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# *Pathogenesis of Acne Vulgaris and New Therapeutic Progresses*

**Zishu Mao[1,a,*]**

[1]*Beijing No.4 High School International Campus, Beijing, China*
*a. zisiselainemmm@gmail.com*
**corresponding author*

***Abstract:*** Acne vulgaris (AV) is a prevalent inflammatory skin condition that bothers a range of people, appearing in lots of areas of our body. This paper examines the various factors contributing to AV development, including hormone levels, dietary influences, environmental triggers, and stress-related pathways. Through analyzing recent findings on topical and oral drug therapies, as well as non-invasive treatments such as photodynamic therapy, the study identifies key treatments that reduce different levels of AV and AV scars. Additionally, the paper discusses the promising results of combining vitamin C and vitamin A (or retinoid) products ("morning C, evening A") for their antioxidative and scar-reducing properties. By synthesizing these findings, this study is looking forward to future AV research, focusing on the multi-faceted approach that considers the impact of lifestyle and psychological health. Future research could benefit from investigating the molecular mechanisms underlying these combined treatments and developing more targeted therapies to minimize side effects while effectively addressing the underlying causes of AV.

***Keywords:*** Acne vulgaris, causal factors, topical and oral medications, photodynamic therapies.

## 1. Introduction

Acne Vulgaris (AV) is a type of skin disease that appears among adults and adolescents, affecting areas of the skin rich in sebaceous glands, such as the face, neck, chest, and back, leading to various forms of lesions, including comedones, pustules, and nodules. Its repeatability leads to people's anxiety and concern.

Recent studies and journals focus on each different symptom, their corresponding causing factors, and chemical and physical treatments. The Chinese Guidelines for the Management of Acne Vulgaris: 2019 Update categorizes comedones as mild (level 1), inflammatory red papules and pustules as moderate (level 2 and level 3, respectively), and nodules/cysts as severe (level 4) [1]. Factors such as season (temperature), age, and lifestyle all have an impact on provoking AV. The charts from a study show that high milk and sugary food intake, staying up late, negative feelings, and premenstruum hormone disorder are the most common reasons that lead to AV [2]. Treatments for AV involve both chemical and physical methods. Topical agents--including retinoids, benzoyl peroxide, and some of the antibiotics--and oral medications belong to chemical treatments. A sensitization test is required before using topical agents. Physical interventions involve using acne tools and photodynamic

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therapies [3]. For example, the light of photon rejuvenation can penetrate deep into the dermis and stimulate collagen production, covering the original AV scars [4].

The ongoing research on AV holds great significance in its potential to alleviate the physical and psychological burdens associated with the condition. With the increasing prevalence of antibiotic resistance and allergy, it is necessary to explore alternative therapeutic options. Furthermore, given that AV can result in AV scars that are hard to eliminate, early and effective treatment is essential not only for reducing current symptoms but also for preventing long-term damage. As more studies continue to emerge linking acne to diet, hormones, and environmental factors, there is a growing need for combined approaches that can have the most effective results. This study aims to summarize the different pathogenesis of AV and critically evaluate the recent advancements in AV treatment, specifically focusing on currently used therapies such as topical agents, medical beauty techniques, hormone regulation, and lifestyle adjustments. By synthesizing findings from contemporary research, this paper will offer a comprehensive overview of the most efficacious strategies for managing AV, coupled with providing novel therapies that contribute to addressing specific allergic problems.

## 2. Pathogenesis of AV

The pathogenesis of AV has not been fully understood. The contributing factors are comprehensive, including hormone imbalance, genetic problems, environmental factors, and psychological and emotional fluctuations. The most common examples will be provided to explain each factor.

### 2.1. Hormones

Excessive secretion of androgen during puberty can lead to an overproduction of sebum due to hyperplasia of sebaceous glands (SGs), which is one of the most common causes of AV. Interestingly, research from Harvard Medical School has found that women are more likely to develop AV after the age of 20 compared to men. This difference is attributed to the fluctuation of women's hormones, particularly during their menstrual cycles and when consuming dairy products and taking sex hormone-related medications, which can affect sebum production. When it comes to daily dietary habits, the data shows that dessert consumption has the highest frequency, followed by milk intake. [2]. It’s worth noting that numerous desserts are rich in refined sugars and processed carbohydrates, both of which necessitate insulin regulation. Furthermore, milk is a significant source of whey protein and casein protein, which have been associated with increased insulin production and levels of Insulin-Like Growth Factor-1 (IGF-1), respectively [5].

### 2.2. Microorganisms

The skin is divided into three categories based on its microenvironments: sebaceous/oily, moist/humid, and dry. AV appears especially in sebaceous body areas, such as the face and back, where the skin microflora primarily comprises Cutibacterium acnes (C. acnes) [6]. This bacterium thrives on decomposing sebum and plays a role in maintaining the balance of the skin microbiota. A decrease in C. acnes and an increase in other bacteria from the staphylococcus family can disrupt the facial microbiome and cause AV.

### 2.3. Environmental factors

Environmental factors impacting the skin can be broadly categorized into seasonal changes and daily habits. The transition from summer to autumn, for instance, often results in skin dehydration, leading to an upsurge in sebum production. Consequently, the skin barrier becomes vulnerable, rendering it more prone to inflammation. Notably, the formation of AV during summer differs slightly from its

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occurrence in winter. In terms of daily habits, staying up late is a prevalent factor contributing to the onset of AV [2]. In the Sleep journal, research found that the body increases blood circulation to the skin to facilitate the healing of skin damage during deep sleep stages [7]. As a result, a lack of sleep can also lead to a decreased ability of metabolism, which serves as an indirect reason for melanin hyperpigmentation, making the AV scars hard to eliminate. Wearing face masks for extended periods can also lead to skin issues. Throughout the pandemic, many individuals have experienced "maskne" (mask-induced acne) on their cheeks and around their noses. This is due to masks trapping heat, moisture, and sweat against the skin, creating a warm, humid environment ideal for the growth of acne-causing bacteria. Additionally, the constant friction from wearing masks can disrupt the skin barrier and cause inflammation in the pores [8]. Another factor can be low exercise frequency: AV breakouts occur when toxins and harmful substances are blocked in pores instead of being excreted through sweat during exercises [9].

### 2.4. Psychological factors

The skin and brain are intricately connected through a complex system known as the skin-brain axis. Psychological stress prompts the release of neuropeptides, such as substance P, which can worsen inflammation in the skin and contribute to acne lesions. Research indicates a strong correlation between the severity of AV and levels of anxiety and depression [8]. For instance, AV tends to worsen when students are under pressure to prepare for important upcoming examinations. Additionally, AV can lower individuals' self-esteem, leading to increased anxiety about their appearance. This interplay between psychological distress and skin health creates a vicious cycle of problems [9].

## 3. Treatment methods

Treatments for AV can be categorized into drug therapies, which involve chemical treatments, and non-drug treatments, which involve physical treatments. Drug therapies encompass oral medications and topical agents. Oral medications may include antibiotics such as the tetracyclines group, while alternatives for those allergic to tetracycline include topical antibiotics like macrolides. Specifically for mild AV (level 1) -- blackheads, topical products such as Kiehl’s’ rare earth deep pore minimizing clay mask can be effective. Other topical agents for AV may contain ingredients like salicylic acid. Additionally, AV scars can be treated with arbutin, vitamin C, and its derivatives. For persistent and ineradicable AV and AV scars, physical treatments are necessary. Using acne tools, as well as photodynamic therapies, are effective but may be more uncomfortable. A recent popular whitening approach, known as "morning C, evening A," shows effectiveness in eliminating AV and reducing AV scars.

### 3.1. Drug therapies

Antibiotics can be administered orally or topically, but usually, their use is allowed only with a doctor’s prescription. The tetracycline group consists of oral medications, with minocycline and doxycycline being two examples. Erythromycin, a specific type of macrolide, is a commonly used topical antibiotic for treating AV. Inflammation is one of the causal factors of acne, and tetracyclines have been found to help inhibit this process. Additionally, tetracyclines, as a class of antibiotics, have been reported to have more than ten different anti-inflammatory effects. However, it's important to note that antibiotics should not be used as the sole long-term treatment and should be complemented with topical agents such as benzoyl peroxide and retinoids [10].

For mild AV (level 1), clay mask products containing Amazonian White Clay, which is rich in elements like magnesium and silica, can effectively help with basic acne and blackhead removal. Due to its pH being very similar to that of the skin, it is ideal for absorbing oil without causing dryness.

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Additionally, it serves as an excellent anti-inflammatory ingredient [11]. It is necessary to clean with facial cleanser and completely dry the water before applying it to the blackhead area (usually, the common area to clean the clay mask is the nose), and make sure that the area is completely covered with a thick layer of clay mask. Then, wait for approximately 20 minutes or until the clay mask is entirely dry and cracks to rinse it off. Lastly, apply a moisturizing lotion or cream to avoid skin flaking off. If the symptoms are not severe, this process can be repeated twice a week.

The products of salicylic acid, azelaic acid, benzoyl peroxide, and retinoids on the market are usually intended for topical use only. Before initial use, it's important to conduct allergy tests to prevent their potential side effects. These products are commonly available in the form of cream, gel, or wet cotton pads, which can be purchased at pharmacies and clinics. After washing face, ensure it is dry before applying a pea-sized amount to the affected areas rather than the entire face to avoid skin irritation. Common products are available in different concentrations - salicylic acid ranges from 0.5% to 2%, azelaic acid ranges from 10% to 20%, benzoyl peroxide ranges from 2.5% to 10%, and retinoic acid ranges from 0.025% to 0.1% - allowing patients to select the most suitable option based on their specific needs and the severity of their condition.

To cure AV scars, topical whitening products can be effective. New AV scars tend to appear red, while older and more serious scars take on a brown color. Typically, it takes about a month or more to eliminate AV scars. However, using whitening products that contain ingredients such as arbutin and vitamin C, along with its derivatives, can speed up this process. They prevent excessive melanin production, resulting in fewer pigments, fewer dark spots, and a more even complexion [12]. The use method of whitening essence on the market is to use the dropper to drop on the AV scars, smear, and massage to promote absorption. It is also important to note that some whitening essences need to be kept in a dark place. Products containing vitamin C can be used during the day. An interesting method known for its brightening effects can also help reduce the appearance of AV scars. A detailed explanation of its function and principles will be provided in section 3.3.

### 3.2. Non-drug treatments

Non-drug treatments include either using acne tools or adopting medical aesthetic methods, including photodynamic therapies.

Manual comedone extraction, known as acne tools, is an easy way for people to remove comedones, blackheads, and whiteheads. Common tools are acne extractors and tweezers. Different acne has different removal methods, but the first step should always be disinfection with alcohol. Comedones and blackheads are similar small bulges whose presence can be felt because they make the skin very uneven. When looking closer at the mirror, the top part of them exposed to the air is black because they are oxidized. Use an acne extractor with a small circle on that side to make sure the bulge is encircled within it and push slightly so that the comedome or the blackhead inside can be squeezed out. Blackheads on the nose, which are typically less severe than those on the forehead and cheeks, can be effectively removed using the small circular side of an acne extractor or directly pinched with tweezers. For whiteheads, an extra step that can be taken before squeezing is to use the other side of the acne extractor, which is a needle, to puncture toward the whitehead at 45 to 60 degrees. It is normal to have redness and swelling in the area where acne tools have been applied, and moisturizing and repairing creams are recommended to help eliminate those problems.

The expensive treatment is to go to the doctors or cosmetic hospitals to do the photodynamic therapies. Doctors often provide treatments suitable to each individual, that is, the light people face may differ from blue light or red light to intense pulsed light (IPL). Before that, a topical photosensitizer needs to be applied. Before applying a topical photosensitizer, it is necessary. When combined with oxygen, light helps to destroy AV cells and bacteria. Photodynamic therapy also reduces the size and activity of sebaceous glands [13]. According to one research, after 12 months of

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treatment, acne caused by inflammation was reduced by 68%. However, due to its high pain index and adverse effects, such as other skin problems and epithelial exfoliation, around half of the total participants gave up before the second treatment started [14]. Thus, photodynamic therapies also require a high tolerance toward pain and a high acceptance of uncommon light rays.

### 3.3. Innovative therapies

The "morning C, evening A" theory normally represents the lifestyle for young people nowadays, which means drinking coffee and working hard in the morning and drinking alcohol to relax at night. In the beauty and skincare industry, there is also the "morning C, evening A" theory, which refers to using products containing vitamin C in the morning and products containing vitamin A (usually retinol or its derivatives) at night. This is known as a whitening method, but since it is also responsible for anti-oxidation and anti-aging, it can be used to speed up cleaning AV scars.

As mentioned above, vitamin C is a potent antioxidant capable of suppressing melanin production, diminishing pigmentation, and consequently alleviating AV scars. Retinoids can boost the metabolism of skin cells, assist in aging exfoliation, and bring out new skin, making it smoother. When taking this method, the sequence is especially essential because vitamin C is used to protect the skin against daytime environmental hazards, such as UV rays, while vitamin A can be deactivated under light circumstances. Thus, during the day, it is necessary to wear suncream after applying vitamin C products. Additionally, high concentrations of vitamin C and retinol may irritate the skin, so it is recommended to start with low-concentration products and keep an eye on the skin's reaction. If there are no issues, then gradually introduce higher concentrations.

## 4. Conclusions

In conclusion, this paper aims to explain the complex causes of AV, providing people with a deeper insight into factors ranging from lifestyle and psychological effects to endocrine disorders. It also informs clinical treatment and personal skincare methods. Also, considering that a minority of people are allergic to certain chemicals, this paper mentions various options, including topical agents, oral medications, manual comedone extraction, photodynamic therapies, and an emerging concept of skin care, to benefit all AV and AV scars patients with different severity of symptoms. By taking these measures, people can more or less reduce both the physical and mental pain of suffering from AV. However, the methods may not be fully generalizable to the whole population due to individual variations. Some people may find a kind of medication ineffective, so it is necessary to find the most suitable treatment method through continuous trial and experience. Since the side effects have not been listed, it is advisable to inquire about them and use the medications cautiously. In addition, if the symptoms have already reached the situation where they cannot be relieved by any of the above methods, such as grade 4, then the patient should immediately stop abusing the medications in person and seek a professional diagnosis and prescription. It is expected that more innovative treatments can be developed to reduce the side effects of drugs and increase treatment efficiency. Additionally, the psychological effects of acne are often overlooked, and future research should pay more attention to the correlation between skin conditions and mental health to promote the overall health of patients.

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