

Spironolactone for Acne: Practical Strategies for Optimal Clinical Outcomes

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PRACTICE POINTS

- Spironolactone is an effective systemic treatment for women with acne and likely is an underutilized alternative to oral antibiotics.
- We recommend a starting dose of 100 mg/d, which is well tolerated by most patients and has superior effectiveness to lower doses.
- Potassium monitoring is of low usefulness in young healthy women, and an association between spironolactone use and increased risk for cancer has not been identified.

Spironolactone is an effective systemic treatment for acne in women and likely is an underutilized alternative to oral antibiotics. It is used off label for all types of acne and has shown effectiveness for both facial and truncal acne. We recommend a starting dose of 100 mg/d, as most patients can tolerate it and it has superior effectiveness to lower doses. The most common adverse effects of spironolactone are lightheadedness; headache; and menstrual irregularities, which tend to be dose dependent and can be prevented or treated using combined oral contraceptives. Potassium monitoring is of low usefulness in young healthy women, and studies have not identified an association between spironolactone use and increased risk for cancer. This article provides an overview of spironolactone for the treatment of acne, including recent clinical trials and practical strategies for patient selection, dosing, adverse effect management, and monitoring.

Spironolactone is increasingly used off label for acne treatment and is now being prescribed for women with acne at a frequency similar to oral antibiotics.^{1,2} In this article, we provide an overview of spironolactone use for acne treatment and discuss recent clinical trials and practical strategies for patient selection, dosing, adverse effect management, and monitoring (Table).

History and Mechanism of Action

Because sebaceous gland activity is an important component of acne pathogenesis and is regulated by androgens,³ there has long been interest in identifying treatment strategies that can target the role of hormones in activating the sebaceous gland. In the 1980s, it became apparent that spironolactone, originally developed as a potassium-sparing diuretic, also might possess antiandrogenic properties that could be useful in the treatment of acne.⁴ Spironolactone has been found to decrease testosterone production, inhibit testosterone and dihydrotestosterone binding to androgen receptors,⁵⁻⁸ and block 5 α -reductase receptors of the sebaceous glands of skin.⁹

In 1984, Goodfellow et al¹⁰ conducted a trial in which 36 male and female patients with severe acne were randomized to placebo or spironolactone doses ranging from 50 to 200 mg/d. They found that spironolactone resulted in dose-dependent reductions of sebum production as well as improvement in patient- and clinician-reported assessments of acne. In 1986, another placebo-controlled crossover trial by Muhlemann et al¹¹ provided further support for the effectiveness of spironolactone for acne. This trial randomized 21 women to placebo or spironolactone 200 mg/d and found that spironolactone was associated with statistically significant ($P < .001$) improvements in acne lesion counts.

Recent Observational Studies and Trials

Following these early trials, several large case series have been published describing the successful use of spironolactone for acne, including a 2020 retrospective case series from the Mayo Clinic describing 395 patients.¹² The investigators found that almost 66% of patients had a complete response and almost 85% had a complete response or a partial response greater than 50%. They also found that the median time to initial response and maximal response were 3 and 5 months, respectively, and that efficacy was

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observed across acne subtypes, including for nodulocystic acne.¹² In addition, a 2021 case series describing 403 patients treated with spironolactone found that approximately 80% had reduction or complete clearance of acne, with improvements observed for both facial and truncal acne. In this cohort, doses of 100 to 150 mg/d typically were the most successful.¹³ A case series of 80 adolescent females also highlighted the efficacy of spironolactone in younger populations.¹⁴

Adding to these observational data, the multicenter, phase 3, double-blind Spironolactone for Adult Female Acne (SAFA) trial included 410 women (mean age, 29.2 years) who were randomized to receive either placebo or intervention (spironolactone 50 mg/d until week 6 and 100 mg/d until week 24).¹⁵ At 24 weeks, greater improvement in quality of life and participant self-assessed improvement were observed in the spironolactone group. In addition, at 12 weeks, rates of success were higher in the spironolactone group using the Investigator Global Assessment score (adjusted odds ratio 5.18 [95% CI, 2.18-12.28]). Those randomized to receive spironolactone also had lower rates of oral antibiotic use at 52 weeks than the placebo group did (5.8% vs 13.5%, respectively).

In the SAFA trial, spironolactone was well tolerated; the most common adverse effects relative to placebo were lightheadedness (19% for spironolactone vs 12% for placebo) and headache (20% for spironolactone vs 12% for placebo). Notably, more than 95% of patients were able to increase from 50 mg/d to 100 mg/d at week 6, with greater than 90% tolerating 100 mg/d. As observational data suggest that spironolactone takes 3 to 5 months to reach peak efficacy, these findings provide further support that starting at a dose of at least 100 mg/d is likely optimal for most patients.¹⁶

A Potential Alternative to Oral Antibiotics

Oral antibiotics such as tetracyclines have long played a central role in the treatment of acne and remain a first-line treatment option.¹⁷ In addition, many of these antibiotic courses exceed 6 months in duration.¹ In fact, dermatologists prescribe more antibiotics per capita than any other specialty^{1,18-20}; however, this can be associated with the development of antibiotic resistance,^{21,22} as well as other antibiotic-associated complications, including inflammatory bowel disease,²³ pharyngitis,²⁴ *Clostridium difficile* infections, and cancer.²⁵⁻²⁹

In addition to these concerns, many patients may prefer nonantibiotic alternatives to oral antibiotics, with more than 75% preferring a nonantibiotic option if available. For female patients with acne, antiandrogens such as spironolactone have been suggested as a potential alternative.³⁰ A 10-year retrospective study of female patients with acne found that those who had ever received hormonal therapy (ie, spironolactone or a combined oral contraceptive) received fewer cumulative days of oral antibiotics than those who did not (226 days vs 302 days, respectively).³¹ In addition, while oral antibiotics were

the most common initial therapy prescribed for patients, as they progressed through their treatment course, more patients ended up on hormonal therapy than oral antibiotics. This study suggests that hormonal therapy such as spironolactone could represent an alternative to the use of systemic antibiotics.³¹

Further supporting the role of spironolactone as an alternative to oral antibiotics, a 2018 analysis of claims data found that spironolactone may have similar effectiveness to oral antibiotics for the treatment of acne.³² After adjusting for age and topical retinoid and oral contraceptive use, this study found that there was no significant difference in the odds of being prescribed a different systemic treatment within 1 year (ie, treatment failure) among those starting spironolactone vs those starting oral tetracycline-class antibiotics as their initial therapy for acne.

A multicenter, randomized, double-blind trial (Female Acne Spironolactone vs doxyCycline Efficacy [FASCE]) also evaluated the comparative effectiveness of doxycycline 100 mg/d for 3 months followed by an oral placebo for 3 months vs spironolactone 150 mg/d for 6 months among 133 adult women with acne. This study found that spironolactone had statistically significantly greater rates of Investigator Global Assessment treatment success after 6 months (odds ratio 2.87 [95% CI, 1.38-5.99; $P=.007$]).³³ Since spironolactone historically has been prescribed less often than oral antibiotics for women with acne, these findings support spironolactone as an underutilized treatment alternative. The ongoing Spironolactone versus Doxycycline for Acne: A Comparative Effectiveness, Noninferiority Evaluation trial—a 16-week, blinded trial comparing 100 mg/d doses of both drugs—should provide additional evidence regarding the relative role of spironolactone and oral antibiotics in the management of acne.³⁴

Ultimately, the decision to use spironolactone or other treatments such as oral antibiotics should be based on shared decision making between clinician and patient. Spironolactone has a relatively slow onset of efficacy, and other options such as oral antibiotics might be preferred by those looking for more immediate results; however, as women with acne often have activity that persists into adulthood, spironolactone might be preferable as a long-term maintenance therapy to avoid complications of prolonged antibiotic use.³⁵ Comorbidities also will influence the optimal choice of therapy (eg, spironolactone might be preferred in someone with inflammatory bowel disease, and oral antibiotics might be preferred in someone with orthostatic hypotension).

Patient Selection

Acne occurring along the lower face or jawline in adult women sometimes is referred to as hormonal acne, but this dogma is not particularly evidence based. An observational study of 374 patients found that almost 90% of adult women had acne involving multiple facial zones with a spectrum of facial acne severity similar

TABLE. Spironolactone for Treatment of Acne

Recommended dosing	Start at 100 mg/d (either once daily or divided dosing), ^a can begin with 50 mg/d for the first wk and increase to 100 mg/d if no side effects; can increase to 150-200 mg/d at follow-up if not at goal or reduce as acne clears or if side effects occur
Adverse effects	Lightheadedness/dizziness/vertigo, headache, diuresis, menstrual irregularities (more likely with doses >100 mg/d, can prevent or treat with combined oral contraceptives)
Potassium monitoring	Potassium monitoring is of low usefulness for healthy young women—consider monitoring for patients with risk factors for hyperkalemia (eg, age, medications, comorbidities) and check levels 1 wk after starting spironolactone; spironolactone can be safely prescribed with drospirenone-containing combined oral contraceptives as there have been concerns about drospirenone increasing risk of hyperkalemia.

^aA higher dosage may be required for patients with polycystic ovary syndrome. For those with a history of orthostasis, consider a lower starting dose of 25-50 mg/d.

to that in adolescents.³⁶ Only a small subset of these patients (11.2%) had acne localized solely to the mandibular area. In addition, acne along the lower face is not predictive of hyperandrogenism (eg, polycystic ovary syndrome).³⁷ Antiandrogen therapies such as spironolactone and clascoterone are effective in both men and women with acne^{10,38} and in adolescents and adults, suggesting that hormones play a fundamental role in all acne and that addressing this mechanism can be useful broadly. Therefore, hormonal therapies such as spironolactone should not be restricted to only adult women with acne along the lower face.

While spironolactone can be effective for acne treatment in any age group, it may be most effective for adult women with acne. In the SAFA trial, prespecified subgroup analyses showed a statistically significant ($P=.005$) interaction term for age (categorized as <25 years and ≥ 25 years), which suggested that spironolactone might be a more effective treatment for women 25 years and older.¹⁵ In addition, subgroup analyses in the aforementioned 2018 analysis of claims data found that spironolactone was more effective relative to oral antibiotics in adults vs adolescents.³² Despite these limitations, several case series have highlighted that spironolactone is effective among adolescent populations with acne. A case series of spironolactone use in 73 patients aged 19 years or younger found that 68% of patients demonstrated resolution or improvement in their acne after spironolactone treatment.³⁹ Another case series among 80 adolescent females reported 80% of patients experiencing improvement of their acne.¹⁴

For those with more severe acne, spironolactone can be combined with other complementary treatment approaches such as topicals, oral antibiotics, or procedural modalities.⁴⁰

Dosing

We recommend starting spironolactone at a dose of 100 mg/d (the patient can take 50 mg/d for 1 week, then increase to 100 mg/d if there are no adverse effects at the

lower dose). In the 1984 trial by Goodfellow et al,¹⁰ participants were randomized to doses of 50 mg/d, 100 mg/d, 150 mg/d, and 200 mg/d. In this trial, efficacy assessed by objective and subjective outcomes did not plateau until doses of 100 mg/d to 150 mg/d. In addition, a case series of 403 patients found that the most successful dosage of spironolactone generally was 100 mg/d or higher.¹³ Most of the patients who were started at this dosage either stayed at this level or escalated, whereas patients who started at lower dosages (25-75 mg/d) frequently increased their dosage over time. The SAFA trial also highlighted that most patients can tolerate a spironolactone dose of 100 mg/d.¹⁵ For specific populations, such as patients with polycystic ovary syndrome, a higher dose (mean dosage of 143 mg/d) may be required for efficacy.⁴¹ Given the slow onset of efficacy, typically taking 3 to 5 months, and the low rate of adverse effects, we believe the optimal starting dose is 100 mg/d to 150 mg/d. If adverse effects occur or lesions clear, then the dosage may be reduced.

Adverse Effects

Spironolactone generally is well tolerated; in the SAFA and FASCE trials, fewer than 1% of participants discontinued due to adverse effects.^{15,33} Rates of discontinuation due to adverse effects typically have been less than 5% in case series of patients treated in routine clinical practice.¹²⁻¹⁴

Because spironolactone is a diuretic and antihypertensive, the most common adverse effects are related to these characteristics. In the SAFA trial, dizziness, lightheadedness, and vertigo were reported more commonly in the spironolactone group than in the placebo group (19% vs 12%, respectively). Similarly, headaches also were reported more frequently in the spironolactone group than in the placebo group (20% vs 12%, respectively).¹⁵ One case series found that, among the 267 patients on spironolactone whose blood pressure was monitored, the mean reduction in systolic blood pressure was 3.5 mm Hg and the mean reduction in diastolic blood pressure was 0.9 mm Hg.¹³ For those with baseline orthostasis or in those who experience adverse effects related to

hypotension, reducing the dose often can be helpful. Of note, while doses of 100 mg/d to 150 mg/d often are the most effective, randomized trials have found that spironolactone still can be effective for acne at doses as low as 25 mg/d to 50 mg/d.^{10,38}

Menstrual irregularities are another commonly cited adverse effect of spironolactone. While a systematic review found that 15% to 30% of patients treated with spironolactone experience menstrual irregularities, it has been difficult to evaluate whether this is due to the medication or other comorbidities, such as polycystic ovary syndrome.⁴² Notably, in the SAFA trial, rates of menstrual irregularities were equivalent between the spironolactone and placebo groups at a dose of 100 mg/d (32% vs 35%, respectively).¹⁵ In contrast, in the FASCE trial, menstrual irregularities were more commonly reported at a dose of 150 mg/d.³³ These findings are consistent with observational data suggesting that menstrual irregularities are much more common at spironolactone doses greater than 100 mg/d.⁴² Additionally, some evidence supports that for some patients these menstrual irregularities may resolve within 2 to 3 months of continued treatment.⁴³ It has been noted in several studies that menstrual irregularities are less likely to occur in patients who are using combined oral contraceptives; therefore, for patients who are amenable and have no contraindications, combined oral contraceptives can be considered to prevent or address menstrual irregularities.^{13,42,44}

More generally, combined oral contraceptives can be an excellent combination with spironolactone, as they have complementary characteristics. Spironolactone primarily blocks the effects of androgens, while combined oral contraceptives predominantly block the production of androgens. Whereas spironolactone typically causes hypotension and menstrual irregularities, combined oral contraceptives cause hypertension and help to regulate the menstrual cycle.

Spironolactone carries an official US Food and Drug Administration warning regarding possible tumorigenicity that is based on animal studies that used up to 150 times the normal dose of spironolactone used in humans⁴⁵; however, observational studies in humans have not identified such an association when spironolactone is used in normal clinical settings. A systematic review and metaanalysis in 2022 reviewed data from a total population of more than 4 million individuals and found that there was no statistically significant association between spironolactone use and the risk for breast, ovarian, bladder, kidney, gastric, or esophageal cancers.⁴⁶ Additional studies also found no association between spironolactone use and cancers.⁴⁸ A more recent cohort study specifically among patients treated with spironolactone for acne also found no significant increased risk for breast cancer.⁴⁹

Combined oral contraceptives are associated with an increased risk for venous thromboembolisms, and there have been concerns that this risk may be greater

in combined oral contraceptives that contain drospirenone.⁵⁰ Drospirenone is molecularly related to spironolactone, which has prompted the consideration of whether spironolactone use also conveys a risk for venous thromboembolism. Reassuringly, a retrospective study of claims data found that individuals on spironolactone were not more likely to develop a pulmonary embolism or a deep venous thrombosis than matched controls treated with tetracycline antibiotics, with a point estimate favoring decreased risk.⁵¹

Monitoring

Given that one of spironolactone's mechanisms of action is aldosterone antagonism and thus the inhibition of potassium excretion, there have been concerns regarding risk for hyperkalemia. A retrospective study analyzing data from 2000 to 2014 found that, among 974 young women receiving spironolactone therapy, the rate of hyperkalemia was 0.72%, which is equivalent to the 0.76% baseline rate of hyperkalemia in the same population.⁵² Subsequent studies also have found that spironolactone does not appear to be associated with a meaningful risk for hyperkalemia among young healthy patients treated for acne.^{38,53} These studies suggest that routine potassium monitoring is of low usefulness for healthy young women taking spironolactone for acne. The 2024 American Academy of Dermatology guidelines on the management of acne also state that potassium monitoring is not needed in healthy patients but that potassium testing should be considered for those with risk factors for hyperkalemia (eg, older age, medical comorbidities, medications).⁴⁰ Clinicians should still engage in shared decision making with patients to determine whether to check potassium. If potassium is to be monitored, it should be checked 1 to 2 weeks after spironolactone is started.^{45,54}

Since drospirenone also has aldosterone antagonistic properties,⁵⁵ there have been concerns about whether concomitant use of spironolactone and drospirenone-containing combined oral contraceptives might increase the risk for hyperkalemia.⁵⁶ However, a retrospective cohort study analyzing data from more than 1 million women found that drospirenone is not any more likely than levonorgestrel to cause hyperkalemia and that there is no interaction between drospirenone and spironolactone for hyperkalemia.⁵⁷ A subsequent prospective study of 27 women treated with combined oral contraceptives containing ethinyl estradiol/drospirenone and spironolactone also did not find any significant elevations in potassium.⁵⁸ Data from these studies suggest that spironolactone can safely be coadministered with drospirenone-containing combined oral contraceptives.

Reproductive Risks

Despite its utility in treating acne, spironolactone should not be used during pregnancy, and appropriate pregnancy

prevention is recommended. Spironolactone crosses the placenta, and some animal studies have shown feminization of male fetuses.⁵⁹ While human data are limited to a few case reports that did not demonstrate an association of major malformations,⁶⁰ it generally is recommended to avoid spironolactone during pregnancy. Small studies have found that spironolactone has minimal transfer to breastmilk and is not associated with adverse effects in breastfed infants.^{61–63} Accordingly, the World Health Organization considers spironolactone to be compatible with breastfeeding.⁶⁴ Notably, spironolactone may be associated with lactation suppression^{65,66}; therefore, it may be best if lactating patients ensure that their milk production is established prior to starting spironolactone and to increase their water intake to offset the diuretic effects.

Spironolactone also can result in gynecomastia in men and therefore typically is not prescribed for the treatment of acne in this population in oral form¹⁰; however, topical antiandrogens such as clascoterone can be used in both women and men with acne.⁶⁷

Conclusion

Spironolactone is a well-tolerated and effective treatment for women with acne, both in adult and adolescent populations. It is a potentially underutilized alternative to oral antibiotics. Spironolactone also is affordable, fully covered without any requirements in almost 90% of states under Medicaid and with a monthly cost of only \$4.00 when obtained through major retailers in the United States, making it an optimal long-term treatment option for many patients.^{52,68} We recommend a starting dose of 100 mg/d, which can be increased to 150 mg/d to 200 mg/d if needed for better acne control or decreased if adverse effects occur or acne clears. Potassium monitoring is of low usefulness in young healthy women, and studies have not identified an association between spironolactone use and increased risk for cancer.

References

- Barbieri JS, James WD, Margolis DJ. Trends in prescribing behavior of systemic agents used in the treatment of acne among dermatologists and nondermatologists: a retrospective analysis, 2004–2013. *J Am Acad Dermatol*. 2017;77:456–463.e4. doi:10.1016/j.jaad.2017.04.016
- Barbieri JS. Temporal trends in the use of systemic medications for acne from 2017 to 2020. *JAMA Dermatol*. 2023;159:1135–1136. doi:10.1001/jamadermatol.2023.2363
- Strauss JS, Pochi PE, Downing DT. Acne: perspectives. *J Invest Dermatol*. 1974;62:321–325. doi:10.1111/1523-1747.ep12724280
- Luderschmidt C, Bidlingmaier F, Plewig G. Inhibition of sebaceous gland activity by spironolactone in Syrian hamster. *J Invest Dermatol*. 1982;78:253–255. doi:10.1111/1523-1747.ep12506612
- Boisselle A, Dionne FT, Tremblay RR. Interaction of spironolactone with rat skin androgen receptor. *Can J Biochem*. 1979;57:1042–1046. doi:10.1139/o79-131
- Menard RH, Stripp B, Gillette JR. Spironolactone and testicular cytochrome P-450: decreased testosterone formation in several species and changes in hepatic drug metabolism. *Endocrinology*. 1974;94:1628–1636. doi:10.1210/endo-94-6-1628
- Rifka SM, Pita JC, Vigorsky RA, et al. Interaction of digitalis and spironolactone with human sex steroid receptors. *J Clin Endocrinol Metab*. 1978;46:338–344. doi:10.1210/jcem-46-2-338
- Corvol P, Michaud A, Menard J, et al. Antiandrogenic effect of spironolactone: mechanism of action. *Endocrinology*. 1975;97:52–58. doi:10.1210/endo-97-1-52
- Akamatsu H, Zouboulis CC, Orfanos CE. Spironolactone directly inhibits proliferation of cultured human facial sebocytes and acts antagonistically to testosterone and 5 alpha-dihydrotestosterone in vitro. *J Invest Dermatol*. 1993;100:660–662. doi:10.1111/1523-1747.ep12472325
- Goodfellow A, Alaghband-Zadeh J, Carter G, et al. Oral spironolactone improves acne vulgaris and reduces sebum excretion. *Br J Dermatol*. 1984;111:209–214. doi:10.1111/j.1365-2133.1984.tb04045.x
- Muhlemann MF, Carter GD, Cream JJ, et al. Oral spironolactone: an effective treatment for acne vulgaris in women. *Br J Dermatol*. 1986;115:227–232. doi:10.1111/j.1365-2133.1986.tb05722.x
- Roberts EE, Newshean S, Davis MDP, et al. Treatment of acne with spironolactone: a retrospective review of 395 adult patients at Mayo Clinic, 2007–2017. *J Eur Acad Dermatol Venereol*. 2020;34:2106–2110. doi:10.1111/jdv.16302
- Garg V, Choi JK, James WD, et al. Long-term use of spironolactone for acne in women: a case series of 403 patients. *J Am Acad Dermatol*. 2021;84:1348–1355. doi:10.1016/j.jaad.2020.12.071
- Roberts EE, Newshean S, Davis DMR, et al. Use of spironolactone to treat acne in adolescent females. *Pediatr Dermatol*. 2021;38:72–76. doi:10.1111/pde.14391
- Santer M, Lawrence M, Renz S, et al. Effectiveness of spironolactone for women with acne vulgaris (SAFA) in England and Wales: pragmatic, multicentre, phase 3, double blind, randomised controlled trial. *BMJ*. 2023;381:E074349. doi:10.1136/bmj-2022-074349
- Shields A, Barbieri JS. Effectiveness of spironolactone for women with acne vulgaris (SAFA) trial: a critically appraised topic. *Br J Dermatol*. 2023;189:509–510. doi:10.1093/bjd/ljad270
- Xu H, Li H. Acne, the skin microbiome, and antibiotic treatment. *Am J Clin Dermatol*. 2019;20:335–344. doi:10.1007/s40257-018-00417-3
- Knutsen-Larson S, Dawson AL, Dunnick CA, et al. Acne vulgaris: pathogenesis, treatment, and needs assessment. *Dermatol Clin*. 2012;30:99–106, viii–ix. doi:10.1016/j.det.2011.09.001
- Han JJ, Faletsky A, Barbieri JS, et al. New acne therapies and updates on use of spironolactone and isotretinoin: a narrative review. *Dermatol Ther (Heidelb)*. 2021;11:79–91.
- Centers for Disease Control and Prevention. Outpatient antibiotic prescriptions—United States, 2021. Accessed May 21, 2025. <https://archive.cdc.gov/#/details?url=https://www.cdc.gov/antibiotic-use/data/report-2021.html>
- Adler BL, Kornmehl H, Armstrong AW. Antibiotic resistance in acne treatment. *JAMA Dermatol*. 2017;153:810–811. doi:10.1001/jamadermatol.2017.1297
- Walsh TR, Efthimiou J, Dréno B. Systematic review of antibiotic resistance in acne: an increasing topical and oral threat. *Lancet Infect Dis*. 2016;16:E23–E33. doi:10.1016/S1473-3099(15)00527-7
- Margolis DJ, Fanelli M, Hoffstad O, et al. Potential association between the oral tetracycline class of antimicrobials used to treat acne and inflammatory bowel disease. *Am J Gastroenterol*. 2010;105:2610–2616. doi:10.1038/ajg.2010.303
- Margolis DJ, Fanelli M, Kupperman E, et al. Association of pharyngitis with oral antibiotic use for the treatment of acne: a cross-sectional and prospective cohort study. *Arch Dermatol*. 2012;148:326–332. doi:10.1001/archdermatol.2011.355
- Bartlett JG, Chang TW, Gurwith M, et al. Antibiotic-associated pseudomembranous colitis due to toxin-producing clostridia. *N Engl J Med*. 1978;298:531–534. doi:10.1056/NEJM197803092981003
- Carroll KC, Bartlett JG. Biology of *Clostridium difficile*: implications for epidemiology and diagnosis. *Annu Rev Microbiol*. 2011;65:501–521. doi:10.1146/annurev-micro-090110-102824
- Velicer CM, Heckbert SR, Lampe JW, et al. Antibiotic use in relation to the risk of breast cancer. *JAMA*. 2004;291:827–835. doi:10.1001/jama.291.7.827
- Song M, Nguyen LH, Emilsson L, et al. Antibiotic use associated with risk of colorectal polyps in a nationwide study. *Clin Gastroenterol Hepatol*. 2021;19:1426–1435.e6. doi:10.1016/j.cgh.2020.05.036

29. Cao Y, Wu K, Mehta R, et al. Long-term use of antibiotics and risk of colorectal adenoma. *Gut*. 2018;67:672-678. doi:10.1136/gutjnl-2016-313413
30. Del Rosso JQ, Rosen T, Palceski D, et al. Patient awareness of antimicrobial resistance and antibiotic use in acne vulgaris. *J Clin Aesthetic Dermatol*. 2019;12:30-41.
31. Park JH, Bienenfeld A, Orlow SJ, et al. The use of hormonal antiandrogen therapy in female patients with acne: a 10-year retrospective study. *Am J Clin Dermatol*. 2018;19:449-455. doi:10.1007/s40257-018-0349-6
32. Barbieri JS, Choi JK, Mitra N, et al. Frequency of treatment switching for spironolactone compared to oral tetracycline-class antibiotics for women with acne: a retrospective cohort study 2010-2016. *J Drugs Dermatol*. 2018;17:632-638.
33. Dréno B, Nguyen JM, Hainaut E, et al. Efficacy of spironolactone compared with doxycycline in moderate acne in adult females: results of the multicentre, controlled, randomized, double-blind prospective and parallel Female Acne Spironolactone vs doxycycline Efficacy (FASCE) Study. *Acta Derm Venereol*. 2024;104:adv26002. doi:10.2340/actadv.v104.26002
34. Barbieri JS, Ellenberg S, Grice E, et al. Challenges in designing a randomized, double-blind noninferiority trial for treatment of acne: The SD-ACNE trial. *Clin Trials*. 2025;22:66-76. doi:10.1177/17407745241265094
35. Collier CN, Harper JC, Cafardi JA, et al. The prevalence of acne in adults 20 years and older. *J Am Acad Dermatol*. 2008;58:56-59. doi:10.1016/j.jaad.2007.06.045
36. Dréno 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;29:1096-1106. doi:10.1111/jdv.12757
37. Schmidt TH, Khanijow K, Cedars MI, et al. Cutaneous findings and systemic associations in women with polycystic ovary syndrome. *JAMA Dermatol*. 2016;152:391-398. doi:10.1001/jamadermatol.2015.4498
38. Plante J, Robinson I, Elston D. The need for potassium monitoring in women on spironolactone for dermatologic conditions. *J Am Acad Dermatol*. 2022;87:1097-1099. doi:10.1016/j.jaad.2022.01.010
39. Berman HS, Cheng CE, Hogeling M. Spironolactone in the treatment of adolescent acne: a retrospective review. *J Am Acad Dermatol*. 2021;85:269-271. doi:10.1016/j.jaad.2020.11.044
40. Reynolds RV, Yeung H, Cheng CE, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2024;90:1006.e1-1006.e30. doi:10.1016/j.jaad.2023.12.017
41. Basu P. High-dose spironolactone for acne in patients with polycystic ovarian syndrome: a single-institution retrospective study. *J Am Acad Dermatol*. 2021;85:740-741.
42. Layton AM, Eady EA, Whitehouse H, et al. Oral spironolactone for acne vulgaris in adult females: a hybrid systematic review. *Am J Clin Dermatol*. 2017;18:169-191. doi:10.1007/s40257-016-0245-x
43. Yemisci A, Gorgulu A, Piskin S. Effects and side-effects of spironolactone therapy in women with acne. *J Eur Acad Dermatol Venereol*. 2005;19:163-166. doi:10.1111/j.1468-3083.2005.01072.x
44. Patiyasikunt M, Chancheewa B, Asawanonda P, et al. Efficacy and tolerability of low-dose spironolactone and topical benzoyl peroxide in adult female acne: a randomized, double-blind, placebo-controlled trial. *J Dermatol*. 2020;47:1411-1416. doi:10.1111/1346-8138.15559
45. Aldactone (spironolactone) tablets. Prescribing information. Pfizer; 2008. Accessed May 21, 2025. https://www.accessdata.fda.gov/drug-satfda_docs/label/2008/012151s062lbl.pdf
46. Bommareddy K, Hamade H, Lopez-Olivo MA, et al. Association of spironolactone use with risk of cancer: a systematic review and meta-analysis. *JAMA Dermatol*. 2022;158:275-282. doi:10.1001/jamadermatol.2021.5866
47. Mackenzie IS, Morant SV, Wei L, et al. Spironolactone use and risk of incident cancers: a retrospective, matched cohort study. *Br J Clin Pharmacol*. 2017;83:653-663. doi:10.1111/bcp.13152
48. Biggar RJ, Andersen EW, Wohlfahrt J, et al. Spironolactone use and the risk of breast and gynecologic cancers. *Cancer Epidemiol*. 2013;37:870-875. doi:10.1016/j.canep.2013.10.004
49. Garate D, Thang CJ, Golovko G, et al. A matched cohort study evaluating whether spironolactone or tetracycline-class antibiotic use among female acne patients is associated with breast cancer development risk. *Arch Dermatol Res*. 2024;316:196. doi:10.1007/s00403-024-02936-y
50. Jick SS, Hernandez RK. Risk of nonfatal venous thromboembolism in women using oral contraceptives containing drospirenone compared with women using oral contraceptives containing levonorgestrel: case-control study using United States claims data. *BMJ*. 2011;342:d2151. doi:10.1136/bmj.d2151
51. Shields A, Flood K, Barbieri JS. Spironolactone use for acne is not associated with an increased risk of venous thromboembolism: a matched, retrospective cohort study. *J Am Acad Dermatol*. 2023;88:1396-1397. doi:10.1016/j.jaad.2023.02.028
52. Plovianich M, Weng QY, Mostaghimi A. Low usefulness of potassium monitoring among healthy young women taking spironolactone for acne. *JAMA Dermatol*. 2015;151:941-944. doi:10.1001/jamadermatol.2015.34
53. Thiede RM, Rastogi S, Nardone B, et al. Hyperkalemia in women with acne exposed to oral spironolactone: a retrospective study from the RADAR (Research on Adverse Drug Events and Reports) program. *Int J Womens Dermatol*. 2019;5:155-157. doi:10.1016/j.ijwd.2019.04.024
54. Lai J, Zaenglein AL, Barbieri JS. Timing of potassium monitoring in females treated for acne with spironolactone is not optimal: a retrospective cohort study. *J Am Acad Dermatol*. 2024;91:982-984. doi:10.1016/j.jaad.2024.07.1446
55. Muhn P, Fuhrmann U, Fritzemeier KH, et al. Drospirenone: a novel progestogen with antimineralecorticoid and antiandrogenic activity. *Ann N Y Acad Sci*. 1995;761:311-335. doi:10.1111/j.1749-6632.1995.tb31386.x
56. Yaz (drospirenone/ethinyl estradiol) tablets. Prescribing information. Bayer HealthCare Pharmaceuticals; 2012. Accessed May 21, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/021676s012lbl.pdf
57. Bird ST, Pepe SR, Etminan M, et al. The association between drospirenone and hyperkalemia: a comparative-safety study. *BMC Clin Pharmacol*. 2011;11:23. doi:10.1186/1472-6904-11-23
58. Kronic A, Ciurea A, Scheman A. Efficacy and tolerance of acne treatment using both spironolactone and a combined contraceptive containing drospirenone. *J Am Acad Dermatol*. 2008;58:60-62. doi:10.1016/j.jaad.2007.09.024
59. Hecker A, Hasan SH, Neumann F. Disturbances in sexual differentiation of rat foetuses following spironolactone treatment. *Acta Endocrinol (Copenh)*. 1980;95:540-545. doi:10.1530/acta.0.0950540
60. Liszewski W, Boull C. Lack of evidence for feminization of males exposed to spironolactone in utero: a systematic review. *J Am Acad Dermatol*. 2019;80:1147-1148. doi:10.1016/j.jaad.2018.10.023
61. de Jong MFC, Riphagen IJ, Kootstra-Ros JE, et al. Potassium and magnesium in breast milk of a woman with gitelman syndrome. *Kidney Int Rep*. 2022;7:1720-1721. doi:10.1016/j.ekir.2022.05.006
62. Reisman T, Goldstein Z. Case report: induced lactation in a transgender woman. *Transgender Health*. 2018;3:24-26. doi:10.1089/trgh.2017.0044
63. Phelps DL, Karim A. Spironolactone: relationship between concentrations of dethioacetylated metabolite in human serum and milk. *J Pharm Sci*. 1977;66:1203. doi:10.1002/jps.2600660841
64. World Health Organization. Breastfeeding and maternal medication: recommendations for drugs in the eleventh WHO model list of essential drugs. February 25, 2002. Accessed May 21, 2025. <https://www.who.int/publications/i/item/55732>
65. Butler DC, Heller MM, Murase JE. Safety of dermatologic medications in pregnancy and lactation: part II. Lactation. *J Am Acad Dermatol*. 2014;70:417.e1-10; quiz 427. doi:10.1016/j.jaad.2013.09.009
66. Cominos DC, van der Walt A, van Rooyen AJ. Suppression of postpartum lactation with furosemide. *S Afr Med J*. 1976;50:251-252.
67. Hebert A, Thiboutot D, Stein Gold L, et al. Efficacy and safety of topical clascoterone cream, 1%, for treatment in patients with facial acne: two phase 3 randomized clinical trials. *JAMA Dermatol*. 2020;156:621-630. doi:10.1001/jamadermatol.2020.0465
68. Ershadi S, Choe J, Barbieri JS. Medicaid formularies for acne treatments are difficult to access and reflect inconsistent coverage policies. *J Am Acad Dermatol*. 2024;90:1074-1076. doi:10.1016/j.jaad.2024.01.033