Acne vulgaris

Basic Dermatology Curriculum

Last updated January 2015
Module Instructions

• The following module contains a number of blue, underlined terms which are hyperlinked to the dermatology glossary, an illustrated interactive guide to clinical dermatology and dermatopathology.

• We encourage the learner to read all the hyperlinked information.
Goals and Objectives

• The purpose of this module is to help medical students develop a clinical approach to the evaluation and initial management of patients presenting with acne and rosacea.

• By completing this module, the learner will be able to:
  – Identify and describe the morphology of acne vulgaris
  – Explain the basic principles of treatment for acne vulgaris
  – Recommend an initial treatment plan for a patient presenting with comedonal and/or inflammatory acne vulgaris
  – Practice providing patient education on topical and systemic acne treatment
  – Differentiate acne vulgaris from acne rosacea
  – Determine when to refer a patient with acne to a dermatologist
Acne Vulgaris: Epidemiology

- **Acne vulgaris**, often referred to as “acne”, is a disorder of pilosebaceous follicles

  - **Epidemiology**
    - Affects 90% of adolescents
    - All races equally affected
    - Family history is often positive
    - Typically presents at ages 8-12 (often the first sign of puberty), peaks at ages 15-18, and resolves by age 25
    - 12% of women and 3% of men will have acne until their 40s
    - In women, it is not uncommon to have a first outbreak at 20-35 years of age
Acne Vulgaris: Clinical Presentation

• **Distribution**
  – Acne affects mainly the face, neck, upper trunk and upper arms (where sebaceous glands are abundant)

• **Morphology**
  – Acne begins with “clogged pores” (pore = pilosebaceous unit), aka comedones
    • Open comedones = “blackheads”
    • Closed comedones = “whiteheads”
• **Pathogenesis**
  
  – Four factors are involved in the formation of acne lesions
    
    • Increase in sebum production (influenced by androgens)
    
    • Keratin and sebum plug the hair follicle and accumulate leading to hyperkeratosis (comedone formation)
    
    • *P. acnes* (bacteria) proliferates in the sebaceous follicle (releases enzymes and stimulates release of pro-inflammatory cytokines)
    
    • Inflammatory response
Case One

Jim Reynolds
Case One: History

• **HPI**: Jim Reynolds is an 17-year-old healthy teenager who presents to his primary care physician with “pimples” on his face for the last 2 years. He reports a daily skin regimen of aggressive facial cleansing with a bar soap during his morning shower.

• **PMH**: no chronic illnesses or prior hospitalizations

• **Allergies**: no known allergies

• **Medications**: none

• **Family history**: father and mother had acne as teenagers

• **Social history**: lives at home with parents, attends high school

• **ROS**: negative
How would you describe Jim’s skin exam?

a. Mild comedonal acne without presence of scarring
b. Mild inflammatory acne without comedones
c. Moderate mixed comedonal and inflammatory acne with presence of scarring
d. Moderate mixed comedonal and inflammatory acne without presence of scarring
Case One, Question 1

Answer: C
Moderate mixed comedonal and inflammatory acne with presence of scarring

- Open comedo
- Closed comedo
- Pustule
- Inflamed papule
- Scarring
Classification of Acne Vulgaris

• Classification of acne is based on the morphology
  – Comedonal: open and closed comedones
  – Inflammatory: papules and pustules
  – Nodulocystic: nodules and cysts

• It is equally important to describe the severity and the presence of scarring for each patient
  – Each type can be mild to severe depending on the extent and density of acne
Case One, Question 3

Which of the following treatments would you recommend for Jim?

a. Salicylic acid 2% facial wash
b. Tetracycline Oral antibiotic
c. Combination therapy with benzoyl peroxide and topical retinoid cream
d. Combination therapy of oral isotretinoin and hormone therapy
e. No treatment necessary at this time
Case One, Question 3

Answer: c

Which of the following treatments would you recommend for Jim?

a. Salicylic acid 2% facial wash (less effective than BP, combination therapy indicated for moderate acne)

b. Tetracycline oral antibiotic (oral antibiotic monotherapy is not recommended due to possibility of bacterial resistance)

c. Combination therapy with benzoyl peroxide and topical retinoid cream (topical antibiotic could also be added)

d. Combination therapy of oral isotretinoin and hormone therapy (these are used in refractory cases of moderate/severe acne, not first-line)

e. No treatment necessary at this time (treatment of his acne is important in order to prevent scarring)
Acne-Related Changes

- Cystic or scarring acne should be treated aggressively to prevent permanent sequelae
  - Refer patients with difficult to control acne or the presence of scarring to dermatology

- In addition to scarring, patients may develop post-inflammatory hyperpigmentation (hyperpigmented macules that persist following inflammation in the skin)
Topical Retinoids (tretinoin, all trans retinoic acid)

• **Mechanism:**
  – Topical retinoids are vitamin A derivatives that act by normalizing the desquamation of follicular epithelium to prevent formation of new comedones and promote the clearing of existing comedones

• **Common Adverse Effects:**
  – Dryness, pruritus, erythema, scaling, photosensitivity

• **Available forms:**
  – Tretinoin, Adapalene, Tazarotene
  – Cream, gel, lotion, solution
Topical Retinoids (tretinoin, all trans retinoic acid)

Additional considerations:
- Use sunscreen and protective clothing to reduce photosensitivity
- Do not apply at the same time as benzoyl peroxide because benzoyl peroxide oxidizes tretinoin
- Tretinoin and Adapalene are FDA Pregnancy Category C; other agents are preferred for treatment of acne in pregnancy
- Tazarotene is Category X and contraindicated in pregnancy
Benzoyl Peroxide

• **Mechanism:**
  – Benzoyl peroxide is a topical medication with both antibacterial and comedolytic properties
  – Acts via the generation of free radicals that oxidize proteins in the *P. acnes* cell wall

• **Available forms:**
  – Available as a prescription and over-the-counter, as well as in combinations with topical antibiotics
  – Cream, lotion, gel, or wash

• **Common Adverse Effects:**
  – Bleaching of hair, colored fabric, or carpet
  – May irritate skin; discontinue if severe
Topical Antibiotics

• **Mechanism**
  – Reduce the number of P. acnes and reduce inflammation in inflammatory acne

• **Available forms:**
  – Erythromycin 2% (solution, gel)
  – Clindamycin 1% (lotion, solution, gel, foam)

• **Common Adverse Effects:**
  – Topical acne treatments are often irritating and can cause dry skin
    • When using retinoids or benzoyl peroxide, consider beginning on alternate days
    • Use a moisturizer to reduce their irritancy

• **Additional considerations:**
  – Often used with benzoyl peroxide (versus monotherapy) to prevent the development of antibiotic resistance in the treatment of mild-to-moderate acne
Acne Treatment: Patient education

- Patient education and setting expectations are important components of effective acne treatment
  - Physician and patient should develop a therapeutic regimen with the highest likelihood of adherence
  - Acne treatment targets new lesions, not present ones
- Lack of adherence is the most common cause of treatment failure
  - Patients will often stop their topical treatments too early without improvement in their acne
  - Topical agents take 2-3 months to see effect
  - Therapy should be continued for at least 8 weeks before a treatment response can be accurately evaluated
Acne Treatment: Patient education

- Many patients can be non-adherent to topical treatments due to adverse effects including skin dryness, peeling, redness, itching, burning, and stinging
  - Acne-affected skin can be deficient in ceramides, which play an important role in maintaining the skin barrier and preserving its ability to prevent moisture loss
  - Daily use of ceramide-containing moisturizers may improve skin dryness and irritation by repairing and maintaining the skin barrier, leading to improved adherence
Acne Treatment: Patient education

- Patients should use only the prescribed medications and avoid potentially drying over-the-counter products, such as astringents, harsh cleansers or antibacterial soaps, as they are ineffective for acne and potentially drying
  - Overaggressive washing and the use of particulate abrasive scrubs often exacerbates acne and should be avoided
- Cosmetics are often labeled as “non-comedogenic” or “oil-free” if they do not cause or exacerbate acne
- There is some evidence to suggest that diet contributes to acne
  - Low glycemic load diets may improve acne by reducing androgen-induced sebaceous gland activity and keratinocyte growth associated with increased insulin and IGF-1 levels
Case Two

Ryan Townsend
Case Two: History

- **HPI**: Ryan Townsend is a 15-year-old healthy teenager who presents to his primary care physician for evaluation of progressively worsening acne over the last 3 years.
- **PMH**: no chronic illnesses or prior hospitalizations.
- **PSHx**: Torn right achilles tendon 1 year ago.
- **Allergies**: no known allergies.
- **Medications**: OTC 10% Benzoyl Peroxide Wash and topical retinoid.
- **Family history**: Older brother had acne as a teenager.
- **Social history**: lives at home with parents, attends high school.
- **ROS**: negative.
Case Two: Physical Exam

- How would you describe Ryan’s skin?
Case Two: Physical Exam

- Severe nodulocystic acne with presence of scarring
Case Two: Management

Ryan has used a combination therapy of 5% benzoyl peroxide and a topical retinoid for the past year without significant improvement. What other treatment strategies can you consider?

a. Add a topical antibiotic
b. Add an oral antibiotic
c. Add oral isotretinoin
d. Refer to a dermatologist
e. All of the Above
Case Two: Management

Ryan has used a combination therapy of 5% benzoyl peroxide and a topical retinoid for the past year without significant improvement. What other treatment strategies can you consider?

a. Add a topical antibiotic
b. Add an oral antibiotic
c. Add oral isotretinoin
d. Refer to a dermatologist
e. All of the Above

- Severe acne can require combination therapy with oral antibiotics, topical retinoids, benzoyl peroxide, +/- topical antibiotics
- Dermatology referral for treatment with oral isotretinoin is necessary in acne failing other therapies
- Hormonal therapy in pubertal females can also be considered
You decide to prescribe Ryan an oral antibiotic, Minocycline 100 mg PO BID.

Which set of side effects do you want Ryan to be aware of?

a. Depressive symptoms or mood changes  
b. Dizziness, ataxia, nausea and vomiting  
c. GI upset and photosensitivity  
d. Xerosis, cheilitis, elevated liver enzymes, hypertriglyceridemia
Answer: B

Which set of side effects do you want Ryan to be aware of?

- a. Depressive symptoms or mood changes (small number of reported cases with Isotretinoin use, no strong evidence)
- b. Dizziness, ataxia, nausea and vomiting
- c. GI upset and photosensitivity (can be seen with any of the tetracycline antibiotics)
- d. Xerosis, cheilitis, elevated liver enzymes, hypertriglyceridemia (known side effects associated with Isotretinoin)
Oral Antibiotics

- **Mechanism:**
  - Reduce *P. acnes* colonization of the skin and follicles

- **Applications:**
  - Moderate to severe inflammatory acne

- **Available forms:**
  - Tetracycline, doxycycline, minocycline, among others
  - Often combined with benzoyl peroxide to prevent antibiotic resistance

- **Adverse effects:**
  - GI upset (epigastric burning, nausea, vomiting and diarrhea can occur)
  - Photosensitivity (patients may burn easier, which can be easily managed with better sun protection)
    - Sun block with UVA coverage is recommended for all acne patients on tetracyclines
  - Minocycline can cause vertigo, dizziness, and hyperpigmentation

30
Oral Tetracyclines: Patient Counseling

- **Additional considerations:**
  - Contraindicated in pregnancy and in children <8 years old
  - If the patient has not responded after 3 months of therapy with an oral antibiotic, consider:
    - Increasing the dose (if not at max dose)
    - Changing the treatment, or
    - Referring to a dermatologist

- **Patients need clear instructions**
  - If taking for acne, it is okay to take antibiotics with food and dairy products for tolerability of GI side effects
  - Take with full glass of water; prevents esophageal erosions
  - Tetracyclines do NOT interfere with birth control pills
  - It takes 2-3 months to see improvement
Minocycline pigmentation

Timing:
- Pigmentation appears after months to years in a small percentage of patients

Distribution:
- First noticeable on the alveolar ridge, palate, sclera

Morphology:
- Skin deposition can be brown or blue-grey (blue-grey pigmentation may occur in scars)

Additional Considerations:
- Skin pigmentation may not fade after discontinuation
- Patients on long-term minocycline should be screened; if seen on gums or sclerae, discontinue
Oral Isotretinoin

• **Mechanism:**
  – Oral isotretinoin is a retinoic acid derivative that targets all four of the pathophysiologic factors involved in acne

• **Applications:**
  – Severe, nodulocystic acne failing other therapies
    • Typically given in a single 5-6 month course

• **Common Adverse Effects:**
  – Xerosis (dry skin), cheilitis (chapped lips), elevated liver enzymes, hypertriglyceridemia

• **Additional Considerations:**
  – Isotretinoin is teratogenic and therefore absolutely contraindicated in pregnancy
    • Female patients must be enrolled in a FDA-mandated iPLEDGE prescribing program in order to use this medication
    • Female patients must use two forms of contraception during isotretinoin therapy and for one month after treatment has ended
### Acne subtype

| Mild Acne: Comedones with few inflammatory lesions | **Initial**: Topical retinoid or benzoyl peroxide (BP)  
**Alternative**: Combination therapy of BP with topical retinoid and/or topical antibiotic |
|-----------------------------------------------|------------------------------------------------------------------------------|
| Moderate Acne: Comedones with marked number of inflammatory lesions | **Initial**: Combination therapy with topical retinoid and BP +/- topical Antibiotic  
**Inadequate response**: Consider oral antibiotics, dermatology referral, and hormonal therapy for females |
| Severe Acne: Extensive Inflammatory Lesions with diffuse scarring | **Initial**: Combination therapy with oral antibiotic, topical retinoid, and BP +/- topical antibiotic  
**Inadequate response**: Consider oral isotretinoin, dermatology referral, and hormonal therapy for females |
Mini Case

Billy
Mini Case: History

A mother calls the advice line at your primary care practice, and she is concerned that her 5-year-old son, Billy, has “acne.” She says he has “pimples and white heads and red marks” on his cheeks.
Mini Case: History

Which of the following signs would make you most concerned about an underlying systemic abnormality? (Mark All That Apply)

- [ ] Breast Development
- [ ] Craniofacial deformities
- [ ] Facial Hair
- [ ] Fever
- [ ] Food Allergies
- [ ] Itching
- [ ] Increased Muscle Mass
- [ ] Pubic Hair
- [ ] Testicular Growth
- [ ] Wheezing
Mini Case: History

- Acne between the ages of 1 and 7 years-of-age is called “Mid-childhood acne,” and it is very rare.
- These features are all possible sequelae of excess androgens that warrant workup by a pediatric endocrinologist.
- Possible causes include: adrenal tumors, gonadal tumors, congenital adrenal hyperplasia, Cushing syndrome, and precocious puberty.

- [x] Breast Development
- [ ] Craniofacial deformities
- [x] Facial Hair
- [ ] Fever
- [ ] Food Allergies
- [ ] Itching
- [x] Increased Muscle Mass
- [x] Pubic Hair
- [x] Testicular Growth
- [ ] Wheezing
Mini Case: Pediatric acne

Pediatric acne can be categorized by the patients age and pubertal status:

- **Neonatal acne** (Onset birth to 6 weeks)
  - Usually self-limited; not true acne, no comedones

- **Infantile acne** (Onset 6 weeks to 1 year)
  - Usually self-limited; true acne with comedones

- **Mid-childhood acne** (1 year to 7 years)
  - Very uncommon

- **Preadolescent acne** (7-12 years or menarche in girls)
  - Common

- **Adolescent acne** (12-19 years or after menarche in girls)
  - Common
Mini Case: Pediatric acne

Treatment of pediatric acne

• From 1 to 7 years, the primary objective is to rule out an underlying systemic abnormality

• The treatment of preadolescent acne is similar to that in older age groups EXCEPT:
  – Oral tetracyclines are not used in children younger than 8 years of age because of a risk of damage to tooth enamel and developing bones
  – A topical retinoid can be started at any age but is off label in some cases
    • Adapalene and benzoyl peroxide gel 0.1%/2.5% is FDA approved for children 9 and older
    • Tretinoin 0.05% gel is FDA approved from children 10 and older
  – Oral contraceptives for acne unassociated with endocrine abnormalities should be withheld until 1 year after menarche
Case Three

Ms. Emily Garcia
Case Three: History

- **HPI**: Ms. Garcia is a 22-year-old woman who was referred to the dermatology clinic for new onset acne
- **PMH**: no major illness or hospitalizations, no pregnancies
- **Allergies**: allergic to penicillin (rash)
- **Medications**: occasional multivitamin
- **Family history**: noncontributory
- **Social history**: lives in the city and attends college
- **Health-related behaviors**: gained 40 pounds over the past 4 years despite a healthy diet and exercise habits
- **ROS**: new upper lip and chin hair growth, irregular menstrual cycles since menarche, last period was 4 months ago
Case Three: Skin Exam

How would you describe Ms. Garcia’s skin?
Case Three: Skin Exam

- Moderate **comedonal** and **inflammatory** acne of cheeks and jaw line, with scattered terminal hairs on the upper lip and lower chin.

- **Hair loss** noted on frontal and parietal scalp.
Case Three, Question 1

Based on the history and exam, what is the most likely diagnosis?

a. Cushing Syndrome
b. Gram negative folliculitis
c. Polycystic ovarian syndrome
d. S. aureus folliculitis
Case Three, Question 1

Answer: c

Based on the history and exam, what is the most likely diagnosis?

a. Cushing Syndrome (manifestations of excessive corticosteroids, which results in central obesity, muscle wasting, thin skin, hirsutism, purple striae)

b. Gram negative folliculitis (multiple tiny yellow pustules develop on top of acne vulgaris as a result of long-term antibiotic administration)

c. Polycystic ovarian syndrome

d. S. aureus folliculitis (multiple follicular pustules and papules)
Ms Garcia most likely has polycystic ovarian syndrome (PCOS)

– Affected individuals must have two out of the following three criteria:
  • (1) oligo- and/or anovulation,
  • (2) hyperandrogenism (clinical and/or biochemical)
  • (3) polycystic ovaries on sonographic examination*

– In addition to hormonal acne, increased circulating androgens also results in hirsutism

– Women with PCOS also have a greater degree with insulin resistance which can cause acanthosis nigricans

* Based on definition from the Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004
Case Three, Question 1

Ms. Garcia was given spironolactone and her acne improved. Why did this medication work?

a. Spironolactone has anti-androgenic effects
b. Spironolactone has anti-comedonal activity
c. Spironolactone when used appropriately has anti-bacterial activity
d. The diuretic effect of spironolactone eliminated sodium resulting in less sebum
Answer: a
Ms Garcia was given spironolactone and her acne resolved. Why did this medication work?

a. *Spironolactone has anti-androgenic effects*

b. Spironolactone has anti-comedonal activity (not true)

c. Spironolactone when used appropriately has anti-bacterial activity (not true)

d. The diuretic effect of spironolactone eliminated sodium resulting in less sebum (not true)
Androgens in Acne

• In many post-adolescent women, antiandrogen therapy can improve acne
  – These women have hormonal acne; their serum hormone levels are usually normal
  – Hormonal acne lesions are often perioral and along the jaw line
  – Many women report a pre-menstrual flare

• Not all women with hormonal acne are tested for hyperandrogenism
  – It should, however, be considered in the female patient whose acne is severe, sudden in onset, or associated with hirsutism or irregular menses
Treatment of Hormonal Acne

Commonly used agents to treat hormonal acne include:

- **Spironolactone** (50 mg daily to 100 mg twice a day)
  - **Mechanism**: androgen-receptor blocker, inhibitor of 5-alpha reductase
  - **Side effects**: Diuresis, hyperkalemia, irregular menstrual periods, feminization of a male fetus during pregnancy
  - **Additional consideration**: Combination with OCP can reduce irregular periods

- **Oral contraceptives**
  - **Mechanism**: suppress LH production, increase sex hormone binding globulin, inhibit 5-alpha reductase, block androgen receptor
  - **Available forms**: Yaz, Ortho Tri-cyclen, Estrostep are FDA approved for treatment of acne
  - **Side effects**: nausea, vomiting, abnormal menses, weight gain, breast tenderness, increased risk of thromboembolism
Acne Rosacea may look very similar to Acne vulgaris, however, it can be differentiated by an absence of comedones

**Morphology:**
- May present with easy flushing, erythema, telangiectasias, papules and pustules, and/or phymatous changes

**Triggers:**
- Alcohol, sunlight, hot beverages (heat), spicy food, emotional stress
- Unlike acne vulgaris, it is not related to hormones

**Additional Considerations:**
- Many patients with rosacea have ocular involvement

**Treatment:**
- Topical and oral treatments often improve the papules and pustules of rosacea, but will not reverse the underlying erythema and flushing
- All patients with rosacea should use sunscreen and avoid known triggers
Periorificial dermatitis, also known as perioral dermatitis, is another acneiform eruption that can be differentiated from acne vulgaris by an absence of comedones.

**Morphology:**
- Erythematous papules and pustules with scaling
- Usually located around the mouth, nose, and eyes (occasionally involves the chin, cheek, or forehead)

**Clinical features:**
- Occasionally presents with pruritus or burning
- Most patients will have history of prior or current use of topical steroids (rash will often improve with topical steroids and flare with cessation)

**Treatment:**
- Gradually taper use of topical steroids
- Systemic treatments: oral tetracycline for patients ≥ 8 years and oral erythromycin for patients < 8 years
- Topical treatments: metronidazole, erythromycin, and pimecrolimus
Take Home Points: Acne Vulgaris

- **Morphology:**
  - Characterized by open and closed comedones, papules, pustules, nodules, and cysts
  - Severity and presence of scarring must be included when describing acne

- **Pathogenesis:**
  - Related to the presence of androgens, excess sebum production, the activity of *P. acnes*, and follicular hyperkeratinization

- **Treatment:**
  - Systemic and topical retinoids, topical benzoyl peroxide, systemic and topical antimicrobials, and systemic hormonal therapies are the main classes of treatment for acne vulgaris
  - Untreated acne can result in permanent scarring
# Acne Vulgaris Review: Common First-Line Treatments

<table>
<thead>
<tr>
<th>Acne subtype</th>
<th>Management</th>
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<tbody>
<tr>
<td>Mild Acne</td>
<td><strong>Initial</strong>: Topical retinoid or benzoyl peroxide (BP)  &lt;br&gt;<strong>Alternative</strong>: Combination therapy of BP + topical retinoid and/or topical antibiotic</td>
</tr>
<tr>
<td>Moderate Acne</td>
<td><strong>Initial</strong>: Combination therapy with topical retinoid and BP +/- topical Antibiotic  &lt;br&gt;<strong>Inadequate response</strong>: Consider oral antibiotics, dermatology referral, and hormonal therapy for females</td>
</tr>
<tr>
<td>Severe Acne</td>
<td><strong>Initial</strong>: Combination therapy with oral antibiotic, topical retinoid, and BP +/- topical antibiotic  &lt;br&gt;<strong>Inadequate response</strong>: Consider oral isotretinoin, dermatology referral, and hormonal therapy for females</td>
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Acknowledgements

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References


To take the quiz, click on the following link:

https://www.aad.org/quiz/acne-and-rosacea-learners