

Tackling Topical Pharmacotherapeutics: A Case-based and Practical Approach

Skin, Bones, Hearts, and Private Parts

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- No conflicts to disclose
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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

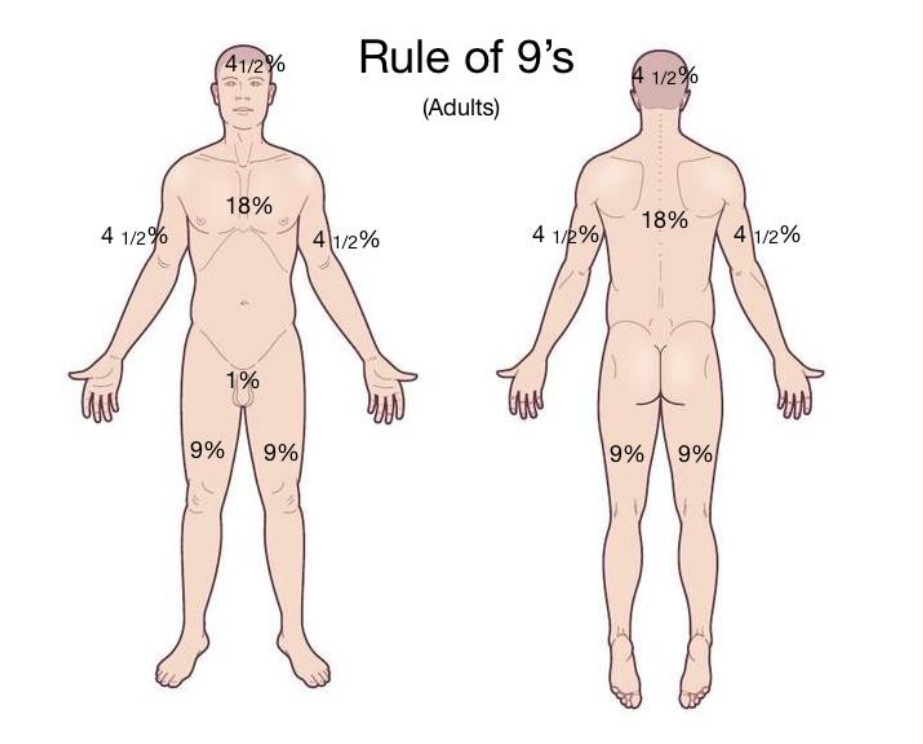


Image source: http://blog.nclexmastery.com/estimating_tbsa/

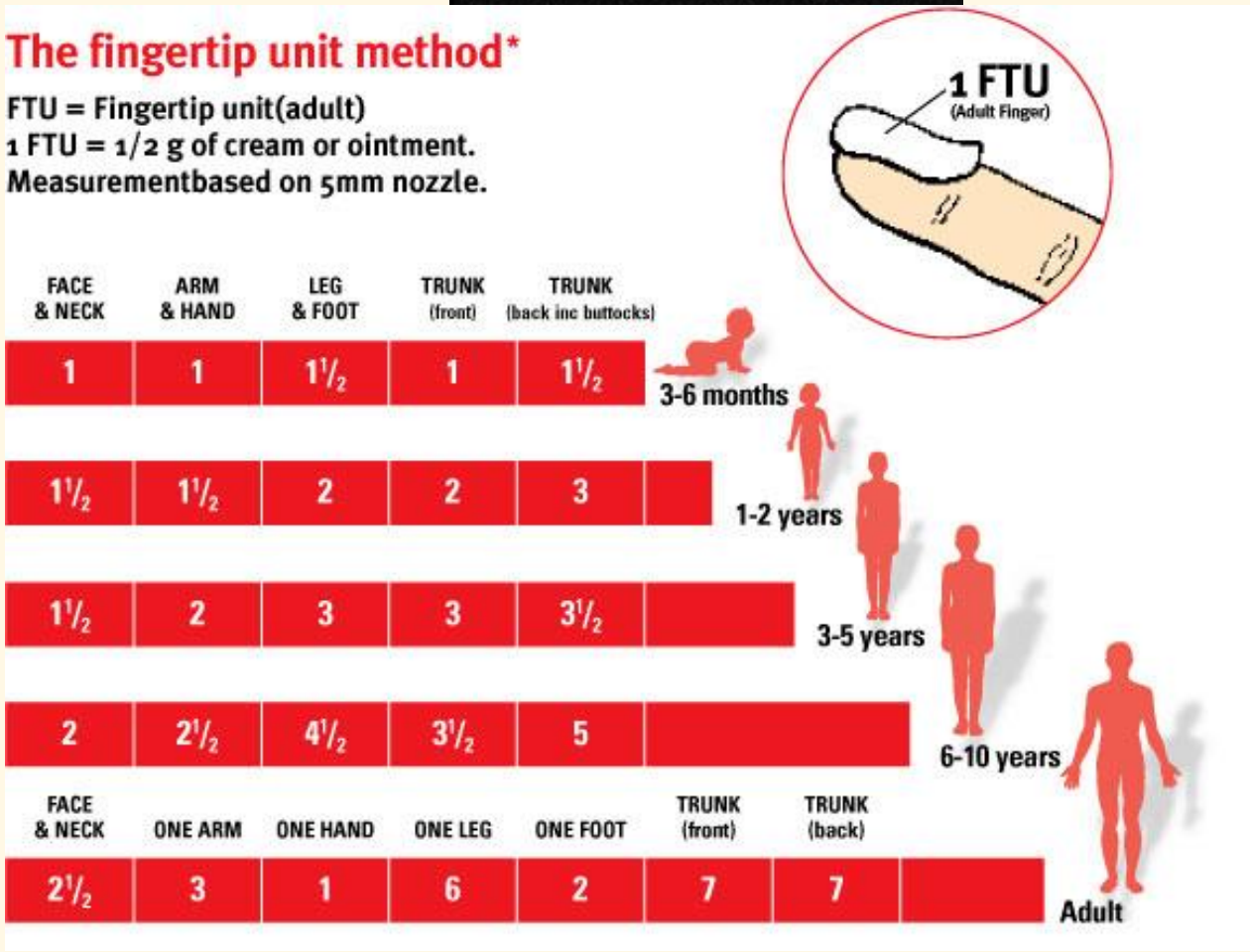
How Much Does the Patient Need?

- 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:
fingertihttp://193.19.159.46/topicalsteroids/measuringsteroidsbyfingertipunit/article/article.asp?ArticleID=77

Rule of the Hand

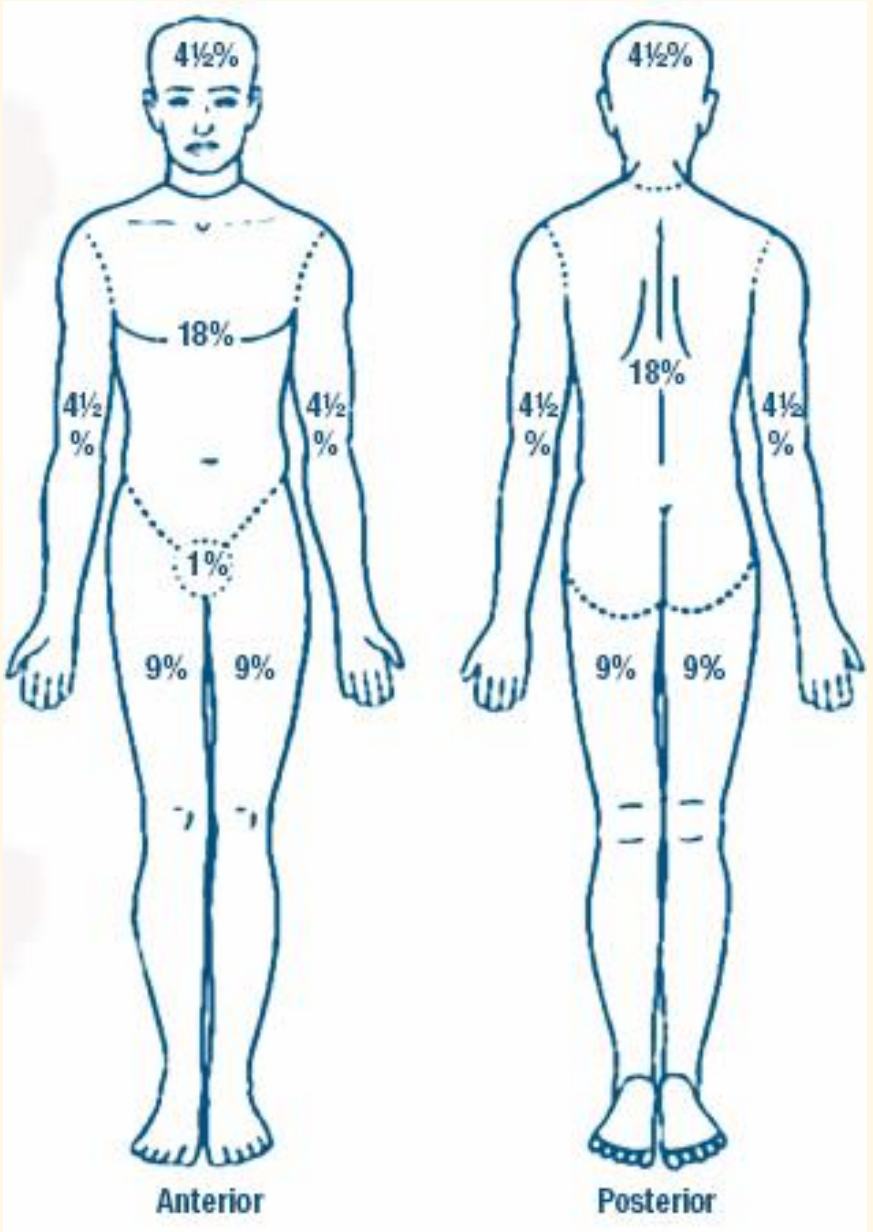
- Hand = 1% BSA
- One hand-sized area (one side) of the skin requires 0.5 FTU or 0.25 g of ointment/cream

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	**0.5**	**0.25**	**3.5**
One leg	6	3	42
One foot	2	1	14

Adapted from Ference JD, Last AR, Choosing Topical Corticosteroids. American Family Physician, January 15, 2009; Vol 79:2, 135-140.

Body Surface Area

Hand = 1%



http://www.uwhealth.org/emergency-room/assessing-burns-and-planning-resuscitation-the-rule-of-nines/12698

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 Topicals in Town

- Topical calcineurin inhibitors
- Topical phosphodiesterase inhibitors
- Topical ivermectin
- Topical efinaconazole
- Topical tavaborole
- Topical minocycline foam
- Topical adapelene 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?

http://www.flickr.com/photos/75491103@N00/239777484/sizes/l/in/faves-jeffnielson/

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

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 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

van Zuuren EJ, Fedorowicz Z, Christensen R, Lavrijsen A, Arents BWM. Emollients and moisturisers for eczema. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD012119. DOI: 10.1002/14651858.CD012119.pub2

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

C=Cream, O=Ointment, L=Lotion, S=Solution

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 non-folded 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, telangiectases
  - 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





http://www.google.com/imgres?imgurl=http://meded.ucsd.edu/clinicalimg/skin_steroid_atrophy3.jpg&imgreurl=http://meded.ucsd.edu/clinicalimg/skin_steroid_atrophy3.htm&usg

http://vgrd.blogspot.com/2010/05/facial-erythema-secondary-to-topical.html

Other Uses for Topical Steroids

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









http://x-medic.net/dermatology/lichen-simplex-chronicus-circumscribed-neurodermatitis/attachment/lichen-simplexchronicus/

http://www.dermis.net/dermisroot/en/14695/image http://organizedwisdom.com/Contact_Dermatitis_Pictures

www.skinsight.com/infant/seborrheicDermatitisPediatric.htmic.htm

Atopic Dermatitis – Rescue the Non-Responders

- Topical calcineurin inhibitors – acute and chronic/proactive treatment
- Topical PDE4 inhibitors – indicated for mild to moderate
- Topical JAK1/2 – on the way!

GG, 19-year-old male



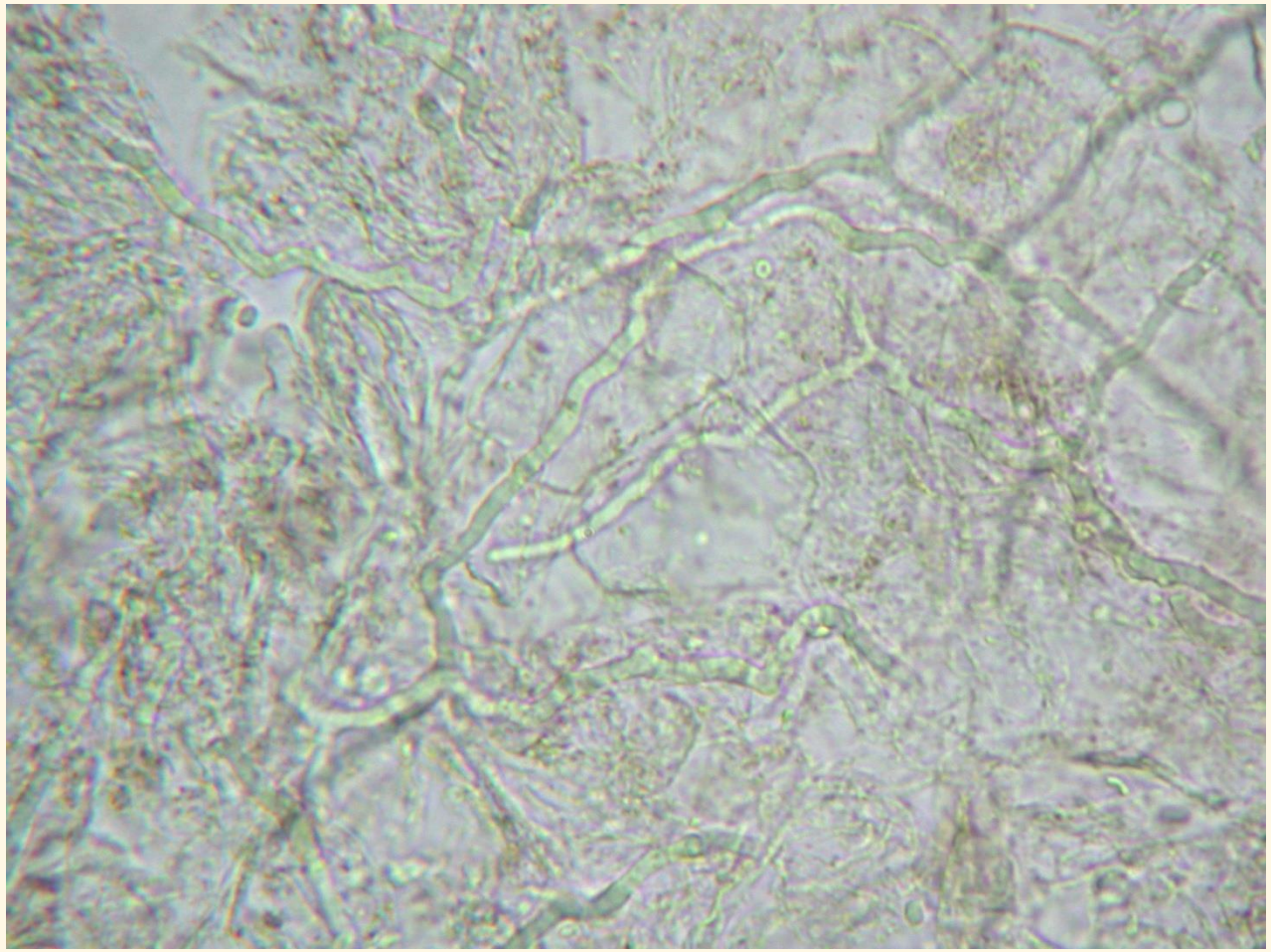
- Developed this rash on thigh over the past 2-3 weeks
- Slightly itchy
- How would you describe it?
- What else might you examine?
- What's in the DDx?

http://kennethgoestoindia.blogspot.com/2009/02/tinea-corporis-aka-ringworm.html

Diagnosis

Tinea corporis

Scrape and KOH it! and Consider a Culture



http://dermatlas.med.jhmi.edu/derm/display.cfm?ImageID=492132121

Prescribe a Topical Antifungal

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

- Some classes are fungistatic and some are fungicidal

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

C=Cream, L=Lotion, S=Solution, G=Gel, O=Ointment, P=Powder

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

- Avoid combination products – beware the steroid and anti-fungal combo…just don’t do it ☺

Other Indications for Topical Antifungals

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







http://drugster.info/img/ail/1679_1691_1.jpg

Topical Anti-fungal Nail Treatment

- Ciclopirox
- Topical efinaconazole
- Topical tavaborole

List of US Food and Drug Administration–approved drugs and respective cure rates at week 48[1]

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)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6600855/

CM, 4-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?

http://www.dfmqueens.ca/intranet/evaluation/resident_project_websites/Amyot/dermatology_basics_006.htm

Diagnosis

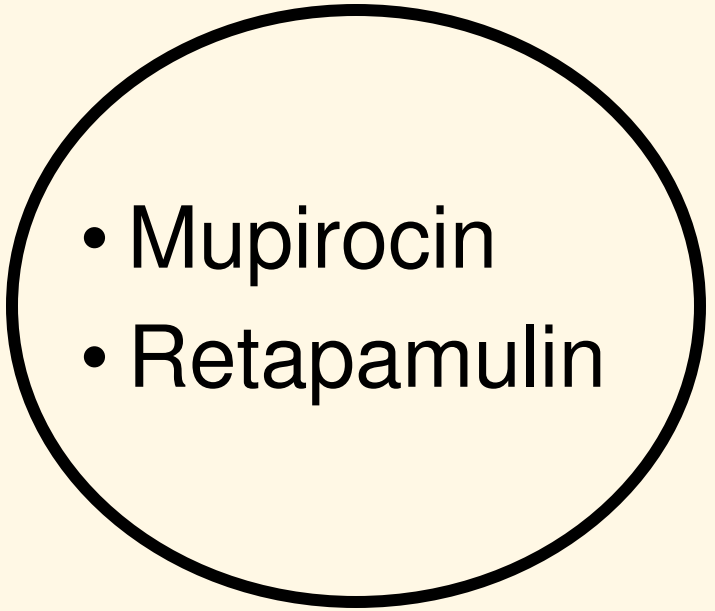
Impetigo

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

Topical Anti-Microbials

- Clindamycin
- Erythromycin
- Minocycline
- Benzoyl peroxide

- Neomycin
- Bacitracin
- Polymixin B



- 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?

https://www.dermnetnz.org/

Diagnosis

Scabies

Antiparasitic Agents

- Permethrin – topical of choice
- Ivermectin – close second
- 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
  - 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
  - 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
- Second-line therapy
  - Oral Ivermectin 200 mcg/kg as single dose (adult)

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?

Diagnosis

Acne VULGARIS

Topical Acne Medications

- **Comedolytic**
  - Salicylic Acid
  - Benzoyl peroxide
  - Retinoids
    - Tretinoin
    - Adapalene
    - Tazarotene
    - Trifarotene
- **Antimicrobials**
  - Benzoyl peroxide
  - Clindamycin
  - Erythromycin
  - Dapsone
  - Sulfacetamide
  - Minocycline

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 6 months
- 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 Retinoids

How Do They Work?

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

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 Antimicrobials

How Do They Work?

- Reduce the number of *P. 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 combination 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

http://www.empr.com/acanya/drug/3285/#acne

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: http://www.uptodate.com/contents/general-principles-of-dermatologic-therapy-and-topical-corticosteroid-use?source=search_result&search=topical+dermatology+therapy&selectedTitle=9%7E150
- Patient-Centered Pharmacology – Dermatology
- Symptom to Diagnosis – Evaluation of a Rash
- Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, Baldwin HE, Berson DS, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016 Feb 15.