

Acne Vulgaris

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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

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

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

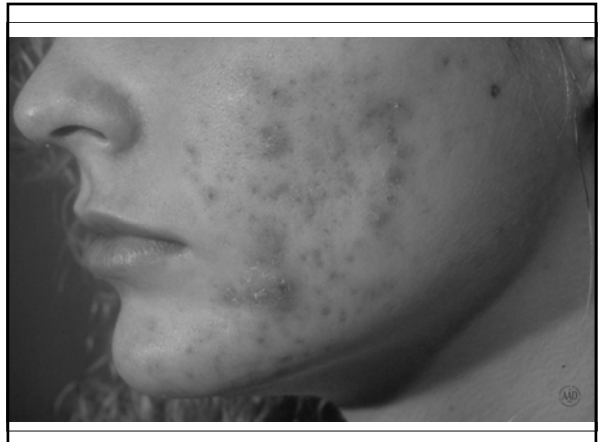
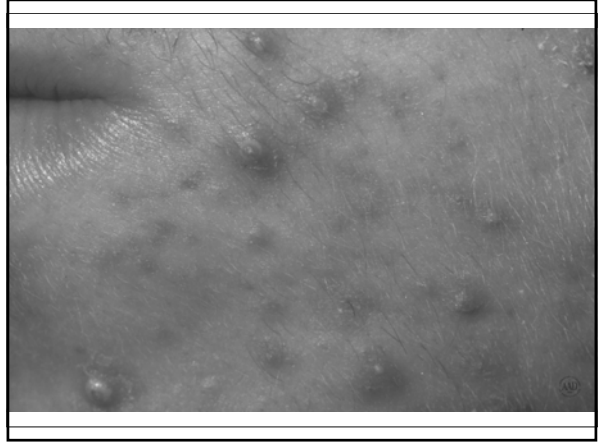
- The formation of the microcomedone is the initial step in development of acne
- The microcomedo begins in keratinized lining of the upper portion of the pilosebaceous follicle, the infundibulum.
- Retention and accumulation of corneocytes produces hyperkeratosis in the proximal infundibulum of the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

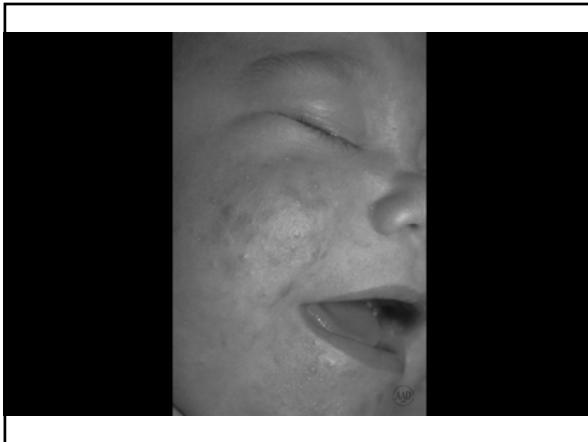


Neonatal Acne

- 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

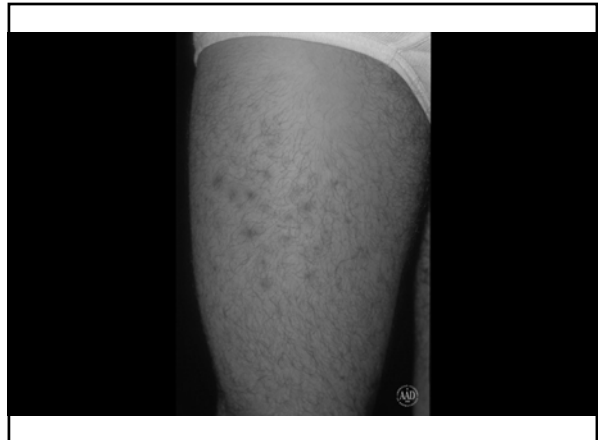


Acne Mechanica

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

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 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)

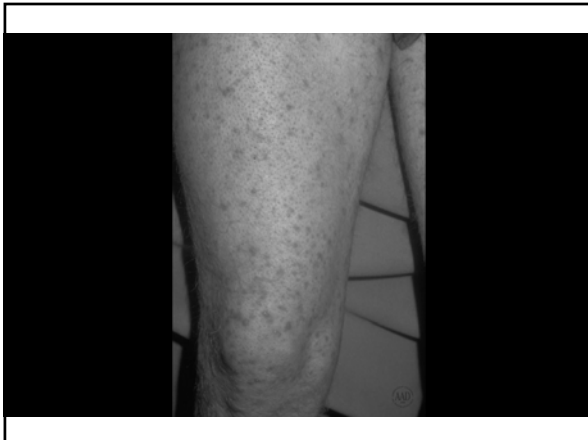


Occupational Acne

- Follicle-occluding substances in the workplace
- Cutting oils, petroleum-based products, coal tar derivatives, chlorinated aromatic hydrocarbons

Chloracne

- Occupational acne caused by exposure to chlorinated aromatic hydrocarbons



Basic Objectives of Acne Therapy

- Reduction of sebum output
- Reduction of bacterial numbers
- Alteration of cell adherence
- Alteration of abnormal keratinization
- Reduction of inflammation

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 teratogenicity
- Caution with sunlight exposure
- May enhance penetration of co-administered medication into the sebaceous follicle
- May have anti-inflammatory effects

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

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

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

Side Effects of Oral Antibiotics

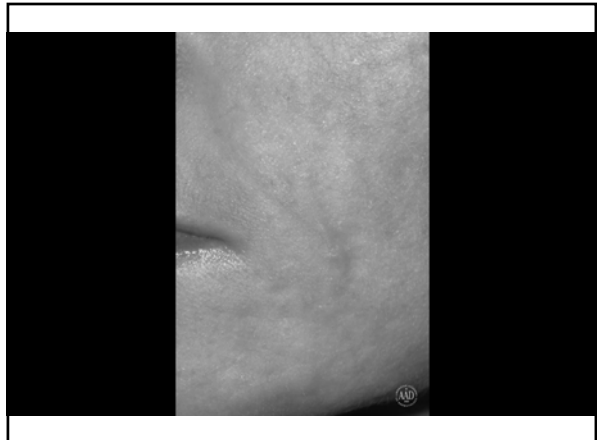
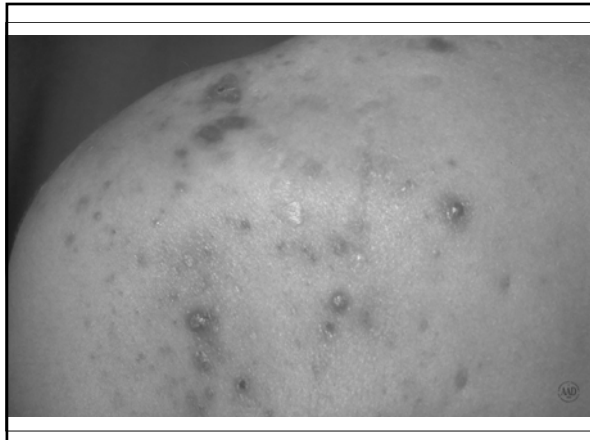
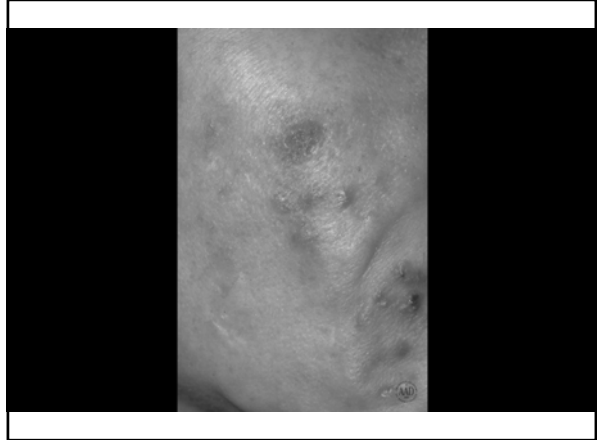
- Minocycline – pseudotumor cerebri, blue discoloration of skin and teeth, vertigo, drug induced lupus, immune hepatitis
- Doxycycline – photosensitivity and epigastric discomfort
- Tetracycline – GI irritation, candidal vaginitis, enamel changes in patients under 10
- Erythromycin – GI upset, hepatotoxicity
- 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, cheilitis, 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.

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.