Dermatologic Therapies for the Nondermatologist

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Financial Disclosures

Amgen

EAISI

P-value communication

Roche

Presentation Overview

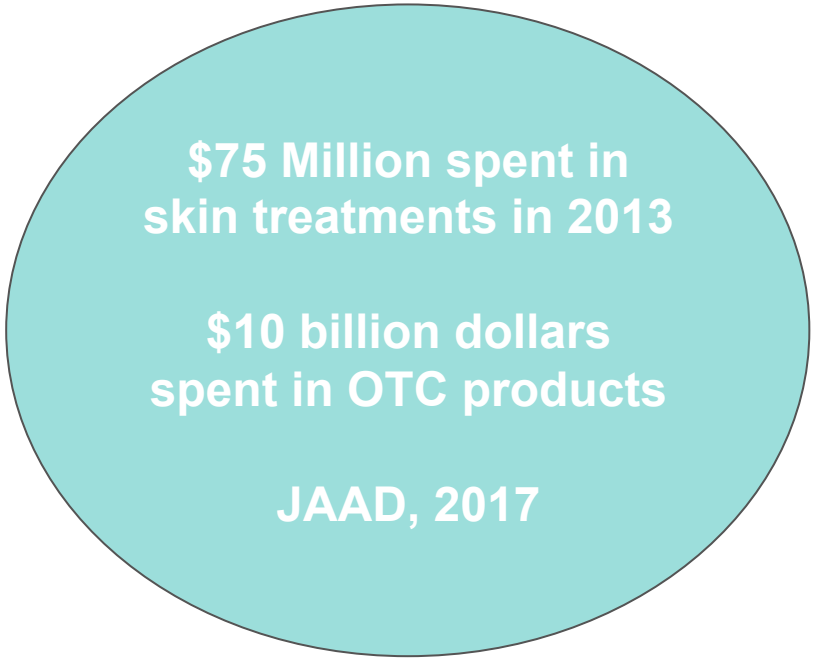
The purpose of this presentation is to review the following topics:

- Burden of skin disease in the United States
- Supportive care Path to Prescription Coverage
- Topical Therapies 101
- Topical Steroids
- Topical Moisturizers
- Topical Antipruritics
- Topical Antibiotics

Burden of skin disease costs…..

How much do people spend on skin treatments/ year?

1. $5 million
2. $10 million
3. $15 million
4. $25 million



Edison & Brod (2017). JAAD, 76(5), 973-974
Lim et al, (2017), JAAD, 76(5), 958-972.e2

Topical Therapy Adherence

Many factors influencing long-term medication adherence:

- Complexity
- Duration
- Cost of treatment
- Patient / physician communication
- Socioeconomic variables
- Values

Patient interviews
Pennsylvania
n=385, 4 practices
Screened for 1^0 adherence

Cost major barrier to initiating therapy

JAMA Derm, 2018

Specific to topical therapies . . .

- Treatment adherence for derm conditions is poor
- Rx redemption only being 65% (psoriasis 50%)
- Following prescribed treatment ranging from 50-60%

Zschocke et al, Arch Dermatol Res. 2014; 306(3): 287–297
Ryskina et al, JAMA Dermatol. 2018 Apr 1;154(4):456-459.

Treatment-Related Toxicities Cost

Ipilimumab Treatment: All toxicities

Table 5 Individual costing per patient

Autoimmune toxicity	Inpatient stay (£)	Diagnostic investigations (£)	Infliximab (£)	Specialist opinion (£)	Cost per patient (£)
Colitis	22 293	2111	2382		26 786
Colitis	13 156	1002			14 158
Colitis	12 425	1033			13 458
Colitis	10 598	187	2382		13 167
Pneumonitis	9095	921		220	10 436
Colitis	7309	1033			8342
Colitis	5116	1033			6149
Colitis	6944	1002			7946
AM, ph	4385	384		440	5209
Colitis	4751	30			4781
Colitis, ph	4385	1320			5705
AM, ph	4385	192		220	4797
ph	3655	348		220	4223
Colitis	2558	1002			3560
Colitis	1827	1033			2860
Colitis	1096	1033			2129
Colitis, rash	731	972			1703
Hepatitis	1462	157			1619
Colitis	1462	61			1523
Colitis	1096				1096
Colitis, hepatitis		1033			1033
Colitis, rash					0
Colitis					0
Rash					0
Rash					0
Rash					0
Rash					0
Rash					0
Rash					0
Total cost					140 680

AM, aseptic meningitis; ph, panhypophysitis.

n = 110
Total: £140,680
Median: £3860

Treatment-related toxicities in cancer setting have been reported to cost thousands of dollars...

TABLE 3
Estimated Costs of Cancer Treatment-related Toxicities Reported by the Northwestern University Costs of Cancer Program*

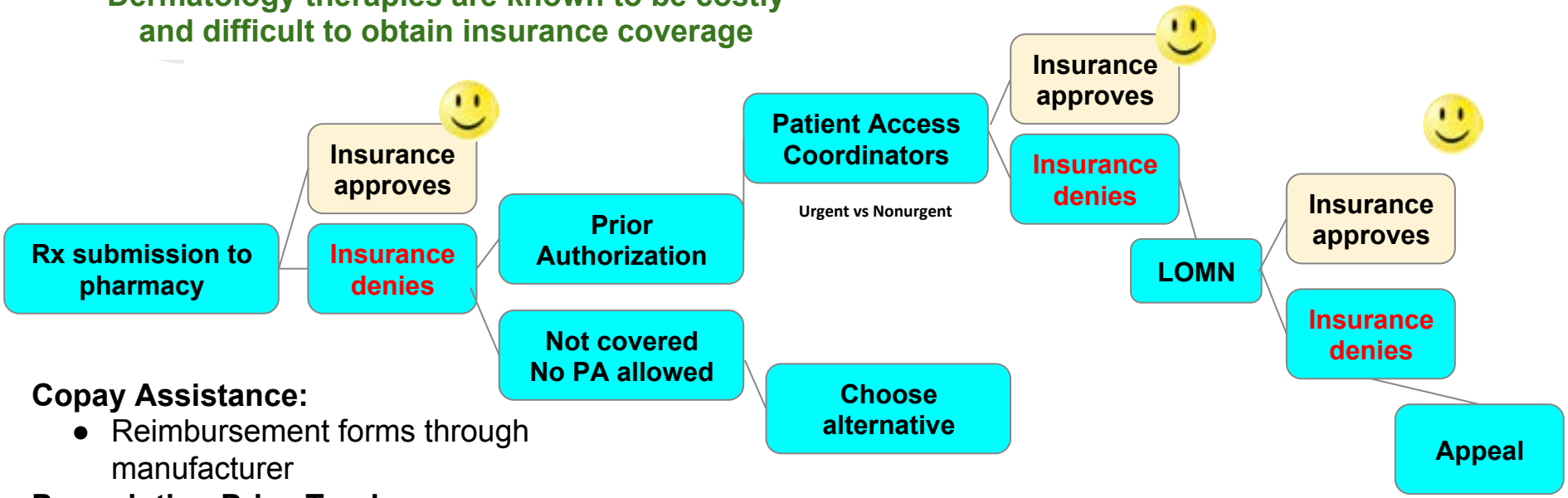
Treatment-related Toxicity (Reference)	Oncology Treatment	Cancer Diagnosis	No. of Patients	Medical Costs, $
Mucositis/pharyngitis (current study)	Radiochemotherapy	Nonsmall cell lung cancer	40	35,960
Neutropenia treated as an inpatient (Albain 2002[9])	Chemotherapy	Lymphoma	11	17,869
Mucositis/pharyngitis (current study)	Radiochemotherapy	Head and neck cancer	99	17,244
Neutropenia treated as an inpatient (Albain 2002[9])	Chemotherapy	Breast cancer	5	10,534
Neutropenia treated as an inpatient (Albain 2002[9])	Chemotherapy	Lung cancer/multiple myeloma	12	10,311
Neutropenia (Calhoun 2001[5])	Cis-platinum	Ovarian cancer	26	7546
Febrile neutropenia (Calhoun 2003[10])	Liposomal daunorubicin	AIDS-related Kaposi sarcoma	166	7138
Febrile neutropenia (Calhoun 2003[10])	Liposomal doxorubicin	AIDS-related Kaposi sarcoma	121	6717
Neutropenia treated as an outpatient (Albain 2002[9])	Chemotherapy	Breast cancer	17	5704
Anemia (Salma 2007[11])	Topotecan	Ovarian cancer	120	5181
Neutropenia (Salma 2007[11])	Topotecan	Ovarian cancer	120	3756
Thrombocytopenia (Calhoun 2001[5])	Cis-platinum	Ovarian cancer	15	3268
Febrile neutropenia treated in an emergency room (Courtney 2007[12])	Chemotherapy	Various	48	1455
Neutropenia treated as an outpatient (Albain 2002[9])	Chemotherapy	Lung cancer/multiple myeloma	14	1329
Neutropenia treated as an outpatient (Albain 2002[9])	Chemotherapy	Lymphoma	12	1201
Neuropathy (Calhoun 2001[5])	Cis-platinum	Ovarian cancer	42	688
Palmar-plantar erythrodysia (Salma 2007[11])	Liposomal doxorubicin	Ovarian cancer	115	104
Stomatitis/esophagitis (Salma 2007[11])	Liposomal doxorubicin	Ovarian cancer	120	101
Nausea and vomiting (Salma 2007[11])	Topotecan	Ovarian cancer	120	83
Diarrhea (Salma 2007[11])	Topotecan	Ovarian cancer	120	58

AIDS indicates acquired immunodeficiency syndrome.
* Calhoun EA, Bennett CL. Evaluating the total costs of cancer. The Northwestern University Costs of Cancer Program. Oncology (Williston Park). Jan 2003;17(1):109-114; discussion 119-121.[13]

Yousaf et al, 2015, *Melanoma Res* 25(3), 259-64
Nonzee et al, 2008, *Cancer*, 113(6), 1446-52

Supportive Care: Path to Prescription Coverage

Dermatology therapies are known to be costly and difficult to obtain insurance coverage



Copay Assistance:

- Reimbursement forms through manufacturer

Prescription Price Trackers:

- http://www.goodrx.com
- https://www.lowestmed.com/

Statewide Assistance Programs:

- https://www.newyorkrxcard.com/

Compound Pharmacies

Topical Therapies 101

Objectives

- Lubricate, medicate
- Treatment or prevention

Choice Depends on

- Disease state and severity
- Skin Turgor
- Anatomic localization of disease
- Patient preference

Excipient

- Inactive substance (vehicle/medium)
- Allowing drug to facilitate through the stratum corneum

Effective Therapy Depends on

- Active Drug
- Properties of vehicle

Importance of Choose Vehicles

- Treatment adherence
- Treatment outcomes

Dermatology Nursing Essentials: A Core Curriculum 2nd Edition, 2003
Weiss, Dermatologic Therapy, Vol. 24, 2011, 471–476

Topical Therapies - Pros/Cons

Vehicle	Pros	Cons
Cream	• Tend to be less irritating • Emollient, cooling, moistening properties • Has elegant appearance and easy application	May be too oily
Foam	• Minimal residue after application • Quick drying, ease of application, lack of fragrance • Spreads easy, helpful if treating larger BSA	Skin reactions Insurance coverage and expensive
Gel	• Cooling affect • Fast onset of action, high patient satisfaction	<1% localized skin reactions. Drying
Lotion	• Most versatile • Have lighter feel – patient prefer • Intertriginous areas preferred • Cooling effect	Skin irritation/burn Not as hydrating Contains alcohol

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Weiss, Dermatologic Therapy, Vol. 24, 2011, 471–476
Adapted from: http://www.skintherapyletter.com
Habif: Clinical Dermatology, 5th Edition 2010

Topical Therapies - Pros/Cons

Vehicle	Pros	Cons
Ointment	• Provides a higher potency • Greater drug penetration • Effective for very dry excoriated skin	Difficult to wash off Insoluble to water Too messy/greasy
Shampoo	• High patient satisfaction = ↑ adherence/TX efficacy • Reduced side effects • Can be used for extended periods of time	Small # of cases with burning, skin atrophy, and telangiectasia Expensive
Solution	• Easy to spread and good use for scalp • Leaves minimal residue	Irritation Messy No emolliating or skin protective properties
Spray	• Can treat larger BSA • Improved QoL scores compared with other formulations	Can produce a small # of localized reactions Insurance coverage and expensive

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Adapted from: http://www.skintherapyletter.com
Habif: Clinical Dermatology, 5th Edition 20

How to Prescribe Topical Therapy?

Measurement of cream to prescribe for patients with skin disease

Adult male: 1 FTU = 0.5gm / Adult female: 1 FTU = 0.4gm

Varies with body part

- One hand: 1 FTU
- One arm: 3 FTU
- One foot: 2 FTU
- One leg: 6 FTU
- Face and neck: 2.5 FTU
- Trunk, front and back: 14 FTU
- Entire body: ~40 FTU

Quantity of med
Dispensed from 5mm nozzle
Placed on finger tip from
Distal tip to DIP joint

Adult Female cream QD to BUE

- 2 arms x 3 FTU x 0.4gm = 2.4gm (QD)
- 2.4gm x 7 = 16.8gm (weekly)
- ~30gm should last 2 weeks

Topical Steroids

Body	**Class I - High** (Clobetasol)
Body	**Mid Potency** (Triamcinolone)
Face and Intertriginous Areas	**Class IV - Low** (Hydrocortisone)

Properties

Anti-inflammatory
Immunosuppressive
Vasoconstrictive
Anti-proliferative

Efficacy/Absorption

Best through **inflamed** and **desquamated** skin

Frequency/Duration

BID x 2-4 weeks course
(1 week of rest → limit side effects and decreased responsiveness)
No more than 45-60gm/week

- Class 1 is 1000 x more potent than class VII
- Steroids within any class are equivalent strength
- Look at the class and not the percentage

Borovicka et al. In: Lacouture ME, Ed. *Dermatologic Principles and Practice in Oncology*. 2014. Habif TP, et al (Eds). *Clinical Dermatology:A Color Guide to Diagnosis and Therapy*. Edinburgh: Mosby Elsevier; 2010. Lacouture ME. Skin Care Guide for People Living with Cancer. 2012.

Topical Steroids Adverse Events

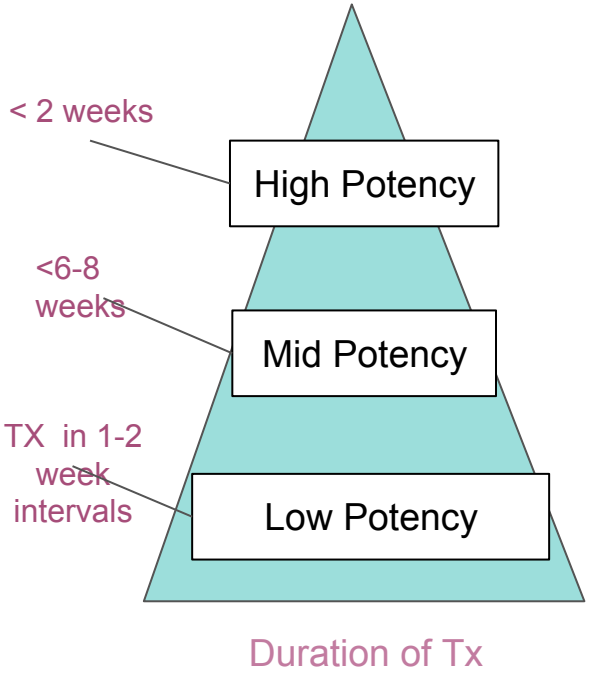
Short Term:

- Burning
- Stinging
- Pruritus
- Erythema
- Irritation

Absorption 0.25-3%

Prolonged:

- Skin Atrophy
- Masking of infection
- Telangiectasias
- Irreversible Striae
- Senile/Solar Purpura
- Hypertrichosis
- Pigmentation Change
- Steroid rosacea
- Periorificial dermatitis



General Principles of Dermatologic Threapy and Topical Steroid Use
[UpToDate 2014] Habif: Clinical Dermatology, 5th Edition 2010

Function of Moisturizing Treatment

Involves…..

- Repair skin barrier
- Retain/increase water content
- Reduce TEWL
- Restore lipid barriers ability to attract, hold, redistribute water
- Maintain skin integrity and appearance

Moisturizers perform these functions by acting as humectants, emollients, and occlusives

Madison, J Invest Dermatol, 121(2), 231-241

Differences in Topical Moisturizers

Occlusive:[1,3]

- Physically block TEWL – hydrophobic barrier
- Allowing skin to retain natural moisture
- "Coat the skin", Best used after bathing

Petrolatum (Aquaphor)

Lanolin, Mineral Oil

Humectants:[1,3]

- Improve hydration of stratum corneum by drawing **TEWL** and in humid conditions the external environment
- **Attracts/retains water**

Ammonium Lactate
Urea 10%

Emollients: [1,3]

- Mainly lipids, and oils
- Fill spaces between skin flaking (corneocytes)
- Hydrate and improve skin softness, flexibility, and smoothness

Cholesterol, Squalene, Fatty Acids

Keratolytics: [3]

- Soften and facilitate exfoliation of epidermal cells (keratin)

Urea 20-40%
Salicylic Acid

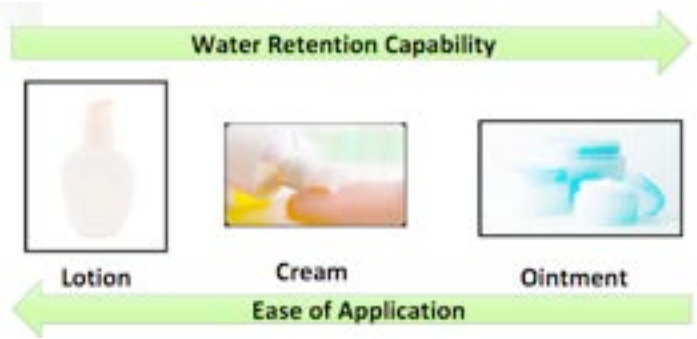
Spencer. (1988). Dry Skin and Moisturizer[1]
http://www.skintherapyletter.com/2005/10.5/1.html[2]
http://www.skintherapyletter.com/2001/6.13/2.html[3]

Moisturizer Education

- Fragrance-free creams
- Gentle soaps with moisturizers
- Applying moisturizer after shower
- Glove or sock occlusion
- Avoiding products containing alcohol.
- Avoid scratching skin
- Monitor for infection with dry and cracked skin
- Use mild, gentle laundry detergent

Medicated Cream | **Moisturizer** | **Sunscreen** | **Cosmetics**

Medication first for best chance of absorption
Moisturizer creates a barrier
Makeup smudges – best to apply last



Adapted from Lacouture ME. Skin Care Guide for People Living with Cancer. 2012.
Caring for Your Dry Skin Patient Education Fact Card http://www.mskcc.org

Topical Antipruritics

- **Pramoxine 1% and Hydrocortisone 2.5%**
  - **Ind**: Inflammatory, pruritic and burning conditions
  - **MOA**: anesthetic and corticosteroid

Cream, ointment, gel
Can cost >$200
Typically BID

- **Doxepin 5%**
  - **Ind**: Pruritus
  - **MOA:** tricyclic antidepressant with potent H1/H2 antagonist effects
  - **Considerations:** Avoid occlusive dressing, risk of drowsiness if applied >10% BSA, inform clinician of pregnancy

Cream only
30-45gm
Can cost up to $500

Pramosone and Doxepin Topical [UpToDate, 2015]

Topical Antipruritics

- **Epiceram**
  - Nonsteroidal controlled release skin barrier
- **MOA:** Replenishes the natural concentrations of lipids in the stratem corneum: ceramides, cholesterol and free fatty acids.

Twice daily
$$ Expensive

- Free of: steroid, fragrance, paraben, propylene glycol and is noncomedogenic

Indications: xerotic and pruritic dermatoses (atopic dermatitis, irritant contact dermatitis and radiation dermatitis)

http://epiceram-us.com/

Topical Antipruritics

Tacrolimus:

- **Indication:** Not commonly used for pruritus unless underlying etiology is inflammatory – used as a second-line approach
- **MOA:**
  - Calcineurin inhibitor
  - Prevents transcription of IL-2 via calcineurin complex binding
  - Suppresses cellular immunity → blocking T Cell activation and proliferation preventing release of T-Cell derived cytokines
  - Antipruritic effect reported to results from reduction of inflammation
- **Considerations**: Re-examined if no improvement <6 weeks. <1% skin cancer and lymphoma development. Avoid use on malignant or premalignant skin conditions or infected areas. Can be safely applied to thinner skin over face and eyelids. Can cause local skin reactions such as burning sensation*

Ointment 0.03% and 0.1%
50-60gm
BID for longer periods of time

Tacrolimus [UpToDate, 2015]

Topical Antibiotics

38% of patients w/EGFR inhibitor therapy (n=221) in 2010
Showing evidence of bacterial, fungal, and viral infections
Most common being staphylococcus aureus and methicillin resistant staph aureus

Variety of Potential Uses:

- Infectious (localized, impetiginized, staph nasal carriage)
- Noninfectious (acne vulgaris)
- Other: post op surgical ppx, chronic wounds based on C&S

Gram (+) Topicals:
Mupirocin ointment 2% (staph / strep)

Gram (-) Topicals
Gentamicin 0.1% (Aerobacter, Escherichia, Klebsiella, Salmonella, Shigella, Proteus + pseudomonas)

Has some G+ activity

Gram (+ / -)Topicals
Silvadene cream (pseudomonas, serratia, enterobacter, klebsiella, e. Coli, proteus mirabilis, morganella, candida, staph, yeast)

Balagula, Lacouture & Ito, 2014 (Lacouture, ME. Ed) Dermatologic Principles and Practice in Oncology
Eilers et al, *JNCI* 2010.

Keypoints

Be aware of skin disease burden, financial impact, influence on topical therapy adherence and clinical outcomes

Be able to appropropriate prescribe the right amount and vehicle of a topical presccription

Be able to describe classes of steroids, types of moisturizers, antipruritics and antibiotics, know their clinical indications, and possible AEs.

Thank you!

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