### Acne Vulgaris in Children: Mental Health, New Treatments, and More

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#### Conflicts of Interest

- Adviser/ Speaker: Incyte, Loreal, Pelthos, Regeneron/ Sanofi, Verrica
- Investigator: Avita, Incyte
- Grants: ACDS, Incyte, PeDRA, Vitiligo Research Foundation

### Mental health

- Depression and acne
- Resilience is protective against depression
- Depression and isotretinoin
- Special populations- Transgender and SOC
- The role of misinformation online

#### Mental health disorders and acne

- Depression 22%
- Anxiety 30%
- Suicidal thoughts in acne patients 12% respectively
- Depression rates peaked in Asia at 42%
- India (53%)
- Saudi Arabia (51%)
- Suicidal thoughts were highest in New Zealand-24%.
  - Chen Y. Clin Exp Dermatol. 2024 Dec 18:llae531. doi: 10.1093/ced/llae531. Epub ahead of print. PMID: 39692772.

## Emotional resilience protects against acne induced depression

- Emotional resilience is associated with better SRQL among patients with acne
- The ability to bounce back from stressful events
- SKINDEX 16

 Stone CJ. J Cosmet Dermatol. 2025 Jan;24(1):e16744. doi: 10.1111/jocd.16744. PMID: 39760180; PMCID: PMC11701875. You can become more resilient in many ways.

Most often, resilience training includes creating healthy habits, such as these:

- Build strong relationships with loved ones and friends.
- Do something that gives you a sense of purpose, such as helping others.
- Be hopeful about the future. Accept that change is part of life.
- Look at what you've used to cope with troubles in the past and build on those strengths.
- Take care of yourself. Tend to your needs and do things you enjoy.
- When you have a problem, don't ignore it. Make a plan and take action.
- Be grateful. Look for the good in your life.
- https://www.mayoclinic.org/tests-procedures/resilience-training/about/pac-20394943

#### Depression and isotretinoin

 Bibliometric analysis
 Emerging articles support the association between severe acne and depression more than with isotretinoin usage

o Ünlü Açıkel S.Clin Exp Dermatol. 2025 Jan 6:llae395.

#### Transgender youth\*

- Up to 9.2% of high school-age adolescents identify as TGDtransgender and gender diverse
- TGD adolescents are at risk for negative social and emotional outcomes secondary to minority stress, discrimination, and rejection by peers and family
- Acne is estimated to affect approximately 85% of adolescents and is associated with negative mental health outcomes, including suicidal ideation, low self-esteem, and depression.
- Zimmer A. Pediatr Rev. 2024 Nov 1;45(11):613-624.

#### Skin of color- concerns are different

- Mental health is a concern for all
- DYSCHROMIA IS THE NUMBER ONE REASON FOR SOC CLINIC VISITS
- Only 3% of clinical trials actually target Fitzpatrick IV-VI
- Only 2.4% include hyperpigmentation as an assessment
- Postinflammatory pigmentary alteration esp hyperpigmentation is a leading concern, often NOT addressed in clinical trials
  - Alexis AF.Cutis. 2007 Nov;80(5):387-94; Kucharik AH. J Am Acad Dermatol. 2022 Jul;87(1):140-142; Swearingen A. J Am Acad Dermatol. 2024 Oct 10:S0190-9622(24)02962-1.

#### Depression, dysmorphia, poor QoL, and Many online hours

Saudi Arabian Study

Excessive social media usage 5+ hours (44%)

Females (76%), Students (58%)

The mean acne duration was 5.75 ± 4.58 years

Hospital Anxiety and Depression Scale=The HADS-A score was 11.14 ± 2.74, whereas the HADS-D score was 11.46 ± 1.78, indicating anxiety and depression symptoms

DLQI scores (6.04 ± 6.05) indicate that acne had a moderate effect on patients' quality of life

Body Dysmorphic Disorder Questionnaire (BDDQ)-The percentage of positive BDD patients is significantly higher than those with negative BDD (p = 0.022)

□Significant association between PAHPI total score and SCAR-S (r = 0.48,  $p \le 0.001$ ) and HADS-D (r = 0.39, p = 0.005) total scores. □ Muzaffar KH. Cureus. 2024 Jul 19;16(7):e64917.

#### Social Media Pros and Cons

Social media can promote unrealistic expected outcome

- Association between poor sleep, social impairment, and mental health disorders, including body dysmorphic disorder (BDD) with acne
- Some positive benefits of information and support but what type of information?

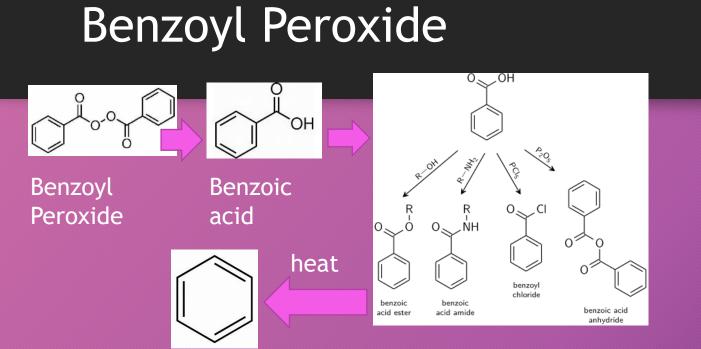
Rieder EA. J Drugs Dermatol. 2023 Aug 1;22(8):817-825.

#### Misinformation online

- Tik Tok platform
- Top 50 acne videos
- Average total DISCERN score was 25.5 (range: 15-57)
- Overall quality is poor 1.7/5 average score on DISCERN
- 6 were not even visible
- Representation fair:Asian (n=5, 11.4%), Black/ African American (n=6, 13.6%), Hispanic (n=11, 25%), White (n=19, 43.2%), and Other (n=2, 4.5%)
- Quality for SOC lower: The scores highest, and the percentage of above-average videos was most significant for videos targeting White patients (average= 1.8/composite DISCERN score: 29.2; 47.7%), followed by Asian (average=1.6/composite DISCERN score: 23.8; 36.4%), African American (average=1.5/composite DISCERN score: 23.7; 15.4%), Hispanic (average=1.5/composite DISCERN score: 23.5; 19%), and Other (average=1.5/composite DISCERN score: 23; 2.5%)
- White videos had higher quality than Black/ Hispanic videos (combined) (p-value=.029132)
- Social media content is of poor quality, especially for those of color
  - Zoltan S, Silverberg NB. Skin, in press

#### Topical therapy- So many classes

- Antibacterials
  Benzoyl peroxide\*
  Antibiotics
  Sodium sulfacetamide/ sulfur\*
  Topical clindamycin\*
  Anti-inflammatory
  - Dapsone
- □Hormonal
  - □Topical clascoterone\*



- 5% of the benzoic acid is absorbed systemically
- □ Excreted by the renal system
- Metabolized by cysteine in the skin, releasing active free-radical oxygen species and oxidizing bacterial
- The peroxide bond of benzoyl peroxide is cleaved to form 2 benzoyloxy radicals.
   Benzoic acid is a significant metabolite of benzoyl peroxide.

Oxidizing agent with BACTERICIDAL and moderate keratolytic properties

Breaks down to benzene

- Avoid letting the product heat up in the car
- $\Box$  After applying 10% benzoyl peroxide daily for 2 weeks  $\rightarrow$  98% C. acnes reduction in follicle
- Bleaches towels and fabrics
- Good antibiotic stewardship
- □ Some ACD/ angioedema extremely rare
  - Cotterill JA. Benzoyl peroxide. Acta Derm Venereol Suppl (Stockh). 1980;Suppl 89:57-63.

#### Sodium sulfacetamide/ sulfur



- □ Sulfacetamide is a Sulfonamide antibiotic
- Inhibits synthesis of folic acid in bacteria
- Bacteriostatic
- Avoid usage is sulfur allergic
- With sulfur has antibacterial, antifungal, and keratolytic activity
- □ Anti-inflammatory effects

Gupta AK. J Drugs Dermatol. 2004 Jul-Aug;3(4):427-31.

#### Topical clindamycin

Anti-inflammatory Effects- prevents PMN chemotaxis

Antibiotic with limited gram negative activity

- □ Targets *C. acnes* well
- □ Inhibits protein translation through binding to the 50S subunit of *C. acnes*
- □ Prevents peptidyl tRNA translocation within the *C*. *acnes* ribosome
- □ Clindamycin binds to the 23S rRNA of the large 50S bacterial ribosomal subunit at the PTC site, with additional proposed effects on aminoacyl-tRNA binding with the A-site
- Drug wih the greatest coverage across all formularies
- Good coverage on Medicaid and CHiP

□Not good antibiotic stewardship alone because it produces rapid resistance formation

Combine with benzoyl peroxide to reduce resistance formation

Colitis concern low, but label supports avoidance

Armillei MK. Antibiotics (Basel). 2024 Mar 17;13(3):270; Kamara M. J Am Acad Dermatol. 2022 Aug;87(2):411-417.

#### Topical clascoterone

□1% cream approved 12 years of age and older

- Excellent efficacy BID- alternative mechanism of action
- **D**Reduces inflammatory and non-inflammatory lesions
- Avoid oral meds
- Limited absorption
- □Slight reduction in sebum
- □4-ring backbone identical to dihydrotestosterone (DHT) and spironolactone, topically applied clascoterone binds androgen receptors (ARs) in the sebaceous glands and hair follicles
- Inhibits sebocyte inflammation

Minimal absorption- avoids effects internally

Rosette C. J Drugs Dermatol. 2019 May 1;18(5):412-418. PMID: 31141847; Basendwh MA. PLoS One. 2024 May 30;19(5):e0298155. doi:

#### Retinoids

#### □RA binds to RARs and RXR- nuclear receptor (NR) superfamily

RAR genes encoding nuclear receptor (RARα, RARß and RARγ)- complex with RXRα, β,
 RARγ Isotretinoin has a low affinity for RAR and RXR, but may be converted intracellularly to metabolites that act as agonists of RAR and RXR

RXR acts as a common heterodimeric partner to a RAR and many other nuclear receptors, such as the thyroid hormone receptor (TR), vitamin D receptor (VDR), liver X receptor (LXR), and peroxisome-proliferator-activated receptors (PPARs)

□First generation: tretinoin binds RAR/ RXR

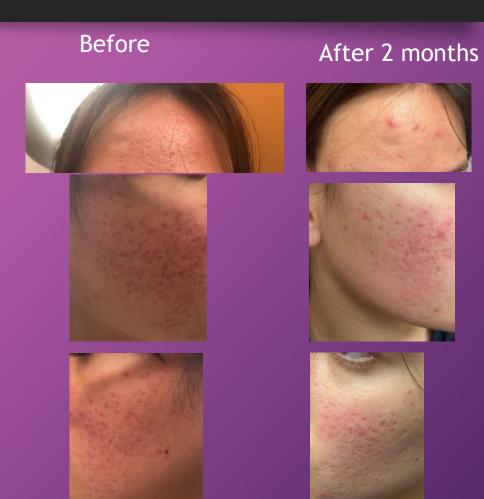
□Third generation: adapalene and tazarotene have higher specificity for RARgamma and RAR-beta and do not interact with RXRs

□Fourth generation: trifaretone-a 20-fold greater affinity for RAR-gamma, the most dominant subtype in the skin, and has no affinity for RXR receptors

Huang P. Chem Rev. 2014 Jan 8;114(1):233-54; Baldwin H. Am J Clin Dermatol. 2021 May;22(3):315-327; Layton A. Dermato-Endocrinology 2009. 1 (3): 162-9; Baldwin H.Am J Clin Dermatol 2021; 22, 315-327;

# Using topicals in the child who can't swallow a pill

- Choose 2 of the following:
  - Tretinoin\*
  - Adapalene
  - Trifaretone or
  - Tazarotene- choose this in darker skin tones



Subfamily 1 NR2B1 (RXR $\alpha$ ) NR2B2 (RXRβ) NR2B3 (RXRy) NR1B1 (RARa) **NR1B2 (RAR**β) NR1B3 (RAR<sub>Y</sub>) NR1A1 (TR $\alpha$ ) NR1A2 (TR $\beta$ ) NR1C1 (PPAR $\alpha$ ) NR1C2 (PPAR $\beta$ ) NR1C3 (PPARy) NR1D1 (REV-ERBα) NR1D2 (REV-ERBβ) NR1F1 (RORa) **NR1F2 (ROR**β) NR1F3 (RORy)

#### New topical therapies

 First triple-combination, oncedaily topical therapy of 1.2% clindamycin, 1.5% adapalene, and 3.1% benzoyl peroxide
 FDA approved once daily
 12 years of age and older
 Drake L. Am J Clin Dermatol 23,

125-136 (2022).



