Peds Rx: Dermatology Pharmacology: Useful Knowledge to Apply in Any Setting

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Disclosure

- Pfizer llc
  - Promotional speaker 2018 to 2019
  - Ad board consultant
- Sanofi
  - Thought leader ad board
  - Speaker for non-promotional educational activities

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Learning Objectives

- A discussion of common pediatric dermatology conditions and appropriate treatments
- Know the mechanisms of action, therapeutic uses and toxicities of topical and/or systemic drugs used to treat pediatric dermatological disorders

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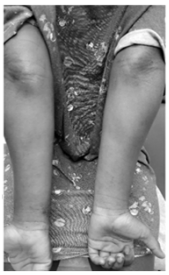
Atopic Dermatitis



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Atopic Dermatitis (AD)

- **Most common skin disorder seen in infants and children**
- **Begins during the first 6 months of life in 45% of children, the first year of life in 60% of affected individuals, and before 5 years of age in at least 85% of affected individuals.**

(Paller, Mancicni, 2011)

- Pruritic (itchy) skin condition
- Typical distribution
  - Age <2: cheeks, forehead, scalp, & extensor surfaces
  - Age >2: flexural areas of neck, elbows, knees, wrists, & ankles
- Chronic relapsing course
- Associated with other atopic conditions (asthma and allergic rhinitis "Atopic March")

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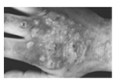
Clinical Pearls



- Typically spares the diaper area and midface including the nose and medial cheeks
- Often overlaps with seborrhea in infancy
- Nipple dermatitis occurs in some infants and children, exacerbated by rubbing on clothing
- In black skin, AD is more papular and follicular-based
- Lymphadenopathy

(Pallor, Mancici 2011)

- Nail dystrophy when finger involvement around the nail matrix (cuticle)
- Secondary staphylococcal infections common
- Prurigo nodularis (thickened papules, most common on the lower legs)
- Post-inflammatory hyper(o)pigmentation
  - Not a scar, resolves over several months
  - Diligent sun protection will help the complexion normalize quicker
- Lichenification

Photos provided by Hansen, Schachner, 2011 6

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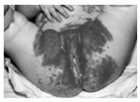
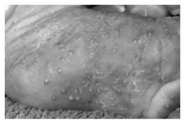
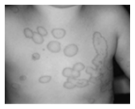
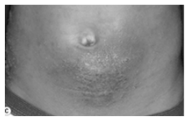
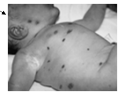
Differential diagnosis

- Psoriasis
- Scabies
- Tinea corporis
- Langerhans cell
- histiocytosis (LCH)
- Contact dermatitis
- Zinc deficiency

Photos provided by Hansen, Schachner, 2011

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Topical corticosteroids

Treatment for inflammatory skin conditions

- Eczema
- Psoriasis
- Genital lichen sclerosis
- Oral lichen planus
- Vesicular stomatitis

Mechanism of Action	Absorption
A naturally occurring glucocorticoid (adrenal corticosteroid) acts as an **anti-inflammatory**, **antipruritic**, vasoconstrictive agent, and has salt-retaining properties.	• Topical: Factors which enhance percutaneous absorption include: (1) degree of skin inflammation, (2) use of occlusive dressings, (3) type of vehicle, (4) concentration of the product

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Topical corticosteroids con't

Medication safety for Clobetasol

Medication Safety

Precautions

Print

See 'In-Depth Answers' for detailed results.

- Avoid: Avoid application to eyes, lips, [29], face, groin, or axillae areas, and avoid ophthalmic, oral, or intravaginal use [8][29][21][1][3][4][2]
- Dermatologic: Local adverse effects (eg, atrophy, striae, telangiectasis, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, secondary infection, and miliaria) may occur and may be irreversible; increased likelihood with occlusive use, prolonged use, or use of high potency corticosteroids [10]; use not recommended with acne vulgaris, rosacea, or perioral dermatitis [21][29][1]
- Dermatologic: Allergic contact dermatitis may occur resulting in failure to heal [8][1][29][21][3][4]
- Dermatologic: Discontinue use in the presence of uncontrolled skin infection [29][1][21][3][4][2]
- Dermatologic: Use on an altered skin barrier or large surface areas may increase risk of systemic absorption [8][29][21][1][3][4]
- Endocrine and metabolic: Latent diabetes mellitus may be unmasked due to systemic absorption [1][21][29]
- Endocrine and metabolic: Hyperglycemia may occur [8][1][21][29], particularly with prolonged use and large doses [8]
- Endocrine and metabolic: Cushing syndrome may occur [1][21][29], particularly with prolonged use and large doses [8]
- Endocrine and metabolic: Suppression of the hypothalamic-pituitary-adrenal (HPA) axis may occur with systemic absorption, even at low doses, with the potential of glucocorticosteroid insufficiency after treatment withdrawal; monitoring recommended and dose adjustment may be required [8][29][21][1][3][4][2]
- Flammable: Avoid fire, flame, and smoking during and immediately after application [8]
- Hepatic: Increased risk of systemic absorption in presence of hepatic failure [8][1][29][21]
- Occlusive dressing: Use of occlusive dressings may increase risk of systemic absorption [8][29][1][21][3][4][2] and should be avoided [8]
- Ophthalmic: Increased risk of glaucoma and posterior subcapsular cataract with use of topical corticosteroids; avoid contact with eyes and consider ophthalmologist referral with report of any visual symptoms [22][23]
- Pediatric: Use of 0.025% cream, foam, lotion, or shampoo is not recommended in patients younger than 18 years of age due to increased risk of systemic toxicity [16][8][29][21]
- Prolonged use: Prolonged use may increase the risk of systemic absorption [8][29][21][1][3][4][2]

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Crisaborole 2% ointment

- Approved for 3 months of age and older
- Adverse effects
  - Application site pain and hypersensitivity reactions
- Mechanism of action
  - Crisaborole is a phosphodiesterase 4 (PDE-4) inhibitor which increases intracellular cyclic adenosine monophosphate (cAMP) levels.
- Directions for use
  - Apply 1-2 times a day anywhere on the body.
    - Not studied on the scalp
    - Don't place in mucous membranes or in mouth

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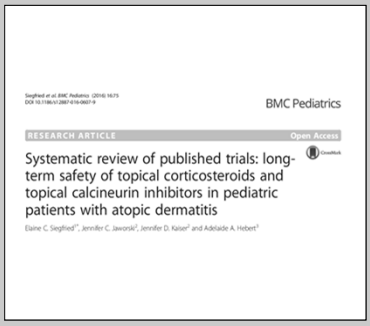
Topical Calcineurin Inhibitors

- Approved for 2 years of age and older for moderate to severe atopic dermatitis-second line therapy
- Directions
  - Apply 1-2 times a day
- Side effects
  - Skin burning and itching
- Safety
  - Data supports safety in topical ointment


Siegfried et al. BMC Pediatrics (2016) 16:75
DOI 10.1186/s12887-016-0607-9

BMC Pediatrics

RESEARCH ARTICLE Open Access

Systematic review of published trials: long-term safety of topical corticosteroids and topical calcineurin inhibitors in pediatric patients with atopic dermatitis

Elaine C. Siegfried[1*], Jennifer C. Jaworski[2], Jennifer D. Kaiser[2] and Adelaide A. Hebert[3]

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Dupilumab

- Systemic treatment for moderate to severe atopic dermatitis and uncontrolled asthma
- Interleukin 4 receptor (IL-4R), human monoclonal antibody
  - Allergic inflammatory pathways driving pathogenesis
  - The centrality of this **pathway in allergic inflammation** stems from the critical role played by IL-4 and IL-13 in orchestrating the allergic response
  - The IL-4/IL-13/IL-4R axis promotes T helper cells type 2 (TH2) differentiation, which **mediate the pro-allergic adaptive immune response**
  - It also activates effector pathways in target tissues including the lung, skin and gut that give rise to the expression of the respective disease attributes 5. These unique properties of the IL-4R axis made it an especially appealing target for
  - Precision medicine intervention that aims to interrupt the allergic inflammatory response and attenuate or abrogate disease chronicity and severity

(Hani, 2020) 12

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Dupimumab considerations

- Parasitic infections
- Conjunctivitis
- Advise continuing asthma medications

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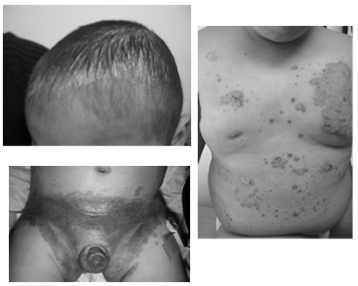
Psoriasis



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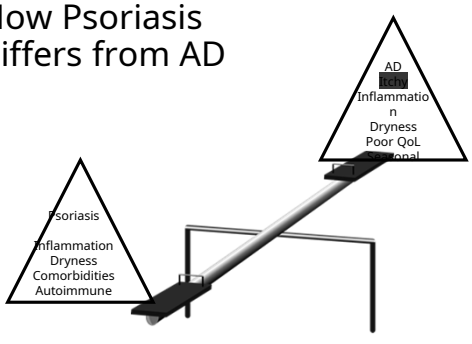
How Psoriasis differs from AD



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Calcipotriene

- Vitamin D-analog
  - Apply in the morning to affected areas of sun exposed skin
  - Treatment of psoriasis may result from inhibition of epidermal proliferation and stimulation of differentiation of epidermal cells
- Side effects: Burning sensation, dermatitis, pruritus
- Contraindications
  - Don't apply on the face
  - Hypercalcemia
  - Vitamin D toxicity
- Precautions
  - Concomitant use of phototherapy

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Biologics

- **Etanercept**
  - 4 years and older
  - SC injections weekly
  - Common AE
    - Upper respiratory infections, pharyngitis, injection site reactions, HA
- **Adalimumab**
  - 4 years and older
  - Weekly or every other week injection
  - Common AD (similar to above)
- **Ustekinumab**
  - 12years and older
  - SC injection week 1, week 4 and every 12 weeks thereafter

Severe side effects: cellulitis, hyperlipidemia, skin carcinoma

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Bacterial infections

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Staph infections

- Mupirocin
- Cephalexin
- Dilute bleach baths

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Mupirocin

- Apply twice a day for 5 days (per Micromedex)
- Mupirocin has been shown to be active against most strains of methicillin-resistant S. aureus
- Contraindications: None

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Cephalexin

- First line for skin infections where MRSA is not of concern
- 500 mg every 12 hours for 7 days
- Severe infections: Up to 4 g/day in 2-4 equally divided doses for 7-14 days

Bacterial culture before oral antibiotics

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Antibacterial practices

- Dilute bleach baths.
  - Data suggests mild bleach and water solution can decrease inflammation, itching and potentially the amount of Staphylococcus aureus bacteria on the skin
- Vinegar soaks
  - Better for gram – infections
- Hibiclens
  - Don't get in eyes or in ears
- CLN wash
  - Gentle cleansers for skin prone to eczema, acne, rash, infection
  - Sodium hypochlorite body wash and shampoo products

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Tinea and Yeast Infections

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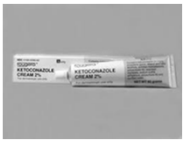
Topical treatments

- Topical treatments run the risk of irritant or contact dermatitis (erythema, pruritus, stinging, burning, rash)
- No specific monitoring required



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Ketoconazole shampoo

Treatment for dandruff
In children 12 years or older, apply ketoconazole 1% shampoo to wet hair, generously lather, rinse thoroughly, and repeat. Use every 3 to 4 days for up to 8 weeks; then as needed to control dandruff

Mechanism of Action	Absorption	Contraindications	Considerations
Ketoconazole exhibits antifungal activity, similar to its predecessors clotrimazole and miconazole • Another possible mechanism of ketoconazole is inhibition of the transformation of yeast forms	• Not detected in plasma in patients who washed with ketoconazole shampoo 4 to 10 times/week for 6 months (n=39) or 2 to 3 times/week for 3 to 26 months (mean, 16 months; n=33) • Following chronic or single application of 2% ketoconazole shampoo, plasma concentrations of ketoconazole were undetectable with no hepatic function test abnormalities	• None for shampoo	• Alcohol-based (may sting with application) • Assess for severe skin irritation, pruritus, stinging, and contact dermatitis

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Oral medications

- Griseofulvin
  - Should be given with fatty food to enhance absorption
  - Affects absorption of other medications such as OCP's, Coumadin and phenobarbital
  - Increases photosensitivity
  - Contraindicated in pregnancy , porphyria, and liver disease
  - Cross reactivity with PCN allergy
  - Long term therapy may monitor with CMP (liver and kidney) and CBC
  - Monitor for therapeutic response

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Oral medications

- Terbinafine
  - Should not be used with chronic or active liver disease
  - Drug interactions with other medications (CYP2D6)
  - Increase in photosensitivity
  - Increase in adverse effects of caffeine if taken concurrently (HA, insomnia, agitation and diuresis)
  - Is not available in liquid form and so will need to be crushed –do not use acidic foods to mix
  - Therapy for fingernails is usually 6 weeks in duration and toenails may be up to 12 weeks, consider LFT's if tx is greater than 6 weeks or sx of liver disease
  - CBC recommended with hx of immunodeficiency for tx>6 weeks

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Oral medications

- Fluconazole
  - Avoid concurrent use of EES
  - Metabolized thru CYP2C9 and CYP3A4 with some meds or electrolyte imbalance may cause prolongation of QT or torsades de pointes
  - If renal or hepatic injury dose may need adjustment or monitor (CMP)

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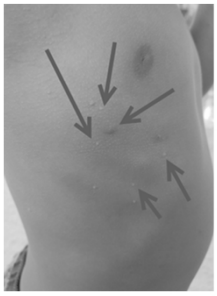
Molluscum



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Molluscum

- Common cutaneous viral infection in children caused by a member of the poxvirus family
- Most common in school-aged children, especially under 8 years old
  - Rarely congenital, but possible via vertical transmission
- Spread from contact, swimming pools, fomites (ie. Sponges, towels)
- Can last 1-2 years
- Common sites of involvement
  - Axillae
  - Side of trunk
  - Lower abdomen
  - Thighs
  - face

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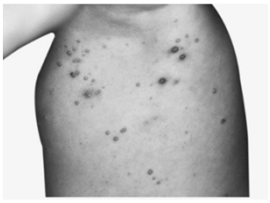
Clinical Pearls



Photos provided by Hansen, Schachner, 2011

- Flesh-colored to pink papules with appearance of translucence
- Central umbilication
- “pimple” appearing
- Fluid filled
- Start small and grow, may appear like a blister
- May develop a surrounding rash (Molluscum dermatitis)
- May become inflamed and appear like an abscess/furuncle

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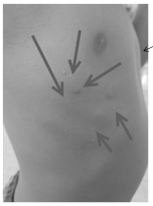
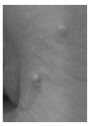
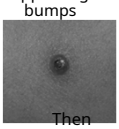


When gone, they look like dried out bumps

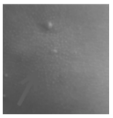


Start as small, pimple appearing bumps

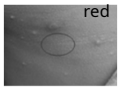


The phases of molluscum

Some can appear infected



Then enlarge and become red



Some can cause dry skin or rashes

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Treatment optio

Tips:

- No bathing with other siblings
- Don’t share the same towels
- Keep out of heated pools and spas and shower vs baths (Schachner, Hansen, 2011).

Pediatric Dermatology

CORRESPONDENCE | Token Access

Imiquimod cream for molluscum contagiosum: Neither safe nor effective

Kenneth A. Katz MD, MSc, Hywel C. Williams DSc, Johannes C. van der Wouden PhD

- Cantharidin (Akharia et al, 2018)
- Topical
  - Several over the counter products
  - Retinoid
- Curettage

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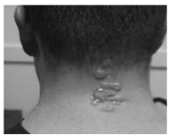
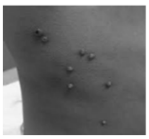
Cantharadin

- Cantharidin is an odorless, colorless fatty substance of the terpenoid class, which is secreted by many species of blister beetles.





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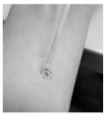
Retinoids

- Retinoids such a tretinoin cause redness, peeling and irritation.
  - Apply to molluscum to incite an immune response



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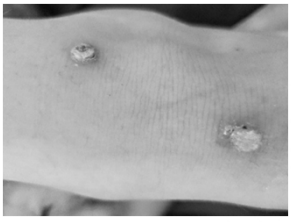
Warts



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Cutaneous Warts

- HPV virus (over 150 subtypes)
- Types
  - Verruca vulgaris (common wart)
  - Verruca plantaris (plantar warts)
  - Verruca plana (flat warts)
- Takes several years to resolve
  - Dry protective layer shields wart virus
  - Virus stays invisible to the immune system
- Treatment may not be necessary.
  - Self-resolves in children (can take several years)
- Common reasons for treatment:
  - Pain, discomfort, functional impairment
  - Patient concern for social stigma
  - Immune suppression

(UpToDate, 2017)

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Treatment in YOUR practice

<u>Destructive therapies</u>

- Cryotherapy

<u>Topical therapy</u>

- Salicylic acid with or without duct tape

<u>Patient education</u>

- Set up expectations

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Table 1

Various agents used in immunotherapy of warts

Agents	Indication, dosage and administration
Topical agents	
Imiquimod	For genital and cutaneous warts, 5% cream, 3 times a week, for 16 week
Sinecatechins	For cutaneous warts, 10% ointment 3 times a day for maximum 16 weeks
BCG	For cutaneous and genital warts, applied topically on the warts in normal saline or salicylic acid, washed after 2 hours, weekly treatment for 6 to 12 weeks
Intralesional (IL) agents	
Mu vaccine	For cutaneous warts, 0.1 ml intradermal into 3-5 warts or all warts, followed by 0.1 ml intralesional, 2-4 weekly, maximum 10 sittings
BCG vaccine	For cutaneous and genital warts, 0.1-0.5 ml intralesional injection in largest wart, in 2 weeks interval in 5 sittings.
PPD	For genital warts, 0.1 ml weekly intradermal injection in the forearm for 12 weeks
MMR vaccine	For cutaneous warts, 0.1-0.5 ml into single largest wart fortnightly for up to 5 sittings
Candidal extract	For cutaneous warts, 0.1-0.3 ml injected into the largest wart at first sitting, then 3 weekly intralesional injections
Trichophyton antigen	For cutaneous and genital warts, 0.3 ml injected into largest wart every 3 weeks, maximum of 5 sittings
Tuberculin	For cutaneous warts, 2.5 units into few warts every 2 weekly
Vitamin D3	For cutaneous warts, 0.2 ml of 7.5 mg/ml, Vitamin D intralesional, 3 sittings 4 week apart
Interferon alpha 2B	For genital warts, 1-2 million units 3 days/week (Monday-Wednesday-Friday) for 3 weeks
Systemic	
Zinc	For cutaneous warts, 10mg/kg/day (2.5 mg/kg/day elemental zinc) for 2 months
Cimetidine	For cutaneous warts, 20-40 mg/kg/day for 3-4 months
Levamisole	For cutaneous warts, 2.5-3 mg/kg/day, 2-3 consecutive days every 2 weeks for 4-5 months.
Echinacea	For cutaneous warts, 600 mg single oral dose (single study)
Propolis	For cutaneous warts, 500 mg single oral dose (single study)
HPV vaccines	For cutaneous warts, 0.5 ml intramuscularly, at 0, 2 and 6 months (2 dose or 3 dose regimen) may be followed

(Thappa & Chiramel, 2016)

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Imiquimod

- Treatment for anogenital condyloma and adult skin cancer
- Apply up to 1 packet topically to warts once daily at bedtime until clearance or for up to 8 weeks

Medication Safety

Adverse Effects

Print

See 'In-Depth Answers' for detailed results.

Common

- **Dermatologic:** Application site reaction (28% to 33%), Burning sensation (5% to 26%), Edematous skin (41% to 78%), Erythema (all grades, 96% to 100%; severe grade, 10% to 31%), Peeling of skin (58% to 93%), Pruritus (16% to 32%), Scab of skin (79% to 93%), Skin discharge (22% to 51%), Skin ulcer (30% to 62%)
- **Immunologic:** Influenza-like symptoms (up to 4%)
- **Neurologic:** Headache (2% to 8%)
- **Respiratory:** Upper respiratory infection (3% to 15%)

Serious

- **Cardiovascular:** Cardiac dysrhythmia, Heart failure, Henoch-Schönlein purpura, Myocardial infarction, Syncope
- **Dermatologic:** Erythema multiforme, Erythroderma
- **Hematologic:** Idiopathic thrombocytopenic purpura
- **Neurologic:** Cerebrovascular accident
- **Reproductive:** Genital edema, female
- **Other:** Angioedema

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Cimetidine

- Oral cimetidine has been reported to be successful in treating recalcitrant warts in more than 80% of children when dosed 30-40 mg/kg 3 times a day over a 6 to 12 week period.
- Side effects include many cytochrome P450 interactions, gynecomastia and stomach upset.

(Silverberg, 2019)

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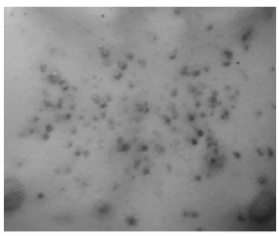
Acne



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Acne

- Acne, or acne vulgaris (typical teenage acne), is a common, usually self-limited chronic inflammatory condition of the pilosebaceous unit.
- The pathogenesis involves multiple factors, including (1) increased sebum production, (2) follicular hyperkeratinization, (3) proliferation of the bacterium Propionibacterium acnes, and (4) inflammation.
- Typically begins at puberty as a result of androgen stimulation

(Visual DX, 2017)

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Pre-assessment considerations

- Type
  - Comedonal, papulopustular, mixed, nodular, cystic?
  - Scarring?
- Skin type
  - Oily, dry
  - Post-inflammatory hyperpigmentation present?
- Menstrual cycle history
- Current skin care regimen and acne treatment history
- History of acne promoting products and medications
- Psychologic impact of acne

(UpToDate, 2017)

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Clinical Pearls

- Education is key
- Treatment is three-pronged
  - Benzoyl Peroxide
  - Retinoid
  - Antibacterial
- Moisturize or suffer
- Don't forget about sunscreen (SPF 30 or higher)
- Use non-comedogenic, oil free, acne-free products
- Clinical effectiveness not seen until 3 months of consistent use

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Benzoyl Peroxide

- Benzoyl peroxide has antibacterial action against Propionibacterium acnes [6] in treatment of acne vulgaris. Benzoyl peroxide improves both inflammatory and noninflammatory lesions of acne.The medication also has some keratolytic effect, which produces comedo lysis, as well as drying and desquamative actions that contribute to its efficacy
- Apply 2.5% to 10% concentration TOPICALLY once or twice daily
- Precautions
  - Bleaching effect on textiles
- Adverse effects
  - Dryness, erythema, hypersensitivity

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Retinoids

- Treatment for acne, fine wrinkles and roughness
- Apply once daily at night
- Precautions
  - Irritation, dryness, peeling, photosensitivity

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Topical antibiotics

- Topical treatment for acne
  - Clindamycin, erythromycin, minocycline (Amzeeq-$420)
- Apply once a day
- Available as **lotion**, **gel**, solution, foam and pad
- Precautions
  - Site irritation
  - Dryness

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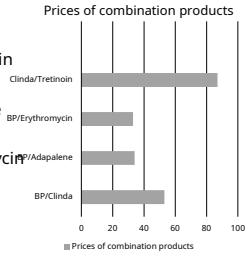
Combination products

- Benzaclin, Duac, Onexton
  - Benzoyl peroxide and clindamycin
- Epiduo
  - Benzoyl peroxide and adapalene
- Benzamycin
  - Benzoyl peroxide and erythromycin
- Ziana
  - Clindamycin and tretinoin



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Other acne medications

- Azelaic acid
  - Treatment of mild to moderate acne and rosacea
  - Additionally thought to help with hyperpigmentation
- Apply 20% cream topically 1-2 times a day
- Precautions:
  - Burning, stinging, pruritus

Cost=$46 lowest on www.Goodrx.com

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