Disclosures

- I have no relevant disclosures
- Off-label treatments will be discussed
Overview

- Pathophysiology
- Types of acne lesions
- Treatments
- Cases
- Special circumstances
Introduction

- At least 85% of individuals between ages of 12 and 24 have some form of acne
- Associated with anxiety, depression, and social isolation
- Physical scarring
- Familial tendency
- Chronic
- Pediatricians are in a key position to treat acne
Pathophysiology of Acne

- Understanding the pathophysiology of acne is key to developing an effective treatment plan for acne.
- The microcomedone is the precursor lesion in acne so reduction and prevention of new ones is critical to the management of acne.
- Treatment should be based on patient’s pimple profile (comedonal, inflammatory, both) and secondary changes.
- Acne is a multifactorial disease so combination therapy results in more rapid and successful clearance.
Pathogenesis of Acne

- Key players
- Pilosebaceous unit
- Androgens produced by the adrenal glands and gonads
- *Propionibacterium acnes* (*P. acnes*)
- Innate immune system
Pathogenesis of Acne

- Sebaceous hyperplasia and seborrhea
- Follicular keratinocyte proliferation and abnormal desquamation
- Proliferation of *P. acnes*
- Immune response and inflammation
Treatment of Acne

- **Sebum production**
  - Isotretinoin
  - OCPs/spironolactone
  - Laser/PDT

- **Follicular hyperkeratosis**
  - Isotretinoin
  - Topical retinoids
  - BPO
  - Salicylic acid

- **P. acnes Proliferation**
  - BPO
  - Antibiotics
  - Retinoids (indirectly)
  - Lasers/PDT

- **Inflammation**
  - Isotretinoin
  - Topical retinoids
  - Oral antibiotics
  - BPO
  - Salicylic acid
Progression of Acne Lesions

Diagram showing:

- **Microcomedone**
  - Epidermis
  - Sebaceous lobule
  - Follicular epithelium

- **Comedone**
  - Epidermis
  - Sebaceous lobule
  - Follicular epithelium
Progression of Acne Lesions

Papule/pustule

Nodule
Noninflammatory Lesions

Closed comedones “whiteheads”

Open comedones “blackheads”
Inflammatory Lesions

Papules and pustules

Nodules and cysts

Source: www.derm101.com
Secondary Lesions
Treatment of Acne

- Consider lesion morphology ("pimple profile")
- Assess severity
- Severity may NOT correlate with patient’s perception of severity
- Look for pigmentary changes and/or scarring
- Assess how bothered patient is by acne
- Past acne treatments
- Allergies or past reactions to treatments
- Insurance coverage 😞
“Doorway Test”
Salicylic Acid

- Present in numerous OTC acne treatments 0.5 – 2 %
- Many different formulations
- Mildly comedolytic
- Less effective than benzoyl peroxide
- Effective as monotherapy for mild acne
- Adverse effects: erythema, peeling
Benzoyl Peroxide (BPO)

- FDA ≥ 12 years
- Monotherapy for mild acne or combination therapy for all acne types
- Bactericidal, mildly comedolytic and anti-inflammatory
- No evidence of *P. acnes* resistance
- **Protects against development of bacterial resistance when co-administered with long-term (> 2 months) antibiotics**
- 2.5% formulations have similar kill rate as 10%, with less irritation
- Adverse effects: irritant or allergic contact dermatitis, photosensitivity, bleaches hair and textiles
Tips to choosing a BPO

- > 100 of products to choose from 2.5 – 10%
- Various formulations (creams, gels, lotions, washes, foams)
  - Base choice on skin type
- Leave-on products: more effective, more irritating, bleach clothing
- Wash-off products: less effective, less irritating, convenient
- All monotherapy products OTC
- Combination products: BPO + erythromycin (BenzaMycin), BPO + clindamycin (generic, BenzaClin, Duac, Acanya), BPO + adapalene (EpiDuo)
But it worked for P-Diddy!

- Proactiv®
  - “Elegant” formulation of benzoyl peroxide and salicylic acid
  - 3-step process (cleanser, toner, lotion)
  - Great marketing
Topical Retinoids

- FDA ≥ age 12
- 1st line and maintenance for all types of acne
- Adapalene, tretinoin, tazarotene
- Comedolytic, anti-inflammatory
- Reduce and prevent formation of microcomedones and comedones
- Reduce inflammatory lesions
Topical Retinoids

- **Efficacy**
  - > 16,000 patients in clinical trials
  - 50% (on average) reduction acne lesions at 12 weeks

- **Adverse Effects**
  - Erythema, desquamation, burning, pruritus
  - More common in patients with dry skin or eczema
  - Increased sensitivity to sun
  - Initial flare of acne
  - Pregnancy category C (tazarotene category X)
Retinoid Effect on Acne Lesions

Topical Retinoids

- **Tips to improve compliance**
  - Pea-sized amount to entire face (not spot treating)
  - Mild soap-free cleanser
  - Ok to use an oil-free emollient
  - Start every other day and increase as tolerated
  - Apply an oil-free sunscreen SPF > 15 every morning
  - May initially worsen acne
  - 50% improvement at 3 months
Topical Retinoids

- **Adapalene** (FDA ≥ 12)
  - Generic: 0.1% cream and gel
  - Differin: 0.1% cream, gel, lotion; 0.3% gel
  - Combination (EpiDuo FDA ≥ 9): 0.1% gel / BPO 2.5%

- **Tretinoin** (FDA ≥ 12)
  - Cream: 0.025%, 0.05%, 0.1%
  - Gel: 0.01%, 0.025%, 0.04%, 0.1%
  - Microsphere gel (Retin-A Micro): 0.04%, 0.1%
  - Polymerized gel (Avita): 0.025%
  - Emollient gel (Atralin): 0.05%
  - Combination (Veltin, Ziana): 0.025% + 1.2% clindamycin

- **Tazarotene** (FDA ≥ 12)
  - Tazorac cream: 0.05%, 0.1%
  - Tazorac gel: 0.05%, 0.1%
Topical Retinoids

- **Tips to choosing a topical retinoid**
  - Many formulations and strengths
  - Sensitive skin: cream not gels; lower strengths; special formulations
  - Oily skin: gels; higher strengths
  - Generic tretinoin is degraded by sunlight – has to be applied at night
  - Tretinoin and tazarotene degraded by benzoyl peroxide
Antibiotics

- Topical and oral
- Antibacterial and anti-inflammatory
- Inflammatory acne
- Should NEVER be used as monotherapy
- Increasing concerns over bacterial resistance
Antibiotics

- **Topical**
  - Mild to moderate inflammatory acne
  - Clindamycin 1% solution, lotion, gel
  - Erythromycin 2% solution, gel
  - Combination products
    - BPO
    - Tretinoin 0.025% gel (Ziana)
  - Local irritation, allergy, rarely diarrhea with clindamycin
  - Never use as monotherapy
Antibiotics

- Oral
- Moderate to severe inflammatory acne
  - Tetracycline, doxycycline, minocycline (FDA > 8; D)
  - Erythromycin (< 8; B)
- Average dose:
  - Doxycycline or minocycline: 50 - 100 mg QD – BID
  - Extended release minocycline (Solodyn): 1 mg/kg/day
  - Need 6 – 8 weeks to assess response
  - Stop 1 month after cessation of new inflammatory lesions
- Adverse effects: photosensitivity, GI, headache, pseudotumor cerebri
  - Minocycline: vertigo, blue-gray hyperpigmentation, DRESS, drug-induced lupus, serum sickness
Antibiotics & Resistance

- Antibiotic resistance is becoming a major public health concern
- Need to limit antibiotic use (topical and oral) for acne
- Add BPO when long-term (> 2 months) antibiotic use is needed
- Resistance associated with treatment failures
- Resistance of more pathogenic bacteria a major concern
- Resistant *P. acnes* spread to close contacts
**Antibiotics & Resistance**

- **Tips to limit antibiotic resistance**
  - Avoid monotherapy with antibiotics – co-prescribe a BPO when possible
  - Co-prescribe a topical retinoid early for maintenance
  - Stop antibiotic once inflammatory lesions no longer appearing
  - Avoid concurrent use of oral and topical antibiotics, especially if chemically different
  - Use original antibiotics for relapses
  - Consider OCPs / isotretinoin for patients unable to stop antibiotics
Hormonal Therapy

- Decreases sebum production

- Combination oral contraceptives (ethinyl estradiol + progestin) suppress ovarian androgen production
  - Ortho Tri-cyclen (EE 35 μg / norgestimate)
  - Estrostep (EE 20-35 μg / norethindrone acetate)
  - Yaz (EE 20 μg / drospirenone)

- Spironolactone blocks androgen receptors and inhibits 5α-reductase
  - Dose 25 – 200 mg/day; often with an OCP

- Progestin-only OCPs can worsen acne
Isotretinoin

- Claravis, Amnesteem, Zenatane, Absorica (Accutane off the market)
- Indicated for severe nodular acne, scarring acne, unresponsive moderate to severe acne, and chronic acne prone to relapse
- Isotretinoin monotherapy remains treatment of choice for severe acne
- Targets all 4 pathogenic factors
- Most potent inhibitor of sebum
- 85% completely clear, 20% need a second course
Isotretinoin

- Dry skin, lips
- Nosebleeds
- Headaches
- Sun sensitivity
- Decreased night vision
- Myalgias, arthralgias
- Elevated LFTs, TG
- Depression, suicidal ideation
- IBD
- Birth defects (I-pledge, don’t share, don’t give blood, monthly UPT, OCP)

Bottom Line – Close Monitoring, but Effective
CASES
Neonatal Acne

- Onset < 6 weeks
- Papules, pustules, NO comedones
- May be due to colonization with *Malassezia* sp.
- Face, neck, upper chest
- Self-limited
- Ketoconazole 2% cream
Infantile Acne

- Infantile acne
  - Onset 6 weeks – 12 months of age
  - More common in males
  - Comedones, inflammatory lesions
  - Typically cheeks and chins
  - Can scar
  - Look for other signs of hyperandrogenism
  - Work-up if other signs or severe and recalcitrant
  - Marker for more severe acne in adolescence
Infantile Acne

- Treatment of infantile acne
  - Topical retinoids
  - BPO
  - BPO/antibiotic
  - Oral erythromycin (cyclines contraindicated!)
  - Isotretinoin if severe
Childhood Acne

- Childhood acne (1 – 6 years)
  - Very uncommon
  - Warrants a work-up for hyperandrogenism due to adrenal, gonadal/ovarian pathology
  - Signs include accelerated growth, advanced bone age, body odor, seborrhea, axillary or pubic hair, genital maturation
  - Studies: bone age, FSH, LH, testosterone, DHEAS, prolactin, cortisol, 17-alpha-hydroxyprogesterone
  - Referral to an endocrinologist
Drug Induced Acne

- Drug-Induced Acneiform Eruptions
  - Corticosteroids
  - Anabolic steroids
  - Anticonvulsants (phenytoin, phenobarbital)
  - Isoniazid
  - Lithium
  - Progestin-only contraceptives
  - Epidermal growth factor receptor inhibitors (erlotinib, cetuximab)
Summary

- Acne is a chronic, multifactorial disease.
- Acne can cause physical and psychological scarring.
- Treatment choices should be based on type and severity of acne.
- Treatments should target the microcomedone, which is precursor of comedonal and inflammatory acne.
- Antibiotics should never be used as monotherapy.
- Acne in young children should increase suspicion for underlying hyperandrogenism.
Any Questions?

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