

Future of Pediatrics: Management of acne vulgaris

Kaiane Habeshian, MD
Assistant Professor of Dermatology and Pediatrics
George Washington University School of Medicine/Children's National

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- No conflicts to disclose:
 - No financial or business interest, arrangement or affiliation that could be perceived as a real or apparent conflict of interest in the subject (content) of my presentation.
 - No unapproved or investigational use of drugs, commercial products or devices.

Speaker Bio



Kaiane Habeshian, MD

Assistant Professor of Dermatology and Pediatrics

- Co-Director, Vulvar Dermatology Clinic
- Associate Program Director, Pediatric Dermatology Fellowship
- Course Director, DC Dermatology Resident Consortium Conference, Pediatric Section

Objectives

- To know when to start oral antibiotics and refer to dermatology for scarring, moderate to severe inflammatory, or nodulocystic acne
- To review special circumstances including the treatment “hormonal acne” and acne in pre-adolescents and in patients with depression
- To provide reference material for tips and tricks for the effective treatment of mild to moderate acne vulgaris

Case 1

What is the best course of action for this patient?

1. Topical retinoids
2. Topical benzoyl peroxide wash
3. Oral doxycycline
4. Refer to dermatology
5. All the above





Oral antibiotics

- Moderate to severe inflammatory, scarring, and/or recalcitrant inflammatory acne
- Doxycycline 100 mg BID for most patients; doxycycline 50 mg BID for pre-adolescents
 - Side effects: nausea, vomiting, esophagitis, headaches, photosensitivity, rare mood changes, contraindicated in pregnancy
 - Take with food and water, sit upright after taking, use sunscreen
- Sarecycline, a novel tetracycline with narrow-spectrum activity, is FDA-approved (October 2018) for the treatment of moderate to severe inflammatory acne in patients age 9 years and older x 12 weeks
 - Cost is often prohibitive (\$1,141/month); manufacturer coupon for non-federal commercial insurance \$15-125/month
- Avoid minocycline 2/2 risk of liver failure, DRESS, drug-induced lupus
- Derm and ID guidelines: limit use to 3-6 months to minimize antibiotic resistance

Oral antibiotics

- Prescribe in combination with first line topical therapies (see reference material)
- Oral antibiotics indicated if there is scarring or significant post inflammatory hyperpigmentation (PIH), likely as a bridge to isotretinoin or hormonal treatment
- Bottom line:
 - Feel comfortable treating mild to moderate acne w/ topicals and oral antibiotics; counsel on proper use, set expectations, provide handouts
 - If there is scarring or significant PIH, start topical retinoid, benzoyl peroxide product, and doxycycline and refer to dermatology for consideration of isotretinoin

Case 2

This healthy 16 yo has flares of inflammatory acne on the lower face monthly before periods. She is diligent w/ topical retinoids. Benzoyl peroxide burned her skin. A prior course of doxycycline was temporarily helpful. Her mom declines COCs. She doesn't want to wait until her dermatology appointment to discuss isotretinoin. What is the best next step?

1. Add topical clindamycin
2. Prescribe another round of doxycycline
3. Discuss oral spironolactone
4. No further treatment is available



Oral spironolactone

- Potassium-sparing diuretic, anti-androgenetic (decreases testosterone production, blocks androgen receptors in skin)
- Use in patients who are post-menarchal >1 year for “hormonal” acne
 - Lower face predominance - chin and jaw – and/or pre-menstrual flaring
- Acne doses: 100 mg (start @50 mg → 100 mg if tolerated in a week) to 200 mg daily
- Maximum benefit seen 3-6 months after initiation
- Side effects: increased urination, menstrual irregularity (reduced w/ COCs), breast tenderness, breast enlargement, dizziness, headache, fatigue
- Contraindications: Acute renal failure, Addison disease, hyperkalemia, anuria, concomitant eplerenone or triamterene use, significant renal impairment



Oral spironolactone – safety

- Two retrospective studies revealed no increased risk of hyperkalemia in healthy acne pts aged 18-45 years
 - 2019 review: hyperkalemia in 1/112 patients <45 yrs of age v. 2/12 patients 46-65 yrs
 - 2015 case-control study: hyperkalemia in 13/1802 (0.72%) of patients
 - Baseline hyperkalemia rate in this population was 0.76%
 - Authors' conclusion: Screening for hyperkalemia is not necessary in young, healthy patients who are not on potassium-elevating medications
- Discuss minimizing high potassium foods, coconut water, low sodium processed foods
- May be used safely with drospirenone-containing COCs
- Bottom line: most of our acne patients do NOT need K⁺ level monitoring
- Three large retrospective cohort studies showed no increased risk of breast or gynecologic cancers
 - Black-box warning–avoid off-label use given oncogenicity in animal studies

Topical clascoterone

- Winlevi (Clascoterone 1% Cream) – novel topical androgen blocker
- FDA approved for the treatment of moderate-to-severe hormonal acne in patients 12 years and over (August 2020)
- Applied twice daily; minimal side effects – redness, scaling, dryness, itching
- Cost: \$655/60 g tube
- WINLEVI Co-Pay Program: eligible non-federal commercially-insured patients pay \$25-50/month

Case 3

You are evaluating this isotretinoin candidate and ask if has been struggling with depression, low mood, or sadness. The patient denies these feelings but then scores an 11 on the PHQ-9 Modified for Teens, consistent with moderate depression. Which of the following is the truest statement?

1. Isotretinoin is contraindicated in depression
2. Isotretinoin is associated with a statistically significant increase in suicide risk
3. Isotretinoin has no effect on mood
4. Isotretinoin is an appropriate option in patients with moderate depression if proper counseling and monitoring is in place



Acne vulgaris and mood

- Increased hospital admissions for a mental health disorder in pts w/ acne c/w those without acne (adjusted OR = 13.02) (Singam 2019)
 - The presence of 1 or more mental health disorder is more common in inpatients with acne versus those without acne (43.7% vs. 20.0%, respectively)
- Acne and post-inflammatory hyperpigmentation negatively impact self-perception, social interactions and quality of life scores (Darji 2017) and self-esteem and self-identity in adolescents (Nguyen 2016)
- Acne is a/w higher rates of unemployment and has a detrimental impact on social, emotional, and psychological function comparable to that of asthma and epilepsy (Gollnick 2003)
 - Treatment of acne can improve quality of life

Isotretinoin and depression

- Case reports of suicide while on isotretinoin led to bad press
- Review of psychiatric adverse events with isotretinoin as the primary suspect drug in the FDA's Adverse Event Reporting System from 1997 through 2017:
 - “(The reported suicide) rates are lower than reported national suicide rates in the United States for these years.”
- 2019 BMJ metanalysis:
 - “This study suggested an association of the use of isotretinoin in patients with acne with significantly improved depression symptoms.”
- 2021 prospective study including patients w/ mild, moderate, and severe depression:
 - “Compared to the baseline, patients using isotretinoin showed a significant reduction in depression scores at 3 months (2.64 ± 6.17 ; p-value < 0.001), 6 months (1.99 ± 5.08 ; p-value < 0.001), and across all follow-up points (p-value < 0.001).”

Our approach

- We screen all isotretinoin candidate with the PHQ-9 Modified for Teens (available in Spanish and other languages)
- Mild depression – proceed with isotretinoin, encourage follow up with mental health provider
- Moderate to severe depression or recent suicidality – evaluation by our clinic psychologist Dr Julie Heier, PhD; further recommendations and consideration of isotretinoin based on recommendations
- Bottom line: Treating bad acne with isotretinoin improves mood in patients with and without depression

PHQ-9: Modified for Teens

Name: _____ Clinician: _____ Date: _____

Instructions: How often have you been bothered by each of the following symptoms during the past **two weeks**? For each symptom put an "X" in the box beneath the answer that best describes how you have been feeling.

	(0) Not At All	(1) Several Days	(2) More Than Half the Days	(3) Nearly Every Day
1. Feeling down, depressed, irritable, or hopeless?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Little interest or pleasure in doing things?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Trouble falling asleep, staying asleep, or sleeping too much?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Poor appetite, weight loss, or overeating?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Feeling tired, or having little energy?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Feeling bad about yourself – or feeling that you are a failure, or that you have let yourself or your family down?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Trouble concentrating on things like school work, reading, or watching TV?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you were moving around a lot more than usual?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Thoughts that you would be better off dead, or of hurting yourself in some way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
In the past year have you felt depressed or sad most days, even if you felt okay sometimes? <input type="checkbox"/> Yes <input type="checkbox"/> No				
If you are experiencing any of the problems on this form, how difficult have these problems made it for you to do your work, take care of things at home or get along with other people? <input type="checkbox"/> Not difficult at all <input type="checkbox"/> Somewhat difficult <input type="checkbox"/> Very difficult <input type="checkbox"/> Extremely difficult				

Has there been a time in the **past month** when you have had serious thoughts about ending your life?
☐ Yes ☐ No

Have you **EVER**, in your **WHOLE LIFE**, tried to kill yourself or made a suicide attempt?
☐ Yes ☐ No

***If you have had thoughts that you would be better off dead or of hurting yourself in some way, please discuss this with your Health Care Clinician, go to a hospital emergency room or call 911.*

Office use only: Severity score: _____

Total Score

Depression Severity

0-4

No or Minimal depression

5-9

Mild depression

10-14

Moderate depression

15-19

Moderately severe depression

20-27

Severe depression

Case 4

This 9 year old presents with her mother, who is surprised to learn that her child has acne (she doesn't have her period yet) and is curious if it is treatable. Which of the following is true regarding acne treatment in preadolescents?

1. No available treatment is safe
2. There are no FDA approved treatments
3. Treatments are not as effective
4. Medicated washes and topical retinoids are first line



PMID:19282599

Acne in pre-adolescents

- First line treatment for mild-moderate comedonal and mild inflammatory acne is essentially the same as in teenagers
- Patients may do best with a wash
 - Hands-on parents can apply a topical retinoid cream for the child
- FDA approved treatments:
 - Topical retinoids:
 - Benzoyl peroxide 2.5%/adapalene 1% gel—age 9 years and up
 - Tretinoin 0.05% gel—age 10 years
 - Tazertene 0.1% cream—age 9 years
 - Trifarotene cream—age 9 years (no generic available)
 - Sarecycline tablets—age 9 years, weight-based dosing (no generic available)
- Commonly used agents:
 - Salicylic acid wash
 - Benzoyl peroxide wash
 - Topical retinoids
- Refer dermatology if oral agent is required for moderate inflammatory acne

Reference material

Topical retinoids

- Topical retinoids are first line; they work but compliance is a major issue
- Commonly used: adapalene 0.1% (OTC), 0.3%; tretinoin 0.025%, 0.05%, 0.1% cream
- Use tiny amounts – half a pea
 - May mix w/ moisturizer to limit amount used
- Apply twice weekly or every other night until skin acclimates (2+ weeks), then nightly if tolerated
 - Better to use 3x/wk consistently than develop retinoid dermatitis
 - Mild dryness and irritation is expected
- Pick generic retinoid that is on formulary; high PA burden

Topical retinoids

- Use acne-friendly moisturizer scheduled, not PRN
 - In AM, apply moisturizer that contains sunscreen
 - Tinted moisturizer w/ iron oxides provide additional benefit for pigmentary alteration, especially important in skin of color
 - In PM, use moisturizer to face before or after retinoid
 - Moisturizer is OTC – must pay out of pocket; emphasize benefit for improving post inflammatory hyperpigmentation and scarring
 - Provide handout with options
- Set expectations; slight flare initially, 4-6 weeks to note max benefit, preventative so use on whole field, avoiding waxing/chemical peels
- Gradual introduction of benzoyl peroxide products
 - Eg. Start with use on chest and back, allow skin of face to adjust to topical retinoid first



\$11.87 (\$3.96/Oz)



\$13.89 (\$4.63/Oz)



\$18.49 (\$6.16/Oz)

anal.



\$14.22 (\$5.69/oz)



\$27.50 (\$11.00/oz)



\$43.00 (\$12.29/oz)



\$38.50 (\$14.25/oz)



\$36.00 (\$18/oz)

Benzoyl peroxide

- Formulations include wash off (cleanser) and leave on (spot treatments)
- Use as a cleanser facilitates treatment of a wider surface area including the chest, shoulders, back, face
 - BP wash is covered by some insurance plans, but those formulations are poorly tolerated
 - Contact time 2+ min with the skin prior to rinsing maximizes antimicrobial benefits but increases risk of irritation
- Risks: dryness, irritation, bleaching of clothing and linens, inactivation of tretinoin
- Reducing side effects:
 - Lower concentrations between 2.5 and 5% are less irritating
 - Start 2-3 times per week, work up slowly
 - Rinse off well, use old pillow covers or towels
- Combination formulations with antibiotic or retinoid improve compliance but \$\$\$



\$9.01 (\$1.50/Oz)



\$9.99 (\$2.38/Oz)



\$12.61 (\$2.52/Oz)

ational.

Topical antibiotics

- Although technically considered first line therapy, I do not use these often because of very high rates of antibiotic resistance
 - This includes cutaneous *staph* species
- Topical clindamycin gel/lotion can be added in combination with benzoyl peroxide (leave on or wash off product) as a spot treatment for occasional inflammatory breakouts
 - Do not use without BP product – latter helps prevent antibiotic resistance

Thank You!



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