

Advances in Acne Management

Advances and Controversies in Pediatrics 2011

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ABP Objectives for ACNE

- Plan for the treatment of acne vulgaris with first-line topical medications, retinoic acid, and benzoyl peroxide (BPO)
- Know when to prescribe systemic antibiotics for acne and which antibiotics to use

Case 1



You see a 14 yo girl for a health maintenance visit. Her mother asks about treatment for her acne.

Case 1:

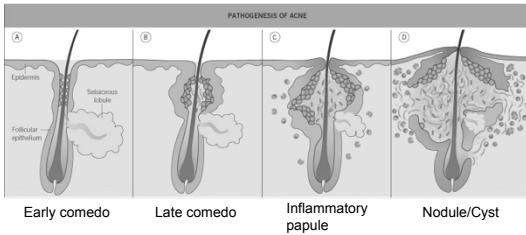
What is the best treatment for her acne?

1. Benzoyl peroxide gel
2. Clindamycin solution
3. Salicylic acid wash
4. Tretinoin cream
5. No treatment

Acne: Background



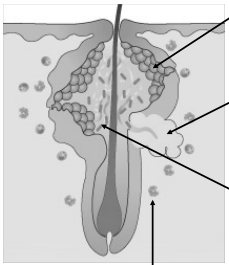
Acne Pathogenesis



- 4 key components:**
- Abnormal shedding of follicular keratinocytes
 - Increased production of sebum
 - Resident bacterial overgrowth
 - Inflammation
- } Driven by Androgens

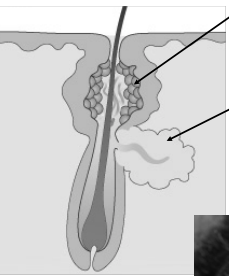
Bolognia, Jorizzo & Rapini: Dermatology 2e, copyright 2008 Elsevier, Ltd.*

Targeted Acne Therapy

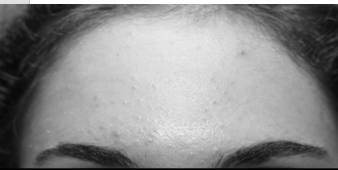


- Follicular Hyperkeratosis**
 - > Retinoids
 - > Benzoyl Peroxide (BPO)
 - > Salicylic Acid
- Increased sebum**
 - > Retinoids
 - > OCPs
 - > Spironolactone
 - > Isotretinoin
- P. Acnes proliferation**
 - > Topical Antibiotics
 - > Systemic Antibiotics
 - > BPO
- Inflammation**
 - > Antibiotics
 - > Salicylic acid
 - > BPO

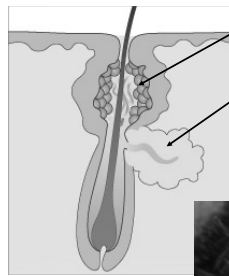
Comedonal Acne



- Follicular Hyperkeratosis**
- Increased sebum**

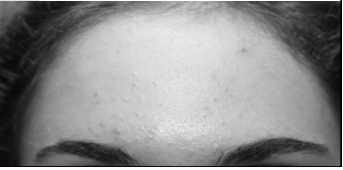


Case 1: Comedonal Acne



- Follicular Hyperkeratosis**
 - > Tretinoin
- Increased sebum**
 - > Tretinoin

Treatment regimen:
Tretinoin Cream QHS



Topical Retinoids

- Vitamin A derivatives
- Tretinoin, Adapalene, Tazarotene
- *Potent* comedolytics & anticomedogenics
- Side effects:
 - peeling and dryness
 - increased sun sensitivity

Topical Retinoids

- Tricks of the trade:
 - Start with the lowest concentration
 - Cream is less irritating than gel
 - Use a pea-sized amount for the whole face
 - Dot it all over a *dry* face, then rub it in
 - Start every other night, increase to nightly as tolerated
 - Apply a moisturizer under or over the medication if excessive irritation

Preadolescent Acne

- Most commonly comedonal acne in midfacial area
- Develops in association with onset of adrenarche (6-7yrs in girls, 7-8 in boys)
- 1st line: BPO
- 2nd line: infrequent retinoid



Eichenfield LF et al. (2010) Pediatrics. 125(6):e1316-23.

Benzoyl Peroxide



- Antimicrobial: kills bacteria via non-specific oxidation
- *Weakly* comedolytic and anti-inflammatory
- Side effects
 - irritation, bleaches clothing/hair, contact dermatitis
- Use the lowest strength available
 - 2.5, 5, and 10% BPO are equally effective
 - Lower strength is less irritating

Case 2

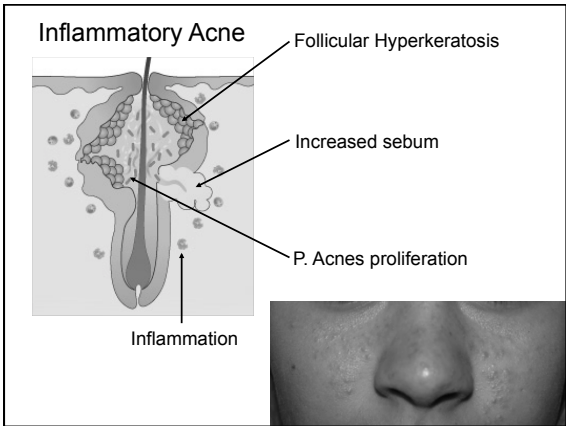


This 15-year-old girl has papules on her forehead, cheeks and nose. She gets occasional pustules. She has no scarring.

Case 2:

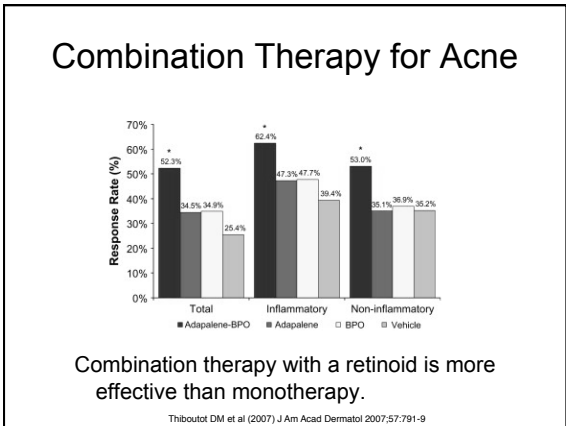
The MOST appropriate initial management strategy is

1. BPO gel
2. BPO/clindamycin gel
3. Tretinoin cream
4. BPO/clindamycin gel + tretinoin cream
5. Doxycycline by mouth



Case 2: Mild Comedonal/Inflammatory Acne

- Mild Inflammatory and Comedonal Acne
- Treatment plan:
 - Benzacilin or Duac (BPO 5% + Clinda 1%) QAM
 - Tretinoin 0.025% Cream QHS
 - f/u in 3 months



Case 3



A 15 year-old girl requests treatment for her acne. She has used BPO without significant benefit. She has early scarring.

Case 3:

The most appropriate treatment to initiate is:

1. topical BPO/clindamycin + topical tretinoin
2. topical tretinoin alone
3. oral doxycycline, topical tretinoin and BPO
4. oral minocycline, topical tretinoin and BPO
5. oral tetracycline, topical tretinoin and BPO

Case 3



- Moderate inflammatory acne
 - Treatment Regimen:
 - > Doxycycline + Tretinoin + BP
 - or
 - > Doxycycline + Epiduo
 - 6-8 weeks for initial improvement, 3 months to see maximal effect

Why prescribe an oral antibiotic?

- For moderate to severe inflammatory acne with potential to scar
- When acne causes severe psychosocial distress
- When inadequate improvement with topicals

Doxycycline

- First line oral antibiotic for acne
- Antimicrobial and anti-inflammatory
- Usual dose: 100mg Qday - BID
- Lower risk of serious side effects than minocycline

Doxycycline

- Side Effects:
 - Stomach Upset - *take with food*
 - Esophageal erosions - *take >1 hr before bedtime*
 - Photosensitivity - *sun avoidance, sunscreen!*
 - Dental staining if used in <8yo or pregnancy

Minocycline

- Use in patients with
 - Moderate/severe acne
 - photosensitivity or high risk of sunburn if given doxycycline
- Side effects: vertigo, pigment deposition, hypersensitivity
- 6x greater risk of serious side effects than doxycycline

Why Benzoyl Peroxide?



- Resistance to antibiotics is increasing in *P. acnes* and other bacteria
- BPO prevents resistance to oral and topical antibiotics

Thiboutot D, et al (2009) J Am Acad Dermatol. S1-50.

How to use Benzoyl Peroxide

- Treatment regimens
 - Daily or pulse therapy (one week per month)
 - Use on face, chest, and back
 - Don't use at same time of day as retinoid
- Tell patients that the purpose of BPO is to keep their other medicines working well
- Combo products (EpiDuo, Benzaclin, Duac, Acanya) improve adherence

Other Strategies to Prevent Antibiotic Resistance

- Don't use oral or topical abx as monotherapy
 - *Always use combination therapy!*
- Prescribe BPO with antibiotics
- Avoid using oral and topical antibiotics at the same time
- Try not to switch antibiotics
- Use topical retinoids for maintenance therapy, with BPO if needed

Thiboutot D, et al. J Am Acad Dermatol. 2009 May; 61:50.

Case 4



This 16-year-old boy has been on minocycline, tretinoin and BPO for 3 months. He has pitted scars.

Case 4:

What should you do next?

1. Wait another 3 months for the minocycline to start working
2. Change to tetracycline
3. Change to doxycycline
4. Prescribe isotretinoin yourself
5. Refer to dermatology

When to refer to dermatology



- Severe, scarring, nodulocystic acne
- Inadequate response to first-line antibiotics
- Atypical acne
- Significant parental or patient concern

What will derm do?

- Second line antibiotics
 - Cefadroxil, cephalixin
 - Septra
 - Amoxicillin
- Hormonal therapies for girls
 - Spironolactone
 - OCPs
- Isotretinoin
- Refine topical regimen
- Acne surgery





Take Home Points

- Combination retinoid based therapy is first line treatment for almost all patients with acne
- Even mild acne can have psychosocial effects - offer treatment
- Doxycycline is the first line abx for moderate acne
- Help limit antibiotic resistance - always use BPO when using another antibiotic

References

Preadolescent Acne

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Antibiotic Resistance

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Benzoyl Peroxide

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Does isotretinoin cause IBD?

1982: Isotretinoin approved by FDA

1982: "isotretinoin-induced IBD" reported

- litigation: \$12.9 million awarded to 3 patients
- result: IBD warning added to package insert

2006: FDA MedWatch 1997-2002

- 85 patients
- only 4 (5%) are highly probable associations

Crockett SD et al (2009) *Am J Gastroenterol*, 104(10):2387
Reddy D et al (2006) *Am J Gastroenterol*, 101:1569

Does isotretinoin cause IBD?

2010: 2 important studies

- Crockett et al (2009) *Am J Gastroenterol*
 - 8,199 patients with IBD
 - Only UC is strongly associated with prior isotretinoin
 - OR 4.36, 95% CI 1.97-9.66
 - Increasing dose of isotretinoin associated with elevated risk of UC (20mg dose, OR 1.50)

Sewell JL, Mahadevan U (2009) *Gastroenterol*, ePub ahead of print
Murphy CL et al (2009) *Am J Gastroenterol*, 104(9):2370
Crockett SD et al (2009) *Am J Gastroenterol*, 104(10):2387

Does isotretinoin cause IBD?

2010: 2 important studies

- Bernstein et al (2009) *Am J Gastroenterol*
 - U of Manitoba IBD database 10:1 case-control
 - no significant difference
 - med before IBD: OR, 1.16, 95% CI 0.73-1.77
 - med after IBD: OR, 1.25, 95% 0.77-1.94

Sewell JL, Mahadevan U (2009) *Gastroenterol*, ePub ahead of print
Murphy CL et al (2009) *Am J Gastroenterol*, 104(9):2370
Bernstein CN et al (2009) *Am J Gastroenterol*, 104(11):2774

Tetracyclines and IBD?

- Margolis et al (2010) *Am J Gastroenterol*
 - UK Health Improvement Network database
 - Possible association between IBD and tetracyclines
 - 94,487 individuals with acne
- Any IBD, Any tetracycline: HR 1.39, 95% CI 1.02-1.90
- Crohns-specific data
 - Minocycline: HR 1.28, 95% CI 0.72-2.30
 - Tetracycline: HR 1.61, 95% CI 0.995-2.63
 - Doxycycline: HR 2.25, 95% CI 1.27-4.00

Margolis DJ et al (2010) *Am J Gastroenterol*, 105(2):2610

What is the link between IBD and acne?

Acne may be a manifestation of systemic inflammatory disease

Acne in the setting of systemic inflammatory disease may require distinct treatment.

Are isotretinoin and tetracyclines associated with IBD?

- Maybe - further study is needed
- I have not changed my routine pre-abx counseling
- I take a careful family history and discuss the conflicting data on IBD and isotretinoin prior to starting isotretinoin
