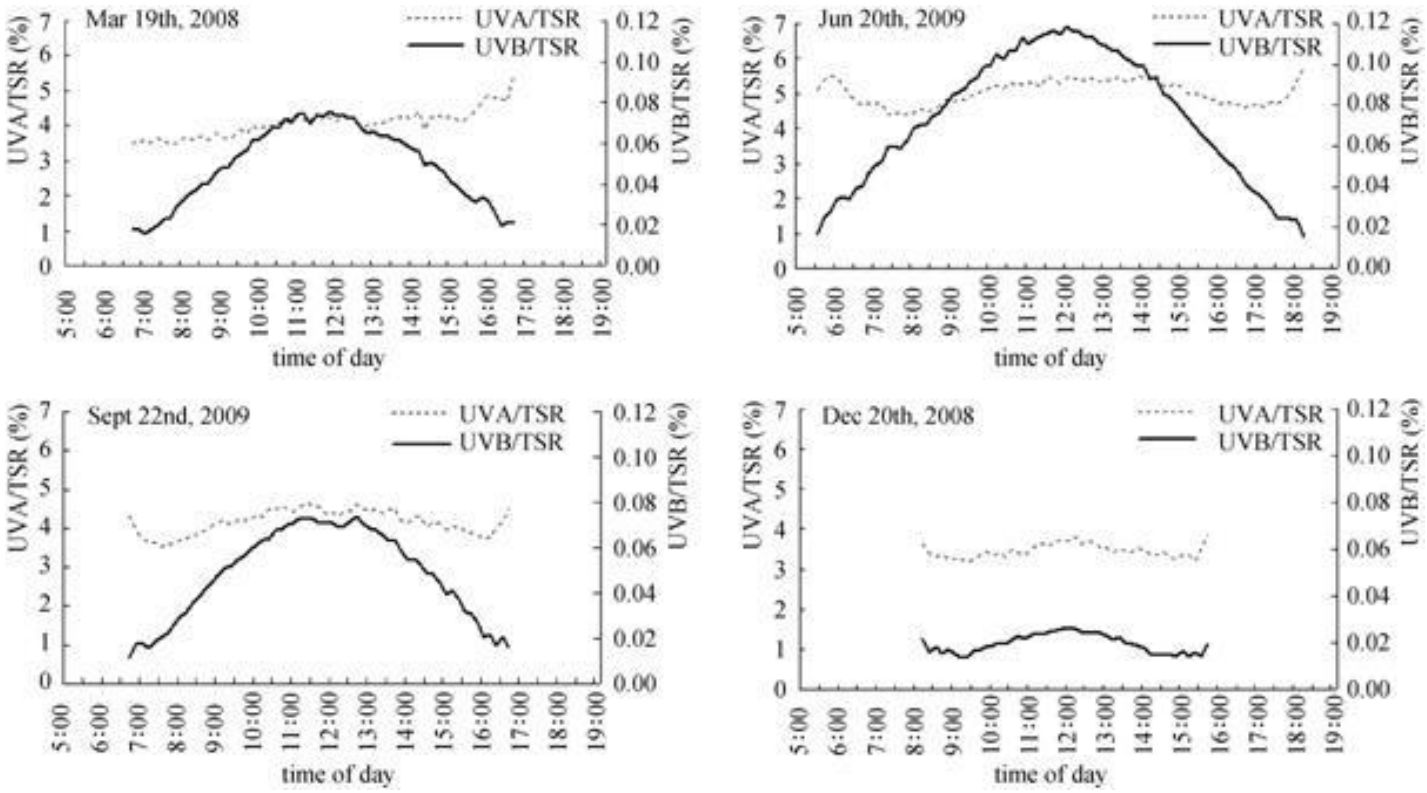


Figure 79. Comparison of the percentage increase in serum 25(OH)D levels of healthy adults who were in a bathing suit and exposed to suberythemal doses (0.5 MED) of UV B radiation once a week for 3 mo with healthy adults who received either 1000 IU of vitamin D_2 or 1000 IU of vitamin D_3 daily during the winter and early spring for a period of 11 weeks. Fifty percent increase represented approximately 10 ng/ml from baseline 18 ± 3 to 28 ± 4 ng/ml. Skin type is based on the Fitzpatrick scale: Type II always burns, sometimes tans; type III always burns, always tans; type IV sometimes burns, always tans; type V never burns, always tans. Data are means ± SEM. Holick, copyright 2008. Reproduced with permission.

Source

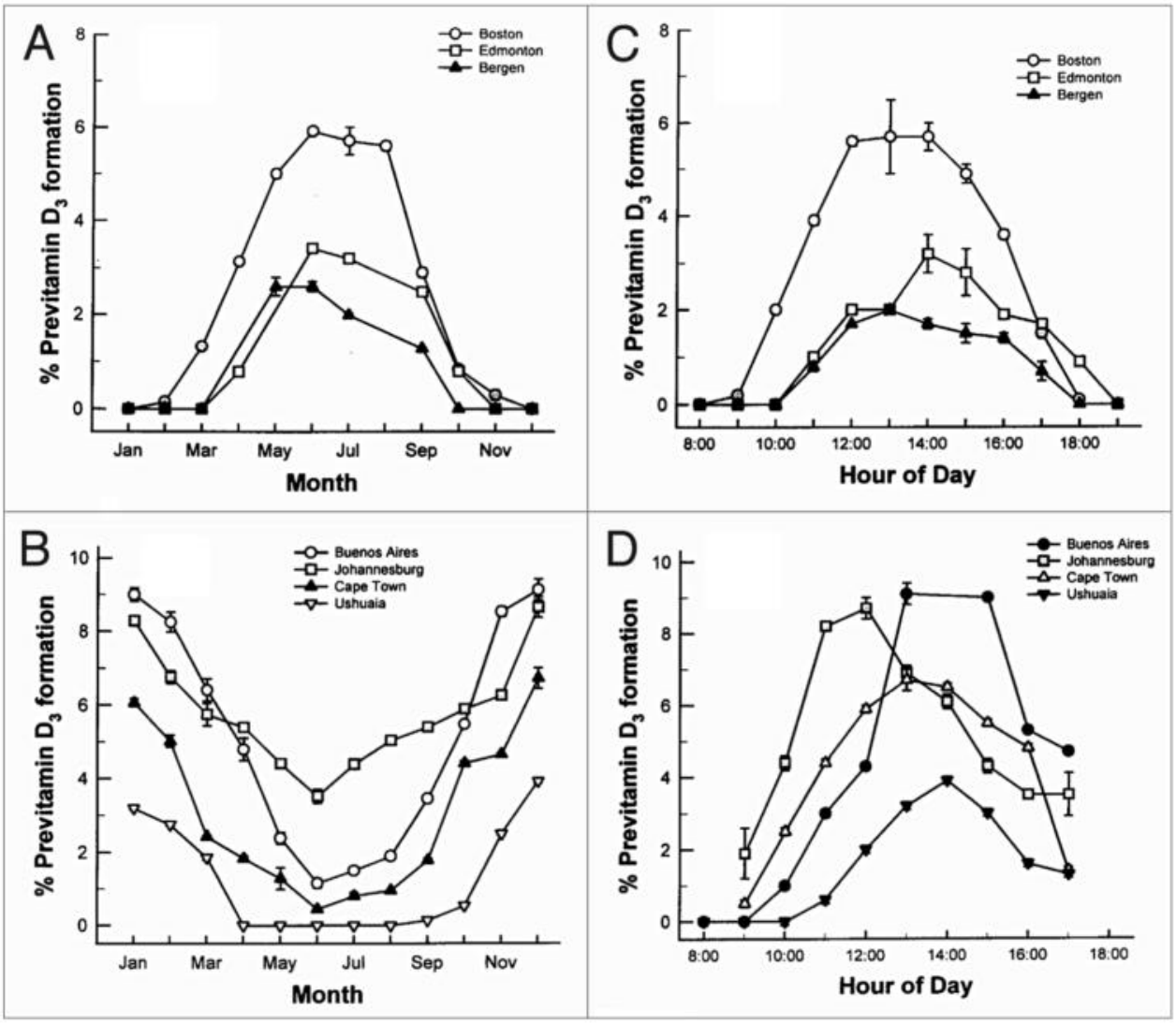
Facial skin does not contribute much to vitamin D protection. The face's skin is also relatively sensitive to skin damage, cancer and wrinkling. As such, it's advisable to protect the face more from sunlight than other body parts.

Vitamin D production from sunlight is highest when the sun is at its peak. The higher the sun, the greater the UVB radiation. See the image below.



The percentage of UVB (solid graph line) to total sunlight radiation (TSR) generally peaks around noon, while the contribution of UVA (dotted graph line) is relatively constant across the day.

More UVB means more vitamin D. The total amount of vitamin D production depends on your location (latitude), the season (seen in the figure above), and what time of day it is. You can find the average monthly UV index in several major cities of the world here. A UV index below 3 is minor; above 7 poses high risks. All of these factors influence the height of the sun and how much vitamin D your skin produces after sun exposure. Basically, brighter sunlight is more effective to get high vitamin D production.



Vitamin D synthesis in response to sunlight across time of day, season and climate.

Problematically, as we discussed earlier, while UVB radiation is responsible for vitamin D production, it can also directly damage your DNA. As such, peak sunlight hours are a good time to quickly get the health benefits of sunlight, but they are not a good time for prolonged tanning. Tanning is better done in the morning or afternoon when you can get tanned with less risk of skin damage (although it will also take longer to get tanned). While UVA also has potential damaging effects, at least you only get highly exposed to one UV wave type instead of the double whammy of UVA plus UVB.

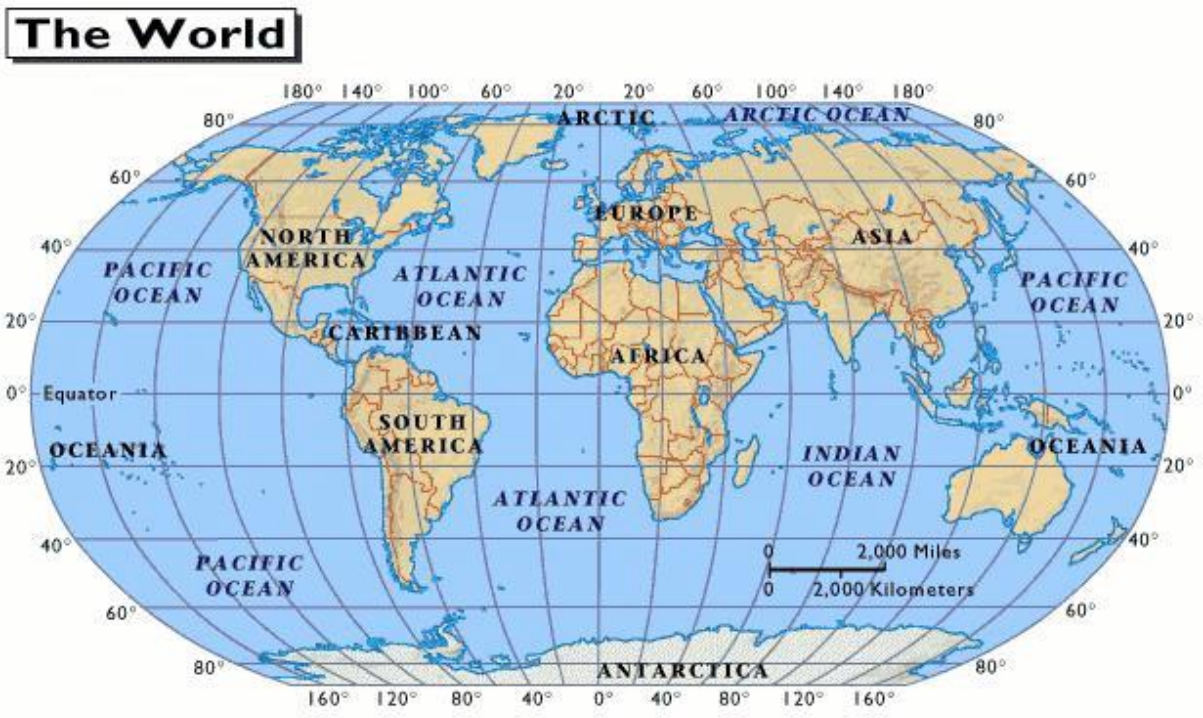
Since sunlight has both positive as well as negative health effects, how much sun exposure should you get?

Finding the cost-benefit sweet spot of sun exposure

Problematically, the factors that increase vitamin D production are largely the same factors that make you more susceptible to skin damage. Spending more time in the sun, exposing more of your body and a higher UV radiation intensity all increase vitamin D production but also the risk of skin damage.

Your skin phenotype strongly determines how much sun exposure you benefit from. Having ‘pale’ (blue or grey) eyes, blonde or red hair, facial freckling as a child and fair skin is significantly associated with increased skin cancer risk from sun exposure. Most gingers are painfully aware of how quickly they sunburn with minimal tanning effect to boot. They also synthesize vitamin D very quickly normally, so the optimal amount of sun exposure for their health is generally measured in minutes per day.

Your location also determines your risk. The closer you live to the equator, the larger your risk. The risk at high latitudes is lower than at low latitudes.



Latitude refers to how far a location lies from the equator on either side. 0° latitude refers to the equator (tropical climates). 90°latitude refers to the Arctic or Antarctica.

A large body of literature has looked at how much sun exposure is ideal, controlling for phenotype and latitude [1, 2, 3, 4, 5, 6, 7]. Since the optimal amount of sunlight is very individual, it's good to keep in mind 3 benchmarks for yourself to know when you certainly had too much sun exposure.

1. Getting sunburned is unequivocally bad. Research already consistently finds significantly increased risk of cancer in individuals that have gotten sunburned just once in their lives.
2. Any reddening of your skin after being in the sun (erythema) indicates skin damage, which is again unequivocally a bad sign. Photodamage sets in before the skin turns red.
3. If you didn't tan at all, you're probably not at risk, unless you have extremely white skin (e.g. ginger).

Assuming no sunburn or erythema, the optimal amount of sun exposure may be quite high for individuals living at higher latitudes and countries where it can freeze during winter. In the UK the risk of melanoma (cancer) is lowest in individuals with a weekday sun exposure of around an hour a day in summer and over 1.5 hours in winter.

Weekend sun exposure seems to be particularly protective with an optimum around 4.5 hours a day even in the summer. Holiday sun exposure also seems protective. These findings and others suggest chronic sun exposure is more damaging than intermittent sun exposure. However, this finding may be confounded by socio-economic status. Individuals that can afford to spend time in the sun in the weekend or go on holiday may be better off than those that can't in many other ways. Plus, most of the benefits were mediated by vitamin D level, so with vitamin D supplementation the optimum sun exposure is significantly lower.

Indeed, when all data were averaged out, anything over 2 hours of sunlight a day increased the risk of skin cancer. So all in all, with vitamin D supplementation, more than an hour of intense sun exposure a day is a risk for most individuals.

Other meta-analytic research supports a relatively clear dose-response risk of cancers with both sunbathing activity and overall outdoor activity regardless of latitude: the more time you spend sunbathing or being outdoors, the higher your risk. Outdoor workers also tend to be at higher risk of cancer than individuals with indoor occupations, although some data find the opposite: it probably depends on if the sun exposure is low enough that the skin can naturally adapt to it or not.

In conclusion, most people are better off with up to an hour of sun exposure a day than no sun exposure. The sweet spot seems to be around half the sun exposure that would result in sunburn.

Tanning beds

Tanning beds are human toasters. Uh, we mean, tanning beds function by emitting mostly UVA radiation at values 10-15 times higher than that of the mid-day sun. There is some UVB radiation, but it's reduced to less than 10%. Since UVB radiation is the more damaging of the two, being directly associated with a carcinogenic effect, tanning beds are theoretically a healthier way to tan than sunbathing is, though vitamin D production is also reduced. In support of this, 10 sessions of indoor tanning resulted in a lower total UV radiation exposure than a 2-week sunbathing holiday, even with sunscreen being applied during the holiday and no sunburns. However, it was a hardcore sunbathing holiday in this study with 6-8 hours of tanning a day and the estimate was that using liberal sunblock would have shifted the UV exposure to below the tanning bed course level.

Tanning beds still pose great risk though. Both UVB and UVA exposure induce DNA damage. While UVB has the direct link, UVA has an indirect effect on DNA via the creation of reactive oxygen species (ROS). Emerging evidence also suggests a direct carcinogenic effect of UVA radiation. It's very easy to overdo indoor tanning due to the high intensity of most tanning beds. Frequent tanning bed use (starting at 4 times per year) has been associated with more than double the risk of developing skin cancer [2]. The younger you start, the higher the risk.

Tanning beds, like sunlight, also improve your mood [1, 2, 3]. The impact on well-being is so strong that frequent tanners can enter a tanning bed blindfolded, and based on how their mood changes, get an idea of the UV radiation intensity. Brain reward pathway activation is not as strong without UV light. In fact, some research shows the dopamine release from tanning is so powerful that resistance develops with further use, causing physical as well as psychological addiction. So again, it's easy to overdo it.

In conclusion, when used appropriately, tanning beds are an effective and relatively safe alternative to sunbathing. Just be careful to work up gradually and stay under half the exposure that would get you a sunburn.

Sunscreen

Sunscreen blocks UV radiation and thereby reduces skin damage. Less UV radiation into the skin also means less tanning, so if your goal is to get tanned, sunscreen in large part just makes you need more sun exposure to reach the same endpoint. However, lighter sunscreens only reduce UVB penetration into the skin, like tanning beds, thereby allowing you to still get tanned without as much risk of skin damage (but also reducing vitamin D production). Broad spectrum 'sunblocks' also reduce UVA penetration, thereby offering more complete protection but also less tanning effect.

Importantly, no sunscreen actually 'blocks' UV radiation completely: it just provides a protective layer that reduces penetration to a certain extent. The extent of protection is measured by the Sun Protection Factor (SPF). The SPF is theoretically a multiplication factor of the time it takes to get sunburned, so factor 50 would delay the time of a sunburn by 50-fold. If it normally takes an hour before you get sunburned, then factor 50 sunscreen *should* make it take 50 hours, but in practice, anybody with any sunburn experience can tell you sunscreen doesn't work that way. For one, regular sunscreen only protects against UVB radiation, so UVA damage can still occur.

More importantly, in order to obtain the listed protection, sunscreen has to be applied at 2 mg/cm of skin^2. In practical terms, that comes down to smearing sunscreen with this thickness on most of the body at least twice per day. You would need about a third of a 200 ml bottle *per day*. You know the people that are literally covered in sunscreen with a thick, pasty white layer over their whole body? Well, these are the only people actually using the recommended amount of sunscreen. Most people only apply sunscreen at a fourth of the advised density, which means you should take the fourth root of the label's SPF for the actual SPF. Factor 50 is then actually factor 2.7; 25 is 2.2 and 15 is 2. Moreover, wind, physical contact, sweat and water can all dilute the sunscreen, further reducing its effectiveness.

Since the real life SPF is far lower than what the label suggests, most sunscreen users overestimate the protection they get and compensate by increasing the duration they're in the sun, thinking they're protected, while actually ending up with more skin damage and a higher risk of cancer(!) Still, SPFs of 15+ tend to reduce the risk of cancer more than SPFs below 15.

In addition to providing only very limited protection, sunscreens have been found to offer protection against only certain kinds of cancer but not all of them.

The labeling gimmick, misuse of sunscreen and inflated protection are probably the reasons why in practice, an abundance of research finds no relation between frequency of sunscreen use and the risk of skin cancer.

In conclusion, sunscreen is theoretically helpful to avoid skin damage when you need to be in the sun longer than your skin can naturally handle, but the offered protection is far lower than what the label suggests. If you're sunbathing primarily to get tanned, sunscreen is only theoretically protective and in large part just makes you need more time in the sun to reach the same stimulus for the skin.

Spray tans

The tan-in-a-can offers a safe alternative to sunbathing for when you want a strong tan, notably contest prep. The tan required for maximal muscle definition during a physique competition is not achievable with natural sunbathing for most people, so a spray tan is virtually a must.

Tanning lotions work similarly, but they are generally far less effective.

Both contain dihydroxyacetone (DHA) as the active ingredient, which reacts with amino groups of skin proteins to turn the skin brown (note: DHA contained in sunless tanning products should not be confused with the omega-3 acid DHA, which is the abbreviation for docosahexaenoic acid).

While DHA exhibits some protective function against UV radiation, it can't prevent sunburn or sun-induced skin damage. In fact, the first 24 hours after application of DHA increases the formation of UV-induced ROS, which potentiates the skin-damaging effect of UV radiation.

DHA is safe when externally applied to the skin, but can be hazardous when inhaled, ingested or in contact with eyes [2]. Many spray tan booths don't use protective measures to prevent inhalation or eye contact, so in these cases, spray tanning may actually pose a health risk.

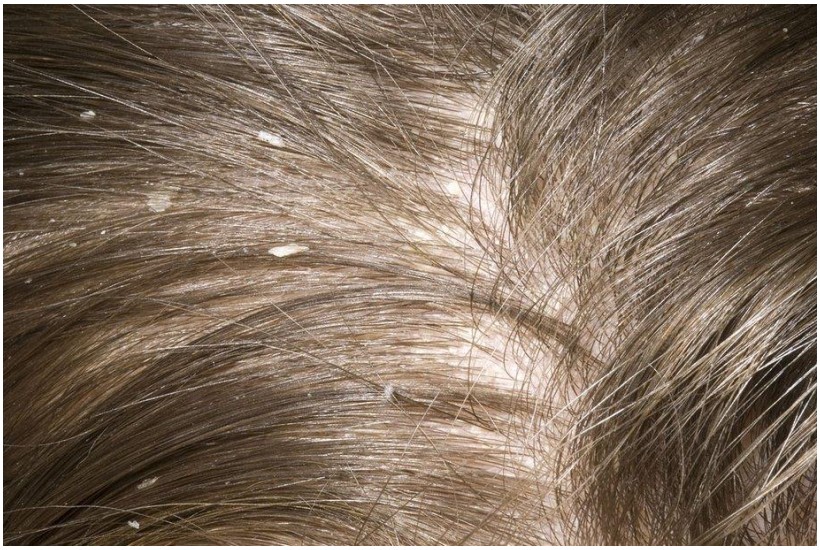
Summary on tanning

- UV radiation in sunlight can damage the skin and cause cancer. However, sunlight also offers several health benefits, notably vitamin D production and a better mood.
- For optimal health, you only need about 50% of the sun exposure that it would take to get a sunburn in at least 20% of your body. This duration is generally measured in minutes. The darker your skin, the more sun exposure you need.
- Vitamin D production results from UVB exposure, which is highest midday when the sun is at its peak. However, UVB is also more damaging for the skin than UVA, so if your goal is primarily to get tanned, the mornings and afternoons are safer.
- Anything over ~2 hours a day of sun exposure and particularly any kind of skin reddening or sunburn majorly increases your risk of skin cancer.
- Tanning beds offer a theoretically safer option to get tanned due to their relative lack of UVB radiation. They also provide similar mood improving effects as sunlight. However, it's incredibly easy to overdo tanning because of the high intensity.
- Sunscreen offers only limited protection against photodamage. Beware of compensation! You need liberal amounts of Sun Protection Factor 15+ applied regularly to get significant protection.
- When a strong tan is desired, consider spray tanning as a safer alternative to sunbathing. For physique competitions a spray tan is virtually mandatory.

DANDRUFF

What is dandruff?

Dandruff is a skin condition that leads to flaking of the skin and often an itchy, scaly scalp. Skin layers continually replace themselves. When this happens, the cells are pushed outwards. Afterwards, the cells die and flake off. Normally, skin cell turnover takes about a month and the skin flakes are too small to be visible. However, people with dandruff have very fast cell turnover: it takes their skin cells only a short time to mature and die compared to normal skin cells. Because of the rapid turnover, dandruff sufferers shed their dead skin cells in large, white, oily flakes, which may then become visible on the scalp, skin and clothes.



Dandruff.

Dandruff affects about half of all people in the United States and can cause serious emotional distress, as it is often perceived as unattractive. Let's find out what causes dandruff and how to get rid of it.

Cause

A yeast-like fungus, Malassezia causes dandruff when there is excess colonization [2, 3, 4]. The fungus feeds on the sebum produced by the skin and releases certain fatty acids that increase skin cell turnover and irritate the skin with dandruff as the result.

Sebaceous gland activity is under hormonal control. High androgen levels increase oil production, which is why dandruff is more prevalent during adolescence and less prevalent in the elderly.

Seborrheic dermatitis often co-present with dandruff. Seborrheic refers to sebaceous glands that produce sebum on the skin, dermal refers to skin and -itis refers to inflammation, so seborrheic dermatitis means there's irritation of the skin and its oil producing glands. Seborrheic dermatitis is essentially a worse form of dandruff. Dermatitis is similar in cause and pathology but also has inflammation and isn't restricted to the scalp like dandruff. Seborrheic dermatitis may affect other areas rich in oil glands, such as the eyebrows, the sides of the nose, the backs of the ears, the breastbone (sternum), the groin area and sometimes the armpits.

Seborrheic dermatitis/dandruff can also affect men's beards. 'Beard itch' is thus in fact often essentially facial dandruff and should be treated as such. The use of commercial beard oils and balms may actually exacerbate it by feeding the Malassezia fungus.

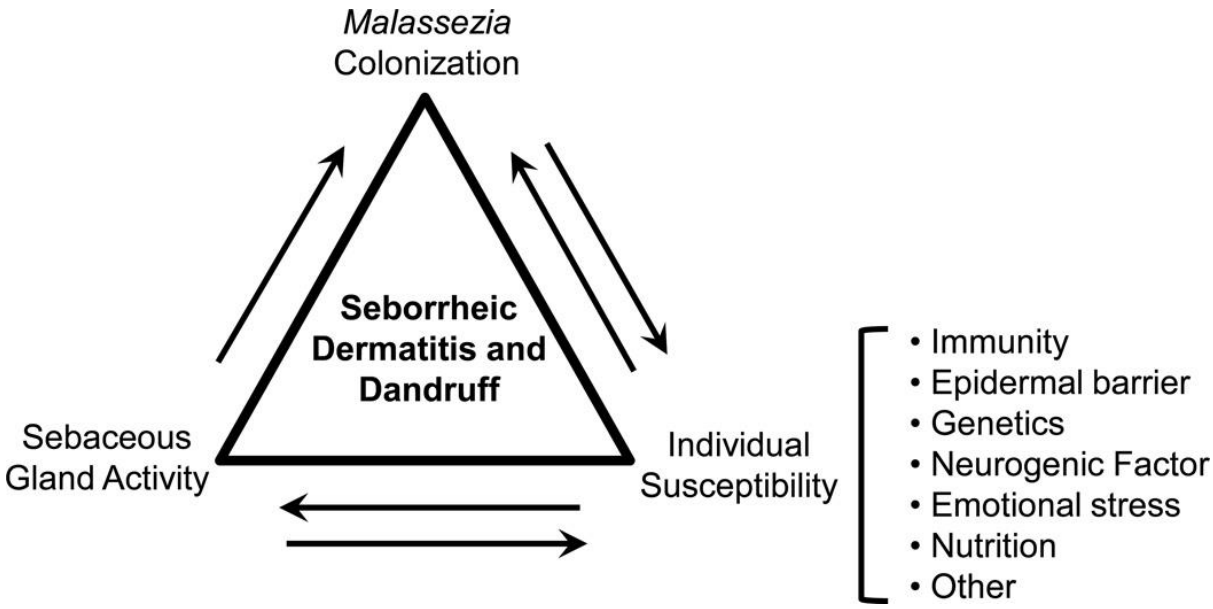
The table below adapted from Borda & Wikramanayake (2015) illustrates the differences and similarities between dandruff and seborrheic dermatitis.

	Seborrheic Dermatitis	Dandruff
Epidemiology	Up to 40% of infants within 3 months of age, 1–3% of the general adult population.	50% of adult population.
Location	Scalp, retro-auricular area, face (nasolabial folds, upper lip, eyelids, eyebrows), upper chest.	Scalp.
Presentation	Erythematous patches, with large, oily or dry scales.	White to yellow flakes dispersed on the scalp and hair; without erythema.
Histology	Acanthosis, hyperkeratosis, spongiosis, parakeratosis, *Malassezia* yeasts.	
	Vasodilation and perivascular and perifollicular inflammatory infiltration; “shoulder parakeratosis”.	Subtle neutrophil infiltration or no inflammatory infiltration.
Treatment	Antifungal shampoos and topical.	
	Topical corticosteroids, immune modulators, phototherapy, systemic treatment.	
Predisposing Factors and causes	Sebaceous gland activity, fungal colonization, and individual susceptibility (epidermal barrier integrity, host immune response, genetic factors, neurogenic factors and stress, nutrition, etc.).	

The following factors can exacerbate the effects of Malassezia colonization, which helps explain why dandruff is more prevalent in the winter months:

- Dry or irritated skin can increase sebum production and the inflammatory effect of the fungus.
- Certain haircare products can cause contact dermatitis, which in turn causes seborrheic dermatitis and dandruff.
- A weakened immune system, either due to illness or emotional distress, can also exacerbate dandruff.

- Sun exposure has been found to trigger dandruff, yet sunlight is anti-inflammatory in moderate amounts and sunlight has been found to kill the Malassezia fungus, so it's unclear if sun exposure is overall beneficial.



Dandruff and seborrheic dermatitis are both caused by colonization of the Malassezia fungus and aggravated by higher sebum production and poor skin health. Source

Treatment

The easiest and widest-spread treatment for dandruff is anti-dandruff shampoo [2]. These shampoos generally have anti-fungal activity, which means they kill the Malassezia fungi and thereby get rid of the root cause of the dandruff. We can classify dandruff shampoos according to the active ingredients they contain:

- Zinc pyrithione [2]. Commonly available and effective.
  Product examples: Head & Shoulders, Jason Dandruff Relief 2 in 1.
- Tar-based shampoos help against SD and dandruff in a similar way as zinc pyrithione. If you have light-colored hair, some tar-based shampoos may cause discoloration and this is probably not a good treatment option.
  Product example: DHS Fragrance Free Tar Shampoo.

- Selenium sulfide shampoos. For natural dark-haired individuals only, as selenium sulfide can discolor blond, gray or chemically colored hair.
  Product example: Selsun Blue.
- Ketoconazole shampoos [2] have broad-spectrum antifungal activity and inhibit fungal cell wall synthesis. Ketoconazole is often recommended as a first-line treatment for dandruff and seborrheic dermatitis. However, note that it has anti-androgenic activity, so it may not be desirable to use on your beard if you're a man and you want a full beard (see section on hair loss).
  Product example: Nizoral.
- Salicylic acid shampoos. Their efficacy for seborrheic dermatitis is not very well studied, however.
  Product example: Neutrogena T/Gel.

Many of these ingredients are also available in oral form, such as itraconazole, but topical application is preferable because oral consumption results in systemic side-effects as opposed to only local ones. Orals should thus only be used as a last resort in consultation with a dermatologist.

Some other treatment options, such as tea tree oil shampoo, show promise for the treatment of dandruff, but the evidence for them is still weak and most people needn't bother with them given the established options mentioned above.

Corticosteroids, generally in cream form, are sometimes recommended for the management of seborrheic dermatitis, but they are effectively no more than a band-aid to manage the side-effects, as they don't address the root cause, which is the fungal overgrowth. They can also present with serious side-effects, such as skin atrophy and hypopigmentation.

The following table from Borda & Wikramanayake (2015) summarizes the established treatment options.

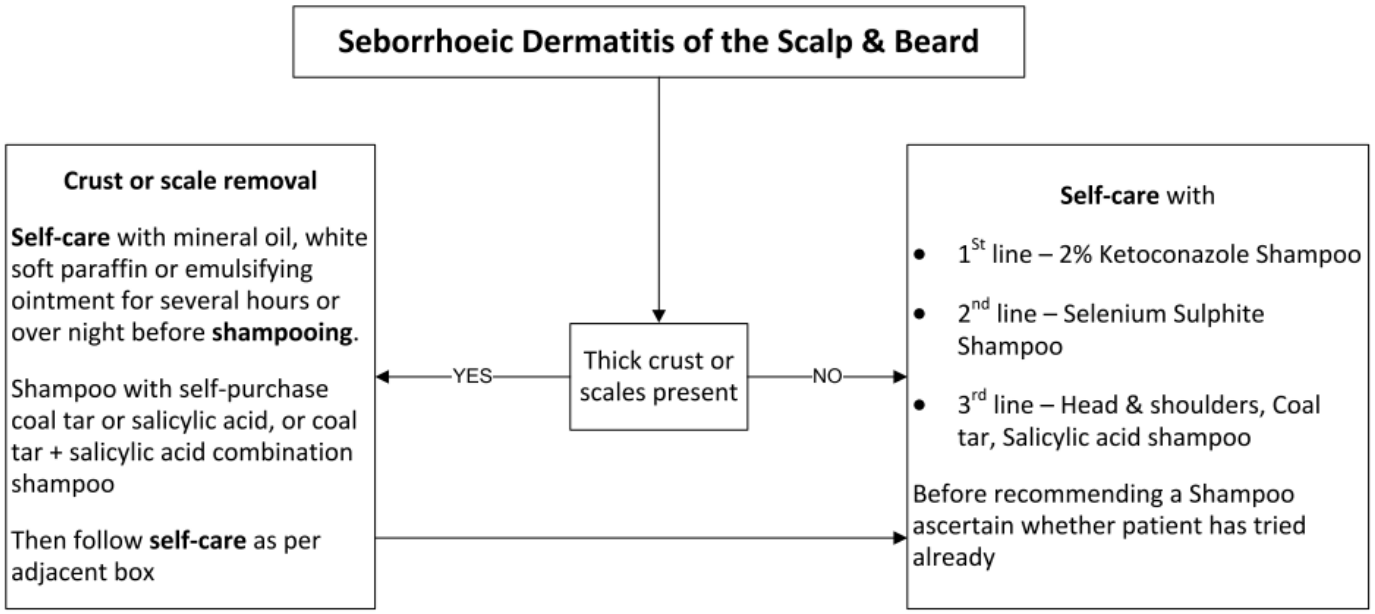
Medication			Dose/ Formulation	Regimen	Mechanisms	Side Effects	References
TOPICAL	Antifungals	Ketoconazole	2% Shampoo, cream, gel or foam	Scalp or skin: Twice/ week × 4 weeks, then once/week for maintenance.	Inhibition of fungal cell wall synthesis.	ICD† in <1% of patients. Itching, burning sensation and dryness in 3% of patients.	[2,8,26,97–101]
		Bifonazole	1% shampoo, cream or ointment	Scalp: every other day or once daily. Skin: once daily.		ICD in 10% of patients.	[8,26,99,102]
		Miconazole	Cream	Skin: 1–2 times daily.		ICD, itching, burning sensation.	[47,97,103]
		Ciclopirox Olamine	1.5% shampoo, cream, gel or lotion	Scalp: 2–3 times/week × 4 weeks, then once/ week for maintenance. Skin: twice daily.	Inhibition of metal-dependent enzymes.	ICD in <1% of patients. Itching, burning sensation in 2% of patients.	[8,47,97,99,104,105]
		Selenium sulfide	2.5% shampoo	Scalp: Twice/week × 2 weeks, then once/week × 2 weeks. Repeat after 4–6 weeks.	Cytostatic and keratolytic.	ICD in ~3% of patients. Orange-brown scalp discoloration.	[8,97,106,107]
		Zinc Pyrithione	1% shampoo	Scalp: 2–3 times/week.	Increased cellular copper interferes with iron-sulfur proteins.	ICD in ~3% of patients.	[8,97,99,101,108,109]
	Cortico-steroids	Hydrocortisone	1% cream	Skin: 1–2 times daily.	Anti-inflammatory, anti-irritant.	Risk of skin atrophy, telangiectasias, folliculitis, hypertrichosis, and hypopigmentation with prolonged use.	[8,9,97,99,103,108]
		Betamethasone dipropionate	0.05% lotion	Scalp and skin: 1–2 times daily.			[8,47,110]
		Desonide	0.05% lotion, gel	Scalp and skin: 2 times daily.			[8,111–113]
		Fluocinolone	0.01% shampoo, lotion or cream	Scalp or skin: Once or twice daily.			[7,114]
	Immuno-modulators	Pimecrolimus	1% cream	Skin: 1–2 times daily.	Inhibition of cytokine production by T-lymphocyte.	Risk of skin malignancy and lymphoma with prolonged use.	[47,98,115–118]
		Tacrolimus	0.1% ointment	Skin: 1–2 times daily × 4 weeks, then twice/ week for maintenance.			[26,97,109,118–120]
	Miscellaneous	Coal tar	4% shampoo	Scalp: 1–2 times/week.	Antifungal, anti-inflammatory, keratolytic, reduces sebum production.	Local folliculitis, ICD on fingers, psoriasis aggravation, skin atrophy, telangiectasias, hyper-pigmentation. Risk of squamous cell carcinoma with prolonged use.	[4,8,47,117,121]
		Lithium gluconate/succinate	8% ointment or gel	Skin: twice daily × 8 weeks.	Anti-inflammatory via increased IL-10 and decreased TLR2 and TLR4 in keratinocytes.	ICD in <10% of patients.	[8,122–124]
		Metronidazole	0.75% gel	Skin: twice daily × 4 weeks.	Anti-inflammatory via inhibition of free radical species.	Rare contact sensitization with prolonged use.	[5,47,125,126]
		Phototherapy	UVB: Cumulative dose of 9.8 J/cm2	Three time/week × 8 weeks or until clearing.	Immuno-modulation and inhibition of cell proliferation.	Burning, itching sensation during/ after therapy. Risk of genital tumor with prolonged use.	[26,127–129]
SYSTEMIC		Itraconazole	Oral: 200 mg	Once daily × 7 days, then once daily × 2 days/month for maintenance.	Inhibition of fungal cell wall synthesis. Anti-inflammatory via inhibition of 5-lipoxygenase metabolites.	Rare liver toxicity.	[97,130,131]
		Terbinafine	Oral: 250 mg	Once daily × 4–6 weeks or 12 days monthly × 3 months.	Inhibition of cell membrane and cell wall synthesis.	Rare tachycardia and insomnia.	[132–134]

Note: Shampoos, foams and lotions are better suited for treating seborrheic dermatitis and dandruff on the scalp; gels, creams and ointments are used to treat seborrheic dermatitis on body locations other than the scalp.

Most people should only need 1% zinc pyrithione or 2% ketoconazole shampoo. Either generally clears dandruff within a matter of days. Lather the shampoo into your hair liberally and leave it in for several minutes before rinsing it out. Use the shampoo daily until the dandruff is gone for several days. You can then stop using the shampoo, but if you are very susceptible to dandruff, you may want to taper down the usage to every other day for a few days, followed by once a week for a few more weeks.

It's possible that a certain type of shampoo stops being effective, possibly due to the development of resistance or growth of a different type of Malassezia species. In this case, switch to a shampoo with a different active ingredient.

If you have not just dandruff but also serious seborrheic dermatitis, consult the following decision tree from the UK National Health Service.



Severe itchy scalp

- **Advise self-care & co-prescribe 4 weeks of treatment with a potent topical corticosteroid scalp application** such as betamethasone valerate 0.1% (BETACAP™) or hydrocortisone butyrate 0.1%,(Locoid Crelo)
- **Potent topical corticosteroid scalp applications are not suitable for application to the beard**, because of adverse effects such as thinning of the skin on the face.
- **Do not prescribe more than 4 weeks topical steroid treatment.** Topical corticosteroids are not appropriate for continuous long-term use, and their use as maintenance treatment is not recommended.
- Seek specialist advice if symptoms have not resolved after 4 weeks, or sooner if response to treatment is poor.

If you don't respond well to shampoo treatment, the dandruff symptoms worsen or signs of an infection are present, specifically crusting, oozing or bleeding, then seek further medical advice from a dermatologist.

HAIR LOSS

What causes hair loss?

Hair loss can have many causes, but 3 of them explain the majority of hair loss: telogen effluvium, androgenetic alopecia and alopecia areata.

Telogen effluvium

A fancy name for what is in essence a rather simple condition: stress. Stress can shorten the growth phase of your hair, causing it to fall out and shed across the entire scalp without there being any scarring or inflammation. The growth cycle of hair is generally characterized by 3 distinct phases.

1. Anagen: The growth phase, lasting 2 to 8 years.
2. Catagen: The involuting or regressing phase, lasting 2 to 6 weeks.
3. Telogen: The resting or quiescent phase ending with the hair falling out of the follicle, lasting 2 to 4 months.

Some researchers argue that hair loss – exogen – should be called a separate hair growth phase, as should the interval between exogen and anagen, in which the hair follicle is empty – ketogen.

The timeline of these phases varies from individual to individual and also from bodypart to bodypart. These phases normally result in you losing 100-150 hairs per day from your scalp, which maintains your hair density. During telogen effluvium, the growth phase of hair is shortened and the catagen phase is prematurely triggered, causing the 'outflow' (effluvium) of hair during the telogen phase.

The hair loss pattern of telogen effluvium is typically diffuse, but most hair loss tends to be in the form of so called bitemporal recession, meaning your hairline recedes at both temples. Telogen effluvium is characterized by a positive hair pull test. Grab ~50 hairs on your scalp with your thumb and index finger and firmly but non-aggressively pull on them. Normally this results in only a handful of hairs being pulled out. Greater than 10% hair loss from the pull suggests shedding.

The stress that triggers the shedding can take many forms. It can be entirely psychological stress, a mixture of physical and physiological stress, such as childbirth or surgery, or it can be mostly physical, such as malnutrition or a certain disease. Iron deficiency may cause hair loss, for example and is very plausible in cutting women, as you learned in the module on micronutrition. The following table lists known causes of telogen effluvium.

Physiological causes	**Postpartum effluvium (telogen gravidarum)**
	Physiological effluvium of newborn
Febrile states	Typhoid
	Malaria
	Tuberculosis
	HIV infection
Stress	Severe febrile illness
	Emotional stress
	Serious injuries
	Major surgery
	Difficult labor
	Hemorrhage
	Starvation
	Crash diet
Drugs	Oral retinoids (etretinate and acitretin)

	Oral contraceptives
	Antithyroid drugs
	Anticonvulsants
	Hypolipidemic drugs
	Heavy metals
	Beta blockers
	Captopril
	Amphetamines
Endocrine	Hyperthyroidism
	Hypothyroidism
Organ dysfunction	Renal failure
	Hepatic failure
Disorder of hair cycle	Short anagen syndrome
Nutritional	Iron deficiency anemia
	Acrodermatitis enteropathy
	Acquired zinc deficiency
	Malnutrition
Local cause	Hair dye application
Others	Syphilis
	Systemic lupus erythematosus

There can be a delay of 2-3 months after the stressful event or condition before the hair loss starts. It typically lasts less than 6 months and much of the lost hair can regrow.

Treatment of telogen effluvium comes down to addressing the root cause of the stress. Anything else is at best a band-aid. That said, a pilot study has shown promise of nigella sativa oil to reduce hair loss during telogen effluvium. The active ingredient seems to be thymoquinone.

The nigella sativa flower.

Alopecia areata

The story of alopecia areata (AA) is short and bitter. AA is an auto-immune condition with a strong genetic predisposition. It leads to recurring episodes of hair loss patches that can occur all throughout the body but often affect the scalp. The hair loss can be permanent, but often some of it grows back over time. AA seems to affect individuals with other immune system conditions more but can otherwise occur in everyone.

Alopecia areata.

There's no established treatment for AA. Practically everything that has been tried so far has failed. However, in some individuals AA seems to be triggered by foods intolerances that trigger the immune system. In these cases, removing the trigger food, such as wheat, from the diet can be a complete cure of AA.

Fortunately, AA isn't common with a life-time risk estimate of 1.7%.

Androgenetic alopecia

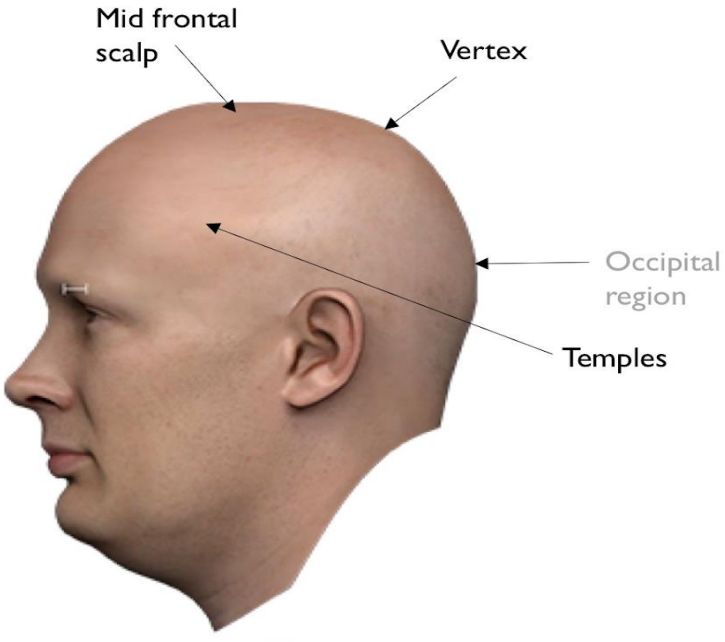
By far the most common type of hair-loss condition is androgenetic alopecia (AGA), also known as male-pattern baldness. As the name suggests, androgenetic alopecia is baldness generated by androgens, such as testosterone. Unsurprisingly then, it mostly affects men, but women are also affected with a different baldness pattern.

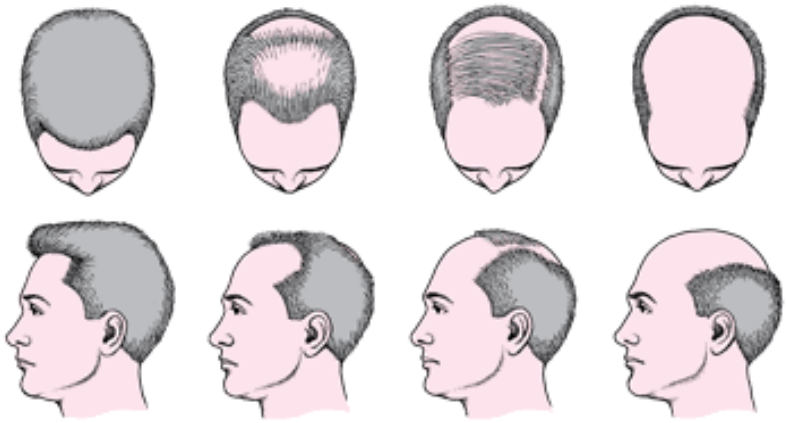
Androgenetic alopecia is more prevalent in white men compared with other nationalities. The condition significantly worsens with age: the prevalence in white males is 12% in their 20s, 50% in their 40s and over 90% by age 80.

The lifetime prevalence of AGA is around 70% in men and 40% in women.

Symptoms & differential diagnosis

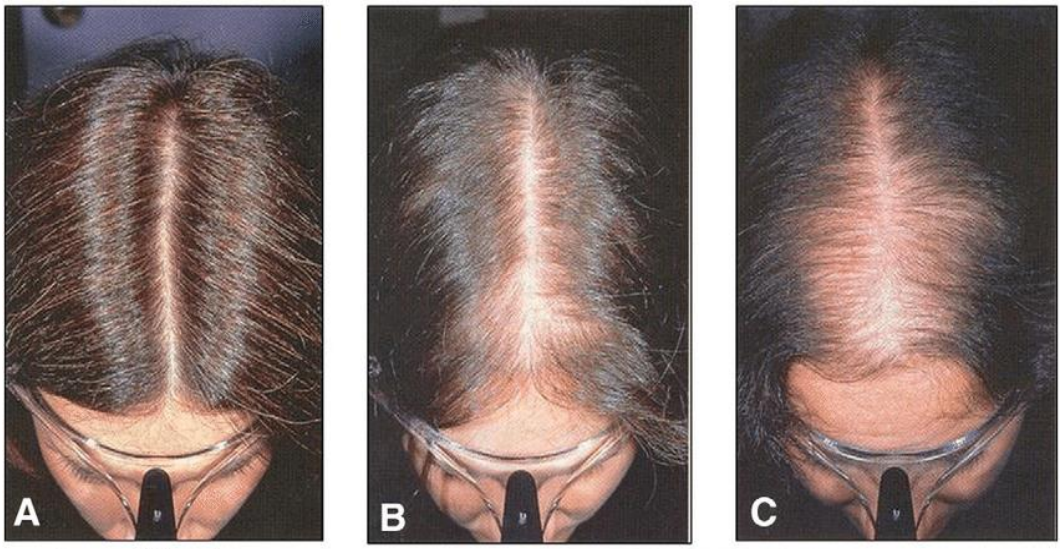
AGA is characterized by a distinct hair loss pattern often seen in older men, hence the name male-pattern baldness. Certain areas are preferentially affected in men: the temples, vertex and mid frontal scalp. Other areas like the occipital region are generally unaffected.





Male-Pattern Baldness

Women will typically develop more of a diffuse thinning over the top of the scalp, yielding a ‘christmas tree’ pattern with more thinning towards the front while the frontal hairline is generally maintained (merry Christmas!).



Normal density

Progressive stages of AGA

If you suspect you have androgenetic alopecia, here’s a flowchart to perform a differential diagnosis of AGA. AGA is characterized by gradual hair loss over time in the absence of any skin conditions. The hair cannot be pulled out easily.

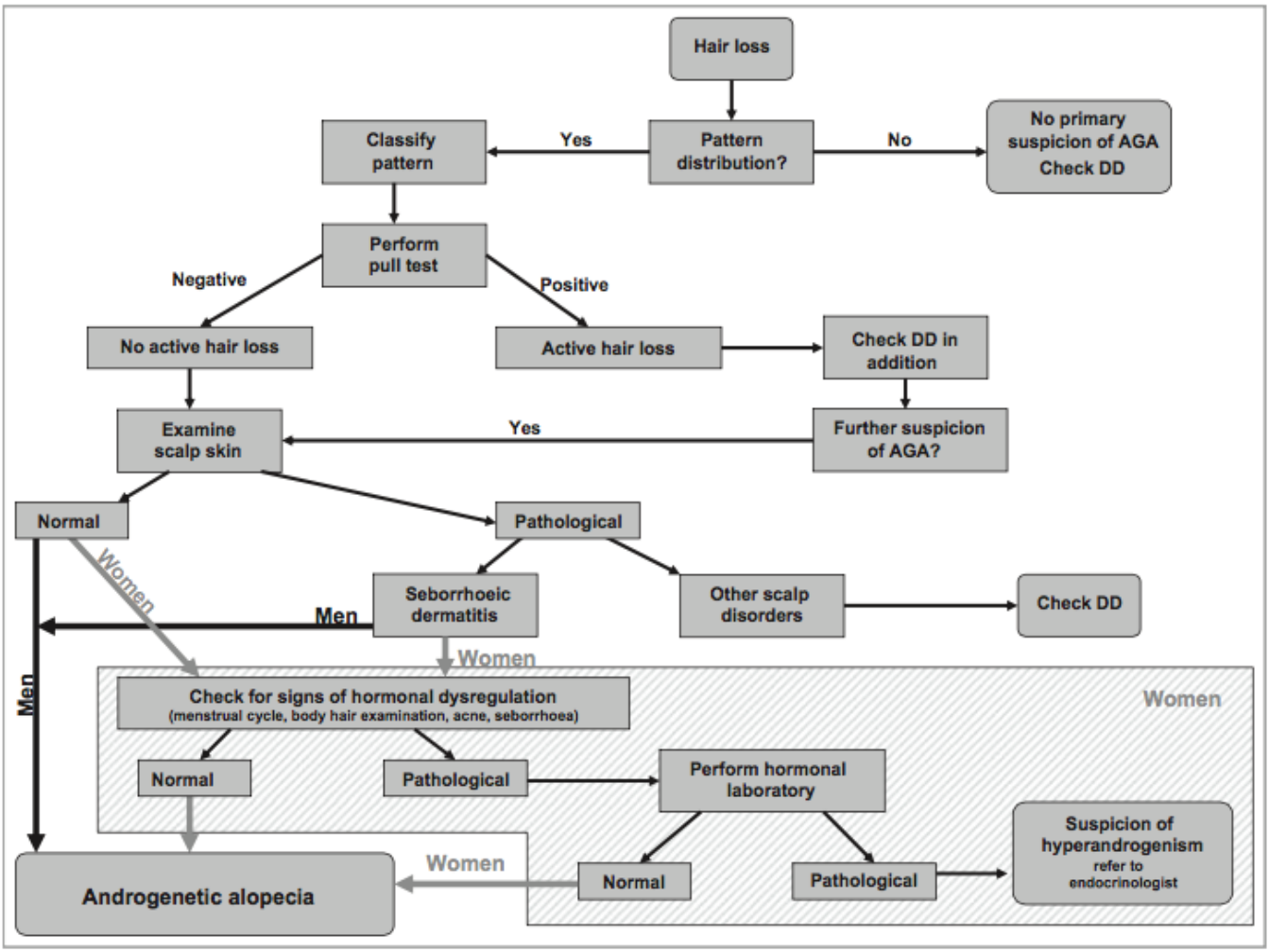
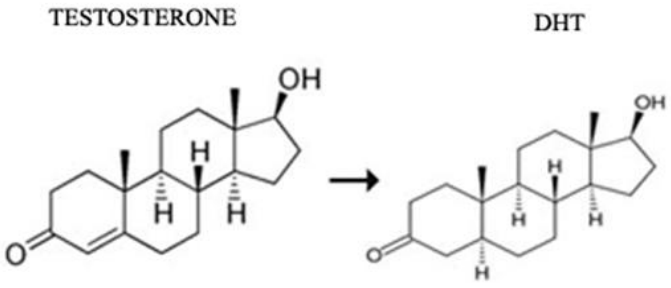


Fig 6. Clinical algorithm for the diagnosis of androgenetic alopecia (AGA). DD, differential diagnosis.

Causes of AGA

Androgenetic alopecia is, as the name suggests, strongly correlated with androgen levels, specifically 5a-dihydrotestosterone (DHT). DHT has a higher affinity to androgen receptors in the skin than testosterone, from which it is converted by 5a-reductase.



Testosterone is converted to DHT by 5 alpha reductase

The extent of androgenetic alopecia is strongly correlated with scalp DHT levels. Castrated men do not bald. Neither do pseudo-hermaphrodites, who lack the enzyme to convert testosterone to DHT. DHT also explains why women do not suffer as much from AGA as men and why anti-androgens and DHT blockers help prevent the onset of AGA. As such, we can quite safely say that AGA is caused by DHT.

However, this poses a paradox for what causes AGA, as DHT is normally responsible for hair growth. DHT explains why men grow body hair during puberty, why men are hairier than women and why testosterone administration increases body hair growth in both genders. How can DHT have the normal function of increasing hair growth yet cause hair loss in the scalp? The conventional theory put forth to explain this paradox is convulated. Supposedly, certain scalp hairs grow androgen independently but are extra androgen sensitive because of an unidentified set of genes and this pattern coincides exactly with the male baldness pattern.

A more elevant theory is that male pattern baldness is caused by the pressure between the skull and the scalp that compresses the hair follicles. This pressure is cushioned by subcutaneous fat tissue. However, DHT decreases subcutaneous fat levels, thereby increasing the pressure on the hair follicles, which over time causes progressive miniaturisation (shrinking) of the hair follicle. This theory explains why hair is lost only from the top of the scalp in AGA: that's where gravity compresses the hair follicles on the scalp.

Regardless of which theory is correct, it's clear that the root cause (no pun intended) of AGA is related to scalp DHT levels, so the treatment of AGA should address this.

Treatment of AGA

Various treatments have been studied for AGA. Overall, none of them offer a true cure. Treatment only slows down the progression of hair loss, typically by reducing scalp DHT levels. With continued therapy, this can have very significant effects though.

Diet

A healthy diet can help reduce hair loss. Several micronutrients contribute to hair growth. However, once all micronutrient requirements are met and the diet is overall anti-inflammatory and health promoting, there is probably nothing further that can be done diet wise to slow down hair loss.

Finasteride

By far the most established treatment option for AGA is finasteride. It is a synthetic type 1 and type 2 5a-reductase inhibitor: it acts by reducing the conversion of testosterone to DHT. 0.5-5 mg of finasteride reduces scalp and blood DHT levels by 50-70%.

The following photo illustrates the efficacy of finasteride in two twins, one of which took finasteride while the other did not.

While finasteride is great for hair loss prevention, it comes with considerable side-effects to have your DHT levels blocked by that amount in your entire body. These are typically classified as trivial or rare, as the medical community is traditionally concerned primarily with life and death and less so with wellbeing, but anecdotally, it's not uncommon to experience quite some odd random side-effects from it. The most common side-effect of systemic 5-AR inhibitors is sexual dysfunction, often associated with lower overall wellbeing [2, 3, 4, 5]. Especially at higher doses, finasteride can in some cases pretty much kill your libido, make you impotent and reduce your ejaculate. Side-effects are usually caused by excessive dosages, but they should be taken seriously, because the side-effects persist even after cessation of use in a small subgroup of users, a phenomenon known as post-finasteride syndrome [2, 3, 4, 5]. In finasteride's defense, it's hard to understand mechanistically how the side-effects could be permanent from a physiological point of view. Neither duration of treatment nor the duration of side-effects correlates with the persistence of the sexual dysfunction, so it's plausible that the erectile problems cause mental health problems and the resulting insecurity is what causes the problems to persist later on when physiologically there is nothing wrong anymore. However, post-finasteride syndrome shares many features with post-SSRI sexual dysfunction, so there may be a physiological basis for the side-effects.

You may think that reducing DHT levels will also affect your gains, but not to worry. Testosterone levels rise during 5a-reductase therapy as less testosterone is converted to DHT [2], or they stay unaffected. Total androgen levels thus tend to stay the same, which means finasteride does not affect your strength or body composition [2, 3, 4].

Fortunately, there is in fact a very straightforward solution to the problem of blood DHT suppression: topical finasteride. By applying the finasteride in a low-dose cream form directly on the skin, you get a ~50% decrease in DHT concentration in the scalp with only a ~25% decrease in the blood. Topical finasteride is just as effective as oral finasteride to reduce hair loss and has a better safety profile [2]. The effective dosage is only 100 microliter of 0.25% topical finasteride cream equating to 0.2275 mg applied once per day or 0.1% applied twice daily. Higher doses or application frequencies mainly further decrease blood and not scalp DHT levels, thus worsening the risk-reward. Going up to 2.3 mg per day of cream or 1% topical concentrations will result in the 50-70% blood and scalp DHT suppression also seen with 1 mg oral finasteride [2, 3, 4].

The main disadvantage of topical finasteride is that you have to apply it at least daily and it needs to be left on the scalp for multiple hours to fully absorb. This is the same downside as with topical minoxidil, so if you use one, you generally might as well use the other for maximum effectiveness without greater effectiveness. Both can be combined in the same product.

If you do decide to go the oral route, oral finasteride should be dosed at 0.2-5 mg per day, depending on the severity of the hair loss and response to treatment. Doses above 0.2 mg have only marginally greater benefits with ~5% greater DHT suppression but significantly increased side-effects, so it's prudent to start with a relatively low dose and only increase it if no major side-effects present. Dosages above 1 mg per day are generally not advisable, especially not for women. One notable exception is that lifters on high doses of testosterone may benefit from higher dosages due to the greater amount of testosterone that needs to be prevented from converting to DHT.

Finasteride treatment should be continued for as long as prevention of hair loss is desirable, as cessation of therapy will result in the progression of hair loss just like it did before therapy.

In general, both minoxidil and finasteride are most effective in improving hair growth in the vertex area of the scalp and less at the anterior scalp or at the hairline.

Finasteride is generally only available with a prescription. Popular brand names are Proscar and Propecia.

Pregnant women should generally not take 5a-reductase inhibitors because of the potential feminizing effects on the fetus.

Ketoconazole

2% ketoconazole shampoo may offer a milder, safer alternative to finasteride. While primarily marketed as an anti-fungal medication for dandruff and dermatitis, ketoconazole also functions as an anti-androgen, similar to finasteride: it seems to inhibit 5a-reductase. According to at least one study, 2% ketoconazole is similarly effective as 2% minoxidil to improve hair growth during androgenic alopecia. They can also be combined: ketoconazole improves the efficacy of finasteride. Ketoconazole shampoo also reduces hair loss during telogen effluvium and stimulates hair growth in mice.

Side-effects are rare and generally trivial. Some people experience skin irritation when they leave the shampoo in too long or use it too frequently.

Given the potential side-effects of finasteride, 2% ketoconazole shampoo applied twice daily and ideally not rinsed out is a reasonable first-line therapy for AGA you can often try without a prescription. Finasteride should be considered only if ketoconazole shampoo fails to result in the desired effect within 3 months or if the hair loss is severe.

Ketoconazole shampoo is frequently available over the counter. A popular brand name is Nizoral.

Dutasteride

Dutasteride does the same thing as finasteride essentially, but it has a dose-response effect in the 0.1-2.5 mg/d dosage range. 2.5 mg was more effective than 5 mg of finasteride in fact in one study. However, there is far less research about dutasteride than about finasteride and the effective dosage of dutasteride is 5 times as high as what is used and studied for prostate health. Given the potential for side-effects, the more established finasteride is recommended over dutasteride when available.

Minoxidil

After finasteride, minoxidil is the most established treatment for AGA. Minoxidil does not address the root cause of AGA, DHT, but instead it basically just makes your hair grow faster by promoting vasodilation (enlargement of blood vessels), angiogenesis (growth of new blood vessels) and cell proliferation. It takes a few months before you notice the new hair growth and up to 40% of people don't seem to respond to minoxidil. For high-responders, the effect is very noticeable even when they didn't know they were on minoxidil. Before the new hair growth, you may experience excess shedding, which can unfortunately make you balder for a short period. This may cause follicles in the telogen phase to shed, which are then replaced by thicker hairs in a new anagen phase, so it's crucial to continue using the shampoo at this point to promote new hair growth. Unfortunately, cessation of usage will result in all newly grown hairs that relied on minoxidil's effects to fall out over the next few months, so your hair count drops back to what it would have been without treatment. Minoxidil treatment is therefore for life (or until you accept balding).

Minoxidil is available over-the-counter in many countries and is available in many topical forms, including shampoos, foams, sprays and creams. However, minoxidil shampoos are not as established to work, because minoxidil normally needs to be applied to dry

skin and left to absorb. The effect is determined by how much minoxidil is absorbed into the scalp and it takes over 4 hours before minoxidil is fully absorbed into the skin. A dosage of 1 ml of 5% solution twice daily on each affected region is recommended for men [2, 3, 4]. For women, 2% bidaily or 5% once-daily is generally enough with no benefits seen above this dosage. The dosage should be reevaluated after 6 months of treatment depending on the response. Common side-effects include contact dermatitis and a transient shedding during the first 4 months of use. There are more side-effects at higher doses.

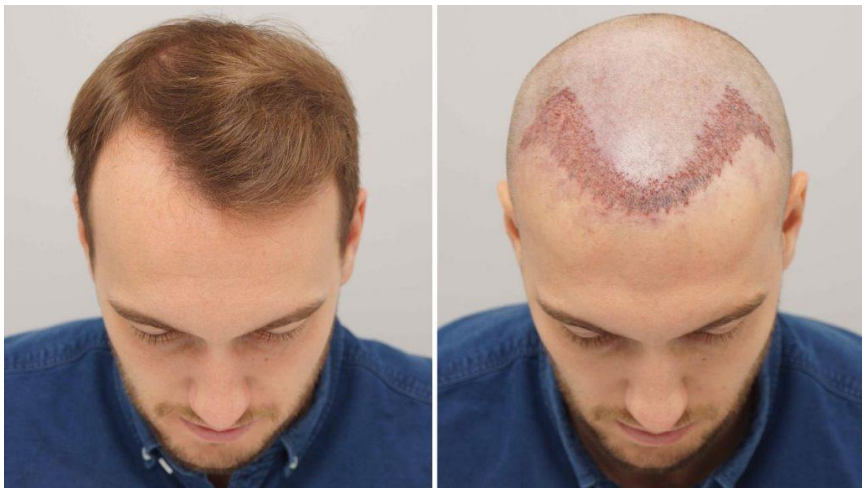
Topical minoxidil can be made more effective with the use of topical tretinoin. Once daily application of 5% minoxidil with 0.01% tretinoin is as effective as bidaily application of 5% minoxidil. The tretinoin improves the absorption of the minoxidil.

Minoxidil is also available in oral (pill) form, but this causes more side-effects. Moreover, you'll get the extra hair growth in your entire body, including your face, groin, armpits, everywhere. Oral use should thus generally be a last resort. Oral minoxidil was actually designed to lower blood pressure rather than to improve hair growth. Water retention from increased electrolyte retention is also common. Oral dosage recommendations range from 0.25 to 2.5 mg daily for women and 1.25 to 5 mg daily for men, depending on the severity of hair loss.

Surgical treatment

A more permanent solution to the loss of hair follicles is to plant new ones. That's essentially what hair transplantation surgery does: take hair follicles from one part of your body and put them on your head. Follicular unit transplantation (FUT) actually works. It's very expensive though with treatment costs often ranging between 5-20k USD. These costs may decrease in the future, as it's mainly this expensive because people have to literally transplant one hair follicle at a time. Robots can automate this process.

Another downside of surgery is that you need to shave your head beforehand. And afterwards, you first look like this:



Hair transplantation is the only solution to hair loss when the hair follicles are fully gone and is therefore the only recommended treatment approach at this point. However, it's likely that over time you will again lose the hair follicles when the root cause of the hair loss is not addressed. Moreover, your hair loss pattern may become very unnatural, as you'll keep losing your hair in other places while the transplanted hairs typically don't fall out as quickly. Multiple transplants may thus be needed over time.

In addition to the above established treatment options for AGA (5a-reductase inhibitors, minoxidil and hair transplantation), there are many treatments that show promise but still lack research support.

Cell mediated treatment

Research is looking into injecting cultured cells for hair follicle insertion. Alternatively, certain growth factors may be injected or platelet rich plasma (PRP), which is isolated from whole blood. Platelets have multiple growth factors associated with them as well as other potentially stimulatory mediators and shows promise for user after hair transplants.

Prostaglandin analogues

The prostaglandin F2alpha analogues latanoprost and bimatoprost are typically used to treat ocular hypertension and glaucoma. A side effect when using them for these conditions was that they increased eyelash hair growth. Bimatoprost can indeed be used to increase eyelash growth. However, side-effects include eyelid swelling, blood seeping into the eye chamber, itching and irritation. As such, it may not be worth it.

One study has also found that daily application of 0.1% latanoprost over 24 weeks can stimulate hair growth during AGA. However, not enough research is available to make treatment recommendations, especially not considering the other established treatments and the fact prostaglandin analogues do not seem to address the root cause of AGA.

Laser treatment

It's unclear how laser treatment results in hair growth, but certain types do seem to be effective [2, 3]. Treatment is often prohibitively expensive and time-consuming, however.

Serenoa Repens

As an alternative to oral finasteride, Serenoa Repens could be a promising approach. The berries of this plant are highly enriched with fatty acids, phytosterols and flavonoids which have anti-androgenic activity through the competitive and nonselective inhibition of 5-alpha reductase type I and II [2].

In the first study, 6 out of 10 patients with AGA showed response to treatment with serenoa.

In the second study, 100 men were treated for 24 months with either 320 mg serenoa or 1mg finasteride. 38% of patients treated with serenoa repens showed improvements and 68% of those treated with finasteride.

A side effect of consumption can be stomach discomfort, which can be alleviated by taking it after consuming food.

While interesting, the same problems of oral finasteride treatment apply in that systemic DHT reductions are not generally desirable.

Hair thickening fibers

While not a true solution, hair thickening fibers can give you the apperance of having more hair than you do. These artifical fibers bind to your hair to blend in. There are many brands and colors available.

Conclusion on AGA

Androgenetic alopecia is a progressive hair loss problem caused by scalp DHT. 2% ketoconazole shampoo is recommended as first-line therapy to address the root cause. 2-5% minoxodil is a more effective alternative but entirely temporary in effect. If hair loss persists, low-dose 0.25% topical finasteride or else 0.2 mg oral finasteride may be added, noting the possibility of serious sexual side-effects. When the hair follicles are completely gone, only hair transplantation remains as an option, but given its cost and invasiveness, a wig may be preferable.