

Tackling Topical Pharmacotherapeutics: A Case-based and Practical Approach

Skin, Bones, Hearts, and Private Parts Kara N. Roman, MMS, PA-C Associate Director & Assistant Professor George Fox University PA Program Newberg, OR

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Learning Objectives

- Review some of the most common dermatologic conditions encountered in primary care and the topical therapy indicated for treatment of these conditions.
- Discuss the various vehicles for delivery of topical medications including creams, lotions, ointments, powders and others.
- Demonstrate the proper prescribing practices for topical medications including dosing, duration, and safety issues.

General Principles of Topical Therapy

- Good news
 - Skin disease is accessible
 - Can be treated with locally applied medications
 - Limits systemic effects of medications
- The efficacy of any topical medication is related to:
 - Vehicle **
 - Active ingredient and concentration
 - Anatomic location of application hydration, skin temperature, vascular supply
 - Acceptability
 - If the patient won't use it, even the best drug won't do any good!

**The vehicle of generics and brand name products may differ and may not be of equal efficacy

Vehicles: Driving the Active Ingredient

Ointment

 Greases with little or no water, translucent, more lubricating, most effective at penetrating and delivering medication to skin

Cream – most commonly used

 Oil in water emulsions, less greasy, usually white in color and vanishes when rubbed in, can be used in any area including intertriginous

Lotion

 Liquids or solutions of diluted creams, contain alcohol, cooling and drying effect

Gel

Semi-solid, greaseless, propylene glycol based with alcohol or water

Foam/Aerosol

 Agent suspended in base and delivered under pressure, useful for scalp or hair-barren areas

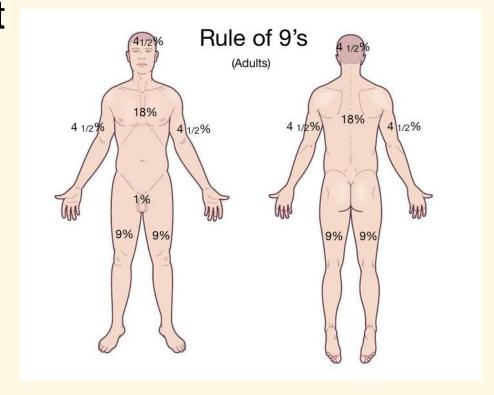
When is topical treatment generally acceptable?

If the patient has a skin disorder covering < 30% BSA

that still sounds like a lot

Generally, 5-10 % can be consistently treated with topical

therapy by a reasonable patient

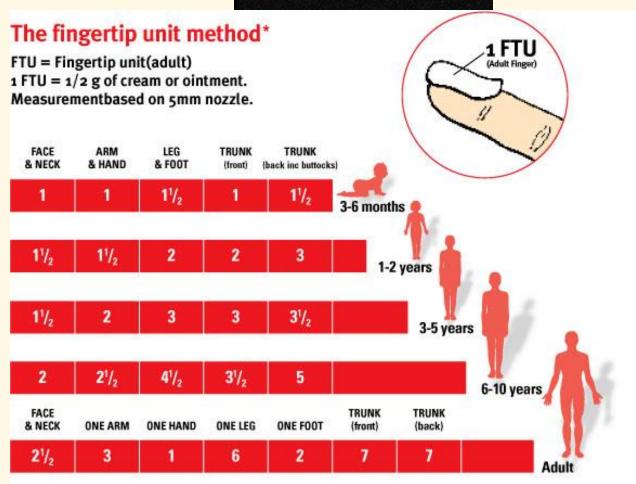


How Much Does the Patient Need?

- Finger tip unit
- Rule of the hand
- Rule of 9's: BSA

Fingertip Unit (FTU)

- Amount that can be squeezed from the fingertip to the first crease
- 1 FTU = 0.5 g



Adapted from:

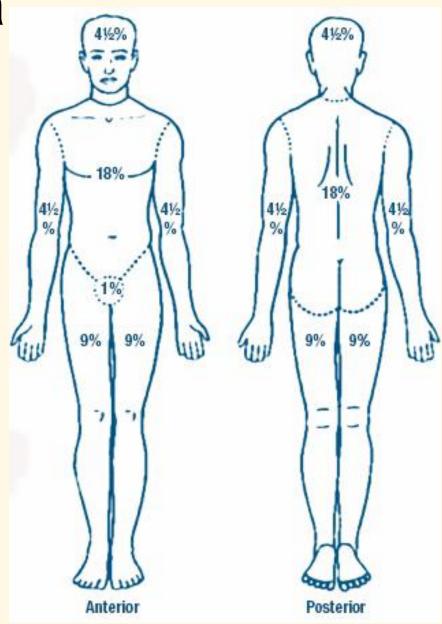
Rule of the Hand

- Hand = 1% BSA
- One hand-sized area (one side) of the skin requires 0.5 FTU or 0.25 g of ointment/cream

Area of body	FTU required for one application	Wt required for one application (g)	Wt required for an adult to treat BID for 1 week (g)
Face and neck	2.5	1.25	17.5
Trunk	7	3.5	49
One arm	3	1.5	21
One hand	<u>0.5</u>	<u>0.25</u>	<u>3.5</u>
One leg	6	3	42
One foot	2	1	14

Body Surface Area

Hand = 1%



How Much Comes in a Tube/Tub?

- Most topical medications are dispensed as
 - 15 gram
 - 30 gram
 - 45 gram
 - 60 gram
- In general, 30 grams of medication will cover the whole body once
- Sometimes you will need a tub, not a tube (1 lb)
 - Triamcinolone 0.1% cream/ointment
 - Hydrocortisone 1% cream

Common Topical Therapeutics in Primary Care

- Skin cleansers, sunscreens, emollients, moisturizers
- Corticosteroids and other anti-inflammatory agents
- Antimicrobials
 - Antibiotics
 - Antifungals
 - Antivirals
 - Antiparasitic agents (insecticides)
- Acne and rosacea medications
 - Retinoids
 - Benzoyl peroxide
 - Antibiotics
 - Combination products
- New agents you may see

New(er) Topicals in Town

- Topical calcineurin inhibitors
- Topical phosphodiesterase inhibitors crisaborole, roflumilast
- Topical JAK inhibitors ruxolitinib
- Topical ivermectin
- Topical efinaconazole
- Topical tavaborole
- Topical minocycline foam
- Topical adapalene gel OTC!!!
- Topical trifarotene

LG, 9-year-old female

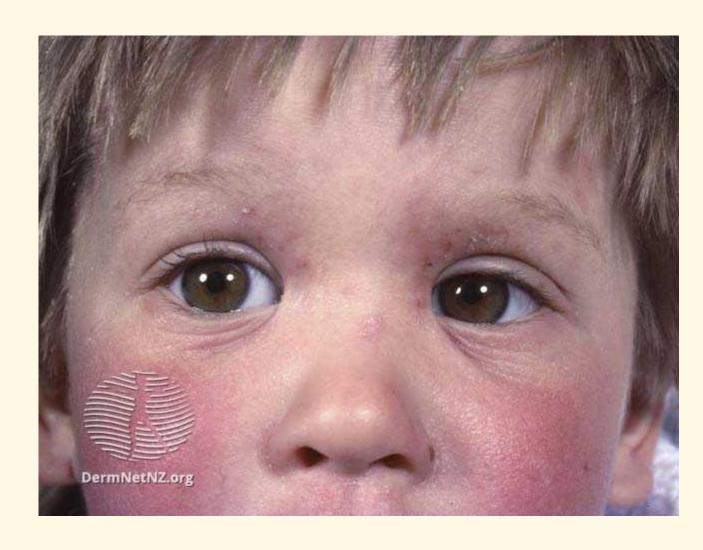




- History of recurrent pruritic skin lesions in the popliteal and anti-cubital fossa b/l
- Flares in winter months
- Skin is really dry and intensely itchy and rash seems to worsen with scratching
- How would you describe it?
- What's in the DDx?

What additional historical or PE findings would support your suspected diagnosis?

- Personal of FH of atopy
- Hyper linearity of palms
- Dennie-Morgan folds
- Other flexural rashes



It Can Look Like This





Or This





Diagnosis

Atopic dermatitis

Topicals to Tx: Atopic Dermatitis

- Emollients/moisturizers/barrier creams
 - Backbone of therapy
- Topical corticosteroids
 - Treat the flares
- Topical calcineurin inhibitors
 - Rescue the non-responders
- Topical PDE4 inhibitors
 - Rescue the non-responders
- Topical JAK inhibitors
 - Rescue the non-responders
- Topical antibiotics
 - For secondary infections if necessary

Emollients: Repair the Barrier

- Backbone of effective AD management
- 10-15 minute lukewarm bath, pat dry, apply immediately, at least once daily
- Good options:
 - Petrolatum-based emollients
 - Aquaphor, Vaseline
 - Lipid-rich, ceramide-containing ointments/creams
 - CeraVe
 - TriCeram
 - Atopiclair

Emollient Choices

- Ideal ingredients: Occlusive agent (petroleum, mineral oil, dimethicone, lanolin), Humectant (urea, glycerol, lactic acid), Lubricant (glyceryl stearate, soy sterols)
- Improve skin barrier function
- Free of irritants and allergens
- Low cost
- Easy to use
- Some other good options: CeraVe, Curel Itch Defense Lotion, Aveeno Eczema Therapy, Theraplex Barrier Balm, Vanicream/Vaniply, Gold Bond Eczema, Cetaphil Cream, Aquaphor

Emollient enhancement of the skin barrier from birth offers effective atopic dermatitis prevention Simpson, Eric L. et al. October 2014

Journal of Allergy and Clinical Immunology, Volume 134, Issue 4, 818 - 823

Evidence for Emollients (Cochrane 2017)

- A 2017 systematic review of 77 studies including 6603 participants (mean age 19 years)
 with mostly mild to moderate eczema evaluated the efficacy of emollients and
 moisturizers in reducing the signs and symptoms of eczema and the frequency of flares:
 - Based on both physician and patient assessment, the use of any moisturizers reduced eczema severity and itch compared with no use, resulted in fewer flares, and reduced the need for topical corticosteroids.
 - In three studies, patients found that a moisturizer containing glycyrrhetinic acid (a natural antiinflammatory agent) was four times more effective than vehicle in reducing eczema severity.
 - In four studies, patients using a **cream containing urea** (a humectant agent) reported improvement more often than those using a control cream without urea.
 - Three studies assessed a **moisturizer containing glycerol** (a humectant agent) versus control. More patients in the glycerol group experienced skin improvement, both by physician and patient assessment.
 - Four studies examined **oat-containing moisturizers** versus no treatment or control. No significant difference in skin improvement was noted between groups, although patients using oat moisturizers tended to have fewer flares and reduced need for topical corticosteroids.

Topical Corticosteroids (TC): Treat the Flares How Do They Work?

- Anti-inflammatory, immuno-suppressive
 - Inhibit transcription and thereby protein synthesis
 - Regulation of cytokine production
 - Rebalance T-helper cell type 1 to type 2 ratio
 - Suppression of endothelial cell and lymphocyte function
 - Decrease vascular permeability
- Anti-proliferative
 - T-lymphocytes
- Vaso-constrictive
 - Inhibit capillary dilation

Topical Corticosteroids: Strength

- Seven classes: I-VII
- Within each class, strength is essentially equivalent, unrelated to percentage
- Multiple Vehicles: Ointments, Creams, Lotions, Foams
- Potency classified based on vasoconstrictor assay (degree of blanching in healthy persons)
 - Classes I-III ultra-high potency
 - Classes IV-V medium potency
 - Classes VI-VII low potency

Some Examples of Steroids

http://www.empr.com/dermatological-disorders/section/1982/

- Classes I-III
 - Clobetasol proprionate 0.05% C, O
 - Halobetasol propionate 0.05% C, O
 - Betamethasone dipropionate 0.05% O
 - Triamcinolone diacetate 0.5% C
- Classes IV-V
 - Mometasone furoate 0.1% C, O, L
 - Triamcinolone acetonide 0.1% O
 - Fluticasone propionate 0.05% C
- Classes VI-VII
 - Alclometasone dipropionate 0.05% C, O
 - Hydrocortisone 0.5 to 2.5% C, O, L
 - Fluocinolone acetonide 0.01% C, S

Principles for TC Application

- Steroid phobia is real address it upfront
- Most patients can be managed with low-med potency steroids
- Lower potency: face, eyelids, intertriginous areas
- Select appropriate vehicle, occlude if needed
- Switch to another class of potency rather than increase the percentage of the same drug
- How to dose:
 - For 3 weeks or less, 1-2 times per day, with steroid-free intervals
 - Generally safe to use for the number of weeks equal to the class in nonfolded or mucous membrane containing areas
 - Prophylactic therapy 1-2 times per week has been shown to be more effective than emollients alone

Increased Steroid Potency = Increased Adverse Effects

- Atrophy
 - Bruising, telangiectasias
 - Fragile skin
 - Striae (not reversible)
- Steroid-induced acne
- Pigment changes
- Steroid rebound, tachyphylaxis
- Masking signs of infection or an underlying disease (fungal infections, lupus, cutaneous T-cell lymphoma)
- Cataracts, glaucoma
- HPA axis suppression

SE of Topical Steroid (Over)Use





Other Uses for Topical Steroids

- Atopic dermatitis
 - Nummular eczema
 - Pomphylox
- Contact dermatitis
- Seborrheic dermatitis
- Psoriasis
- Lichen planus
- Lichen simplex chronicus









Atopic Dermatitis – Rescue the Non-Responders

- Topical calcineurin inhibitors acute and chronic/proactive treatment
 - Pimecrolimus 1% cream 3 months and up
 - Tacrolimus 0.03 to 0.1% ointment 2 yo and up
- Topical PDE4 inhibitors indicated for mild to moderate
 - Crisaborole 2% ointment 3 months and up
- Topical JAK inhibitor short-term tx of mild to moderate
 - Ruxolitinib 0.75% to 1.5% cream 12 yo and up

GG, 19-year-old male

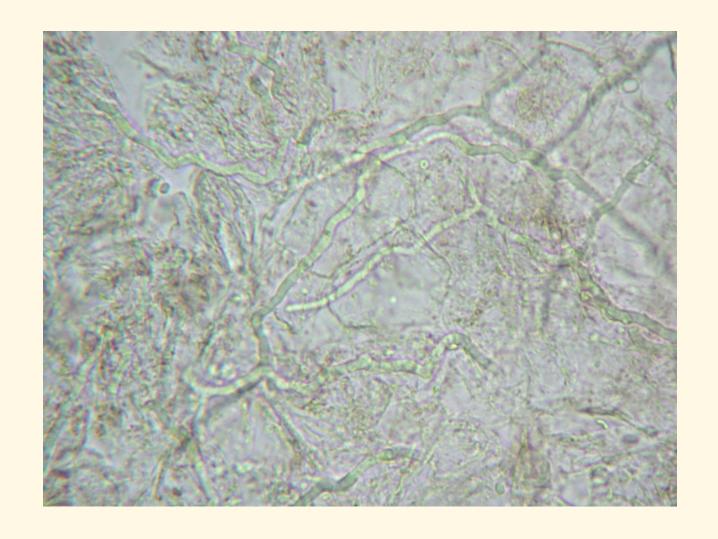


- Developed this rash on thigh over the past 2-3 weeks
- Slightly itchy
- How would you describe it?
- What else might you examine?
- What's in the DDx?

Diagnosis

Tinea corporis

Scrape and KOH it! and Consider a Culture



So you don't cause this...Tinea incognito





Or this...Majocchi's granuloma



Prescribe a Topical Antifungal

- There are several classes of topical antifungal medications
 - Azoles
 - Allylamines
 - N-hydroxypyridinone
 - Ciclopirox
 - Oxaborole
 - Polyene
 - Nystatin

Some classes are <u>fungistatic</u> and some are <u>fungicidal</u>

Azoles

- Azoles are a good choice if you are unsure if your patient has a yeast or fungus infection
- Azoles (fungistatic)
 - Clotrimazole (OTC) C, L, S
 - Miconazole (OTC) C, L, S, P
 - Ketoconazole (OTC) C, S
 - Sulconazole C **
 - Econazole C **
 - Oxiconazole C, L **
 - Sertaconazole C **
- **Newer azoles feature once daily application and have some antibiotic and anti-inflammatory properties

Allylamines

- Allylamine (fungicidal, anti-inflammatory activity)
 - Terbinafine (OTC)
 - 1% cream, 1% solution
 - Butenafine (OTC)
 - 1% cream
 - Naftifine
 - 1% cream, 1% gel
- Generally more effective than azoles
 - Higher cure rates, especially at 4-6 weeks of use
 - Lower relapse rates
 - High bioavailability, stay in stratum corneum longer

Principles of Topical Antifungal Application

- Treat for long enough they are more effective with time
 - 2-4 (6) weeks of tx are generally required
 - Treat for 1 week after clearing
 - Apply to the affected area and to 2 cm of normal skin surrounding lesion once or twice daily

Vehicles

- Lotions intertriginous and hairy areas
- Creams non-oozing, moderate scaling
- Ointments hyperkeratotic lesions
- Powders and sprays may be used to prevent re-infection

Principles of Topical Antifungal Application

- Manage concomitant overhydration and secondary bacterial infections in tinea pedis
- May need to add a topical keratolytic for tinea pedis with significant moccasin keratosis
- Avoid combination products beware the steroid and antifungal combo...just don't do it ©
 - Exception in the case of super itchy tinea where a low-dose TCS can be added for first week

Other Indications for Topical Antifungals

- Onychomycosis
- Tinea of trunk and extremities
- Candidal intertrigo
- Paronychia
- Tinea versicolor
- Seborrheic dermatitis







Topical Anti-fungal Nail Treatment

Mild to moderate (up to 50-60% of nail)

- Ciclopirox 8% hydro lacquer applied once daily
 - Used for 7 days in a row then removed with alcohol
 - Must be used in conjunction with monthly trimming by health care provider
- Efinaconazole 10% solution applied once daily
 - Triazole antifungal, approved FDA 2014



Boron-based antifungal agent, approved FDA 2014



List of US Food and Drug Administration—approved drugs and respective cure rates at week 48¹

Drug	Mycological cure	Complete cure
Oral medications		
Terbinafine	70%	38%
Itraconazole	54%	14%
Topical medications		
Tavaborole	31.1%	6.5%
Efinaconazole	53.4–55.2%	15.2–17.8%
Ciclopirox	29–36%	5.5-8.5%

^{1.} Gupta AK and Stec N. Recent advances in therapies for onychomycosis and its management [version 1; peer review: 2 approved] F1000Research 2019, 8(F1000 Faculty Rev):968 (https://doi.org/10.12688/f1000research.18646.1) First published: 25 Jun 2019, 8(F1000 Faculty Rev):968 (https://doi.org/10.12688/f1000research.18646.1)

CM, 6-year-old female



- Presents with multiple lesions on face
- 2 siblings with similar lesions
- No systemic symptoms
- How would you describe these lesions?
- What's in the DDx?

It Can Look Like This





Or This





Diagnosis

Impetigo

11 million SSTI annually (that's a lot of infections)

Topical Anti-Microbials

- Clindamycin
- Erythromycin
- Minocycline
- Benzoyl peroxide
- Neomycin
- Bacitracin
- Polymixin B

- Mupirocin
- Retapamulin

- Metronidazole
- Ivermectin

Topical Antibiotics for Impetigo

- Mupirocin 2% ointment, cream
 - Covers S pyogenes, methicillin-susceptible S aureus
- Retapamulin 1% ointment
 - Additionally covers erythromycin-resistant S pyogenes, some MRSA coverage

Principles for Topical Antibiotic Application

- At least 1 week of treatment is required (5-7 days)
- Frequency of application
 - Mupirocin 3 times per day for 5-7 days
 - Retapamulin twice a day for 5 days
- Remove crust before application, keep washcloths separate and launder often
- Cover lesions with gauze/dressing if needed
- Keep tube/jar clean
- If more than a few lesions or large areas (10 lesions or >2% BSA), consider an oral antibiotic
 - Dicloxacillin, Cephalexin

Other Indications for the Use of Topical Antibiotics

- Superficial impetigo
- Folliculitis
- Prophylaxis of wound infection
- Acne
- Rosacea

- Abscesses are a different story
 - Topicals generally ineffective
 - I & D is key
 - Culture and sensitivity
 - Oral TMP/SMZ, doxycycline, or clindamycin if suspect MRSA

SM, 6-year-old female



- Multiple lesions
- Wrists, ankles, between fingers and toes
- Intensely pruritic, especially at night
- Several family members with the same symptoms
- How would you describe these lesions?
- What's in the DDx?

Or This





Diagnosis

Scabies

Antiparasitic Agents

- Permethrin topical of choice
- Ivermectin close second, oral, easy, not in pregnancy or kids < 15 kg
- Topical sulfur is considered safe in infants <2mo
- Lindane doesn't even cross the finish line...
 - CNS toxicity, bone marrow suppression
- Malathione, Pyrethrin, Benzyl benzoate, Ivermectin
 - Used for pediculosis

Application of Antiparasitic Agents

- Permethrin 5% cream, 1% lotion or liquid
 - Treatment of choice for scabies
 - Indicated for pts 2 months of age and up, including pregnant and lactating
 - Apply to the entire body neck and below and rinse off in 8-14 hours
 - Massage cream thoroughly into the skin
 - Include areas under the fingernails and toenails
 - 30 grams sufficient for average adult
 - For those under 2 yo scalp involvement is common so apply to scalp and face in this population
 - A second application 1-2 weeks later may be beneficial

Adjuncts to Scabicides

- Treat the family and all close contacts at once
- Low-Medium potency corticosteroid may be added after permethrin to tx hypersensitivity reaction
- May need to treat the itch with antihistamines
- Second-line therapy
 - Oral Ivermectin 200 mcg/kg as single dose, may need to be repeated in 7-10 days

MB, 16-year-old female



- Facial lesions for several years
- Has had oily skin since she was 12-years-old
- Lesions seem to worsen the week prior to menses
- How would you describe these lesions?
- What's in the DDx?

It Can Look Like This





Or This





Diagnosis

Acne VULGARIS

Topical Acne Medications

- Comedolytic
 - Salicylic acid
 - Benzoyl peroxide
 - Retinoids
 - Tretinoin
 - Adapalene
 - Tazarotene
 - Trifarotene

- Antimicrobials
 - Benzoyl peroxide
 - Clindamycin
 - Erythromycin
 - Dapsone
 - Sulfacetamide
 - Minocycline
- Anti-androgens
 - Clascoterone

General Principles of Acne Management

- Be patient treatment is preventative, not curative it takes at least 4 weeks to affect a change and improvement may continue for up to <u>6 months</u>
- Pay attention to the vehicle
 - Start with a cream, change to a gel if not effective and change to a lotion if cream is too irritating
- Apply stepwise approach to topical therapy management
 - OTC comedolytic, topical retinoid, topical antibiotic/comedolytic, oral antibiotic/topical comedolytic
- Retinoids are good for maintenance

Topical Retinoid Formulations

- Tretinoin
 - 0.025%, 0.05%, 0.1% cream
 - 0.01%, 0.025%, 0.05% gel
 - Microencapuslated 0.04%, 0.1% gel
 - Contains glycerin and dimethicone to help repair epidermal barrier and increase skin moisturization
- Adapalene best tolerated AND NOW OTC!!!
 - 0.1% cream
 - 0.1%, 0.3% gel
- Tazarotene most effective, most irritating
 - 0.05%, 0.1% cream
 - 0.05%, 0.1% gel
- Trifarotene
 - 0.005% cream

Topical RetinoidsHow Do They Work?

- Act by down-regulating TLR2 and CD14 messenger RNA, reducing cell surface expression and resulting in <u>anti-inflammatory activity</u>
- Inhibit comedone formation by <u>normalizing keratinocyte</u> <u>activity</u>

Application of Topical Retinoids

- Used for all types and grades and as monotherapy
- Skin irritation is common
 - Start low and go slow, every 2-3 days at first
 - Use only a pea-sized amount to cover the whole face, not for spot treatment
 - Can wash off after 20-30 minutes and then increase as tolerated
- Apply at night as sun exposure causes degradation
- Microsphere technology reduces irritation and has greater photostability
- Not for use in pregnant patients

Topical AntimicrobialsHow Do They Work?

- Reduce the number of *C. acnes* colonizing the skin, reduce the inflammatory response
- Recommended for the treatment of inflammatory acne

Topical Antimicrobial Formulations

- Benzoyl peroxide
 - 2.5% 10% gels, lotions, creams, pads, masks, cleansers
 - Causes bleaching of hair/clothing
 - 2.5% generally most effective
- Erythromycin
 - 2% gel, solution
- Clindamycin
 - 1% gel, solution, lotion, foam
- Minocycline
 - 4% foam

Application of Topical Antibiotics in Acne Management

- Should be used in <u>combination</u> therapy
- All applied once to twice daily
 - Antibiotic in AM
 - Retinoid in PM

New Combos

- Adapalene 0.1%/BPO 2.5% gel
- Clindamycin 1.2%/Tretinoin 0.025% gel
- Clindamycin 1.2%/BPO 2.5% gel
- All combos used once daily, tretinoin product at bedtime
- Clindamycin/BPO gel contains glycerin and dimethicone to improve skin moisturization
- Triple-combination clindamycin 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%
- New Guidelines Jan 2024

Topical Anti-Androgen

- Clascoterone 1% cream androgen receptor inhibitor
 - Applied twice a day
 - Ages 12 and older
 - Can be used as monotherapy or in combination
 - \$600 for a 60 g tube

Management of Acne Vulgaris Adults, adolescents, and preadolescents (≥ 9 years) with acne vulgaris Evaluation SEVERITY ASSESSMENT: Routine · Acne objective severity should be assessed consistently, using the Physician microbiological Global Assessment (PGA) or other scales and endocrine · Assess satisfaction with appearance, extent of scar / dark marks, treatment testing are not satisfaction, long-term acne control, and impact on quality of life. indicated to severe SYSTEMIC ANTIBIOTICS **TOPICAL TREATMENTS** Limit systemic antibiotic use when possible to reduce the Multimodal therapy combining multiple mechanisms of development of antibiotic resistance and other action is recommended antibiotic-associated complications. Use concomitant BP and other topical treatment **Topical retinoids** Doxycycline BP Minocycline **Topical antibiotics** Monotherapy is not recommended Sarecycline **Multimodal Topical Therapy Topical antibiotic & BP** Doxycycline over azithromycin **Topical retinoid & BP HORMONAL AGENTS Topical retinoid Combined oral contraceptives** & antibiotic · Concomitant use of BP can prevent the Spironolactone development of antibiotic resistance. Potassium monitoring is of low usefulness in patients without risk factors for hyperkalemia (e.g., older age, medical comorbidities, medications). Clascoterone Intralesional corticosteroids Salicylic acid Adjuvant treatment for larger acne papules or nodules at risk of acne scarring or for rapid improvement in Azelaic acid inflammation and pain. **ISOTRETINOIN PHYSICAL MODALITIES** Isotretinoin Pneumatic broadband light · Patients with psychosocial burden or scarring should added to adapalene be considered candidates for isotretinoin. We recommend monitoring only LFT and lipids Population-based studies have not identified increased risk of neuropsychiatric conditions or Strong recommendation in favor of the intervention inflammatory bowel disease with isotretinoin. Conditional recommendation in favor of the intervention · For persons of pregnancy potential, pregnancy Strong recommendation against the intervention prevention is mandatory. Conditional recommendation against the intervention Daily dosing over intermittent dosing Abbreviations: BP: Benzoyl peroxide LFT: Liver function test Either lidose-isotretinoin or standard isotretinoin



Topical Take-Home Points

- Many dermatologic conditions in primary care can be managed safely and effectively with topical medications
- Prescribe the right vehicle and the right amount
- Provide patient education to help ensure compliance

Selected Resources/References

- American Academy of Dermatology Education Modules https://www.aad.org/education/basic-derm-curriculum
- UpToDate General Principles of Dermatologic Therapy and Topical Corticosteroid Use: <a href="http://www.uptodate.com/contents/general-principles-of-dermatologic-therapy-and-topical-corticosteroid-use?source=search_result&search=topical+dermatology+therapy&selectedTitle=9%7E150
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