Acne

Richard P. Usatine, MD, FACP
Professor, Family and Community Medicine
Professor, Dermatology and Cutaneous Surgery
Medical Director, University Skin Clinic
University of Texas HSC, San Antonio

Disclosure Statement:

- Co-President, Usatine Media
  - medical app development company
- Author, medical books

Objectives

- Evaluate the different etiologies of acne.
- Utilize appropriate criteria to diagnose acne as mild, moderate or severe.
- Formulate treatment plans for acne and modify therapies as necessary to minimize adverse side effects
Acne Vulgaris

- acne is an inflammatory disease of the pilosebaceous unit
- sebaceous follicles - produce small hairs and have large sebaceous glands
- sebum - complex lipid mixture to maintain hydration of skin

Steps in Acne Pathogenesis

1. obstruction of the sebaceous follicle with sebum and desquamated cells
2. disruption of follicle wall occurs
3. extrusion of P. acnes, sebum, hair, and cells into dermis causes inflammation
   - P. acnes causes inflammation not an infection

Four major pathophysiologic features

1. sebum overproduction
2. abnormal desquamation of the follicular epithelium (keratin plugging)
3. P. acnes proliferation
4. inflammation
Noninflammatory lesions are

- Closed comedones (whiteheads)
- Open comedones (blackheads)

Inflammatory lesions

- Papules and Pustules (<5mm)
- Nodules and Cysts (>5mm)

Cysts

- large deep inflammatory nodules are referred to as cysts
- most of these are not true epithelial cysts
Major Causes/Exacerbating Factors

- Genetics
- Androgens
- Stress
- Diet?

EBM – Diet and Acne

- Milk - excessive skim milk intake may increase acne in teenaged boys.
- Chocolate and fried food have no effect on acne.
- Glycemic index?

EBM #2 – Diet and Acne

- Higher glycemic index diet may worsen acne but studies are mixed1,2

Chocolate has no effect on acne.
Chocolate lovers need not despair over acne.
Studies of facial cleansing and sun exposure reveal mixed results on acne.


Other causes/Exacerbating Factors

- Excessive friction- ex. sweat bands, helmet straps
- Medications - ex. Li, INH, corticosteroids and some OCPs.
- oil-based cosmetics

Classification is essential

- obstructive vs inflammatory- use morphology of lesions
- by severity - mild, moderate, severe
- useful for deciding upon the therapeutic approach
EBM RECOMMENDATION # 2

- Topical clindamycin, erythromycin, benzoyl peroxide, tretinoin, oral tetracycline, and oral norgestimate/ethinyl estradiol work for acne.
- Benzoyl peroxide at various strengths was equally efficacious in mild/moderate acne.
- Seidler EM and Kimball AB, JAAD, 2010, 63(1), 52-62

Topical Medications for Acne Therapy

- Antimicrobial effect- benzoyl peroxide and azelaic acid (Azelex)
- Topical antibiotics - clindamycin and erythromycin
- Keratolytic agents – retinoids and azelaic acid

EBM - Benzoyl peroxide

- Kills *P. acnes* by direct toxic effect
- Use 2.5% to 5% (gel, cream, lotion)
- 10% is more irritating and no more efficacious
- Lotion is less irritating than alcohol based solutions

http://www.ncbi.nlm.nih.gov/books/NBK33218/
Topical antibiotics

- Erythromycin - solution, gel, cream
- Clindamycin (Cleocin-T) - solution, gel, lotion
- Combination products:
  - Benzamycin gel
  - BenzaClin (Duac) gel

Benzamycin or BenzaClin

- Erythromycin or Clindamycin with Benzoyl peroxide - effects are synergistic
- Defers development of resistance of P. acnes to antibiotics
- Appears to cause less irritation than most benzoyl peroxide only preparations

BenzaClin Gel or Duac Gel

- Clindamycin 1%, Benzoyl peroxide 5%
- Although not significant, one study demonstrated a trend for greater efficacy with a BenzaClin compared to a Benzamycin (Leyden et al., 2001).
- BenzaClin is somewhat less expensive
Topical retinoids

- Tretinoin – Retin-A
- adapalene gel – Differin gel
- tazarotene gel – Tazorac gel,
  - Decreases abnormal follicular keratinization
  - Expect some redness and scaling
  - May make acne worse during the first 2 weeks
  - Maximal effect seen in 3-6 months

Azelaic Acid Cream

- 20% Azelaic Acid cream (Azelex)
- uniquely has antibacterial and keratolytic effects
- first used for benign hyperpigmentation

Azelaic Acid Cream Clinical Efficacy for Acne

- As effective as:
  - Retin-A, Benzoyl peroxide, 2% Erythromycin
  - Less scaling, erythema and irritation than:
    - Retin-A, Benzoyl peroxide

  - Gibson, Cutis. January 1996
Dapsone gel is effective, safe, and well tolerated with a rapid onset of action.\textsuperscript{1}
No evidence of hemolytic anemia noted in G6PD-deficient subjects with acne vulgaris.\textsuperscript{2}


Benzoyl peroxide 2.5% + Adapalene 0.1% (Epiduo)

- Combination gel more effective than monotherapies, with differences as early as 1 week.\textsuperscript{1}
- Adverse event frequency and tolerability were similar to adapalene 0.1%, BPO 2.5%, or BPO 10%. Tazarotene 0.1% gel was more irritating than other test products. \textsuperscript{1,2}

2) Losche C, et. al. Adapalene 0.1% and benzoyl peroxide 2.5% as a fixed-dose combination gel is as well tolerated as the individual components alone in terms of cumulative irritancy. Eur J Dermatol. 2008 Sep-Oct;18(5):524-6.

Clindamycin 1.2% + Tretinoin 0.025% (Ziana)

- Combination gel reduced lesion counts and improved patients' overall appearance vs monotherapies.
- Discontinuation rates due to adverse events < 1%.

Systemic Antibiotics for Acne

- Doxycycline 50mg -100mg qd-bid - inexpensive, well tolerated, increases sun sensitivity
- Minocycline 50mg qd-bid – more expensive, effective, no significant photosensitivity, dizziness
- Erythromycin 250mg -500mg bid- inexpensive, frequent GI disturbance
- Trimethoprim/Sulfa – risk of Stevens-Johnson s.
- Azithromycin – weekly dosing – no better than others

Mild Comedonal Acne

- Try monotherapy
- Topical retinoid or azelaic acid
- Add OTC acne cleanser
  - Either BPO 4-5% or Salicylic Acid 2-3%

Mild-moderate Inflammatory

"Triple therapy"

1) Benzoyl Peroxide
2) Topical Clindamycin
3) Topical Retinoid

Can be achieved with any number of the combination products to increase compliance in those that can afford the combination products
Moderate to Severe Papulopustular Acne

- "Triple Therapy" + Oral antibiotics are essential - especially if the back or trunk is involved

- In women – may also add:
  - spironolactone 50-100mg qd-bid
  - OCPs – Ortho TriCyclen, Yaz, others

- If good response after 3 mo, consider tapering or stopping oral antibiotics (e.g, bid→qd, or 7-10 days of month when flaring)
Severe Nodular or Scarring Acne

- when acne has not responded to the above treatments, consider:
  - hormonal treatment for women
  - Isotretinoin - the nuclear option

Severe Nodular or Scarring Acne

- Isotretinoin - 0.5 - 1mg/kg day for 20 weeks
  - treats all the mechanisms for acne production
  - teratogenic

Indications for Accutane

- Severe nodulocystic acne
- Moderate inflammatory acne that fails to improve after 3-6 months of combination topical and systemic therapy
- Moderate acne with significant scarring or significant psychological distress
- Acne fulminans
- Acne conglobata
- Gram-negative folliculitis – rare complication of long-term oral antibiotic use
Severe Acne
16 yo boy

After prednisone then isotretinoin

Acne conglobata
Acne Fulminans

FIGURE 106-10 Rapidly worsening truncal acne in a 15 year-old-boy with a WBC of 17,000.

Isotretinoin (Accutane) Risks

- Birth defects – major teratogen
- Depression
- Suicide?
- Inflammatory bowel disease!

- Consent forms that emphasize these risks
- Must take mental health history

iPledge Program

- You must input information online (including pregnancy test results) on a monthly basis for all patients
- Need to use two separate, effective forms of contraception at least one month before, during, and for one month following therapy
Before and after Isotretinoin

Hormonal Therapy for Women with Acne

- Can treat acne of any type/severity with OCP
- FDA approved for acne: Ortho Tri-Cyclen, Estrostep, Yaz, Yasmin, Beyaz
- “Yazes” contain the progestin drospirenone
Spironolactone

- For women – especially if hirsutism exists
- 50 to 200 mg per day
- Must use birth control

Yasmin and spironolactone

- Small prospective study of 27 women with severe papular and nodulocystic acne.
- Combination of EE/DRSP (Yasmin) and spironolactone 100 mg daily
- 85% of subjects were entirely clear of acne lesions or had excellent improvement
- No significant elevation of serum potassium


Oral contraceptive failure rates and oral antibiotics

- Women taking antibiotics had oral contraceptive pill failure rates of 1.6% versus 1% without.
- Although this difference was not statistically different, consider warning patients about the slight chance that daily antibiotics may interfere with the efficacy of oral contraceptives.

Helms SE, et al. Oral contraceptive failure rates and oral antibiotics. JAAD. 1997 May;36
In summary

- Tailor therapy to morphology, distribution and severity of the acne
  - Comedonal vs. inflammatory
- Use combination therapy for most types
- Consider hormonal therapy for women
- Know when to use or refer for isotretinoin treatment

Objectives for Cases

- Discuss how to individualize acne treatment for patients by type of acne and severity
- Describe the use of topical retinoids for treating acne.
- Discuss use of systemic antibiotics for acne.
- Describe how to do acne injections and acne surgery.
- Discuss the risks and benefits of isotretinoin in acne.
Conclusion

- Give the patient hope
- Have follow-up at the onset of treatment to increase compliance and efficacy (4-6 weeks)
- Keep titrating and adjusting medications until good results are achieved