ABSTRACT

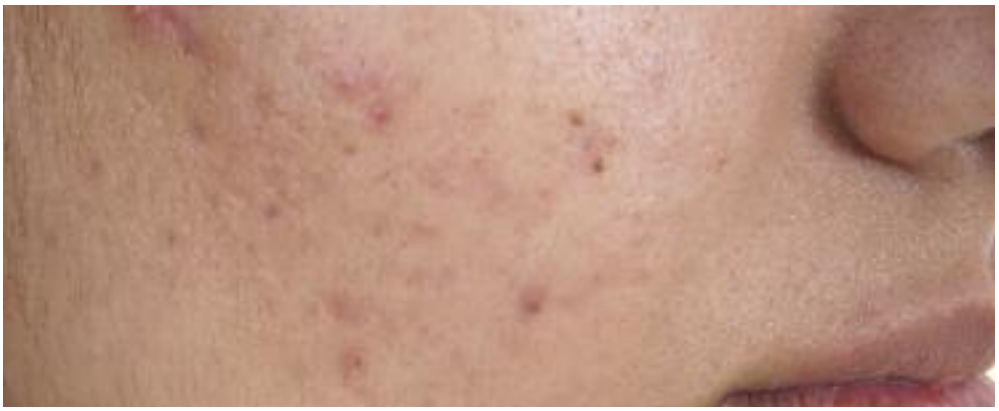
Acne vulgaris (acne) is a common affliction in adolescence and is a growing problem in adult women. Despite an increasing awareness of acne in the adult female population, there is a lack of good prospective studies assessing the severity, distribution, and differential response to treatment in this group. The long-held dogma that acne in adult women develops on the lower one-third of the face has been recently challenged, and here the authors critically review data from available literature. Moreover, while adult female acne has traditionally been defined as disease in women over age 25, it is the authors' experience that this group is subdivided into women ages 25 to 44 years, separate from perimenopausal patients, ages 45 years and up. While there is no data specifically comparing these two groups, the authors will review the existing data and provide practical recommendations based on our experience in treating these groups of patients. Finally, while there is a lack of data on this subject, it is the group's opinion that adherence to medication regimens is likely higher in women than men, which influences therapeutic outcomes.

J Clin Aesthet Dermatol.
2017;10(1):37–46

REVIEW

Emerging Issues in Adult Female Acne

[a]JOSHUA A. ZEICHNER, MD; [b]HILLARY E. BALDWIN, MD; [c]FRAN E. COOK-BOLDEN, MD; [d]LAWRENCE F. EICHENFIELD, MD; [d]SHEILA FALLON-FRIEDLANDER, MD; [e]DAVID A. RODRIGUEZ, MD
[a]Mount Sinai Hospital, New York, New York; [b]Morristown, New Jersey; [c]Skin Specialty Dermatology, New York, New York; [d]University of California, Rady Children's Hospital, San Diego, California; [e]Dermatology Associates/Research, Coral Gables, Florida; [c]Redwood Dermatology Research, Santa Rosa, California



ACNE VULGARIS IS A COMMON skin disease and is increasingly seen in adult women.[1,2] Almost twice as many women seek help for their acne than men,[3] and one third of total acne office visits are made by women over 25 years old.[4] The objective of this article is to review the published data on adult female acne and its treatment, with a particular focus on topical therapy. The authors provide management recommendations based on critical appraisal of the data and their clinical experience.

Adult female acne has been traditionally defined as acne in women over 25 years of age and is broadly divided into persistent, new-onset, or recurrent disease. Persistent acne represents disease that presented in adolescence and continues into adulthood. New onset acne presents for the first time in adulthood. Finally, recurrent disease is acne that is present in adolescence, clears for a variable amount of time, then returns in adulthood.[5–7] Some practitioners suggest a further categorization of adult female acne into women 45 years of age and older with acne around the perimenopausal period. It is the opinion of the group that women 18 to 24 years old are more similar to adolescents than adult women with acne, and should not

Disclosure: The authors report no relevant conflicts of interest.
Author correspondence: Joshua A. Zeichner, MD; E-mail: joshua.zeichner@mountsinai.org

be included in the adult female population.

Persistent acne is the most common history observed in adult females, seen in 75 to 85 percent of cases.[7–9] Late-onset acne is much less common, developing in a reported 20 to 40 percent of women.[7,8,10]

Recurrent acne is poorly described in the literature and the least understood, but is likely much more common than reported. Current epidemiological surveys ask the age of acne onset, but rarely ask about whether there is a recurrence after a clear period after adolescence. What is also unclear is whether the clinical distribution of the acne is the same during these two periods or whether teenage acne morphs into another form in the adult female. Another unanswered question is whether severity of teenage acne impacts the reporting of recurrence, especially if initial acne was mild and not bothersome. In those cases, perhaps patients would not report previous acne.

While most studies in the literature report that acne in older women tends to be mild, the members of this group agree that the average patient they see has at least moderate disease. Moreover, they observe that many adult female acne patients present with a perioral or mandibular distribution of lesions, while younger patients do not necessarily have this clinical presentation.

WHAT CAN WE LEARN FROM SURVEYS?

Clinically based, multicenter surveys with high numbers of patients and global representation provide the best insights into skin diseases. Unfortunately, there is no definitive, prospective study categorizing the severity, distribution, type, or differential response to therapy for adult female acne. The available acne surveys use widely different age ranges and methodologies. While there are large differences among surveys, they all support the ideas that adult female acne is commonplace, more prevalent than in adult males, and may persist beyond menopause. Stress appears to be a major influence, and depression is a common comorbidity in affected women.

One large epidemiologic acne study utilized data from an administrative claims database of more 80 public and private healthcare plans and 9.6 million unique patients. Importantly, these data include only patients who sought treatment for their acne.[3] Investigators found that 61.9 percent of acne patients were over 18 years of age, with the average age being 25 years old. Two-thirds of visits (65.2%) were made by women. Depression was reported in 10.6 percent of females, compared with 5.3 percent in men, and seen most commonly in patients over 36 years old.[3] While it is unclear whether acne is the precipitating factor for depression, it is important to address it as a part of patient management.

A community-based survey of 749 patients at least 25 years old also found that acne affected women more frequently than men. Fifty-four percent of women and 40 percent of men reported having some form of acne. Moreover, acne was more severe in women. Using the Leeds Acne Grading Scale, acne with at least grade 0.75 was seen in 12 percent of women, as compared to three percent of men ($P<0.001$).[11] They also noted that acne persisted into middle age, with no substantial decrease in prevalence until after 44 years old ($P<0.001$).

A university-based survey of 1,013 subjects ages 20 years and older (mean age 48.0±16.7) reported that 73.3 percent of patients suffered some form of acne in their lifetime. While data may be biased by patients who were long-term acne sufferers, the study showed that women were more likely to report having had acne than men, with statistically significant differences across all age groups studied.[12] The majority of women (53.3%) reported that their acne improved after their teenage years. However, 50.9 percent of women 20 to 29 years old and 35.2 percent of women 30 to 39 years old reported acne. Increased severity in post-teenage years was reported in 13.3 percent of women. About a quarter of women (23.6%) reported never having acne. Of the group of premenopausal women surveyed (N=225), 62.2 percent noted that their acne got worse around the time of menstruation.[12]

Results of a self-administered, dermatologist-validated questionnaire of 3,305 women ages 25 to 40 years in France suggested that total acne prevalence was 41 percent of the population. Adult onset acne was reported by 41 percent of women. Stress was listed as a precipitating factor for acne in

half of the women surveyed.[5]

A photo-based survey of 2,895 women in the general population ages 10 to 70 years showed that 55 percent of patients had some form of acne. Of those judged to have clinical acne, half had predominantly inflammatory lesions and the rest predominantly comedonal acne. Women with inflammatory acne tended to be younger than those with comedonal acne ($P \leq 0.001$). Postmenopausal women had less acne than their age-matched peers ($P < 0.0001$). While acne peaked in teenage years, 45 percent of women aged 21 to 30, 26 percent aged 31 to 40, and 12 percent aged 41 to 50 had clinical acne.[8] Clinical acne was also more prevalent in people of color than those with lighter skin types.[13] It was also suggested that Asian women may have predominantly inflammatory acne, and Caucasians comedonal acne, but this is confounded by sampling issues. Patients were evaluated in only four cities, with some ethnicities from only a single city. Moreover, being a photographic study, acne in skin of color may have been over-represented because of the presence of hyperpigmentation in photos.

Acne is the most common diagnosis seen in United States dermatology ambulatory practices. It is uncertain whether there is truly an increase in prevalence or whether increased awareness is driving patients into the office to seek care.[11] In any case, the authors perceive a higher prevalence of adult female patients compared to the past in their practices. They also observe a higher prevalence of hormonal issues, specifically polycystic ovary syndrome (PCOS). The community-based survey conducted more than 15 years ago suggested the overall mean age of acne has increased from 20.5 to 26.5 years over a 10-year period.[11] Similarly, the ambulatory medical care survey carried out about the same time reported a mean age of acne patients at 24.3 years, with 10 percent of patients between 35 and 44 years.[14] Likely, an increase in post-adolescent patients seeking acne treatment is skewing the data. See Table 1 for a summary of data from different surveys.

PATHOGENESIS AND ETIOLOGY

Acne traditionally has been attributed to four main pathogenic factors: sebum production, *Propionibacterium acnes* colonization, follicular hyperkeratosis, and inflammation. While the same are likely involved in the development of acne in adult women, specific factors leading to new onset or recurrence in this population are unclear. Hormonal fluctuations, genetics, cosmetics, diet, tobacco use, and stress have all been attributed to causing acne in adult women and need further evaluation.[1,15]

Adult female acne is commonly referred to as "hormonal acne." However, in reality, all acne is hormonally mediated. The initial development of acne in adolescence coincides with adrenarchy, an increase in androgen production during puberty leading to a rise in sebum production. Using the term "hormonal acne" to reference adult females is a misnomer. A more appropriate term for this population would be "cyclical" or "premenstrual" acne, as all acne patients are hormone-sensitive.

Monthly hormone fluctuations across the menstrual cycle likely play a key role in acne flares. Up to 85 percent of adult women report a worsening of their acne in the days before menstruation.[5,12,15–17] The rate of premenstrual acne flares has been found to be significantly higher in women over 30 years of age compared to younger women ($P=0.03$). While some women have frank hormonal abnormalities, including hyperandrogenism or PCOS, many women are found to have hormonal levels within the range of normal. The authors theorize that in some patients, acne may be a manifestation of end-organ hypersensitivity. While androgen levels appear normal, they may be high in that particular patient. In addition, while the literature suggests that excessive skin greasiness (seborrhea) in adult women may indicate hormonal or genetic abnormalities associated with acne,[7] in clinical practice, many adult female acne patients actually present with dry skin. So the question must be raised whether excessive oiliness is truly a main factor in all adult female acne cases.

In the authors' practices, they observe a growing population of women being treated for acne in the perimenopausal period. Clinically, most of these women do not exhibit any signs of virilization. They generally have androgen levels within the normal range. However, the mean androgen levels of these women exceeds that of of age-

Table 1: Prevalence of Adult Female Acne

STUDY TYPE	NUMBER OF SUBJECTS, AGE, AND GENDER	PREVALENCE
Large-scale epidemiology survey (Yentzer et al)	Claims database representative of 9.6 million patients male and female (all age ranges)	Two-thirds (65.2%) of visits made by females Older patients (>18y) comprised 61.9% patients with acne Depression more common in females (10.6% versus 5.3% in men)
Community-based clinical examination (Gouldon et al)	749 subjects male and female (>25 years)	Clinical grade acne seen in 12% of women and 3% of men. Acne prevalence presists until after 44 years
University campus and medical complex (Collier et al)	1,103 subjects male and female (20+ years)	73.3% suffered acne at some stage Age 20–29y: 50.9% women and 42.5% men Age 30–39y: 35.2% women and 20.1% men Age 40–49y: 26.3% women and 12.0% men Age 50y and older: 15.3% women and 7.3% men
General population survey (Stern)	20,749 residents male and female (15-44 years)	Active acne in 27% of women and 34% of men
General population survey (Perkins et al)	2,895 female only (10–70 years) US (photo study)	55% had some form of acne (27% clinical acne) Age 21–30y: 45% women had clinical acne Age 31–40y: 26% women had clinical acne Age 41–50y: 12% women had clinical acne
General population survey (Poli et al)	3,305 female only (25-40 years) France	41% of women with high proportion of late-onset acne (41%). Stress main cause of acne

matched controls without acne.[8] Acne in the perimenopausal period may represent a "tipping point," a period in which ratios of hormones are such that there is excess sebaceous gland stimulation. In this case, falling estrogen levels may give rise to a relative increase in androgen levels, and this imbalance may result in acne flares.

There is likely a genetic predisposition to developing adult female acne. Two-thirds of cases report a history of at least one first-degree relative who also suffers from acne.[18] Moreover, data suggest that the daughters of adult female acne patients are at a significantly higher risk of developing acne as an adult ($P<0.001$)[19] It must be acknowledged that the true role of genetics may be clouded, as the estimated background lifetime risk of developing acne is 85 to 90

percent.[20]

Cosmetic camouflage of acne and related spots using makeup has been shown to be the single most important coping mechanism for adult female patients with acne. Educating women on the use of cosmetics has been shown to improve self-esteem and may increase adherence to medical regimens.[21] However, data suggests that cosmetics trigger acne in as many as 62 percent of cases.[7] Therefore, the use of proper, non-comedogenic and non-acnegenic cosmetics is of the utmost importance in order to avoid acne flares. Moreover, one study found that discontinuing cosmetics use was not associated with a regression of post-adolescent acne.[22] In addition to makeup itself, skin care products, such as moisturizers are commonly used along with acne medications. Limited information exists on the use of moisturizers with acne medications. One study has shown that application of a moisturizer before topical acne medications did not interfere with efficacy and enhanced tolerability of the drug.[23] Less is known about compatibility of products such as toners and sunscreens.[24]

Cigarette smoking may increase acne risk, as there is a great prevalence of acne among smokers compared to nonsmokers.[25] In addition, adult women ages 25 to 50 years who are smokers have been shown to have a higher prevalence of comedonal acne.[26] It is not known whether tobacco worsens pre-existing acne or triggers new acne in those with a genetic predisposition. Moreover, some suggest that smoking eases stress and question why it would not actually improve acne severity in those patients. There are many unanswered questions that must be further researched.

Stress-related worsening of acne is a common complaint in our practices, particularly in adult female patients. However, the role of stress in acne is poorly understood. Clear data exist that acne is associated with significant psychological stress in patients, but less decisive research shows that stress itself triggers acne. In one observational study, daily stress was shown to exacerbate acne in a third of adult female patients.[7] The theory on how stress affects the skin is linked to an increase in cortisol and androgens from the stress response associated with a rise in sebum production and resulting comedogenesis.[2,27]

There has been much media and patient attention to the association between diet and acne. While data are somewhat limited, studies have suggested that high glycemic index diets and consumption of cow's milk (particularly skim milk) may be associated with acne flares in predisposed individuals.[28,29] Foods with a low glycemic index (low in sugar and starch) as well as cow's milk substitutes like almond milk have been suggested as alternatives in concerned acne patients. In addition, a high prevalence of acne has been reported in patients with anorexia nervosa and bulimia nervosa at the time of weight gain.[28,29] The mechanisms by which this occurs is unclear. There are conflicting data on body weight and the presence of acne. While a recent study has suggested that acne is associated with a low body mass index (BMI),[30] other studies have shown a low BMI to have a reduced risk of acne.[31] More specifically, data addressing the impact of diet and acne in adult women is needed before definitive conclusions can be drawn. See Table 2 for main factors suggested to be associated with adult female acne.

Table 2: Factors suggested to be connected with adult female acne

Hormones
Genetics
Cosmetics
Diet and dieting
Tobacco
Stress

CLINICAL PRESENTATION

Adult female acne is considered by this group to be a different type of acne than that seen in adolescents. It has traditionally been described as mild-to-moderate inflammatory papules along the mandible, a so-called "surgical mask distribution."[1,10] Recently, this stereotype has been challenged, with the suggestion that adult female acne is in fact similar to that of adolescents.[32]

An international observational study concluded that the clinical presentation of acne in adult women is commonly characterized by low levels of mixed comedones and

inflammatory papules across all facial zones.[32] Three hundred seventy-four adult female acne patients (≥25 years) found that almost 90 percent of cases were similar to those seen in adolescent acne, with lesions on the cheeks, forehead, mandible, and temples, with a range of acne severity. Only 6.4 percent of women had inflammatory lesions, and a minority of patients (11.2%) had acne localized specifically to the mandibular area. While facial acne is most common, truncal lesions are found in up to 50 percent of women.[7,32]

Despite the results found from this study, the authors do not see this pattern in their clinical practices. There is a distinct group of adult women with mandibular acne, or mandibular acne along with other facial areas, which the authors feel is much more common than the 11.2 percent of cases recently reported. Moreover, they find a much higher percent than 6.4 of women have predominantly inflammatory lesions. There are many factors that have influenced these findings, including severity of patients seen and clinical history (e.g., new onset, persistent, or recurrent disease). Future studies must be performed to validate these findings.

BURDEN OF DISEASE

Acne confers a significant impact on quality of life. Adult female patients in particular often report frustration, embarrassment, and distress over acne. It is a common misconception among patients that acne does not persist past the teenage years,[21] and patients who suffer with it are not only impacted from a psychosocial perspective, but also are asking for an explanation on why it is occurring. In fact, acne may have a more significant impact on quality of life in adult female acne patients as compared to younger acne patients.[16,34]

TREATMENT OF ADULT FEMALE ACNE

The nature of the adult female acne and variability in response determine management. With frequent relapses, initial treatment with long-term maintenance is needed to keep the skin clear.[4] Moreover, treatment selection depends on the patient's childbearing potential, skin sensitivity and dryness, personal concerns about tolerability and irritation, and compatibility with current skin-care regimen.[34] Despite the prevalence of adult female acne, there are little data comparing different treatments and evaluating combination regimens. However, there are many studies demonstrating efficacy of particular products in this patient population. In the following, the authors provide guidance based on the available literature and their clinical experiences in using topical and oral treatments for adult women with acne.

TOPICAL THERAPIES

The same topical medications used for adolescents are helpful in treating adult women. These include topical retinoids, benzoyl peroxide, antibiotics, and dapsone as well as various fixed-dose combinations of these actives. Their use, however, must be adapted to the specific needs of the adult women and their skin type.

In the authors' experience, it is not uncommon to see adult women with acne and dry skin, which may be the result of decreased sebum production in this population. Tolerability is an extremely important issue in managing adult female acne patients, as topicals are commonly used in combination with cosmetics. Local side effects of topical therapy, such as cutaneous irritation, erythema, dryness, peeling, and scaling, can lead to poor adherence.[35,36]

While studied in psoriasis patients and not in acne patients, studies have shown that better regimen adherence ultimately results in better efficacy.[37]

Treatment guidelines suggest the use of topical retinoids in adult female patients as monotherapy for patients with mild comedonal acne, or as part of a combination regimen for moderate-to-severe disease.[38,39] Their use, however, must be adjusted to the skin of older patients, who produce less sebum and may be more susceptible to irritation. For this reason, perhaps lower concentrations and emollient formulations may be beneficial.[6,34] In addition, education on the use of appropriate moisturizers and gentle, non-soap cleansers with pH close to skin should be a part of the patient's treatment plan.[30]

Several topical retinoids have been evaluated specifically in the adult female acne population. A *post hoc* analysis of two Phase 2 and 3 studies with adapalene 0.3% gel (N=74) showed greater efficacy than vehicle in reducing total lesion

counts in women aged 18 to 41 years (P=0.045), similar to the results seen in the overall study population. The median percent reductions in inflammatory and comedonal lesions (61.2% and 50.7%) favored adapalene 0.3% gel, but differences were not significant.[40] In addition, a subgroup analysis of the pooled results from three pivotal studies with clindamycin 1.2%-tretinoin 0.025% gel in patients over 18 years old reported greater median percent reductions in inflammatory and comedonal lesions in adult female patients compared to adult male patients (72.4% and 55.2% versus 66.7% and 53.3%, respectively).[41] In females patients (N=471), clindamycin 1.2%-tretinoin 0.025% was significantly more effective than the monads or vehicle in reducing inflammatory lesions (P<0.03), but only significantly more effective than clindamycin in reducing comedonal lesions (P<0.02).[41]

Benzoyl peroxide is comedolytic and antimicrobial, with activity against *Priopionbacterium acnes*.[42] It is commonly prescribed as part of a fixed-dose combination drug alongside a topical antibiotic or retinoid. Several fixed combinations have been evaluated in the adult female population.

Subpopulation analysis of the pivotal Phase 3 clinical trial with clindamycin 1.2%-benzoyl peroxide 3.75% gel found statistically greater improvements in female compared to male patients. In moderate-to-severe acne, the mean percent reduction in inflammatory and comedonal lesions was 65.3 percent and 55.7 percent in females (N=123), compared with 55.8 percent and 48.1 percent in males (N=130), respectively (P=0.049 for inflammatory lesions; P=0.084 for comedonal lesions).[43] An additional *post hoc* analysis of the 72 adult female patients ages 25 and older found a mean percent reduction in inflammatory and comedonal lesions of 68.7 percent and 60.4 percent after 12 weeks of treatment (P=0.019 and P=0.020 versus vehicle, respectively). No substantive differences were seen in cutaneous tolerability compared to vehicle.[44]

A meta-analysis of 254 patients from three Phase 2 and 3 clinical studies with adapalene 0.1%-benzoyl peroxide 2.5% gel evaluated use in adult women ages 25 years and up (N=130). A median percent reduction in inflammatory and comedonal lesions of 73.0 percent and 70.0 percent was found in adult women at 12 weeks (P<0.001 and $P\leq$0.016, versus vehicle).[45]

A pooled analysis of two Phase 3 studies with dapsone 5% gel reported statistically significant lesion reductions in women compared to men. In women 18 years and up, the mean percent reductions in inflammatory and comedonal lesions were 46.6 percent and 39.8 percent, respectively (compared with 35.8% and 28.5% in males, P<0.001).[46] The vehicle appeared to have a greater effect in females, which in our opinion also contributes to the overall effect of the drug. In addition, a *post hoc* analysis of the female patients compared efficacy in adolescents (12–17 years) to adult female (>18 years old) patients. Reductions in comedonal lesions were greater in the adult female patients compared to adolescent female patients (P<0.0001), but there was no statistical differences in inflammatory lesion reductions between the subpopulations.[47] A summary of the clinical trials in adult female acne are shown in Table 3.

ORAL AGENTS

Oral antibiotics, isotretinoin, and hormonal therapies are all commonly used agents to treat acne in adult women. A comprehensive discussion of all oral agents is beyond the scope of this paper. Here, the authors focus on hormonal options, both oral contraceptive pills and spironolactone.

Several large studies have documented the usefulness of oral contraceptive pills (OCPs) containing ethinyl estradiol in combination with several different progestins to treat acne in women.[48] There are four OCPs currently United States Food and Drug Administration (FDA) approved to treat acne, without any significant efficacy differences among them. While OCPs may increase the risk of deep vein thrombosis (DVT), the overall risk remains low (2–4/10,000, compared to 1 in 10,000 for non-users). Products containing drospirenone, desogestrel, and gestodene appear to increase the risk of DVT slightly more than other OCPs; however, their DVT risks are still lower than the DVT risk in pregnant women. While not all of the opinion leaders involved in this

Table 3. Clinical trials in adult female acne (*post hoc* analyses and meta-analyses)

STUDY	ADULT FEMALE GROUP (AGE/TOTAL N)	MEAN BASELINE INFLAMMATORY LESIONS	MEAN BASELINE NONINFLAMMATORY LESIONS	MEAN PERCENT (%) CHANGE IN INFLAMMATORY LESION COUNTS ACTIVE/VEHICLE*	MEAN PERCENT (%) CHANGE IN NONINFLAMMATORY LESION COUNTS ACTIVE/VEHICLE*
Clindamycin 1.2%-benzoyl peroxide 3.75% gel (Zeichner et al)	>25 yrs of age (N=72)	25.3	34.8	68.7 *(73.1)*/39.7 *(41.8)*	60.4 (67.7)/34.0 (45.4)
Adapalene 0.1%-benzoyl peroxide 2.5% gel (Stein Gold et al)	>25 yrs of age (N=254)	24.25	40.0	*(73.0)* /*(41.0)*	*(70.0)*/*(45.0)*
Dapsone 5% gel (Del Rosso et al)	≥18 yrs of age (N=434)	27	42.3	60.0/56.8	47.4/42.3
Adapalene 0.3% gel (Berson et al)	18-41 yrs of age (N=117)	Unknown	Unknown	*(61.2)*/*(45.8)*	*(50.7)*/*(34.8)*
Clindamycin 1.2%-tretinoin 0.025% gel (Dreno et al)	≥18 yrs of age (N=1194)	Unknown	Unknown	*(72.4)*/*(55.7)*	*(66.7)*/*(38.7)*

* Data in brackets and italics are median % change in lesion counts

publication prescribe OCPs themselves, all advocate their use.

Standard of care for prescribing OCPs requires a thorough history and physical examination to rule out other conditions that increase risk for thromboembolism. Risk factors include migraine headaches with aura, cardiovascular disease with hypertension, and a family or personal history of thromboembolic disease. Cigarette smoking and increasing age (>35 years old) are also contraindications as they increase the risk of thromboembolic events. In addition, all patients should have a blood pressure reading and negative pregnancy test prior to initiating therapy.

In the event that a practitioner is not comfortable prescribing OCPs, or if the patient is high risk, the authors advise involving gynecology.

While spironolactone is not FDA approved to treat acne, it has been used off-label for decades in treating adult women. It is a weak diuretic with anti-androgen properties that competes with testosterone for binding the androgen receptor on the sebaceous gland. Typical dosage ranges from 50 to 200mg per day, taken with food to enhance absorption. The consensus of the group is to prescribe the drug in two divided doses during the day. Common side effects include dose-related breast tenderness and menstrual irregularities. When spironolactone is used along with OCPs, the OCP mitigates any effect on the menstrual cycle. Spironolactone is a potassium-sparing diuretic, and salt substitutes, other potassium-sparing anti-hypertensives, and potassium-rich coconut water should be avoided. Of note, drospirenone is a spironolactone relative, and drospirenone containing OCPs offer a potassium-sparing effect. While there is no consensus on requirements for routine blood monitoring, a recent study of healthy women on spironolactone found the risk of hyperkalemia to be less than one percent, similar to that of the general population.[49] While some of the group monitor all patients regularly, it is particularly appropriate for patients on higher doses (e.g., 100mg/day), those with risk factors, or those on other drugs that may raise potassium levels.

CONCLUDING REMARKS

Adult female acne is common in dermatology practice. Unfortunately, clinical studies specifically evaluating prevalence, presentation, and treatment of this population are lacking in the literature. The guidance provided in this paper comes from the few studies currently available, along with the authors' personal experiences as key opinion leaders in treating acne.

The authors suggest that adult female acne should be sub-

categorized into the following two distinct groups: post-adolescent patients ages 25 to 44 years and older and perimenopausal patients, ages 45 years and older. In the authors' experience, while some adult female acne patients do have acne similar to that of adolescents, there is a large, distinct group who suffer from inflammatory disease localized to the lower one-third of the face and neck. Moreover, just as the treatment needs of adult women are different than adolescents, the needs of patients in these two distinct adult female groups are likely different as well.

Treatment outcomes rely heavily on drug tolerability and adherence to a prescribed regimen. As many women self-treat with a variety of OTC products and cosmetics, it is important for a prescription to fit into an existing skin-care regimen. It is also important to elicit a history of skin sensitivity, dryness, and personal preferences to select an appropriate medication. Whether the regimen involves a single topical drug, a combination regimen, or concurrent use of an oral agent, up-to-date knowledge of adult female acne along with appropriate patient education optimize the chance for a good therapeutic outcome.

ACKNOWLEDGMENT

The authors acknowledge Brian Bulley, MSc, of Konic Limited for medical writing support. Valeant Pharmaceuticals North America LLC funded Inergy's activities pertaining to this manuscript.

REFERENCES

1. Preneau S, Dreno B. Female acne—a different subtype of teenager acne? *J Eur Acad Dermatol Venereol.* 2012;26(3):277–282.
2. Knaggs HE, Wood EJ, Rizer RL, et al. Post-adolescent acne. *Int J Cosmet Sci.* 2004;26(3):129–138.
3. Yentzer BA, Hick J, Reese EL, et al. Acne vulgaris in the United States: a descriptive epidemiology. *Cutis.* 2010;86:94–99.
4. Zeichner JA. Evaluating and treating the adult female patient with acne. *J Drugs Dermatol.* 2013;12:1416–1427.
5. Poli F, Dreno B, Verschoore M. An epidemiological study of acne in female adults: results of a survey conducted in France. *J Eur Acad Dermatol Venereol.* 2001;15:541–545.
6. Williams C, Layton AM. Persistent acne in women: implications for the patient and for therapy. *Am J Clin Dermatol.* 2006;7:281–290.
7. Dumont-Wallon G, Dreno B. Specificity of acne in women older than 25 years. *Presse Med.* 2008;37:585–591.
8. Perkins AC, Maglione J, Hillebrand GG, et al. Acne vulgaris in women: prevalence across the life span. *J Womens Health* (Larchmt). 2012;21:223–230.
9. Kim GK, Michaels BB. Post-adolescent acne in women: more common and more clinical considerations. *J Drugs Dermatol.* 2012;11:708–713.
10. Holzmann R, Shakery K. Postadolescent acne in females. *Skin Pharmacol Physiol.* 2014; 27(Suppl. 1): 3–8.
11. Goulden V, Stables GI, Cunliffe WJ. Prevalence of facial acne in adults. *J Am Acad Dermatol.* 1999; 41: 577–580.
12. Collier CN, Harper JC, Cantrell WC, et al. The prevalence of acne in adults 20 years and older. *J Am Acad Dermatol.* 2008;58:56–59.
13. Perkins AC, Cheng CE, Hillebrand GG, et al. Comparison of the epidemiology of acne vulgaris among Caucasian, Asian, Continental Indian and African American women. *J Eur Acad Dermatol Venereol.* 2011;25:1054–1060.
14. McConnell RC, Fleischer AB Jr, Willford PM, et al. Most topical tretinoin treatment is for acne vulgaris through the age of 44 years: an analysis of the national ambulatory medical care survey, 1990–1994. *J Am Acad Dermatol.* 1998;38:221–226.
15. Shaw JC, White LE. Persistent acne in adult women. *Arch Dermatol.* 2001;137(9):1252–1253.
16. Goulden V, Clark SM, Cunliffe WJ. Post-adolescent acne: a review of clinical features. *Br J Dermatol.* 1997;136:66–70.
17. Lucky AW. Quantitative documentation of a premenstrual flare of facial acne in adult women. *Arch Dermatol.* 2004;140:423–424.
18. Lasek RJ, Chren MM. Acne vulgaris and the quality of life of adult dermatology patients. *Arch Dermatol.* 1998;134:454–458.
19. Goulden V, McGeown CH, Cunliffe WJ. The familial risk of adult acne: a comparison between first-degree relatives of affected and unaffected individuals. *Br J Dermatol.* 1999;141:297–300.
20. Danby FW. Acne: causes and practical management. John Wiley & Sons Ltd.; 2015.
21. Tanghetti EA, Kawata AK, Daniels Sr, et al. Understanding the burden of adult female acne. *J Clin Aesthet Dermatol.* 2014;7:22–30.
22. Williams C, Layton AM. Persistent acne in women: implications for the patient and for therapy. *Am J Clin Dermatol.* 2006;7:281–290.
23. Zeichner JA, Patel RV, Haddican M, et al. Efficacy and safety of a ceramide containing moisturizer followed by fixed-dose clindamycin phosphate 1.2%/benzoyl peroxide 2.5% gel in the morning in combination with a ceramide containing moisturizer

followed by tretinoin 0.05% gel in the evening for the treatment of facial acne vulgaris. *J Drugs Dermatol.* 2012;11(6):748–52.
24. Bhatia N, Pillai R. Randomized, observer-blind, split-face compatibility study with clindamycin phosphate 1.2%/benzoyl peroxide 3.75% gel and facial foundation makeup. *J Clin Aesthet Dermatol.* 2015;8(9):25–32.
25. Schäfer T, Nienhaus A, Vieluf D, et al. Epidemiology of acne in the general population: the risk of smoking. *Br J Dermatol.* 2001;145:100–104.
26. Capitanio B, Sinagra JL, Ottaviani M, et al. "Smoker's acne": a new clinical entity? *Br J Dermatol.* 2007;157:1070–1071.
27. Kligman AM. Post adolescent acne in women. *Cutis.* 1991;48:75–77.
28. Gupta MA, Gupta AK. The psychological comorbidity in acne. *Clin Dermatol.* 2001;19:360–363.
29. Danby FW. Nutrition and acne. *Clin Dermatol.* 2010; 28(6):598–604.
30. Yang JH, Weng SL, Lee CY, et al. A comparative study of cutaneous manifestations of hyperandrogenism in obese and non-obese Taiwanese women. *Arch Gynecol Obstet.* 2010;282(3):327–333.
31. Di Landro A, Cazzaniga S, Parazzini F, et al. Family history, body mass index, selected dietary factors, menstrual history, and risk of moderate to severe acne in adolescents and young adults. *J Am Acad Dermatol.* 2012;67:1129–1135.
32. Dreno B, Thiboutot D, Layton AM, et al. Large-scale international study enhances understanding of an emerging acne population: adult females. *J Eur Acad Dermatol Venereol.* 2015;29(6):1096–1106.
33. Tan JK, Li Y, Fung K et al. Divergence of demographic factors associated with clinical severity compared with quality of life impact in acne. *J Cutan Med Surg.* 2008;12:235–242.
34. Marks R. Acne and its management beyond the age of 35 years. *Am J Clin Dermatol.* 2004;5:459–462.
35. Akomeah FK. Topical dermatological drug delivery: Quo Vardis? *Curr Drug Deliv.* 2010;7(4):283–296.
36. Castro GA, Ferreira LA. Novel vesicular and particlulate drug delivery system for topical treatment of acne. *Expert Opin Drug Deliv.* 2008;5(6):665–679.
37. Zaghloul SS, Goodfield MJ. Objective assessment of compliance with psoriasis treatment. *Arch Dermatol.* 2004;140(4):408–414.
38. Thiboutot D, Gollnick H, Bettoli V, et al. New insights into the management of acne: an update from the Global Alliance to Improve Outcomes in Acne group. *J Am Acad Dermatol.* 2009;60:S1–S50.
39. Nast A, Dreno B, Bettoli V, et al. European evidence-based (S3) guidelines for the treatment of acne. *J Eur Acad Dermatol Venereol.* 2012;26(Suppl. 1):1–29.
40. Berson D, Alexis A. Adapalene 0.3% for the treatment of acne in women. J Clin Aesthet Dermatol. 2013;6(10):32–35.
41. Dreno B. Treatment of adult female acne: a new challenge. *J Eur Acad Dermatol Venereol.* 2015;29(Suppl 5):14–19.
42. Tanghetti E. The evolution of benzoyl peroxide therapy. *Cutis.* 2008;5(Suppl):5–11.
43. Harper JC. The efficacy and tolerability of a fixed combination clindamycin (1.2%) and benzoyl peroxide (3.75%) aqueous gel in patients with facial acne vulgaris: gender as a clinically relevant outcome variable. *J Drugs Dermatol.* 2015;14(4):381–384.
44. Zeichner JA. The efficacy and tolerability of a fixed combination clindamycin (1.2%) and benzoyl peroxide (3.75%) aqueous gel in adult females with facial acne vulgaris. *J Clin Aesthetic Dermatol.* 2015;8(4):21–25.
45. Stein Gold L, Dreno B, Kerrouche N, et al. Adapalene-benzoyl peroxide gel is efficacious and safe in adult female acne. Presented at Maui Derm; Maui, Hawaii; January 2015.
46. Tanghetti E, Harper JC, Oefelein MG. The efficacy and tolerability of dapsone 5% gel in female vs. male patients with facial acne vulgaris: gender as a clinically relevant outcome variable. *J Drugs Dermatol.* 2012;11(12):1417–1421.
47. Del Rosso JQ, Kircik L, Gallagher CJ. Comparative efficacy and tolerability of dapsone 5% gel in adult versus adolescent females with acne vulgaris. *J Clin Aesthet Dermatol.* 2015;8(1):31–33.
48. Arowojolu AO, Gallo MF, Lopez LM, et al. Combined oral contraceptive pills for treatment of acne. *Cochrane Database Syst Rev.* 2012;Jun 13;6:CD004425.
49. Plovanich M, Weng QY, Mostaghimi A. Low usefulness of potassium monitoring among healthy young women taking spironolactone for acne. *JAMA Dermatol.* 2015;151(9):941–944.