

Acne and Pregnancy: A Clinical Review and Practice Pearls

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PRACTICE POINTS

- The management of acne in pregnancy requires careful consideration of therapeutic choices to guarantee the safety of both the mother and the developing fetus.
- The use of topicals should be observed as first-line therapy, but consideration for systemic therapy in cases of treatment failure or more severe disease is warranted.
- Discussion of patient expectations and involving them in decision-making for therapeutic choice is crucial.

Acne vulgaris is a common condition that routinely affects females of childbearing age. Taking into consideration the reproductive journey of women when treating acne is of paramount importance given the safety concerns to both the mother and the fetus associated with certain medications. Therefore, careful consideration of therapeutic choices during pregnancy is crucial. Herein, we summarize the safety of acne treatments during pregnancy and offer practical clinical pearls for routine dermatology practice.

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Acne vulgaris, or acne, is a highly common inflammatory skin disorder affecting up to 85% of the population, and it constitutes the most commonly presenting chief concern in routine dermatology

practice.¹ Older teenagers and young adults are most often affected by acne.² Although acne generally is more common in males, adult-onset acne occurs more frequently in women.^{2,3} Black and Hispanic women are at higher risk for acne compared to those of Asian, White, or Continental Indian descent.⁴ As such, acne is a common concern in all women of childbearing age.

Concerns for maternal and fetal safety are important therapeutic considerations, especially because hormonal and physiologic changes in pregnancy can lead to onset of inflammatory acne lesions, particularly during the second and third trimesters.⁵ Female patients younger than 25 years; with a higher body mass index, prior irregular menstruation, or polycystic ovary syndrome; or those experiencing their first pregnancy are thought to be more commonly affected.⁵⁻⁷ In fact, acne affects up to 43% of pregnant women, and lesions typically extend beyond the face to involve the trunk.^{6,8-10} Importantly, one-third of women with a history of acne experience symptom relapse after disease-free periods, while two-thirds of those with ongoing disease experience symptom deterioration during pregnancy.¹⁰ Although acne is not a life-threatening condition, it has a well-documented, detrimental impact on social, emotional, and psychological well-being, namely self-perception, social interactions, quality-of-life scores, depression, and anxiety.¹¹

Therefore, safe and effective treatment of pregnant women is of paramount importance. Because pregnant women are not included in clinical trials, there is a paucity

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of medication safety data, further augmented by inefficient access to available information. The US Food and Drug Administration (FDA) pregnancy safety categories were updated in 2015, letting go of the traditional A, B, C, D, and X categories.¹² The Table reviews the current pregnancy classification system. In this narrative review, we summarize the most recent available data and recommendations on the safety and efficacy of acne treatment during pregnancy.

Topical Treatments for Acne

Benzoyl Peroxide—Benzoyl peroxide commonly is used as first-line therapy alone or in combination with other agents for the treatment of mild to moderate acne.¹³ It is safe for use during pregnancy.¹⁴ Although the medication is systemically absorbed, it undergoes complete metabolism to benzoic acid, a commonly used food additive.^{15,16} Benzoic acid has low bioavailability, as it gets rapidly metabolized by the kidneys; therefore, benzoyl peroxide is unlikely to reach clinically significant levels in the maternal circulation and consequently the fetal circulation. Additionally, it has a low risk for causing congenital malformations.¹⁷

Salicylic Acid—For mild to moderate acne, salicylic acid is a second-line agent that likely is safe for use by pregnant women at low concentrations and over limited body surface areas.^{14,18,19} There is minimal systemic absorption of the drug.²⁰ Additionally, aspirin, which is broken down in the body into salicylic acid, is used in low doses for the treatment of pre-eclampsia during pregnancy.²¹

Dapsone—The use of dapsone gel 5% as a second-line agent has shown efficacy for mild to moderate acne.²² The oral formulation, commonly used for malaria and leprosy prophylaxis, has failed to show associated fetal toxicity or congenital anomalies.^{23,24} It also has been used as a first-line treatment for dermatitis herpetiformis in pregnancy.²⁵ Although the medication likely is safe, it is better to minimize its use during the third trimester to reduce the theoretical risk for hyperbilirubinemia in the neonate.^{17,26-29}

Azelaic Acid—Azelaic acid effectively targets non-inflammatory and inflammatory acne and generally is well tolerated, harboring a good safety profile.³⁰ Topical 20% azelaic acid has localized antibacterial and comedolytic effects and is safe for use during pregnancy.^{31,32}

Glycolic Acid—Limited data exist on the safety of glycolic acid during pregnancy. In vitro studies have shown up to 27% systemic absorption depending on pH, concentration, and duration of application.³³ Animal reproductive studies involving rats have shown fetal multisystem malformations and developmental abnormalities with oral administration of glycolic acid at doses far exceeding those used in humans.³⁴ Although no human reproductive studies exist, topical glycolic acid is unlikely to reach the developing fetus in notable amounts, and the medication is likely safe for use.^{17,35}

Clindamycin—Topical clindamycin phosphate is an effective and well-tolerated agent for the treatment of mild to moderate acne.³⁶ Its systemic absorption is minimal, and it is considered safe for use during all trimesters of pregnancy.^{14,17,26,27,35,37}

Erythromycin—Topical erythromycin is another commonly prescribed topical antibiotic used to target mild to moderate acne. However, its use recently has been associated with a decrease in efficacy secondary to the rise of antibacterial resistance in the community.³⁸⁻⁴⁰ Nevertheless, it remains a safe treatment for use during all trimesters of pregnancy.^{14,17,26,27,35,37}

Topical Retinoids—Vitamin A derivatives (also known as retinoids) are the mainstay for the treatment of mild to moderate acne. Limited data exist regarding pregnancy outcomes after in utero exposure.⁴¹ A rare case report suggested topical tretinoin has been associated with fetal otocerebral anomalies.⁴² For tazarotene, teratogenic effects were seen in animal reproductive studies at doses exceeding maximum recommended human doses.^{41,43} However, a large meta-analysis failed to find a clear risk for increased congenital malformations, spontaneous abortions, stillbirth, elective termination of pregnancy, low birthweight, or prematurity following first-trimester

FDA Pregnancy Labeling for Drugs

Discontinued	PLLR as of 2015 ¹²
A: No risk in first, second, or third trimester	(Drug name) is not absorbed systemically following (route of administration) and maternal use is not expected to result in fetal exposure to the drug
B: No risk in second or third trimester; first trimester studies not available	
C: Human data not available, animal studies adverse fetal effects	OR
D: Evidence of human fetal risk	Risk summary including:
X: Contraindicated	1. Risk statement based on human data ^a
	2. Risk statement based on animal data ^a
	3. Risk statement based on pharmacology
	4. Background risk information in general population ^a
	5. Background risk information in disease population

Abbreviations: FDA, US Food and Drug Administration; PLLR, Pregnancy and Lactation Labeling Rule.

^aRequired information.

exposure to topical retinoids.⁴⁴ As the level of exposure that could lead to teratogenicity in humans is unknown, avoidance of both tretinoin and tazarotene is recommended in pregnant women.^{41,45} Nevertheless, women inadvertently exposed should be reassured.⁴⁴

Conversely, adapalene has been associated with 1 case of anophthalmia and agenesis of the optic chiasma in a fetus following exposure until 13 weeks' gestation.⁴⁶ However, a large, open-label trial prior to the patient transitioning from adapalene to over-the-counter treatment showed that the drug harbors a large and reassuring margin of safety and no risk for teratogenicity in a maximal usage trial and Pregnancy Safety Review.⁴⁷ Therefore, adapalene gel 0.1% is a safe and effective medication for the treatment of acne in a nonprescription environment and does not pose harm to the fetus.

Clascoterone—Clascoterone is a novel topical antiandrogenic drug approved for the treatment of hormonal and inflammatory moderate to severe acne.⁴⁸⁻⁵¹ Human reproductive data are limited to 1 case of pregnancy that occurred during phase 3 trial investigations, and no adverse outcomes were reported.⁵¹ Minimal systemic absorption follows topical use.⁵² Nonetheless, dose-independent malformations were reported in animal reproductive studies.⁵³ As such, it remains better to avoid the use of clascoterone during pregnancy pending further safety data.

Minocycline Foam—Minocycline foam 4% is approved to treat inflammatory lesions of nonnodular moderate to severe acne in patients 9 years and older.⁵⁴ Systemic absorption is minimal, and the drug has limited bioavailability with minimal systemic accumulation in the patient's serum.⁵⁵ Given this information, it is unlikely that topical minocycline will reach notable levels in the fetal serum or harbor teratogenic effects, as seen with the oral formulation.⁵⁶ However, it may be best to avoid its use during the second and third trimesters given the potential risk for tooth discoloration in the fetus.^{57,58}

Systemic Treatments for Acne

Isotretinoin—Isotretinoin is the most effective treatment for moderate to severe acne with a well-documented potential for long-term clearance.⁵⁹ Its use during pregnancy is absolutely contraindicated, as the medication is a well-known teratogen. Associated congenital malformations include numerous craniofacial defects, cardiovascular and neurologic malformations, or thymic disorders that are estimated to affect 20% to 35% of infants exposed in utero.⁶⁰ Furthermore, strict contraception use during treatment is mandated for patients who can become pregnant. It is recommended to wait at least 1 month and 1 menstrual cycle after medication discontinuation before attempting to conceive.¹⁷ Pregnancy termination is recommended if conception occurs during treatment with isotretinoin.

Spironolactone—Spironolactone is an androgen-receptor antagonist commonly prescribed off label for mild to severe acne in females.^{61,62} Spironolactone

promotes the feminization of male fetuses and should be avoided in pregnancy.⁶³

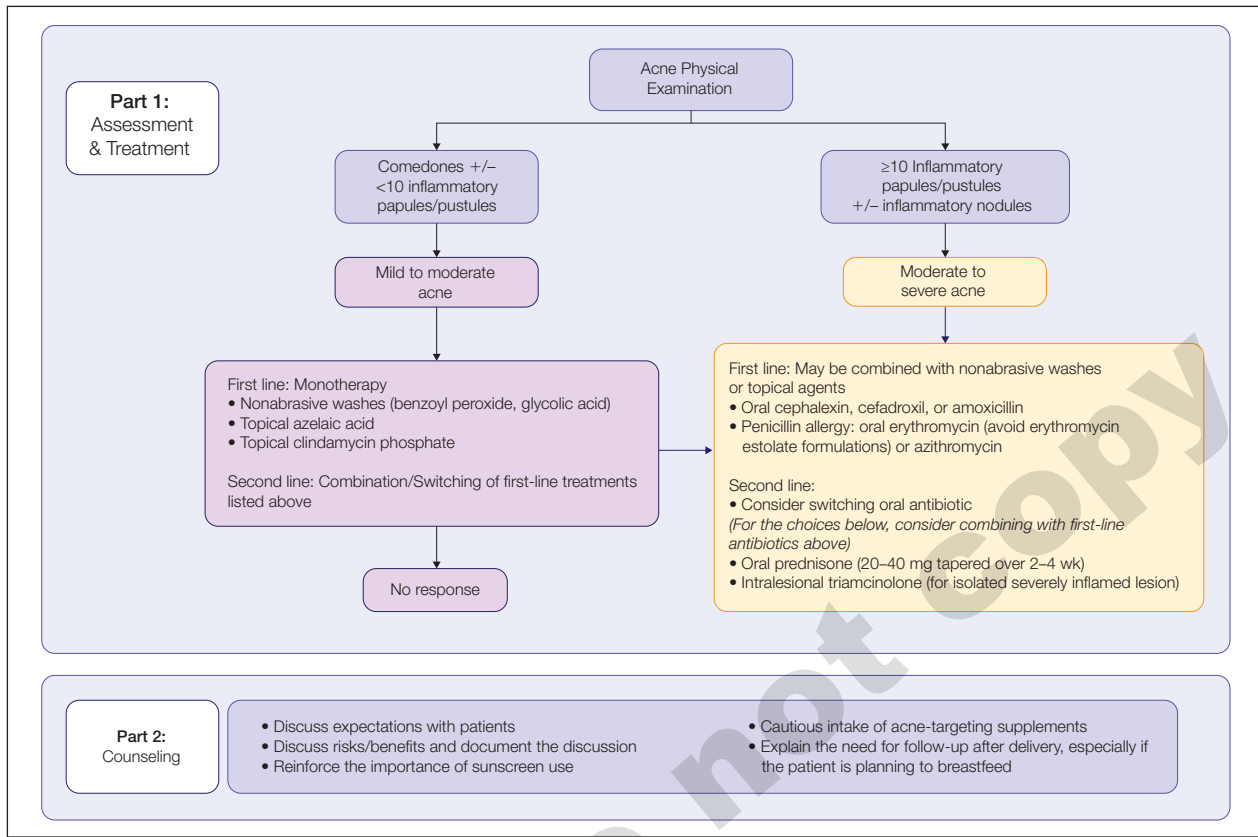
Doxycycline/Minocycline—Tetracyclines are the most commonly prescribed oral antibiotics for moderate to severe acne.⁶⁴ Although highly effective at treating acne, tetracyclines generally should be avoided in pregnancy. First-trimester use of doxycycline is not absolutely contraindicated but should be reserved for severe illness and not employed for the treatment of acne. However, accidental exposure to doxycycline has not been associated with congenital malformations.⁶⁵ Nevertheless, after the 15th week of gestation, permanent tooth discoloration and bone growth inhibition in the fetus are serious and well-documented risks.^{14,17} Additional adverse events following in utero exposure include infantile inguinal hernia, hypospadias, and limb hypoplasia.⁶³

Sarecycline—Sarecycline is a novel tetracycline-class antibiotic for the treatment of moderate to severe inflammatory acne. It has a narrower spectrum of activity compared to its counterparts within its class, which translates to an improved safety profile, namely when it comes to gastrointestinal tract microbiome disruption and potentially decreased likelihood of developing bacterial resistance.⁶⁶ Data on human reproductive studies are limited, but it is advisable to avoid sarecycline in pregnancy, as it may cause adverse developmental effects in the fetus, such as reduced bone growth, in addition to the well-known tetracycline-associated risk for permanent discoloration of the teeth if used during the second and third trimesters.^{67,68}

Erythromycin—Oral erythromycin targets moderate to severe inflammatory acne and is considered safe for use during pregnancy.^{69,70} There has been 1 study reporting an increased risk for atrial and ventricular septal defects (1.8%) and pyloric stenosis (0.2%), but these risks are still uncertain, and erythromycin is considered compatible with pregnancy.⁷¹ However, erythromycin estolate formulations should be avoided given the associated 10% to 15% risk for reversible cholestatic liver injury.⁷² Erythromycin base or erythromycin ethylsuccinate formulations should be favored.

Systemic Steroids—Prednisone is indicated for severe acne with scarring and should only be used during pregnancy after clearance from the patient's obstetrician. Doses of 0.5 mg/kg or less should be prescribed in combination with systemic antibiotics as well as agents for bone and gastrointestinal tract prophylaxis.²⁹

Zinc—The exact mechanism by which zinc exerts its effects to improve acne remains largely obscure. It has been found effective against inflammatory lesions of mild to moderate acne.⁷³ Generally recommended dosages range from 30 to 200 mg/d but may be associated with gastrointestinal tract disturbances. Dosages of 75 mg/d have shown no harm to the fetus.⁷⁴ When taking this supplement, patients should not exceed the recommended doses given the risk for hypocupremia associated with high-dose zinc supplementation.



An algorithm-based approach for the management of acne during pregnancy.

Light-Based Therapies

Phototherapy—Narrowband UVB phototherapy is effective for the treatment of mild to moderate acne.⁷⁵ It has been proven to be a safe treatment option during pregnancy, but its use has been associated with decreased folic acid levels.^{76–79} Therefore, in addition to attaining baseline folic acid serum levels, supplementation with folic acid prior to treatment, as per routine prenatal guidelines, should be sought.⁸⁰

AviClear—The AviClear (Cutera) laser is the first device cleared by the FDA for mild to severe acne in March 2022.⁸¹ The FDA clearance for the Accure (Accure Acne Inc) laser, also targeting mild to severe acne, followed soon after (November 2022). Both lasers harbor a wavelength of 1726 nm and target sebaceous glands with electrothermolysis.^{82,83} Further research and long-term safety data are required before using them in pregnancy.

Other Therapies

Cosmetic Peels—Glycolic acid peels induce epidermolysis and desquamation.⁸⁴ Although data on use during pregnancy are limited, these peels have limited dermal penetration and are considered safe for use in pregnancy.^{33,85,86} Similarly, keratolytic lactic acid peels harbor limited dermal penetration and can be safely used in pregnant women.^{87–89} Salicylic acid peels also work

through epidermolysis and desquamation⁸⁴; however, they tend to penetrate deeper into the skin, reaching down to the basal layer, if large areas are treated or when applied under occlusion.^{86,90} Although their use is not contraindicated in pregnancy, they should be limited to small areas of coverage.⁹¹

Intralesional Triamcinolone—Acne cysts and inflammatory papules can be treated with intralesional triamcinolone injections to relieve acute symptoms such as pain.⁹² Low doses at concentrations of 2.5 mg/mL are considered compatible with pregnancy when indicated.²⁹

Approaching the Patient Clinical Encounter

In patients seeking treatment prior to conception, a few recommendations can be made to minimize the risk for acne recurrence or flares during pregnancy. For instance, because data show an association between increased acne severity in those with a higher body mass index and in pregnancy, weight loss may be recommended prior to pregnancy to help mitigate symptoms after conception.⁷ The Figure summarizes our recommendations for approaching and treating acne in pregnancy.

In all patients, grading the severity of the patient's acne as mild, moderate, or severe is the first step. The presence of scarring is an additional consideration during the physical examination and should be documented. A

careful discussion of treatment expectations and prognosis should be the focus before treatment initiation. Meticulous documentation of the physical examination and discussion with the patient should be prioritized.

To minimize toxicity and risks to the developing fetus, monotherapy is favored. Topical therapy should be considered first line. Safe regimens include mild nonabrasive washes, such as those containing benzoyl peroxide or glycolic acid, or topical azelaic acid or clindamycin phosphate for mild to moderate acne. More severe cases warrant the consideration of systemic medications as second line, as more severe acne is better treated with oral antibiotics such as the macrolides erythromycin or clindamycin or systemic corticosteroids when concern exists for severe scarring. The additional use of physical sunscreen also is recommended.

An important topic to address during the clinical encounter is cautious intake of oral supplements for acne during pregnancy, as they may contain harmful and teratogenic ingredients. A recent search focusing on acne supplements available online between March and May 2020 uncovered 49 different supplements, 26 (53%) of which contained vitamin A.⁹³ Importantly, 3 (6%) of these 49 supplements were likely teratogenic, 4 (8%) contained vitamin A doses exceeding the recommended daily nutritional intake level, and 15 (31%) harbored an unknown teratogenic risk. Furthermore, among the 6 (12%) supplements with vitamin A levels exceeding 10,000 IU, 2 lacked any mention of pregnancy warning, including the supplement with the highest vitamin A dose found in this study.⁹³ Because dietary supplements are not subject to the same stringent regulations by the FDA as drugs, inadvertent use by unaware patients ought to be prevented by careful counseling and education.

Finally, patients should be counseled to seek care following delivery for potentially updated medication management of acne, especially if they are breastfeeding. Co-management with a pediatrician may be indicated during lactation, particularly when newborns are born preterm or with other health conditions that may warrant additional caution with the use of certain agents.

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