

Acne Vulgaris
Updates on Approach to Treatment
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Acne Vulgaris

- Most common skin disease presenting to primary care physicians.
- Chronic disease for some patients
- Don't underestimate the social and psychological effect of acne on patients
- Acne is not necessarily a rite of passage

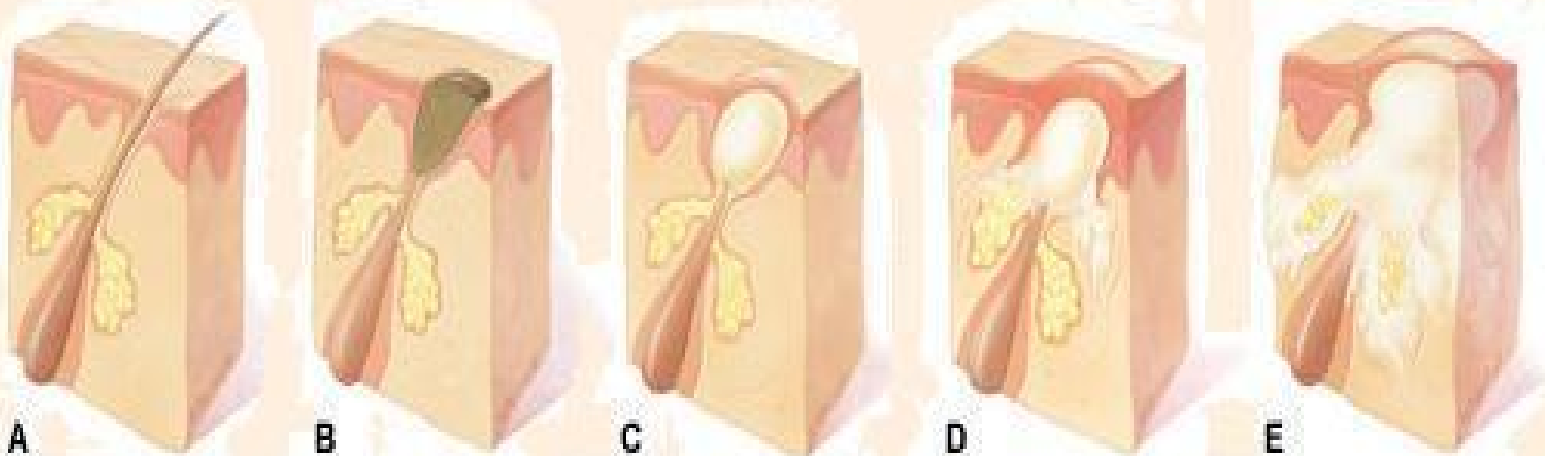
Pathophysiology

- Four primary pathogenic factors which interact in complex manner
 - Sebum production by the sebaceous gland
 - *P. acnes* follicular colonization
 - Alteration in the keratinization process
 - Release of inflammatory mediators into the skin
- Other factors
 - Androgens, stress, occupational exposure, underlying metabolic abnormalities
- Treatment should target these pathogenic factors

Clinical Features

- Non-inflammatory Lesions
 - Open comedones (blackheads)
 - Closed comedones (whiteheads)
- Inflammatory Lesions
 - Pustules/papules
 - Nodules
 - Cysts
- Help determine treatment modalities

Primary Lesions



(A) Normal follicle; (B) open comedone (blackhead);
(C) closed comedone (whitehead); (D) papule; (E) pustule.

Variants of Acne

- Acne cosmetica
- Acne excoriee
- Senile comedones
- Milia
- Acne mechanica
- Gram-negative acne
- Steroid-induced acne
- Occupational acne
- Favre-Racouchot syndrome
- Solid facial edema
- Neonatal acne
- Drug-induced acne

Treatment

- Choice of treatment depends on
 - Type of acne
 - Severity
 - Age
 - Location
 - Patient preference
- Evaluate patient
 - Current medications, allergies
 - Menstrual history
 - Tanning habits, hobbies
 - Expectations, myths, fears
 - Scarring
 - Pregnancy

Treatment

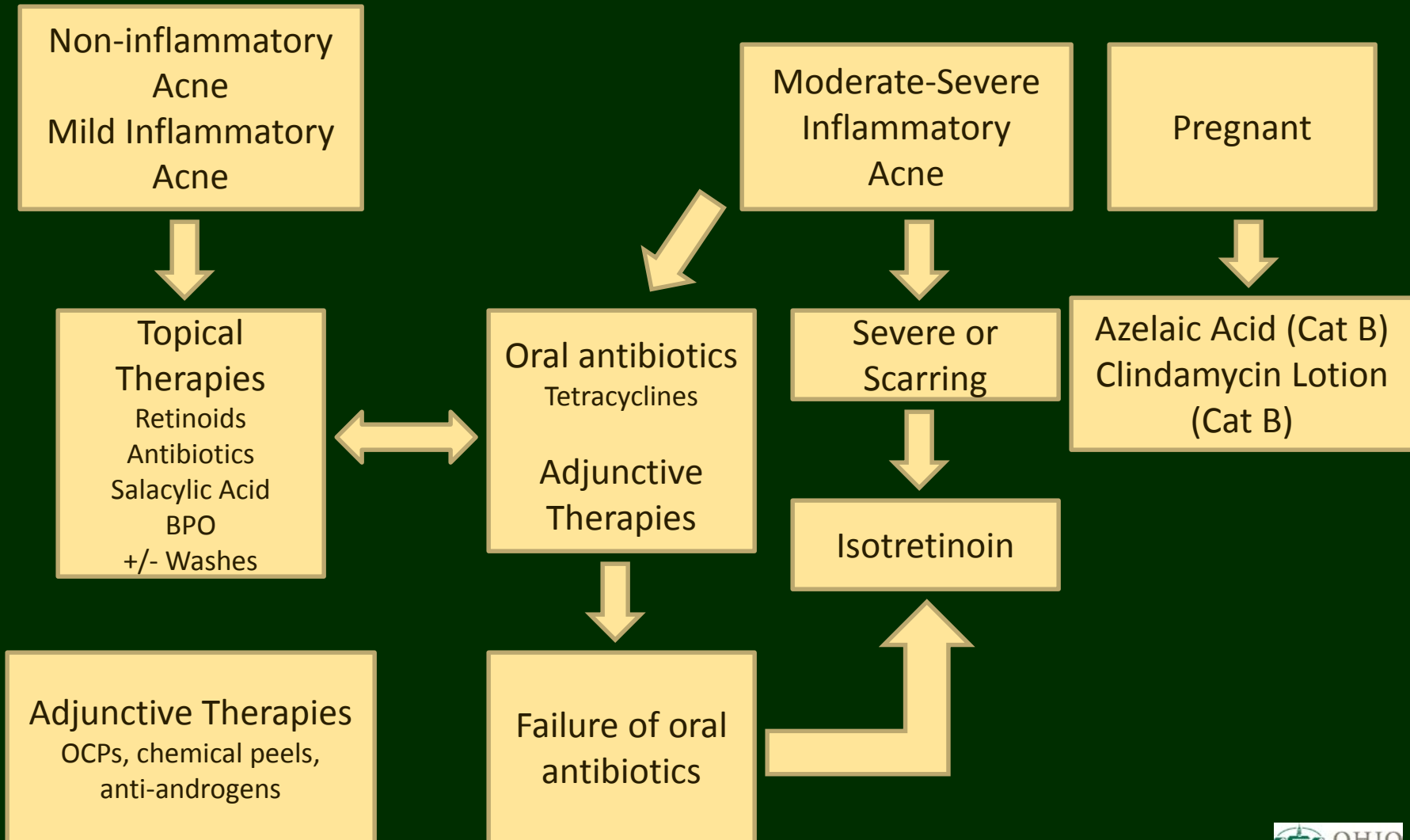
- Approach should be multi-therapy, not monotherapy
- Topicals
 - Antibiotics
 - Retinoids
 - Benzoyl peroxide
 - Combination therapies
 - Other therapies
- Oral therapy
 - Antibiotics
 - Isotretinoin
- Adjunctive therapy
 - Hormonal/anti-androgen therapy
 - Chemical peels
 - Scar treatment

Global Alliance Acne Treatment Algorithm

Acne Severity	MILD → MODERATE → SEVERE				
	Comedonal	Mixed and Papular/pustular	Mixed and Papular/pustular	Nodular(2)	Nodular/Conglobate
1 ST Choice	Topical Retinoid	Topical Retinoid + Topical Antimicrobial	Oral Antibiotic + Topical Retinoid +/- BPO	Oral Antibiotic + Topical Retinoid + BPO	Oral Isotretinoin ⁽³⁾
Alternatives (1)	Alt. Topical Retinoid or Azelaic acid* or Salicylic acid	Alt. Topical Retinoid Antimicrobial Agent + Alt. Topical Retinoid or Azelaic Acid*	Alt. Oral Antibiotic + Alt. Topical Retinoid +/- BPO	Oral Isotretinoin or Alt. Oral Antibiotic + Alt. Topical Retinoid +/- BPO/Azelaic Acid*	High Dose Oral Antibiotic + Topical Retinoid + BPO
Alternatives for Females (1,4)	See 1st Choice	See 1st Choice	Oral Antiandrogen ⁽⁵⁾ + Topical Retinoid/ Azelaic Acid* +/- Topical Antimicrobial	Oral Antiandrogen ⁽⁵⁾ + Topical Retinoid +/- Oral Antibiotic +/- Alt. Antimicrobial	High Dose Oral Antiandrogen ⁽⁵⁾ + Topical Retinoid +/- Alt. Topical Antimicrobial
Maintenance Therapy	Topical Retinoid		Topical Retinoid +/- BPO		

1. Consider physical removal of comedones. 2. With small nodules (<0.5 cm). 3. Second course in case of relapse. 4. For pregnancy, options are limited. 5. For full discussion, see Gollnick H, et al. JAAD. 2003;49 (Suppl):1-37.

Treatment Approach



Treatment Approach

- Early, appropriate treatment is best to minimize potential for acne scars
- Combination of a topical retinoid and antimicrobial agent remains the preferred approach for almost all patients with acne
 - Attacks 3 of the 4 major pathogenic factors of acne: abnormal desquamation, *P. acnes* colonization, and inflammation
 - Retinoids are anticomedogenic, comedolytic, and have some anti-inflammatory effects
 - BPO is antimicrobial with some keratolytic effects and antibiotics have anti-inflammatory and antimicrobial effects

Treatment Approach

- Topical retinoids should be first-line agents in acne maintenance therapy
- Avoid contributing to antibiotic resistance

Benzoyl Peroxide

- Mechanism of action¹
 - Bactericidal for *P. acnes*
 - Inhibits triglyceride hydrolysis
 - Decreases inflammation of acne lesions
- Advantages
 - No resistance demonstrated to date¹
 - When used in combination with a topical antibiotic can help to prevent resistance²
 - Activity is enhanced when combined with other topicals (i.e. clindamycin)^{1,2}
- Formulations
 - OTC & prescription
 - Washes, gels, lotion, solution

1. Wolverton SE. editor Comprehensive Dermatologic Drug Therapy 2nd Ed. Philadelphia: Saunders Elsevier; 2007.

2. Thiboutot D, et al. New insights into the management of acne: An update from the Global Alliance to Improve Outcomes in Acne Group. *J Am Acad Dermatol* 2009;60:S1-50.

Retinoids

- Most important class of drugs used to treat acne
- Topical form of vitamin A
- Mechanism of Action¹
 - Normalize follicular keratinization
 - Act on the microcomedone
- Proper instruction on application is essential to compliance
 - Gradual application with small amount of drug
 - “Training for a marathon”

1. Wolverton SE. editor Comprehensive Dermatologic Drug Therapy 2nd Ed. Philadelphia: Saunders Elsevier; 2007.

Retinoids

- “Least Irritating” (most tolerable)
 - Adapalene gel (Differin® 0.1%, 0.3%)
 - May be appropriate starting point for ethnic and/or sensitive skin
- “Moderately Irritating”
 - Tretinoin (cream, gel)
 - Tretinoin 0.01%, 0.05%, 0.025%
 - Retin-A Micro® 0.1%, 0.04%
- “Most Irritating” (least tolerable)
 - Tazarotene
 - More tolerable in lotion vehicle
 - Trifarotene 0.005% cream (Aklief)
 - Targets retinoid receptor gamma
 - 87% of retinoid receptors found in skin
 - Approved for chest and back as well

Topical Antibiotics

- Erythromycin 2%
 - Gel or solution or cream
 - Resistance of some *P. acnes* strains
 - Usage fallen out of favor
- Clindamycin phosphate 1%
 - Generic, Cleocin T[®] (lotion, gel, solution)
 - Antibiotic-associated colitis very unlikely
 - Work best in combination with BPO
 - Good choice for pregnant women (Pregnancy Category B)
- Azelaic acid
 - Finacea[™]
 - Bacteristatic/bactericidal against *P. acnes*
 - Good choice for pregnant women (Pregnancy Category B)

Topical Antibiotics

- Sodium sulfacetamide/sulfur (10%/5%)¹
 - Keratolytic effects, antibacterial for *P. acnes*
 - Used most commonly for rosacea
- Metronidazole¹
 - Benefit for acne debatable
 - Metronidazole lotion (generic), Metrogel 1%[®]
- Minocycline Foam 4% (Amzeeq)
 - Once Daily
 - Yellow discoloration
- Dapsone gel 5% and 7.5% (Aczone[®])²
 - Approved for moderate to severe acne
 - BID dosing
 - May cause a temporary yellow or orange discoloration of skin and facial hair if used along with BPO
 - Low risk of hemolytic anemia in G6PD deficient patients

1. Wolverton SE. editor Comprehensive Dermatologic Drug Therapy 2nd Ed. Philadelphia: Saunders Elsevier; 2007.

2. Aczone[®] prescribing information. January 2009.

Combination Therapies

- Clindamycin/Benzoyl peroxide
 - Clindamycin phosphate 1%/benzoyl peroxide 5% (Benzaclin[®] Gel)
- Erythromycin/Benzoyl peroxide
 - Erythromycin 3%/benzoyl peroxide 5% (Benzamycin[®])
- Retinoid/Benzoyl peroxide
 - Adapalene 0.1%/benzoyl peroxide 2.5% (Epiduo[™] Gel)
 - Tretinoin 0.1%/benzoyl peroxide 3% (Twyneo Gel)
- Retinoid/Clindamycin
 - Tretinoin 0.025%/Clindamycin phosphate 1.2% (Ziana[®] Gel)

Oral Antibiotics

- Therapeutic role in acne
 - Reduction of *P. acnes*
 - Anti-inflammatory activity
- Dosing
 - Start high then taper down after control is achieved
 - Use PRN during flares
 - Do not use as monotherapy

Oral Antibiotics

- Antibiotic Choice
 - Tetracycline Class (minocycline, doxycycline, tetracycline)
 - Erythromycin (Ery-tab[®])
 - Trimethoprim/sulfamethoxazole
 - Amoxicillin
 - Sarcycline (Seysara) 60mg 100mg and 150mg
 - Low propensity for antibiotic resistance
- Anti-inflammatory antibiotics/no antimicrobial activity
 - Doxycycline 20 mg (Periostat[®])
 - Doxycycline 40 mg (Oracea[®])

How to Prevent Resistance

- Combine a topical retinoid plus an antimicrobial
- Limit the use of antibiotics to short periods and discontinue when there is no further improvement or the improvement is only slight
- Co-prescribe a BPO-containing product or use as washout
- Oral and topical antibiotics should not be used as monotherapy

Hormonal Therapy

- FDA-approved OCPs for acne
 - Ortho Tri-Cyclen[®]
 - Estrostep[®]
 - Yaz[®]
- Anti-androgens
 - Spironolactone
 - Doses range between 50-200mg
 - Not FDA-approved for acne
 - Monitor side effects: menstrual irregularities, hyperkalemia

Hormonal Acne

- Clascoterone 1% (Winlevi)
 - Androgen inhibitor that targets acne hormones in the skin
 - Apply BID
 - Only hormonal treatment for men

Isotretinoin

- Approved for the treatment of severe recalcitrant nodular acne in 1982
- Member of the Vitamin A family
- Effects on acne
 - Normalizes the keratinization process
 - Reduces sebocytes and secretions
 - Reduces inflammation
 - Reduction in numbers of *P. acnes*

Isotretinoin

- Pre-medication counseling
 - Side Effects
 - Contraception
 - Compliance/duration of treatment
 - Laboratory monitoring
 - iPledge registration
- Dosing 1-2 mg/kg/day
 - Goal 120-150 mg/kg over course of treatment

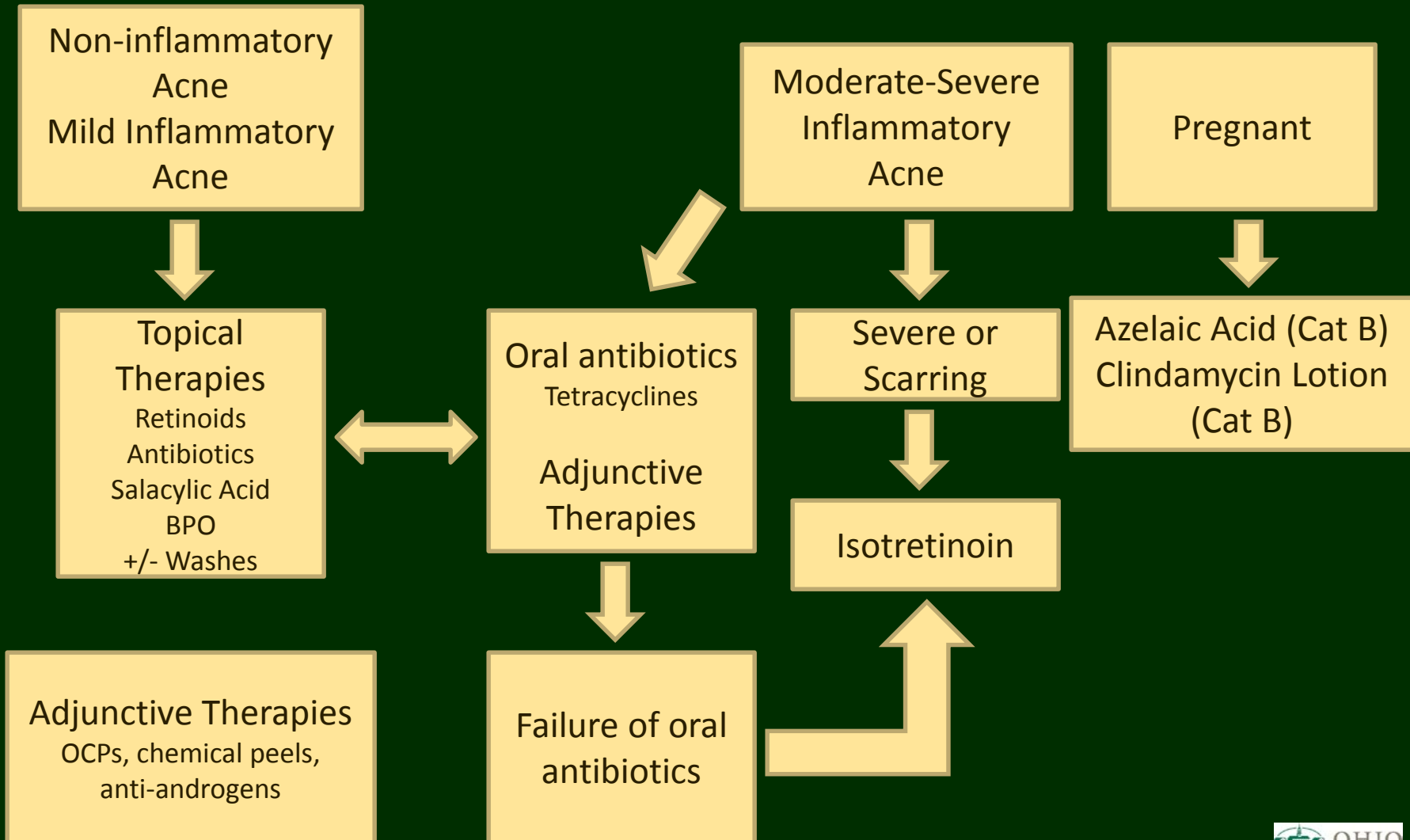
Case Studies

Case One

- 15-year-old male
- Non-inflammatory & inflammatory acne
 - Face only
 - Open/closed comedones
 - Papules
- Treatment Plan?



Treatment Approach

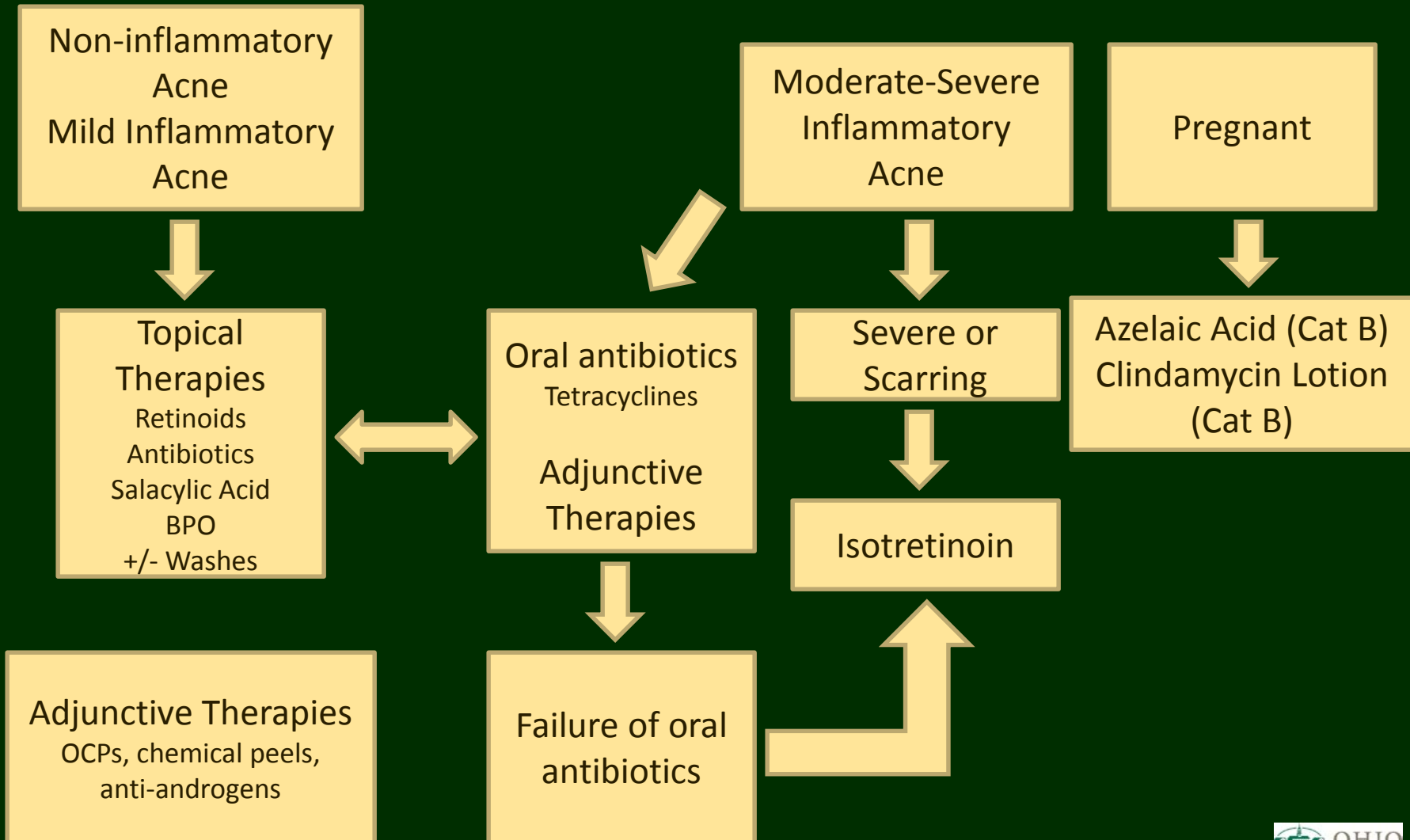


Case Two

- 17-year-old-female
- Inflammatory acne
 - Regular menstrual cycles (-flares)
 - Face, chest, back involved
 - Pustules, papules
 - Open & closed comedones
- Treatment plan?



Treatment Approach

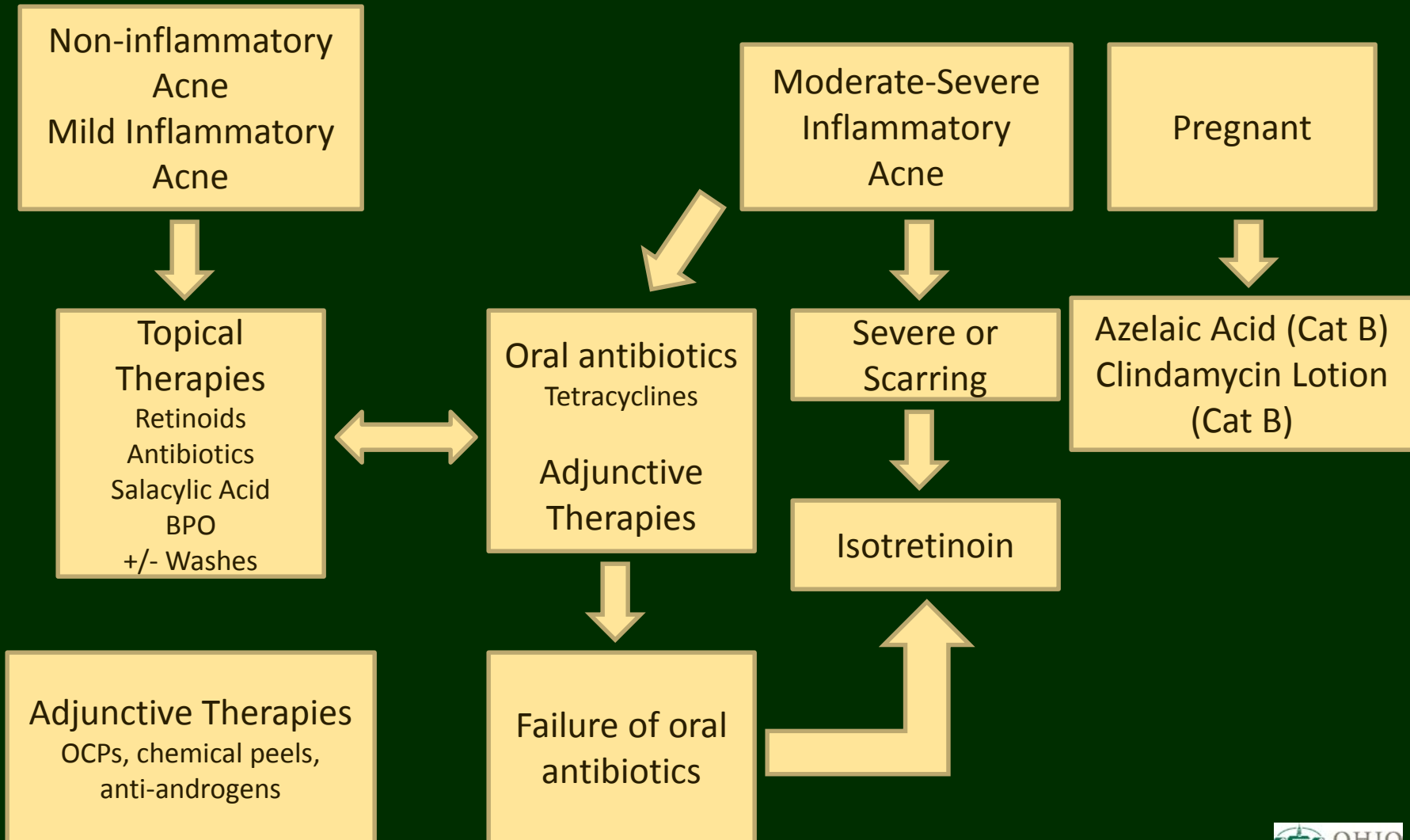


Case Three

- 22-year-old female
- Mild-moderate inflammatory acne
 - Regular menstrual cycles (+ flares)
 - Face involved
 - Chest, back spared
 - Nodular lesions along jawline
 - Comedones
- Treatment plan?

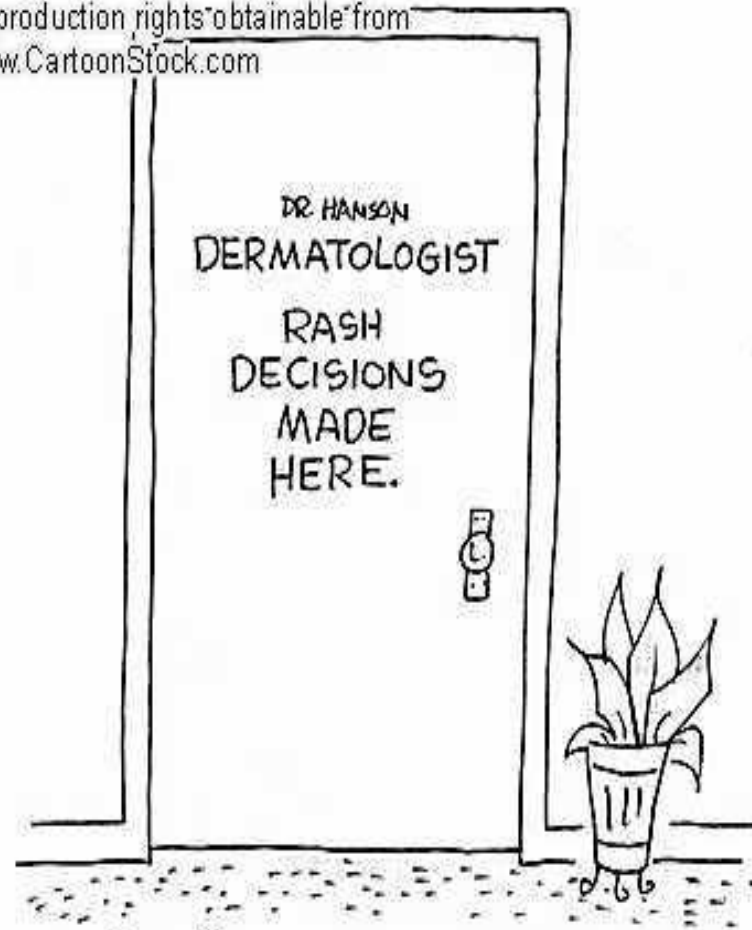


Treatment Approach



Questions?

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