

ACNE IN ADULTS: TREATMENTS AND SKIN CARE

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Article Received on 14/09/2021

Article Revised on 04/10/2021

Article Accepted on 25/10/2021

ABSTRACT

Introduction: The incidence of acne in women over 30 years of age has increased in recent decades, mostly presenting as persistent acne since adolescence. **Objectives:** To understand the causes of the appearance and persistence of acne in women over 30 years of age and the different approaches to care, treatment and prevention in acne-prone skin. **Methodology:** Literature review in the Medline (PubMed) and Scielo databases. **Results:** The aetiopathogenesis and treatment of acne in women over 30 years of age presents aggravating factors compared to other groups (hormonal, stress, obesity, diet, cosmetics, medication...). The response to treatment is usually slow, and mature skin is **more sensitive to topical treatments**. **Conclusions:** The management of acne in mature women is more complex than in adolescents. Hygiene and hydration of the skin are essential, together with an approach that reduces sebum secretion, comedogenesis and inflammation.

KEY WORDS: acne, adult, women, skin, therapeutics.

INTRODUCTION

Acne is a chronic inflammatory disease of the pilosebaceous unit characterized by an increase in sebaceous production induced by:

- Androgenic hormones and the consequent obstruction of the pilosebaceous duct.
- Hyperkeratosis due to retention and hyperproliferation of the cells of the hair follicles.
- Innate inflammation
- The colonization and bacterial proliferation by *Propionibacterium acnes* of the hair follicles.

It is usually located especially on the face and back, but it is also common on the neck and chest.^[1]

This disease is usually accompanied by seborrhea as one of the first symptoms, in addition to being reflected in the form of lesions, mainly comedones that can be open, the so-called blackheads, and closed, known as whiteheads.

Papules, pustules and nodules are characteristic lesions of an inflammatory type acne, as opposed to a non-inflammatory comedonal acne.^[2]

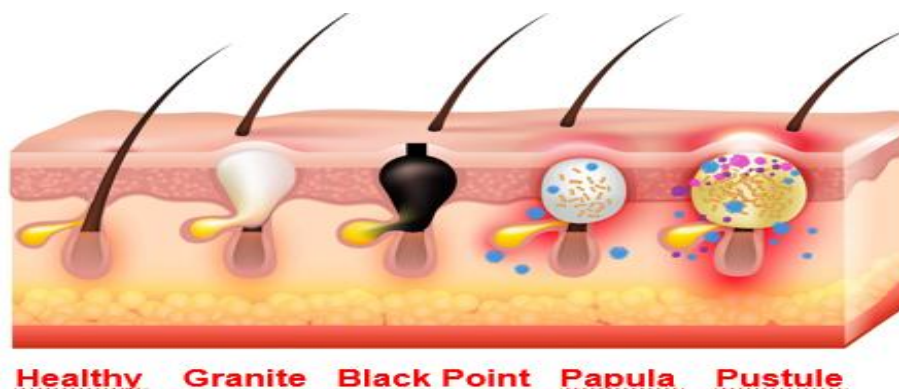


Figure 1: Types of acne lesions.^[3]

Prevalence

The prevalence of this disease is clearly higher in young adults or adolescents, with a peak prevalence of 80-85% of people between 12 and 24 years old and a higher incidence in men. Most cases resolve this pathology during adolescence, but its persistence into adulthood is more and more frequent, especially after the age of 25.

In 12% of women it can persist until after 44 years compared to 3% in men. The incidence of acne in adult

women has increased in the last decades.^[4] Prevalence figures can vary from 14 to 54% of women depending on the studies.^[5]

We know that its incidence is increasing in the last two decades, without being very clear why, it has been attributed to the modern way of life. Most of the cases are persistent acnes from adolescence and only 19% begin in adulthood.^[6]

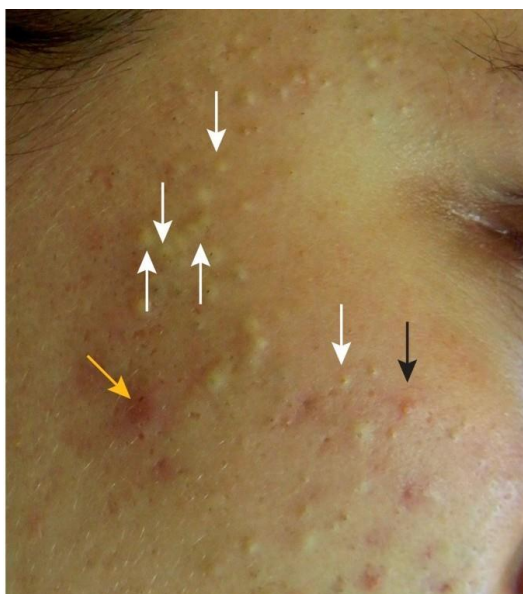


Figure 2: Acne lesions, including comedones (white arrows), papules (yellow arrow), and pustules (black arrow) on facial skin.^[7]

Etiology

The etiology is not entirely known; It is a multifactorial disease, with a clear influence of *P. acnes* and genetic factors, but its triggering or the role of treatments in the course of this disease is not clear.

Diet and various environmental and external factors are also believed to be involved, but have not been proven.

-Aggravating/influencing factors on the etiopathogenesis

In adulthood, it is more difficult to know its etiology, since it is not proven, but various factors are known that predispose or promote the appearance or persistence of these lesions.

There is a greater secretion of sebum in women with persistent acne, which may worsen existing acne or promote its appearance by obstruction of the pilosebaceous units.



Figure 3. Inflammation process and the appearance of acne 3.

Genetics

A high percentage of patients with late acne have been seen with a family history of persistent acne, therefore correlating with a genetic predisposition.^[5] Around 50% of patients have a direct family history of post-adolescent acne, a factor that increases the 3.93% risk of late acne.^[6]

Immunity

There is evidence of the presence of an exacerbated innate immune response to colonization by the *P. acnes* bacteria that contributes to the appearance of acne.^[7]

Tobacco

According to certain studies, tobacco has a high influence on this disease, more as an aggravating factor or promoter of the persistence and exacerbation of this pre-existing disease or trigger in people with a predisposition, specifically non-inflammatory acne, than as the primary cause of these injuries.^[8]

Extrinsic factors

Different drugs or cosmetics are believed to be acne inducers, although they have not been involved in its persistence.^[9]

Topical or general corticosteroids, antiepileptic drugs, vitamins A and B (vit. B12) or psychotropic drugs such as antidepressants, can be the reason for worsening or the primary cause of the appearance of these outbreaks. In these cases there are inflammatory acne lesions (pustules and papules) that usually affect the extremities.

Stress and anxiety are factors that contribute to the worsening of the clinical picture, although it seems unlikely that they induce the formation of new lesions. Emotional stress is increasingly common, directly related to acne.^[10]

When under stress, the body produces different hormones such as cortisol and androgens, neuropeptides such as endorphins and insulin and cytosines responsible for inflammation; which have an influence on the state and behavior of the sebaceous glands and can aggravate the state of acne.^[10]

The association with diet is controversial. A high-fat diet has not been shown to make acne worse; but there are publications that associate the high consumption of carbohydrates. A high glycemic index is associated with a higher incidence of acne, due to the spike in insulin and insulin-like growth factors, which stimulate the sebaceous glands, causing an increase in sebum secretion.

Dairy products, skim or not, have also been correlated with the appearance of acne breakouts and an increase in

the number of lesions. It is believed that it may have a relationship with hormones from cows. However, no studies have been found that directly link it, so subjecting a teenager to a strict fat-free diet does not help improve acne.

Hormonal factors

A hormonal imbalance is directly related to the presence of acne. Many women who suffer from acne present in turn different clinical manifestations caused by hyperandrogenism, as well as menstrual imbalances, androgenic alopecia, hirsutism, etc. For this reason, it is important to carry out a prior clinical evaluation to rule out these possible hormonal disorders, analyzing the levels of different hormones in the laboratory.^[11,12]

Types

Acne vulgaris is one of the most common dermatological conditions in the world, hence the importance of its knowledge. It has been seen that there is an increasing number of patients in adulthood, who present this dermal involvement, and especially women.

Therefore, the clinical manifestation of post-adolescent acne in women is mainly hormone-dependent acne. It is usually mild-moderate acne with a predominance of inflammatory lesions with the presence of papules, pustules and comedones, although to a lesser extent, therefore it is a rather inflammatory acne (9,11).

Two main clinical groups are identified in adult female acne:

- **Persistent acne:** begins in puberty or adolescence with continuous outbreaks until adulthood. It is characterized by the practically constant and daily presence of lesions and also the appearance of more severe premenstrual outbreaks. The lesions are usually papulo-nodular, especially in the lower part of the face, the mandibular part (chin, mouth and beginning of the neck)...

- **Late-onset acne:** appears in ages over 25 years without having had previous acne lesions.

o **Chin acne:** inflammatory lesions concentrated in perioral areas and around the chin. Pustules and papules predominate which, depending on the severity of the patient, can be more or less deep. There are practically no comedones, so it is an inflammatory acne. Its exacerbation is frequent in the premenstrual period. They are usually resistant to treatment and produce post-inflammatory erythema, leaving spots and scars.

o **Sporadic acne:** acute acne outbreaks of fortuitous appearance, without apparent reason or associated with some systemic disease or sign of androgenization. As in the previous case, pustules and inflammatory papules predominate with very few comedones, which can affect any location. Treatment is usually seen in people over 60 years of age.



Figure 4: Acne located on the chin and on the back.^[13,14]

Justification

Acne is a recognized problem in today's society, increased by the enormous importance that is currently given to personal appearance. It is a skin condition that can affect people of any age due to the personal perception of body image, which can produce harmful psychological effects.

In today's society, acne affects a very high percentage of the young or adolescent population, populations in which there are multiple reviews or studies that allow this disease to be addressed specifically and effectively.

In the specific case of adult acne in adult women, we find an increase in the prevalence in recent decades but, unlike in the young population, the information is more limited, with fewer studies available.

Although the pathogenesis or causes of acne in adolescents and adult women are similar, there are differential or aggravating factors in the latter, such as stress, obesity, diet, tobacco, cosmetics, medications, sleep disorders ...

The interest in carrying out this work arises due to the differential factors between acne in adolescents and adult women, together with the increased prevalence in the latter and the limitation of studies in this population.

This work provides a theoretical contribution that reviews the information from bibliographic reviews and different studies referring to a not-so-discussed topic, such as adult acne.

Objective

To know the main causes of the appearance and persistence of acne in adult women and to know the different approaches regarding the care, treatment and prevention of acneic skin in these women.

METHODOLOGY

The bibliographic search was carried out in the Medline information databases (PubMed) in the Pubmed and Scielo databases.

The following search strategy was used using MeSH terms: *Acne, adult women, acne skin, onset and persistence, treatment, skin care, prevention*. The different concepts were combined by means of the

Boolean AND and OR operations.

The search provided initial information with the subsequent aim of delving into the different fields of application, carrying out specific searches for each group.

A total of 322 articles were initially obtained, the vast majority in Medline, those articles in which certain concepts were repeated or that had no relationship with the study topic were discarded. In the end, 41 articles were selected that are those that have been used to carry out the work.

The bibliographic search has been done for the last 25 years, until 2021. The only filter used was the language, searching only articles in Spanish and English.

No additional filter was included as of the publication date, etc., in order not to lose information.

No additional filter was included on publication date, etc., in order not to lose information.

Among the exclusion criteria of the present bibliographic review, those articles that repeated information already described or did not contribute anything new or that already came in the topics of the books consulted were discarded.

The present work is based on studies carried out in humans.

RESULTS

Acne, as already seen, can cause anxiety and detrimental effects on self-esteem in any patient. Specifically, in the group of patients treated in this study, the clinical manifestations that it can leave are permanent sequelae, such as all scars and marks. It is important that patients have as much information as possible about the available treatment options and their expected results.

The response to treatment in this particular group of patients is usually slow, and mature skin is usually more sensitive to topical treatments; Therefore, it is essential to make patients aware of the long duration of treatment, as well as to encourage them to continue complying with the chosen treatment regimen despite the fact that the improvement is not immediate and they may even experience an initial worsening.

The general principles of treatment to be followed in an adult woman do not differ significantly from those of other age groups, but there are some subtle differences that must be taken into account, so an examination of the patient is necessary when establishing treatment more appropriate.

Despite the high influence of androgenic hormones on the appearance of acne, the majority of adult acne patients do not have endocrine system disorders. However, it is an important cause to consider, since hormonal disorders such as hyperandrogenism are responsible for polycystic ovary syndrome, hirsutism, irregular menstruation or infertility among others, which can be the direct causes of severe acne in women and its sudden appearance or late.

One study showed that one in ten patients with late-onset acne has polycystic ovaries or late-onset adrenal hyperplasia.^[12]

Due to this, it would be advisable to always carry out a clinical evaluation prior to the beginning of any therapeutic treatment that consists of a specific hormonal analysis:

- Dehydroepiandrosterone sulfate (DHEAS), which measures the alteration of adrenal hormones and can detect an excess production of androgenic hormones.
- Testosterone, collects ovarian activity.
- Luteinizing hormone/follicle stimulating hormone (LH/FSH), confirming a polycystic ovary.
- Prolactin to determine a pituitary disorder. It is convenient to obtain these laboratory tests during the first 5 days of the menstrual period.^[11,12]

It is also convenient to focus on the different main objectives that are sought when dealing with this disease:

- Decreased sebum secretion.
- Decreased comedogenesis.
- Decreased proliferation and persistence of *P. acnes*.
- Decrease in inflammation.

Topical treatments

Older skin shows different sensitivity to this type of treatment than young skin, specifically, high irritability against retinoids and topical antibacterials, and greater tolerability against the abrasive effects of benzoyl peroxide.^[15]

Currently, the guidelines for topical treatment of acne contemplate the combination of various topical treatments in order to reduce the risk of developing bacterial resistance to antibiotics and to provide faster results than in monotherapy.^[15,16] The use of topical antibiotics, such as erythromycin, and clindamycin, is very recurrent (superior efficacy against non-inflammatory lesions), together with benzoyl peroxide or retinoids, especially in prolonged treatments, due to the high availability of presentations (gel, lotion, cream, soap, wipes or ampoules), which provide the patient with a simplification of the treatment regimen, favoring

adherence to said treatment. These treatments are the first step that is usually resorted to due to their facilities.^[17,18]

- Topical antibiotics

The most widely used topical antibiotics are erythromycin and clindamycin, which act by inhibiting the synthesis of *P. acnes* proteins, preventing sebum from being converted into free fatty acids, which are responsible for stimulating the body's immune response. They also have anti-inflammatory activity.^[19]

Specifically, clindamycin is considered more effective than erythromycin, because the latter has a higher risk of developing resistance. Clindamycin inhibits the production of pro-inflammatory cytokines, such as interleukin-12 and interferon- γ , in peripheral blood cells stimulated by heat-killed *P. acnes*; decreasing the production of microorganisms on the skin surface and comedones. It also has anti-inflammatory activity in sebocytes activated by insulin or peptidoglycans.^[19,20]

One of the drawbacks of the use of antibiotics in long-term treatments is the risk of developing resistance to *P. acnes*, especially when used at low doses, leading to a decrease in their efficacy.^[21]

- Benzoyl peroxide

It is an antimicrobial with activity against *P. acnes* by releasing oxygen free radicals, generating an aerobic environment preventing the proliferation of *P. acnes*. In addition, it has keratolytic activity, producing comedolysis, sebosuppressive and direct anti-inflammatory, making it a very effective active principle against inflammatory skin lesions and comedones. Unlike the previous group, benzoyl peroxide is not associated with antimicrobial resistance, but it can produce cross-sensitivity with estrogens and skin irritations such as allergic dermatitis, erythema or scaling.^[22,23,24]

- Hydroxy acids

They stimulate the production of polysaccharides such as hyaluronic acid, improve the quality of elastin fibers and the density of collagen and increase the production of hyaluronic acid and collagen, achieving greater renewal and thickening of the skin, greater hydration, elasticity and uniformity in the skin tone.

According to their chemical structure and their properties, the following can be distinguished: Alpha hydroxy acids and Beta hydroxy acids. Both produce that stimulation of the exfoliation of skin cells, but they will act at different levels.

- Alpha hydroxy acids are water soluble, so they will exert this exfoliative action on a more superficial level (epidermis). The most used are glycolic and lactic acid.
- Beta hydroxy acids are fat soluble, penetrating deeper layers through the sebaceous follicles, allowing a deeper exfoliation and cleansing of the pore. The most widely

used is salicylic acid.^[25]

- Azelaic acid

It is a dicarboxylic acid of natural origin, effective against comedones and inflammatory acne lesions, as well as hyperpigmentation disorders. There are studies that have shown an efficacy of azelaic acid in the treatment of acne comparable to that of benzoyl peroxide, topical or oral antibiotics such as tretinoin. It is very well tolerated and the only drawback would be local skin irritation.^[26]

- Retinoids

Retinoids are synthetic derivatives of vitamin A with keratolytic and keratoplastic action with evidence of a decrease in comedones and inflammatory lesions due to their multiple actions on the dermal layer.^[27,28]

- They inhibit the formation and reduce the number of comedones (anticomedogenic).
- Reduce mature and closed comedones (comedolytics).
- They reduce inflammatory lesions and anti-inflammatory action, specifically adapalene has proven to be the retinoid with the highest anti-inflammatory activity.
- They promote normal desquamation of the follicular epithelium.
- They facilitate the penetration of other drugs.
- Reduce free fatty acids in microcomedones.

Those indicated for acne are adapalene, tretinoin and tazarotene, which are characterized by maintaining the remission of acne by inhibiting the formation of microcomedones, thus avoiding new lesions. The drawback is the significant irritation they produce on the skin, especially in older skin. It is advisable to start these treatments gradually and progressively.^[22, 29]

Systemic treatment

- **Oral antibiotics:** These drugs inhibit neutrophilic chemotaxis and reduce the amount of free fatty acids, so they have both bacteriostatic and bactericidal activity on *P. acnes* as well as anti-inflammatory.^[30,31]

Doxycycline and minocycline have now replaced tetracycline and erythromycin. Other antibiotics such as azithromycin have a high risk of generating resistance, which is why it is in disuse.^[7]

To reduce the development of antibiotic resistance, the combination of systemic antibiotics with a topical regimen such as retinoids or benzoyl peroxide is recommended, but always avoiding the simultaneous use of oral and topical antibiotics.^[32]

This type of treatment has a fairly slow but effective response in a high percentage of patients, so it must be used for prolonged periods of between 3 and 6 months.^[7,27]

- Oral isotretinoin

Isotretinoin is a retinoid (derived from vitamin A). Its ability to act at the level of the pathophysiological pathways responsible for this disease make it a highly effective treatment to combat severe and recalcitrant acne, as well as to prevent the extensive amount of scars that can form, or in cases of lack of response to other treatments.

It suppresses around 90% the production of sebum, inhibiting the differentiation and proliferation of sebaceous glands and prevents the relapses of acneic lesions. It has antibacterial, anti-inflammatory and anticomedogenic action.^[31,33]

This drug is highly teratogenic, so its administration is contraindicated during pregnancy, the use of contraceptives is strictly necessary during and after this treatment.^[34,35] Adverse effects on the epidermis and mucous membranes, dryness of the lips, skin, eyes. A decrease in night vision, headache, epistaxis, and back pain are also frequent.^[35]

Isotretinoin can also be associated with a mild to moderate elevation of liver enzymes and triglycerides. It is advisable to carry out a follow-up by performing periodic tests of cholesterol, fasting triglycerides and liver function.^[35]

- Oral contraceptives

They are one of the most used hormonal treatments against acne. These decrease the androgenic effect generating an ovarian suppression of androgen production by inhibiting different hormones (luteinizing and stimulating the follicle). Also due to their action they cause an increase in estrogens and a decrease in testosterone levels, decreasing the excessive production of sebum.

There is a high thromboembolic risk, which can be associated with an increased risk of cardiovascular diseases, such as thromboembolic disease, thrombotic stroke and myocardial infarction.

There are contraceptives composed of progestogens that have an intrinsic androgenic activity that can aggravate acne, but at present the 3rd generation progestogens (desogestrel and norgestimate) are more used due to their low intrinsic androgenic activity.

In Spain, the combination of ethinyl estradiol and cyproterone acetate are mainly used as anti-acne treatment.^[33,36] They are used as first-line treatment in hyperandrogenic states associated with polycystic ovary syndrome, and in the treatment of idiopathic hirsutism and acne.^[33]

Recommendations

Given the different possible pharmacological treatments for the treatment of this condition, it is important to

know different methods and recommendations to take into account when preventing the progression of these acneic or scarring lesions and to improve the condition of the skin.

Faced with inflammation, its inadequate control leads to one of the most difficult to address topical complications of this disease, the scar sequela. Given its difficulty to treat in a pharmacological way, it would be necessary to resort to abrasive processes such as laser, dermabrasion or chemical peels that perform a deep exfoliation of the skin, renewing it to gradually eliminate those scar marks.^[37,38]

- **Hygiene:** It is essential to maintain a cleanliness of the areas affected by acne mainly to keep excess sebum under control and eliminate dirt particles from the environment. Cleaning must be delicate and gentle with the skin, so that it does not produce irritations that cause a worsening of the active lesions. Non-soap products with neutral PH are suitable.^[6]

- **Hydration:** For adequate hydration, it is advisable to use non-comedogenic creams. These creams are important to compensate for certain actiacneic treatments that cause dry skin.^[6,39]

- **Photoprotection** To avoid post-inflammatory hyperpigmentation, non-oily sunscreen should be used. Some of the anti-acne treatments produce photosensitivity, so photoprotection is essential.^[4,6]

- **Camouflage** In certain situations it is appropriate to "camouflage" the lesions caused by acne, for which the makeup used must be non-comedogenic or oil-free. Treatment.^[4, 39]

- **Dietetics:** As already mentioned, there are no studies that justify a direct influence of diet with a greater risk of presenting this skin condition, however, a healthy diet and lifestyle will always favor and be reflected throughout our body. It is advisable to maintain a healthy diet, consuming all kinds of foods such as fruits, vegetables, lean meats, avoiding processed foods, saturated fats and any type of excesses as much as possible.

Therefore, there is evidence that diet plays an important role in acne and, although it does not correspond to the definitive treatment, it achieves clinical improvement and helps the effectiveness of medical treatment.

CONCLUSIONS

The prevalence of acne in adult women has increased in recent decades, presenting mostly as persistent acne since adolescence.

The etiopathogenesis of acne in adult women presents aggravating differential factors compared to acne in adolescents and acne vulgaris in other populations, such as hormonal factors or factors related to stress, obesity, diet, the use of drugs and cosmetics, disorders of the dream.... Various etiopathogenic factors and having more sensitive and less oily skin make the management

of acne in mature women more complex than acne in other populations. Hygiene and hydration of the skin is essential, along with an approach that reduces sebum secretion, comedogenesis and inflammation.

Response to treatment is usually slow. Compared to topical treatments, mature skin tends to be more irritable to topical retinoids and antibacterials, and tolerability to the abrasive effects of benzoyl peroxide. Systemic alternatives include oral antibiotics, retinoids, and oral contraceptives. The current trend is to start treatment as early and as effectively as possible to avoid both physical and psychological alterations.

BIBLIOGRAPHY

1. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. *Lancet*. 2012; 379(9813): 361–72.
2. Real Academia Nacional de Medicina. [Internet]. Ediciones Universidad de Salamanca; 2018 [consultado 20 mayo 2021]. p. 195–200. Available in: https://dtme.ranm.es/busador.aspx?NIVEL_BUS=3&LEMA_BUS=acne
3. De puntosnegros [Internet]. Diferencia entre punto negro y espinilla [Internet]. Puntosnegros.org. 2020 Available in: <http://puntosnegros.org/diferencia-entre-punto-negro-y-espinilla/>
4. Dreno B, Bagatin E, Blume-Peytavi U, Rocha M, Gollnick H. Female type of adult acne: Physiological and psychological considerations and management. *J Dtsch Dermatol Ges*. 2018; 16(10): 1185-94.
5. Dréno B. Treatment of adult female acne: a new challenge. *J Eur Acad Dermatol Venereol*. 2015; 29(5): 14-9.
6. Bagatin E, Freitas THP, Rivitti-Machado MC, Machado MCR, Ribeiro BM, Nunes S, et al. Adult female acne: a guide to clinical practice. *An Bras Dermatol*. 2019; 94(1): 62-75.
7. Tuchayi S, Makrantonaki E *et al.* Acne vulgaris. *Nat Rev Dis Primers* [Internet]. 2015 15029. Available in: <https://doi.org/10.1038/nrdp.2015.29>
8. Capitano B, Sinagra JL, Ottaviani M, Bordignon V, Amantea A, Picardo M.
9. «Smoker's acne»: a new clinical entity? *Br J Dermatol*. 2007; 157: 1070-1.
10. Rivera R, Guerra A. Manejo del acné en mujeres mayores de 25 años. *Actas Dermosifiliogr*. 2009; 100(1): 33–7.
11. Jović A, Marinović B *et al.* The impact of psychological stress on acne. *Acta Dermatovenerol Croat* 2017; 25(2): 1133-41.
12. Layton AM, Williams C. Persistent acne in women. Implications for the patient and for therapy. *Am J Clin Dermatol*. 2006; 7: 281-90.
13. Husein-ElAhmed H. Management of acne vulgaris with hormonal therapies in adult female patients. *Dermatol Ther*. 2015; 28(3): 166-72.
14. Rodríguez A. El acné en la mujer adulta [Internet]. 2020 Available in:

- <http://www.amparorodriguez.com/acne-la-mujer-adulta/>
15. Tratamiento del acné de la espalda y del cuerpo [Internet]. 2020 Available in: <https://tratamientoacne.org/tratamiento-acne-espalda-cuerpo>
 16. Marks R. Acne and its management beyond the age of 35 years. *Am J Clin Dermatol*. 2004; 5: 459-62.
 17. Kane A, Niang SO, Diagne AC et al. Epidemiologic, clinical, and therapeutic features of acne in Dakar, Senegal. *Int J Dermatol* 2007; 46: 36-38.
 18. Nast A, Dreno B, Bettoli V, Degitz K, Erdmann R, Finlay AI et al. European evidence-based (S3) guidelines for the treatment of acne. *J Eur Acad Dermatol Venereol*. 2012; 26: 1-29.
 19. Strauss JS, Krowchuk DP, Leyden JJ, Lucky AW, Shalita MD, Siegfried EC, et al. Guidelines of care for acne vulgaris management. *J Am Acad Dermatol*. 2007; 56: 651-663.
 20. Dréno B, Bettoli V, Ochsendorf F, Layton AM, Perez M, Dakovic R. Efficacy and safety of clindamycin phosphate 1.2%/tretinoin 0.025% formulation for the treatment of acne vulgaris: pooled analysis of data from three randomised, double-blind, parallel-group, phase III studies. *Eur J Dermatol*. 2014; 24: 201-9.
 21. Sato T, Shirane T, Noguchi N, Sasatsu M, Ito A. Novel anti-acne actions of nadifloxacin and clindamycin that inhibit the production of sebum, prostaglandin E2 and promatrix metalloproteinase-2 in hamster sebocytes. *J Dermatol*. 2012; 39: 774-78.
 22. Eady EA, Gloor M, Leyden JJ. Propionibacterium acnes resistance: a world-wide problem. *Dermatology*. 2003; 206: 54-6.
 23. Dréno B, Layton A et al. Adult female acne: a new paradigm. *J Eur Acad Dermatol Venereol*. 2013; 27(9): 1063-70.
 24. Benedí J, Saavedra V. Antiacneicos. *Farm prof* [Internet]. 2007; 21(8): 44-8.
 25. Ficha técnica de Peróxido de benzoilo. [Internet]. Centro de información on line de la AEMPS. Available in: https://cima.aemps.es/cima/pdfs/es/ft/57371/57371_ft.pdf
 26. Cosmeceutical Center [Internet]. Cosmeceuticalcenter.com. Available in: <https://www.cosmeceuticalcenter.com/NEW-concepto-los-hidroxiacidos>
 27. Kainz JT, Berghammer G et al. Azelaic acid 20 % cream: effects on quality of life and disease severity in adult female acne patients. *J Dtsch Dermatol Ges*. 2016; 14(12): 1249-59.
 28. Gollnick H, Cunliffe W, Berson D, Dreno B, Finlay A, Leyden JJ, et al. Management of acne: a report from a Global Alliance to Improve Outcomes in Acne. *J Am Acad Dermatol*. 2003; 49: 1-37.
 29. Gold LS, Baldwin H, Rueda MJ, Kerrouche N, DrÉno B. Adapalene-benzoyl Peroxide Gel is Efficacious and Safe in Adult Female Acne, with a Profile Comparable to that Seen in Teen-aged Females. *J Clin Aesthet Dermatol*. 2016; 9(7): 23-9.
 30. Berson D, Alexis A. Adapalene 0.3% for the Treatment of Acne in Women. *J Clin Aesthet Dermatol*. 2013; 6: 32-35.
 31. Muñoz MJ. El acné y su tratamiento. *Offarm*. 2001; 20(8): 71-81.
 32. Bagatin E, Florez-White M, Arias-Gomez MI, Kaminsky A. Algorithm for acne treatment: Ibero-Latin American consensus.. *An Bras Dermatol*. 2017; 92(5): 689-93.
 33. Kircik LH. Fixed Combination of Clindamycin Phosphate 1.2% and Benzoyl Peroxide 3.75% Aqueous Gel: Long-Term Use in Adult Females With Moderate Acne Vulgaris. *J Drugs Dermatol*. 2017; 16(6): 543-6.
 34. Moradi Tuchayi S, Makrantonaki E, Ganceviciene R, Dessinioti C, Feldman SR, Zouboulis CC. Acne vulgaris. *Nat Rev Dis Primers*. 2015; 1(1): 15029.
 35. González-Guerra E, Universidad Internacional de La Rioja. Acné en la mujer adulta. *Más dermatol*. 2018; 30: 19-27.
 36. Haider A, Shaw JC. Treatment of acne vulgaris. *JAMA*. 2004; 292(6): 726-35.
 37. de Bastos M, Stegeman BH et al. Combined oral contraceptives: venous thrombosis. *Cochrane Database Syst Rev*. 2014; (3): CD010813.
 38. Cirigliano M, Kaminsky A. Acné, una mirada al futuro. En: *Acné. Un enfoque global*. Alfaomega grupo editorial; 2012. 339-46. Available in: <https://antoniorondonlugo.com/wp-content/uploads/2014/03/Libro-GILEAen-baja.pdf#page=355>
 40. Di Landro A, Cazzaniga S et al. Adult female acne and associated risk factors: Results of a multicenter case-control study in Italy. *J Am Acad Dermatol*. 2016; 75(6): 1134.
 41. Araviiskaia E, Dréno B. The role of topical dermocosmetics in acne vulgaris. *J Eur Acad Dermatol Venereol*. 2016; 30(6): 926-35.