18 & 19 - Acne

Background:

4 Main Contributing Factors

1. Abnormal keratinization
   - Keratinocytes proliferate too quickly
   - Keratinocytes are more cohesive
2. Excess sebum production
   - Sebum production under hormonal control
   - Androgen receptor on sebaceous glands binds Dihdrotestosterone (DHT) = ↑ sebum production

PEARL: So why do we give oral contraceptives to female patients? **OCPs inhibit ovarian androgen production via negative feedback inhibition = ↓ sebum production.** Also, OCPs **increase sex hormone binding globulin** which **reduces free androgens in serum.**

3. *Propionibacterium acnes* overgrowth
   - Thrives in oily environment
4. Inflammation

PEARL**:** What mechanism does *P acnes* induce inflammation? P acnes activates **toll-like receptor 2**, which are receptors on the surface of keratinocytes and macrophages → causes release of inflammatory mediators like IL-1, IL-8, IL-12, and TNF-alpha.

Additional Triggers

1. **Hormonal** or menstrual flares
   - Look for lesions on the jawline
2. Psychological **stress**
3. **Cosmetic** products
   - Occlusive foundations, hair spray, pomades
   - Consider mineral-based, oil-free noncomedogenic makeups
4. **Mechanical** factors (e.g. sports gear)
5. **Medications**
   - "A PIMPLE": anabolic steroids, prednisone, iodides, marijuana (loose association), progesterone-only contraceptives, lithium, EGFR inhibitors (e.g. erlotinib)
6. **Diet**
   - Theory: High Glycemic Load causes ↑ insulin levels = ↑ androgens
     - Sweet/Fatty Diet → Plant-based/low glycemic load may improve acne

Clinical Presentation:

Types of Acne Lesions

1. Open comedones ("blackheads")

   "Comedone" = plugged hair follicle ("pore")

   Turns black due to air oxidizing oils and debris to black color
2. Closed comedones ("whiteheads")
   - White or fleshy bumps that have no obvious follicular opening
3. Inflammatory papules, pustules, nodules
4. Cysts

Types of Acne Scars

1. Icepick
2. Boxcar
3. Rolling
4. Hypertrophic/Keloidal

Acne Variants

- Acne excoriee
  - Often young acne patient w/ anxiety or OCD who picks at their lesions
- Acne congloblata
  - Nodulocystic acne w/out systemic changes
- Acne fulminans
  - Nodulocystic acne w/ systemic changes
  - Classically: teenage boys w/ fevers, joint pain, and even osteolytic bone lesions

PEARL**:** SAPHO Syndrome: synovitis, acne conglobata, pustulosis (including pustular psoriasis), hyperostosis, and osteitis

Pediatric Acne

- Neonatal Acne (Birth – 1 month)
  - 20% of newborns
  - Usually self-resolves
- Infantile Acne (1 month – 1 year)
  - More comedonal and more resistant than neonatal acne
- Mid-Childhood (1-6 years)
  - Assess for signs of androgen excess (consider endocrine workup)
    - Pubic hair, testicle or clitoral enlargement, breast development, and increased muscle mass
- Prepubertal Acne (7-11 years)

Treatment:

Basic Acne Recommendations

- Counsel to wash face x2 daily and after exercise
  - Use gentle cleansers (e.g. Cerave, Cetaphil, Aveeno, Neutrogena, Vanicream)
  - Benzoyl peroxide (+ topical antibiotic), salicyclic acid, and sulfur-based washes
- Use a daily facial moisturizer w/ > SPF 30
  - Prevents post-inflammatory hyperpigmentation (PIH)
- Refrain from picking → can lead to scarring

Treatment Groups (Severity Stratification)

1. **Over-the-counter treatments** (Listed Above)

PEARL**: If using topical antibiotic, remember to combine with BPO wash** to **↓ antibiotic resistance,** or consider combo topical like clindamycin/BPO

2. **Prescription topical antibiotics or retinoids**

- Topical Antibiotics:
    - Remember your ABCDE's. Azelaic acid, benzoyl peroxide, clindamycin, dapsone (Aczone), erythromycin, sulfacetamide
- Topical Retinoids:
    - Cosmeceuticals (Retinol, Retinal) & prescriptions (tretinoin, adapalene, and tazarotene)
        - Tretinoin: inactivated by UV light (use at night) and oxidized/inactivated by BPO (do not use w/ topical BPO or after BPO wash)
        - Adapalene: 3rd gen. that is light stable and often combined w/ BPO (e.g. Epiduo)
        - Tazarotene: pregnancy category X, strongest topical retinoid

PEARL: Topical retinoids are our most important tx for acne! Target 3 out of 4 components of acne pathogenesis (Normalize keratinocyte hyperproliferation, comedolytic, and anti-inflammatory)

PEARL: Use **pea-sized amount of topical retinoid** and apply throughout acne prone areas. Remind patients that this is NOT spot tx. If dryness, applying every other night working up to nightly + moisturizer!

PEARL: Retinoids tend to be drying so if the pt has oilier skin and isn't too sensitive, you can use a higher strength retinoid

3. **All of the above + oral agents (antibiotics, spironolactone, or oral contraceptives)**

- Oral Antibiotics:
    - Doxycycline (Targadox, Acticlate, Doryx), minocycline (minocin, solodyn), tetracycline
        - Approved for pts 8 y/o and above
        - Patients <8 y/o or tetracycline allergies→ consider erythromycin, azithromycin, or bactrim

PEARL**: Doxycycline Side Effect**: GI (nausea, vomiting, diarrhea, esophagitis)…↓ w/ large glass of water and meal (avoid dairy, calcium decreases absorption), photosensitivity, vaginal candidiasis, photo-onycholysis.

Minocycline Side Effect: GI (above), hyperpigmentation (scars, shins, sun-exposed), vertigo, teeth discoloration, and rarely, lupus-like syndrome or benign intracranial hypertension (pseudotumor cerebri)

PEARL: College-aged female w/ acne that flares on her jawline during menses not willing to use oral antibiotics. Dx? Hormonal acne Tx? Oral contraceptives and spironolactone

- Oral Contraceptives:
    - Ortho Tri-Cyclen (norgestimate w/ ethinyl estradiol)
    - Yaz (drospirenone w/ ethinyl estradiol)
    - Estrostep (norethindrone w/ ethinyl estradiol)

PEARL: How do you screen patients to ensure they are safe on the pill?

Risks outweigh benefits in the following:

1) >35 yo who smoke >15 more cigarettes per day 2) multiple cardiovascular risk factors such as HTN, diabetes, smoking 3) hx of HTN 4) hx of venous thromboembolism 5) hx of ischemic heart dz 6) hx of stroke 7) current breast cancer, hepatocellular adenoma, or malignant hepatoma 8) severe cirrhosis

- Spironolactone:
    - an **aldosterone antagonist, inhibiting 5-alpha reductase** (converts testosterone → more potent DHT).
    - **Dosed 50-200 mg daily.**
    - **Contraindications** include renal insufficiency, hyperkalemia, pregnancy, and abdominal uterine bleeding, and black box warning for personal or FHx of breast cancer.
    - Side effects
        - Hormonal-related: menstrual irregularities, breast tenderness, and gynecomastia
        - Diuretic-related: urinary frequency, orthostatic hypotension, hyperkalemia

PEARL: **Hyperkalemia and Spironolactone**?

Recent literature concluded that routine potassium monitoring in young (18-45 y/o), healthy pts who do not have renal dz, congestive heart failure, or on other RAS medications, is not recommended. Otherwise, potassium checked q3-6 months and w/ dosing changes.

4. **Isotretinoin**

- Referred to its old brand name "Accutane", which is no longer available
- Daily use for ~ 6 months (Goal: 120-150 mg/kg)
- Works on all 4 components of acne
    - May shrink sebaceous glands up to 90%

PEARL: What are the **side effects of isotretinoin** and how are they monitored?

Birth Defects (Craniofacial & Cardiac abnormalities):

- iPledge = ensures 2 forms of contraception + that patients don't share their medicine or donate blood while on isotretinoin
- Monthly negative pregnancy test

Labs: Fasting Lipid panel, LFTs

DRYNESS, including dry skin, lips, eyes (caution pt's wearing contact lenses), nose bleeds: moisturizer, chapstick, eyedrops, Vaseline

Depression: Screening during visits

Inflammatory Bowel Dz: Screen for personal & FHx

Headache: do NOT combine doxycycline w/ isotretinoin → can cause pseudotumor cerebri

Hair loss, myalgias, arthralgias, slow healing (caution about waxing eyebrows; issues with ingrown nails)

Treatment approaches

MILD amount of comedones and inflammatory lesions

- Treated w/ benzoyl peroxide wash and/or topical retinoid
- If compliant, you can escalate treatment if needed by increasing retinoid strength or adding topical antibiotic

MODERATE

- Topical retinoid +/- topical BPO +/- topical antibiotic
- Oral antibiotic or OCP/Spironolactone (for female pt)
- Consider isotretinoin for moderate pt w/ resistance to previous tx plan above, present w/ scarring, or FHx of scarring acne

SEVERE

- Isotretinoin OR..
- Topical BPO + topical antibiotic + topical retinoid + oral antibiotic

***Always ensure compliance before significantly escalating therapy!