# Acne Vulgaris

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## Acne Vulgaris

- A multifactorial disorder of the pilosebaceous unit
- Affects 40-50 million individuals each year in the U.S.
- Peak incidence occurs during adolescence
- May create self-consciousness and social isolation
- Affects 85% of young people 12-24 years of age

## Acne Vulgaris - Onset

- Lesions may begin as early as 8-10 years
- Incidence increases steadily during adolescence
- Girls often develop acne earlier than boys
- Severe acne affects boys 10 times more frequently than girls
- Severe cystic acne may have a family history

## Patients at Increased Risk for Developing Acne

- XYY chromosomal phenotype
- Polycystic ovarian syndrome
- Hyperandrogenism
- Hypercortisolism
- Precocious puberty
Principal Factors in the Pathogenesis of Acne

- Increased sebum production
- Abnormal keratinization of the follicular epithelium
- Proliferation of *Propionibacterium acnes*
- Inflammation

Pathogenesis of Acne

- The formation of the microcomedone is the initial step in development of acne
- The microcomedo begins in keratinized lining of the upper portion of the pilosebaceous follicle, the infundibulum.
- Retention and accumulation of corneocytes produces hyperkeratosis in the proximal infundibulum of the pilosebaceous lumen

Propionibacterium acnes

- Gram-positive, non-motile rod, anaerobic
- Naturally produces porphyrins (Coproporphyrin III), which fluoresces with a Woods light
- Plays a role in production of lipases, enzymes that contribute to comedo rupture and production of several proinflammatory mediators.
- Activates Toll-like receptor 2 (TLR2).

Acne Lesions

- Non inflammatory lesions
  - Closed comedo (whitehead)
  - Open comedo (blackhead)
- Inflammatory lesions
  - Papules
  - Pustules
  - Cysts
  - Abscesses
### Neonatal Acne
- Occurs in more than 20% of healthy newborns
- Lesions appear at about 2 weeks of age and usually resolve by 3 months
- *Malassezia furfur* (yeast organism) may be the etiology
- Inflamed papules over nose and cheeks
- May improve with ketoconazole cream

### Infantile Acne
- Presents at 3-6 months of age
- Comedo formation more prominent
- Cystic acne and scarring may occur
- Reflects hormonal imbalances intrinsic to stage of development of infant
- Infant boys – elevated LH and testosterone
- Infant boys and girls – elevated DHEA

### Acne Fulminans
- The most severe form of cystic acne
- Primarily young men 13-16 years of age
- Painful cysts, hemorrhagic crusts, severe scarring
- Osteolytic bone lesions, fever, arthralgias, myalgias, enlarged liver-spleen
- Isotretinoin, systemic and intralesional steroids, Dapsone
### Acne Conglobata
- Severe nodulocystic acne without systemic manifestations
- Part of the follicular occlusion tetrad – dissecting cellulitis of scalp, hidradenitis suppurativa, and pilonidal cysts
- Isotretinoin, systemic and intralesional steroids

### Acne Mechanica
- Occurs secondary to repeated mechanical and frictional obstruction of the pilosebaceous outlet
- Comedo formation results
- Rubbing of helmets, chin straps, collars
Acne Excoriée

- Comedones and inflammatory papules are neurotically excoriated
- Patients develop crusted erosions that scar
- Many patients have an underlying psychiatric component, anxiety disorder, or obsessive-compulsive disorder
- Antidepressants or psychotherapy may be beneficial.

Drug-induced Acne

- Anabolic steroids
- Corticosteroids
- Phenytoin
- Lithium
- Isoniazid
- Iodides
- Bromides
- Inhibitors of epidermal growth factor receptor (EGFR)
<table>
<thead>
<tr>
<th>Occupational Acne</th>
<th>Chloracne</th>
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<tr>
<td>• Follicle-occluding substances in the workplace</td>
<td>• Occupational acne caused by exposure to chlorinated aromatic hydrocarbons</td>
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<tr>
<td>• Cutting oils, petroleum-based products, coal tar derivatives, chlorinated aromatic hydrocarbons</td>
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<tr>
<th>Basic Objectives of Acne Therapy</th>
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<tr>
<td>• Reduction of sebum output</td>
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<tr>
<td>• Reduction of bacterial numbers</td>
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<tr>
<td>• Alteration of cell adherence</td>
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<tr>
<td>• Alteration of abnormal keratinization</td>
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<td>• Reduction of inflammation</td>
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Management of Acne

- Topical therapies
  - Benzoyl peroxides
  - Topical antibiotics
  - Topical retinoids
  - Salicylic acid
  - Azelaic acid
  - Topical Dapsone
  - Combination topicals

- Systemic therapies
  - Oral antibiotics
  - Isotretinoin
  - Oral contraceptives
  - Spironolactone

Topical Antibiotics

- Bacteriostatic effect on *P. acnes*
- Anti-inflammatory effects
- Bacterial resistance may occur with monotherapy
- Topical agents include erythromycin, clindamycin, sodium sulfacetamide, and sulfur products
- Preparations available as gels, solutions, pledgets, and combined with benzoyl peroxide

Benzoyl Peroxides

- Potent bactericidal effect
- Decreases number of *P. acnes* and FFA
- Due to lack of bacterial resistance, should be an integral part of acne therapy
- May decrease size and number of comedones
- Side effect include contact sensitivity and bleaching of clothes
- Formulations include washes, gels, soap bars, and combinations with topical antibiotics

Combination Antibiotics and Benzoyl Peroxides

- Benzoyl peroxides have been combined with erythromycin and clindamycin
- Combining benzoyl peroxide with erythromycin or clindamycin greatly reduces bacterial resistance to the antibiotic component
## Topical Retinoids

- May help normalize follicular keratinization
- Increase epidermal cell turnover and decreases cell cohesiveness
- Inhibits formation of comedones and helps expel existing comedones
- Minimal risk of tetratogenicity
- Caution with sunlight exposure
- May enhance penetration of co-administered medication into the sebaceous follicle
- May have anti-inflammatory effects

## Tretinoin – Retin A®, Avita®

- First topical retinoid – all trans-retinoic acid
- Product is photolabile – apply at night
- May cause a pustular flare during initial 3-4 weeks
- Most common side effects are topical irritation and increased risk of sunburn
- Available in gels, creams, solutions, and microspheres impregnated with tretinoin

## Adapalene (Differin®)

- A derivative of naphthoic acid
- Receptor specific (RAR-gamma)
- Product is not degraded by sunlight and can be applied at same time as benzoyl peroxide
- May be less irritating and have less comedolytic activity than tretinoin
- Available as gel and cream

## Tazarotene (Tazorac®)

- A synthetic acetylenic retinoid
- Receptor specific for RAR-beta and RAR gamma
- Category X – avoid in pregnancy
- Light stable
- Skin irritation most common side effect
- Available as cream or gel
### Azelaic Acid (Azelex®, Finacea®)
- Dicarboxylic acid derivative
- Antimicrobial, anti-inflammatory, and comedolytic activity
- May help decrease post-inflammatory hyperpigmentation
- More effective when combined with other topicals

### Commonly used oral antibiotics in the treatment of acne
- Tetracycline
- Doxycycline
- Minocycline
- Erythromycin

### Oral Antibiotics
- Suppress the growth of *P. acnes*
- With decrease in *P. acnes*, the FFA levels fall
- Interfere with local chemical and cellular inflammatory mechanisms
- Tetracycline, erythromycin, and clindamycin inhibit neutrophil chemotaxis

### Other oral antibiotics used in acne treatment
- Trimethoprim-sulfamethoxazole
- Trimethoprim
- Cephalosporins
- Ampicillin
- Azithromycin
- Clindamycin
**Spironolactone**

- Blocks binding of androgens to androgen receptors
- Recalcitrant acne in adult women
- Avoid during pregnancy due to effects on male genitalia
- May cause menstrual irregularities, breast tenderness, and hyperkalemia
- Combine with birth control pill

**Isotretinoin (Accutane®, Sotret®)**

- 13-cis retinoic acid
- Indicated for severe nodulocystic acne refractory to conventional treatment
- Exact mechanism of action is not known, but the drug does act on sebaceous glands and reduces sebum production by 90%
- Reduction in *P. acnes* and normalization of follicular keratinization

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**Side Effects of Oral Antibiotics**

- Minocycline – pseudotumor cerebri, blue discoloration of skin and teeth, vertigo, drug induced lupus, immune hepatitis
- Doxycycline – photosensitivity and epigastric discomfort
- Tetracycline – GI irritation, candidal vaginitis, enamel changes in patients under 10
- Erythromycin – GI upset, hepatotoxicity
- Clindamycin – pseudomembranous colitis
- Trimeth-sulfa – TEN, neutropenia, aplastic anemia, liver toxicity

**Isotretinoin**

- Dosing varies from 0.5 – 2.0 mg/kg/day for 16-20 weeks
- Risk of relapse is reduced if cumulative dose reaches 120-150 mg/kg
- Approximately 40% of patients relapse
- Caution when starting in patients with severe inflammatory acne
Isotretinoin Side Effects

- Teratogenic in humans – pregnancy prevention critical
- Possible association with depression and suicide
- Xerosis, chelitis, alopecia, dry eyes, muscle aches, epistaxis
- Pseudotumor cerebri, hepatotoxicity, hypertriglyceridemia, vertebral hyperostosis
**FDA Advisory Panel on Isotretinoin**

- Proposed a new risk management program
- Previous risk management programs did not significantly reduce pregnancies

**Endocrine Abnormalities and Acne-Hyperandrogenism**

- Suspect in female patients with severe acne, hirsutism, irregular menstrual periods, and androgenetic alopecia
- May be associated with insulin resistance and acanthosis nigricans
- Initial tests (off oral contraceptives) include total and free testosterone, DHEAS, and 17-hydroxyprogesterone
- If hypercortisolism is suspected, obtain a morning serum cortisol level.

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**Isotretinoin Pregnancy Risk Management Program (IPRMP)**

- All interested parties have obligations
  - Wholesalers
  - Pharmacy
  - Patients
  - Prescribers
  - Prescribers staff
  - Manufacturers

**Abnormal Endocrine Labs**

- Congenital adrenal hyperplasia
  - DHEAS levels 4000-8000 ng/ml
- Adrenal tumor
  - DHEAS levels > 8000 ng/ml
- Polycystic ovary syndrome
  - Testosterone levels from 150-200 ng/dl
  - LH/FSH ratio > 2-3
- Ovarian tumor
  - Serum testosterone levels exceed 200 ng/dl
### Hormonal Therapy

- Can be effective in women with normal or abnormal androgens
- Therapy works best in women with recalcitrant acne on the lower face and neck
- Blocks ovarian and adrenal production of androgens
- Reduce free testosterone, testosterone conversion
- Most formulations combine an estrogen with a progesterone

### Hormonal Therapy

- Estrogen should be linked with a non androgenic progestogen
- Low androgenic progestins include ethynodiol diacetate, norethindrone, levonorgestrel, desogestrel, and norgestimate
- FDA approved for treatment of acne – Ortho Tri-Cyclen®, Estrostep®, Yaz®
- Yasmin®, Alesse®, Triphasil®, Mircette®, Desogen® may be helpful.