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Review

# What is new in adult acne for the last 2 years: focus on acne pathophysiology and treatments

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## Abstract

Acne affects more than 640 million people worldwide, including about 85% of adolescents. This inflammatory dermatosis affects the entire population, from teenagers to adults, which reinforces the need to investigate it. Furthermore, in adults, acne has serious consequences, including a psychological impact, low self-esteem, social isolation, and depression. Over the last years, the understanding of acne pathophysiology has improved, mainly thanks to the identification of the pivotal role of the microbiota. The aim of this review was to screen the most recent scientific literature on adult acne and the newly tested treatments. Clinically, therapeutic innovations for the treatment of acne have been recently developed, including pre/probiotics, new molecules, and innovative formulations associated, however, with fewer side effects. Moreover, clinical trials are underway to use off-label molecules that seem to be proving their value in the fight against adult acne.

## Introduction

Acne vulgaris is the most common skin disorder worldwide as estimated by global skin disease prevalence studies,[1] and it may persist into or appear during adulthood. This chronic inflammatory skin disease may affect the entire population, regardless of gender, including teenagers and adults.

Serious consequences of acne have been reported in adults, including a psychological impact associated with low self-esteem, social isolation, and depression.

Acne results from the interplay between androgen-induced hyperseborrhea, follicular hyperkeratinization, a loss of skin microbial diversity, and inappropriate inflammatory response.[2] A loss of diversity of *Cutibacterium acnes* subgroups has recently been identified as crucial in the initiation of skin inflammatory responses in acne,[3] and the microbiome appears to play a significant role in the development of inflammatory lesions.[4,5]

Therapeutic innovations for the treatment of acne have been recently developed, including pre/probiotics, new molecules, and innovative formulations associated with fewer side effects.[6,7] Indeed, current first-line treatments target one or two steps in acne pathogenesis, including benzoyl peroxide, topical retinoids, and topical or oral antibiotics.[8] Nevertheless, antibiotic resistance is a concern in acne because it is increasing worldwide, not to forget the problem of resistance in all diseases, which the WHO alerted us to on April 30, 2014.[9] Also, oral isotretinoin is recommended in more severe cases, but it is associated with side effects and should be used with caution in women of childbearing age because of its teratogenic risk. Note, in March 2021, that the Agence nationale de sécurité du médicament et des produits de santé (ANSM - French regulatory authorities) organized a public hearing to help it strengthen the information of patients and health professionals on the teratogenic and psychiatric risks associated with isotretinoin. The ANSM recommends stopping treatment and consulting "as soon as possible" with her physician in the event of a pregnancy occurring during treatment.[10]

### Prevalence and risk factors of adult acne

Though it becomes less common in adulthood than in adolescence, nearly half of people in their 20s and 30s continue to have acne and about 4% continue to have difficulties into their 40s.[11] Regarding acne vulgaris in adult females, it has increased over the past 10 years; it affects currently 15–50% of adult women depending on the studies.[12,13]

A multicenter study conducted in seven European countries (Belgium, Czech and Slovak Republics, France, Italy, Poland, and Spain) has reported an overall high prevalence of self-reported acne in adolescents/young adults; heredity was the main risk factor.[14]

Adult acne prevalence is increasing worldwide.[15] Interestingly, a retrospective cross-sectional study has assessed acne frequency in adults with lactose intolerance in a large population of patients in the United States and investigated the role of insulin-like growth factor 1 (IGF-1) in acne pathogenesis. A significant decrease in acne frequency has been observed in patients with lactose intolerance, and it could be assumed that the increased levels of IGF-1 found in dairy products could play a role by stimulating the proliferation of sebocytes and acne, thus increasing androgen bioavailability and sebum production.[16] On the other hand, consuming milk, sugary drinks, and fatty and sugary products seems to be associated with acne in adults.[17]

In parallel, a recent study has reported that overweight and obesity are inversely associated with acne in young patients, and this association seems to increase with overweight and obesity severity.[18]

Finally, Wertenteil et al. reported a prevalence of acne vulgaris of 15.2% in adults with hidradenitis suppurativa (7315 out of 48,085 subjects) compared with 2.9% in adults without (497,360 out of 16,899,470 subjects) ($P < 0.001$). This finding could help to improve the management of patients with hidradenitis suppurativa with an assessment of their acne status and the optimization of concomitant strategies for managing these two types of dermatoses.[19]

**Microbiome and adult acne**

Cumulative evidence has demonstrated an intimate, bidirectional connection between the gut and the skin, and numerous studies link gastrointestinal (GI) health to skin homeostasis and allostasis.[20] GI disorders are often accompanied by cutaneous manifestations, and the GI system, particularly the gut microbiome, appears to participate in the pathophysiology of many inflammatory disorders. The recent literature points out the pivotal role of the skin microbiome in the pathophysiology of many inflammatory dermatoses, in particular, through its various interactions with the host's innate immunity.[20] Regarding acne, the composition of the skin microbiota is different between acne patients and healthy volunteers[21] and would be different depending on acne grade.[22] However, Li et al. conducted their trial on nine healthy subjects and 67 acne patients, inducing bias in their study. They have shown that the microbiota of patients with mild and moderate acne was similar. In contrast, patients with severe acne had a specific microbiota that significantly differed from the others, with a higher proportion of Gram-negative bacteria (*Faecalibacterium*, *Klebsiella*, *Odoribacter*, and *Bacteroides*).[22]

In parallel, in the era of high-throughput sequencing and with the more precise determination of the skin microbiota composition, the impact of acne treatments on the skin microbiota has been extensively studied. Ahluwalia et al. have recently reported that benzoyl peroxide did not significantly impact the alpha-diversity of the skin microbiota in a study conducted in female patients aged 7 to 12 years.[23] In contrast, systemic antibiotics are associated with significant changes in skin microbiota composition and diversity.[24] Indeed, minocycline was associated with a 1.4-fold decrease in *C. acnes* levels, but these levels returned to their initial value after treatment discontinuation. The impact varied depending on the bacterial genus considered. For instance, a transient 5.6-fold increase in the relative abundance of *Pseudomonas* species was observed immediately after antibiotherapy, as well as a sustained 1.7-fold increase in the relative abundance of *Streptococcus* species and a 4.7-fold decrease in the relative abundance of *Lactobacillus* species 8 weeks after antibiotic discontinuation.[24]

Other treatments used have significant impacts on skin microbiota composition. Kelhälä et al. demonstrated that isotretinoin and a cycline (lymecycline) altered the skin microbiota, in particular by reducing *Cutibacterium* levels, while the levels of several other taxa were significantly higher in treated cheek skin samples compared with untreated samples. Fewer changes were observed in back skin samples. On the other hand, the diversity of the microbiota on the cheek and back skin was significantly increased after acne treatments.[25] In contrast, isotretinoin drastically modified skin microbiota composition, in particular, through a reduction in *Cutibacterium* genus levels,[26] suggesting that the use of isotretinoin could help to select a specific community of healthy skin-associated *Cutibacterium* to restore a healthy skin profile.

Recently, the skin microbiome has been suggested to be regulated by the gut microbiome,[27] probably through the modulatory effect of intestinal commensals on systemic immunity. Some intestinal microorganisms and their metabolites, including retinoic acid, *Bacteroides fragilis* polysaccharide A, *Faecalibacterium prausnitzii*, and bacteria belonging to the *Clostridium* IV and XI clusters, promote the accumulation of regulatory T lymphocytes that facilitate anti-inflammatory responses.[27] Moreover, the impact of the skin-gut-brain axis has been described on acne vulgaris pathogenesis, with a significant effect of psychological stressors on the gut microbiota. As an example, they induce the production of different neurotransmitters such as serotonin, norepinephrine, and acetylcholine or the release of neuropeptides by nearby enteroendocrine cells. These neurotransmitters increase intestinal permeability, leading to intestinal and systemic inflammation that is suspected to play a role in inflammatory dermatoses. Interestingly, stimulation of substance P-containing nerves and a strong expression of this neuropeptide are seen in acne vulgaris and in intestinal dysbiosis.[28]

In focusing on the relationship between the gut microbiome and inflammatory dermatoses, it has been shown that the gut microbiota of acne patients differs from healthy subjects.[29] According to the authors, the mechanisms are based on the

short-chain fatty acids resulting from the fermentation of fibers in the intestine, which would determine the predominance of certain skin microbiome profiles and could consequently influence the mechanisms of the skin immune defense.[29] Within the skin microbiome, *Staphylococcus epidermidis* plays a particularly important role in addition to *C. acnes*.[30] Several subpopulations of *C. acnes* are known to be associated with acne, which is the case for subtype IA1.[30] Furthermore, a diversity loss in these subgroups could induce an inflammatory process in an *in vitro* skin model, highlighting the major role of *C. acnes* phylotype diversity in the maintenance of skin homeostasis.[3] On the other hand, some skin commensal species have recently been identified as able to selectively kill *C. acnes* bacteria, such as *Staphylococcus capitis*, as recently reported by O'Neill et al.[31]

Finally, since the microbiome plays a crucial role in skin homeostasis maintenance, the impact of the environment on the microbiome has been increasingly studied. For instance, ultraviolet radiation has been shown to influence skin microbiome composition,[32] reinforcing the need to use sun protection.[33] Moreover, exposure to certain pollutants such as polycyclic aromatic hydrocarbons has been reported to induce skin dysbiosis, which raises the question of the effect of these pollutants on the pathophysiology of some inflammatory skin disorders in urban areas and in smoking populations.[34]

### Adult female acne

Acne vulgaris in adult females has increased over the past 10 years. A confocal microscopy study conducted on 15 female acne patients has shown specific topographic features on the skin of patients compared with 15 healthy subjects. A stronger hyperkeratinization was observed on the skin of adult women with acne compared to healthy controls, confirming that the presence of microcomedones is crucial in the development of acne lesions. The authors have also shown that the distribution of comedones and microcomedones was heterogeneous with a large number concentrated in the mandibular area where acne lesions were specifically located.[35] Regarding the impact of *Cutibacterium acnes*, some studies have reported that no specific strain was associated with this type of acne.[36]

### Update of adult acne recommendations and treatments

Patients with acne should benefit from careful dermatological and psychopathological monitoring. A consensus has been reached in 2018, gathering the opinions of international acne experts, and the consensus recommendations are summarized below (Table 1).[8,37] Isotretinoin is highlighted while the place of antibiotics in the first-line treatment of acne is changing.

The role of *C. acnes* in acne pathophysiology is still extensively investigated. Patients with acne do not harbor more *C. acnes* than normal individuals.

In addition, certain subtypes of this bacterium are associated with acne and are more often found on the skin of acne patients compared with healthy subjects.[38] This study suggested a role of *C. acnes*-derived biofilms in the increasing antibiotic resistance observed with these bacteria, which represents a new target for future therapies. Antibiotics have long been used for the management of acne. The current international guidelines recommend the use of topical antimicrobials for the treatment of mild and moderate acne, including comedonal and localized papulopustular manifestations. However, their use as a monotherapy is not recommended in European and American guidelines due to the extremely high risk of associated bacterial resistance.[39] Thus, benzoyl peroxide, which has a potent oxidative activity, seems to be the preferred topical antimicrobial agent, mainly based on the data available on the increasing antimicrobial resistance.[8]

Other studies support the use of effective therapeutic alternatives such as emerging topical therapies, diet modifications,

**Table 1** Summary of the international guidelines[9,45]

| Recommendation number | Details explaining each recommendation |
|---|---|
| Recommendation 1 | Retinoids play an essential role in acne treatment. For most patients with inflammatory acne, comedonal acne, or both, the first-line therapy should combine a topical retinoid and benzoyl peroxide. |
| Recommendation 2 | The role of antibiotherapy in acne has changed. Neither topical nor systemic antibiotics should be used as a monotherapy in acne treatment. |
| Recommendation 3 | Oral isotretinoin should be the first-line therapy for very severe (cystic and conglobata) acne. |
| Recommendation 4 | Oral isotretinoin should be continued until full clearance of acne. Additional studies are needed to define a total cumulative dose that allows for maintaining remission. |
| Recommendation 5 | Acne flare should be minimized by initiating low-dose oral isotretinoin. |
| Recommendation 6 | Most patients with acne should receive maintenance therapy with a topical retinoid combined or not with benzoyl peroxide. Topical antibiotics should not be used as acne maintenance therapy. |
| Recommendation 7 | Azelaic acid cream 20% or gel 15% should be used in pregnant women and in patients with acne and postinflammatory hyperpigmentation. |
| Recommendation 8 | Devices, including laser, intense pulsed light, and photodynamic therapy, should not be considered first-line treatments for inflammatory acne. |
| Recommendation 9 | In a minority of women ≥25 years, acne lesions are only located on the lower face. Topical retinoids combined or not with benzoyl peroxide are important components of adult acne treatment. |
| Recommendation 10 | The potential risk of acne scarring should be minimized by the early initiation of effective treatment. |

spironolactone, and oral contraceptives combined with isotretinoin, depending on the clinical context.[40]

Oral contraception is known to exacerbate or minimize acne depending on its composition. Birth control pills combining both estrogen and progestin are used for acne, as progestin-only and contraceptive implants may exacerbate the condition.[41]

The former contraceptive pills (first and second generations) contain a progestogen, derived from the so-called androgenic testosterone (levonorgestrel or norethisterone), with effects close to male hormone and which can therefore aggravate acne. The progestogen prevails over the estrogen, and this pill has a progestational climate and promotes acne in women who are predisposed. However, when the progestogen belongs to the third generation, that is, not androgenic, the androgen/estrogen balance is then modified in favor of estrogen, which reduces acne. For the pills of the fourth generation, an antiandrogenic progestogen has been chosen which neutralizes the androgens. Nevertheless, because of thrombosis risks, ANSM advised physicians, in 2012, to favor systematically the pills of the second generation in the first intention.[42]

The course and severity of the disease could also be due to environmental factors called "exposomes" such as nutrition, medications, occupational factors, pollutants, climatic factors, and psychosocial and lifestyle factors. Recent studies have recommended the identification of these factors by the clinician and the reduction of their impact on adequate acne management.[43] A panel of international experts agreed that off-label acne treatments either as a monotherapy for mild acne or in combination with prescription treatments for more severe acne would respond to a significant unmet need.[44] Note that the direct cost of acne in the United States is estimated to exceed $1 billion/year, with $100 million spent on over-the-counter products.[45]

In clinical practice, new acne treatments include innovative targets such as skin microbiome modulation and newly developed molecules. These new treatments are summarized in Table 2.

Regarding microbiome modulation, Perin et al. have explored this hypothesis by testing the transfer of the skin microbiota from one anatomical site to another in the same host, in four healthy volunteers.[46] The clinical promise of microbiota transfer has been demonstrated with fecal microbiota transplantation that has shown a curative potential, in particular, in colitis induced by *Clostridium difficile*. This proof-of-concept study has shown the possibility to transfer a partial DNA signature from one cutaneous site to another in a given subject. For the clinical development of this treatment, the next step will be to study the viability and efficacy of the colonization of the microbiota transferred from one subject to another in the same location.

One other direction focused on the treatments able to modulate the skin microbiota, in particular using probiotics based on *Lactobacillus reuteri*,[47] known to inhibit the growth of other bacteria such as *C. acnes*, *S. aureus*, and *S. epidermidis*. Finally, regarding the relationships between the gut and skin microbiota, the possibility of using oral probiotic strains in combination with topical probiotics and/or prebiotics is suggested to develop a personalized treatment for skin disorders.[48]

In focusing on *C. acnes* communities, since some phylotypes seem to be associated with acne, the modulation of these phylotypes has recently been explored by Karoglan et al.[49] They have reported encouraging results with a decrease in the number of comedones using a two-phase treatment (benzoyl peroxide followed by the application of a topical probiotic formulation based on different strains of *C. acnes*). A renewed interest is also observed for treatments using bacteriophages, in particular as an alternative to antibiotics and to restore *C. acnes* antibiotics sensitivity. Bacteriophages would be able to target multiresistant bacteria, which represents a promising therapeutic avenue in the management of acne patients. However, additional studies are needed to assess the safety and the best way to use these phages.[50] The possibility of developing a vaccine targeting virulence factors produced by *C. acnes*, including Christie-Atkins-Munch-Peterson (CAMP) factor, has also been studied.[51] The authors have suggested that targeting the CAMP factor produced by *C. acnes* through a public vaccination program in early childhood could prevent the onset of acne while preserving the commensal relationship between the host and these bacteria (Table 2).

Other types of topical treatments based on newly discovered molecules have been recently developed:

- Clascoterone cream 1%, a novel topical androgen receptor inhibitor, has shown its efficacy in a phase III randomized clinical trial. Indeed, it concluded that more patients receiving clascoterone cream, 1%, vs. vehicles achieved treatment success at week 12 (18.4% vs. 9.0%, respectively). The trial shows its safety; the cream had the same safety profile as the vehicle with low rates of adverse events.[52] It competes with androgens for binding to the androgen receptors, leading to an inhibition of sebum production and the activation of pathways involved in proinflammatory cytokine production.[52]
- Tazarotene 0.1% is known to induce severe cutaneous adverse events (e.g., rash), but a new formulation with a lower percentage has been developed to lower down the toxicity. A phase III, randomized, double-blind trial (NCT03168334 and NCT03168321) has compared its new formulation at 0.045% in a polymer emulsion vs. a vehicle. The efficacy was significantly higher compared with the vehicle (at week 12, 30.4% vs. 17.9%; $P < 0.001$), and it was well tolerated in patients with moderate-to-severe acne.[53]
- Trifarotene 50 μg/g cream, a topical retinoid, has been recently developed for back and facial acne. In a 52-week study (NCT02189629), trifarotene was well tolerated and effective on moderate acne of the face and trunk. It is therefore an attractive therapeutic option to include in the clinicians' arsenal.[54]
- Finally, a last interesting perspective has to be mentioned. It is based on the use of an adapalene transferosome gel containing vitamin C.[55] This new formulation enriched with

**Table 2** Summary of innovative targets for skin microbiome modulation and newly developed molecules

| Treatment | Mechanism | Galenic formulation | Ref. |
|---|---|---|---|
| The microbiota | | | |
| Transfer of skin microbiota | • Restore a healthy skin microbiota | Topical | 82 |
| Probiotics containing *Lactobacillus reuteri* bacteria | • Inhibit the growth of other bacteria such as *C. acnes*, *S. aureus*, and *S. epidermidis*<br>• Reduce IL-6 and IL-8 levels and increase aquaporin 3 and laminin A/B levels | Topical | 83 |
| Personalized treatment combining oral probiotic strains with topical probiotics and/or prebiotics | • Pathogenic loop: gut dysbiosis may induce IGF-1 that may trigger a change in the quantity and/or quality of the lipid-rich sebum, favoring the colonization of pilosebaceous unit by different *C. acnes* phylotypes, disturbing the balance between skin microbiota microorganisms<br>• Dual modulation of the IGF1/IGF-1 receptor pathway by the gut and skin microbiota, which is involved in acne pathophysiology | Topical and oral | 84 |
| Application of selected *C. acnes* strains in combination with benzoyl peroxide | • *C. acnes* strains associated with the inflammatory response in acne produce high linoleic acid isomerase levels on the skin. The mechanism of this treatment is based on replacing these strains with others not associated with inflammation to reduce acne severity | Topical | 85 |
| Use of bacteriophages | • Bacteriophages are able to target and destroy multiresistant bacteria<br>• Reduce biofilm formation | Topical | 86 |
| Vaccine | • Vaccine targeting virulence factors secreted by *C. acnes*<br>• Neutralizing these factors may lower the risk of disturbing skin microbiota composition | Injection | 87 |
| Topical treatment | | | |
| Clascoterone cream, 1% | • Novel topical androgen receptor inhibitor.<br>• Competition with androgens, for binding to their androgen receptors. It, therefore, inhibits sebum production and the activation of the pathways involved in proinflammatory cytokine production | Topical | 88 |
| Tazarotene | • The current formulation (0.1%) may cause irritations<br>• A new formulation (0.045%) using a polymeric emulsion technology has been developed to lower these side effects | Topical | 8 |
| Trifarotene | • Anticomedogenic, antipigmenting, and anti-inflammatory properties | Topical | 89 |
| Adapalene-loaded transferosome gel containing vitamin C | • Combination of adapalene (a topical retinoid) and vitamin C<br>• Vitamin C prevents oxidative damage to the skin, scavenges reactive oxygen species, inhibits the activation of melanogenesis (treatment of postinflammatory hyperpigmentation) | Topical | 90 |
| Aldosterone antagonist | | | |
| Spironolactone | • Aldosterone antagonist and inhibitor of five alpha-reductase | Oral (100 mg or 150 mg daily) | 63,74,91 |
| Antiobiotic | | | |
| Sarecycline | • Narrow-spectrum tetracycline-class antibiotics used in moderate-to-severe acne | Oral | 72 |

vitamin C is in the early stages of development, but it is one of the most promising avenues for the management of acne patients.

Among systemic drugs, spironolactone is also prescribed for off-label use. In all the studies published, spironolactone was effective on acne lesions located on the face[56] and/or on the back.[57,58] To note, all these studies were performed in an open setting with no control group.

With regard to antibiotics, sarecycline, a narrow-spectrum tetracycline-class antibiotic, has been recently approved by the Food and Drug Administration (FDA) for use in moderate and severe acne.[59] Indeed, long-term systemic antibiotics are usually used in females and vulgar acne. Since antibiotic resistance is a worldwide and growing phenomenon, spironolactone could be an alternative for the treatment of acne in adult women instead of isotretinoin, which is more complex to manage in a female population. Currently, antiandrogenic hormone therapy, including

 

spironolactone and combined oral contraceptives, is usually not used as a first-line systemic treatment in women with acne. However, a recent study has reported that the use of a hormonal antiandrogen was associated with shorter cumulative antibiotic durations, and the early initiation of this type of treatment could decrease the use of antibiotics for acne management.[60]

## What is the medical impact of these recent data?

### Microbiota modulation

Microbiota modulation-based therapies are currently being investigated. Most articles included in this review have reported encouraging results for the future development of acne treatments. The main advantage of these treatments is to limit the use of antibiotics. However, further clinical studies are needed to investigate their safety and benefit for human skin before being approved by the health authorities of each country.[46–49]

### Spironolactone

Spironolactone is widely prescribed for acne treatment despite the possible risk of hyperkalemia. However, two large observational studies have demonstrated that the hyperkalemia's rate in healthy young women taking spironolactone for acne is equivalent to the baseline rate of hyperkalemia in this population.[61,62] Spironolactone represents an interesting alternative to systemic antibiotics and isotretinoin, more complex to manage in women. Based on the recent clinical data, spironolactone seems to be safe and effective for the treatment of acne in women. Prospective studies must be conducted to further confirm the safety and efficacy of spironolactone in this population.[63]

### Topical agents

Among topical advances, a new tazarotene 0.045% lotion formulation using a polymeric emulsion technology has been developed.[53] As already quoted, this less-concentrated new formulation is associated with fewer side effects than the formula normally used at 0.1%. Also, trifarotene is a new generation of retinoids with selectivity for the retinoic acid receptor (RAR)-$\gamma$ that is strongly expressed in the skin. It is well tolerated and represents a safe and effective option in patients with moderate facial and truncal acne. Finally, clascoterone 1% is a novel topical androgen receptor inhibitor, which is bound with high affinity to the androgen receptor. It has also been found to be four times more potent than progesterone. Recent studies have shown its safety and efficacy in patients with facial acne. Indeed, the treatment resulted between baseline and week 12 in a significant reduction of noninflammatory and inflammatory lesions.[64] This topical treatment is under investigation as a first-in-class therapy for acne treatment, providing an interesting alternative to antibiotics for the management of acne patients.[52]

Recently, Ottaviani et al. suggested that an alteration of the sebocyte differentiation process was related to acne development. The induction of sebocyte differentiation reduces the response to insulin, normalizing the sebum production and decreasing the release of proinflammatory mediators.[65] This induction can be promoted by NAC-GED0507, a specific agent. In a first open-label phase I clinical trial (EUDRACT NUMBER: 2014-005244-17), NAC-GED0507 1% gel treatment was associated with a consequent modification of the sebum composition which leads to a significant reduction of acne manifestations.[66]

## Conclusion

Acne is a common inflammatory dermatosis. New treatments are continuously being developed, and the role of various agents is evolving, with newly identified actors that play crucial roles in the development of acne. Skin microbiome modulation appears to be a promising target for future therapies but still needs to be further investigated. In parallel, antibiotic resistance is increasing worldwide, and there is, therefore, an urgent need to reduce their use, especially in acne management as they have been extensively used in the last 20 years. Through their effect on microcomedones and their preventive action on initial lesions, retinoids may be one of the cornerstones of acne therapy. The variety of acne treatments and diversity of molecules (antiandrogenic hormones, retinoids, antibiotics, etc.) offer great flexibility to dermatologists to personalize patients' therapeutic regimens while achieving good results.

### Questions (answers provided after references)

**1** What is the major bacterium involved in acne physiopathology?
- a Cutibacterium acnes
- b Staphylococcus aureus
- c Escherichia coli
- d Proteus mirabilis

**2** Acne vulgaris of adult females currently affects:
- a 15% to 50% of adult women
- b 20% to 30% of adult women
- c 30% to 50% of adult women
- d 80 to 90% of adult women

**3** "Exposomes" include factors that may be able to impact the course and severity of acne. These factors include
- a nutrition
- b medications
- c occupational factors
- d pollutants
- e climatic factors

**4** Which treatment should be the first-line therapy for very severe (cystic and conglobata) acne?
- a Antibiotics
- b Oral isotretinoin
- c Spironolactone
- d Topical retinoids

**5** Among the following treatments, which are in topical galenic formulation?

a Clascoterone cream, 1%

b Tazarotene

c Trifarotene

d Spironolactone

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## Answers to questions

**1** a
**2** a
**3** a bcde
**4** b
**5** a b c