Learning objectives for this lecture:

- Describe how the physiology of the skin affects drug delivery including the practical aspects of selection of topical dosage forms.
- Understand the importance of initiation of non-pharmacologic therapies first for dermatologic disorders.
- Provide appropriate pharmacotherapy, for both initial and refractory cases, to treat varying dermatologic disorders.
- Compare and contrast the potency of topical corticosteroids.
- Describe the use of calcineurin inhibitors in topical syndromes, as well as emollients, keratolytics, retinoids and other agents mentioned in this lecture.
- Justify the role of topical antibacterial and antifungal agents in various dermatologic conditions.

Outline for this lecture

- Percutaneous drug absorption and drug delivery: topical and transdermal
  - Atopic dermatitis treatment
    - Emollients
    - Topical corticosteroids
    - Topical calcineurin inhibitors
  - Other dermatologic conditions
    - Keratolytics
    - Anthralin
    - Vitamin D3 analogues
    - Coal tar
    - Retinoids
    - Antifungals and antibacterials
- Complementary Alternative Medicine
Stratum corneum provides the greatest protection against chemicals and drugs. Drugs penetrate via passive diffusion. Factors that affect drug absorption are:

- Skin hydration
- Integrity of stratum corneum
- Also:
  - presence of inflammation
  - anatomical site
  - surface area
  - age of patient

In neonates, absorption is increased in rate and extent, due to:

- thinner epidermal layer (stratum corneum) example: transdermal patches - 3x absorption in neonates
- increased skin hydration example: ↑ absorption of ointments
- increased ratio of SA per kg of body weight
Percutaneous absorption...

Associated toxicities
- rubbing alcohol
- hexachlorophene soaps
- salicylate ointments
- boric acid powders
- topical hydrocortisone

Therapeutic uses
- theophylline gel
- clonidine patch
- topical sertraline
- topical betamethasone

Why topical drug delivery?

Advantages:
- Can deliver a drug at a high concentration locally and minimize ADRs
- Non-invasive and easy to use
- Topical agents can provide hydration, protection and delivery

Disadvantages:
- Messy
- Minimal contact time
- Systemic absorption
- Hypersensitivity

...Versus transdermal delivery

Advantages:
- Helpful for certain medications: short half life, poor bioavailability/first pass metabolism
- Patient: better compliance, no need for IV, good for nausea or vomiting or intolerance

Disadvantages:
- Rate-limiting absorption, dose dumping, alteration of patches dangerous
- Very few medications can be delivered this way
- Examples: nitroglycerin, clonidine, estrogen, progesterone
Topical drug delivery depends on dosage form....

Which dosage form has the most effective dermal penetration?

A. creams  
B. ointments  
C. foams  
D. they all have the same dermal penetration

Drug delivery: Emulsions

<table>
<thead>
<tr>
<th>Oil-in-water</th>
<th>Water-in-oil</th>
</tr>
</thead>
</table>
| - Creams in general  
  - Most common  
  - Patients prefer  
  - Must be fully rubbed in  
  - Cetaphil  
  - Keri lotion  
  - Lanaphilic...  
| - Ointments made of inert bases or “water in oil”  
- More greasy/messy  
- High level of skin penetration (very lipophilic)  
- Aquaphor, Eucerin, Lubriderm, Nivea... |
**Emollients**

- Water in oil products
- Apply emollient to skin within 3 minutes of bathing ("soak and seal" method)
- Moisturize at least twice daily to keep skin soft and pliable
- Creams or ointments are preferred


---

**Drug delivery in the skin depends on dosage form**

- **Solutions**
  - Normal saline, aluminum acetate, silver nitrate, acetic acid and potassium permanganate
- **Lotions** - good for scaly/hairy areas
- **Powders**
- **Gels** - cooling effect but can be irritating if in alcohol base
- **Aerosols**
- **Foams** – feel good but not as penetrating

---

**Which dosage form to choose?**

| Acute inflammation: Oozing, weeping, vesication, edema, pruritus | Aqueous vehicles/water, powder solutions, lotions, sprays and aerosols |
| Sub-acute inflammation: Less oozing, pruritus, crusting | Creams, gels |
| Chronic inflammation: Lichenification, dryness, scaling, erythema, pruritus | Ointments |
How we treat topical skin disease:
Through the eyes of a med student...

- If it’s wet, dry it.
- If it’s dry, wet it.
- If it’s ugly, cover it up.
- If you don’t know what it is, put corticosteroids on it.

Steroid pharmacology

- Steroids cause their effects by binding to the glucocorticoid receptor (GR)
- The GR complex up-regulates the expression of anti-inflammatory proteins in the nucleus and represses the expression of proinflammatory proteins
- CS have anti-inflammatory, antiproliferative and immunosuppressant properties

Topical corticosteroids

- Convenient, rapid response, some inexpensive
- Only provide temporary relief and can see tachyphylaxis
  - To avoid use intermittent dosing or “pulse therapy”
- Limit to < 3-4 weeks and wean slowly
Who should not use topical steroids

Patients who:
- Have bacterial, viral or fungal infections
- Are pregnant or breastfeeding
- Have allergies to steroids or vehicle
- Have thin skin

Bacterial skin infection
www.skinrashpictures.com/images

Dosing topical steroids

- Dosed BID
  - Taper to lowest effective dose and potency
  - Best to rub in when skin is moist
  - Dosed via a “FTU”
    - 1 FTU to cover hand, 2 for face/foot, 6 for leg, 14 for trunk...
- Available in many dosage forms:
  - Ointment, gels, creams, lotions/solutions, foams


Topical Corticosteroids: Skin Penetration

- Absorption depends on area:
  - sole 0.05%, palm 0.1%, forearm 1%, armpit 4%, face 7%, eyelids/genitals 30%
- Affects agent of choice:
  - Areas of high penetration (groin, axillae, face, skin folds, or mucous membranes) require lower-potency topical preparations.
  - Areas of poor penetration (elbows, knees, palms, or soles) require higher-potency topical preparations.


22

23

24
Topical Corticosteroids: To occlude or not to occlude?

- Occlusion
  - Increases percutaneous absorption
  - Traps heat and promotes maceration
  - Enhances the potency of corticosteroids by a factor of 10
- In treatment of AD:
  - Best for chronic lesions that are thick & scaly
  - Short periods can be clinically useful
  - Should not be maintained for more than 12 hours in a 24 hour period


Which of following is/are occlusive?

A. Ointments
B. Saran wrap
C. Band-Aids
D. Tight fitting diapers/clothes
E. All of the above

Potency of topical steroids (based on USP standards)

- Low-potency
  - Safe for long term
  - Best for face/intertriginous areas, on children, and with occlusion
  - Example: nonfluorinated agents such as hydrocortisone valerate (Westcort)/butyrate (Locoid) creams
- Medium-potency
  - Use on face/intertriginous areas for limited time
  - mometasone, betamethasone, fluocinolone, triamcinolone

Corticosteroids (Topical) | USP-DX 2001
www.potestoids.org
More on steroid potency

- **High-potency**
  - Reserve for severe dermatoses
  - Betamethasone dipropionate (Diprolene AF, Diprosone, Maxivate)

- **Very high-potency**
  - For short time on small areas, no occlusive dressings
  - Betamethasone dipropionate (Diprolene), clobetasol (Temovate), halobetasol (Ultravate)

- **Product charts available**
- Also a vasoconstrictive potency rating:
  - Class I (highest) – Class VII (lowest)

Topical Corticosteroids: Vasoconstricting Potency Ranking

<table>
<thead>
<tr>
<th>Class I (highest)</th>
<th>Class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Betamethasone dipropionate</td>
<td>Fluocinolone acetonide</td>
</tr>
<tr>
<td>Clobetasol propionate</td>
<td>Flurandrenolide</td>
</tr>
<tr>
<td>Halobetasol propionate</td>
<td>Hydrocortisone valerate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amcinonide</td>
</tr>
<tr>
<td>Desoximetasone</td>
</tr>
<tr>
<td>Diflorasone diacetate</td>
</tr>
<tr>
<td>Flucinolone</td>
</tr>
<tr>
<td>Halcinonide</td>
</tr>
<tr>
<td>Mometasone furoate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Betamethasone benzoate</td>
</tr>
<tr>
<td>Betamethasone valerate</td>
</tr>
<tr>
<td>Fluocinonide propionate</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Betamethasone benzoate</td>
</tr>
<tr>
<td>Betamethasone valerate</td>
</tr>
<tr>
<td>Fluocinonide propionate</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alclometasone dipropionate</td>
</tr>
<tr>
<td>Hydrocortisone butyrate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class VI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desonide</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class VII (lowest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone</td>
</tr>
<tr>
<td>Dexamethasone sodium phosphate</td>
</tr>
<tr>
<td>Hydrocortisone</td>
</tr>
<tr>
<td>Hydrocortisone acetate</td>
</tr>
<tr>
<td>Methylprednisolone acetate</td>
</tr>
</tbody>
</table>

Class I (highest):
- Bethamethasone dipropionate
- Clobetasol propionate
- Halobetasol propionate

Class II:
- Amcinonide
- Desoximetasone
- Diflorasone diacetate
- Flucinolone
- Halcinonide
- Mometasone furoate

Class III:
- Betamethasone benzoate
- Betamethasone valerate
- Fluocinonide propionate
- Triamcinolone acetonide

Class IV:
- Betamethasone benzoate
- Betamethasone valerate
- Fluocinonide propionate
- Triamcinolone acetonide

Class V:
- Alclometasone dipropionate
- Hydrocortisone butyrate

Class VI:
- Desonide

Class VII (lowest):
- Dexamethasone
- Dexamethasone sodium phosphate
- Hydrocortisone
- Hydrocortisone acetate
- Methylprednisolone acetate

Adapted from Pharmacotherapy: A Pathophysiologic Approach. 9th ed. 2013. Table 101-4.

Potency is determined by ability of product to penetrate skin after release from vehicle

Enhance by:
- Using occlusion
- Use of enhancing substances
- Change vehicle
- Modifications of steroid molecule
  - Hydrocortisone → butyrate & valerate
  - Betamethasone valerate → benzoate/dipropionate
  - dipropionate in optimized vehicle
**When corticosteroids are used topically, adverse events are:**

A. Nonexistent  
B. Possible depending on multiple patient specific factors  
C. Possible depending on dosage form used  
D. B and C  

**ADRs of topical steroids**

- Most common:
  - Epidermal/dermal atrophy  
  - Hypopigmentation  
  - Acne, rosacea and perioral dermatitis  
  - Localized hair growth  
  - Telangiectasia/striae  
  - Idiosyncratic/allergic reactions  
  - Rebound flare-up  
  - Systemic effects? (i.e. cushingoid features)  

- Can worsen acne vulgaris, ulcers, scabies, warts, molluscum contagiosum, fungal infections, and balanitis

**Increased risk of ADR's:**

- Longer duration of therapy
- Medication potency
- Patients more at risk:
  - Children/elderly patients
  - Liver dysfunction/failure
- Areas more at risk:
  - Occluded areas
  - Thin-skinned areas

---

**Topical Calcineurin Inhibitors (TCA's or TIMS)**

- Bind to FKBP-12 to inhibit calcineurin, inhibits T-cell activation & prevents release of cytokines
- Effective for AD – second line
- Do not cause skin atrophy, making them good alternatives for face & neck lesions
- Black box warning
  - “Long term safety of topical CNI has not been established... rare cases of malignancy have been reported. Therefore, long-term use of CNI should be avoided... & not indicated in < 2 years”
  - Additional Protopic info: 0.03% approved in 2-15 yrs

---

**Tacrolimus (Protopic®)**

- Decreased immunologic response to antigen
  - Inhibits cytokine production and alters epidermal antigen-presenting dendritic cells
- 0.03% and 0.1% ointment BID
- Most common adverse drug reactions:
  - Burning, erythema, pruritus
Pimecrolimus (Eidel®)

- Immunomodulatory agent
- No systemic absorption
- Better tolerated for long-term therapy
- Approved only > 2 years of age
- 1% cream BID
- Similar ADR's to Protopic


Alternative/Adjunctive Topical Treatments

- Local anesthetics
  - Benzocaine 20% or lidocaine 3-4%
- Antihistamines
  - Doxepin or diphenhydramine are used
  - Can cause skin irritation
- Topical antibiotics
- Non-pharmacologic


Treatment of Severe, Refractory AD

- Wet Dressings
- Phototherapy
- Highly potent topical steroids
- Cyclosporine
- Methotrexate
- Oral steroids
- Azathioprine

Additional pharmacotherapy for other conditions such as:

Keratolytic agents
- May increase penetration of adjunct topical agents
  - Not for use on armpits or genitals
- Associated ADR's
- Specific agents:
  - Topical salicylic acid (up to 10%)
  - T-Sal (3%), Salex Shampoo (6%), Psoriasis Medic Moisturizer lotion (2%), Dermarest Psoriasis moisturizer (2%), Skin Zinc
  - Hydroxy acids
- Inexpensive but minimally effective

Anthralin (dithranol)
- Reduces mitotic rate and proliferation of epidermal cells by inhibiting DNA synthesis
- Considered effective and safe
- Enhanced efficacy when used in combo w/UVB
- Limited patient acceptance (staining & irritating)
- Best if applied nightly at bedtime; or apply stronger preparation for 20 minutes and then rinse off
- Available topically as Drithro-Scalp®, Psoriatec™, Zithranol RR
Coal Tars
- Has anti-inflammatory effects (decreases cell mitosis and scale development)
- Use in psoriasis for flaky scalps/mild forms/severe itching; can also use for AD
  - 2nd line for psoriasis due to limited patient acceptance
- Improved efficacy with UVB
  - Products: (5% most effective)
    - Balnetar®, Neutrogenia T/Gel®, Polytar®, Estar®, Zetar®
    - Psoriasin Gel

Vitamin D₃ analogues (calcipotriene/calcipotriol)
- Synthetic derivative of calcitriol
  - Inhibits cell proliferation and induction of cell differentiation
- Effective as topical steroids
- Use QD – BID; Max effect seen in 6 – 8 weeks
  - Contraindicated in pregnancy
  - Do not use on face or on flexural areas or with salicylic acid
- ADR’s: skin irritation, hypercalcemia
- Dovonex® 0.005% available as a cream, ointment or solution; $$$

Related products
- Taclonex/Taclonex Scalp®
  - Calcipotriene 0.005% and betamethasone dipropionate 0.064%
  - Use topically once daily
    - Not for face, underarms or groin
    - Or for erythrodermic, exfoliative or pustular psoriasis
  - Expensive
- Calcitriol (Vectical®) also available
  - Apply BID, max 200 g/week
- Investigational: becalcidiol
**Topical retinoids**

- Adapalene (Differin), tretinoin (Retin-A...), tazarotene gel (Tazorac)
- Metabolite of vitamin A; binds to RAR
- For mild/moderate plaque psoriasis, acne, photodamaged skin...
- Typically dosed QD; 0.05% BID most effective
  - Category X
- Local reactions are dose/frequency related
  - Primarily cutaneous irritation
  - Reduce by using moisturizers, steroids or QOD treatment

**Antifungal agents**

- Ampho B and nystatin
  - Bind to ergosterol in fungal cell membrane
- Azoles:
  - Clotrimazole, econazole, ketoconazole (Nizoral), miconazole, oxiconazole, terconazole, tioconazole (Vagistat)
- Allylamines:
  - Naftifine and terbinafine (Lamisil)
  - Inhibit sterols biosynthesis by interference with CYP450 enzymes or squalene epoxidase

**TRUE OR FALSE??**

Polysporin and Neosporin when used appropriately, can potentially **prevent** skin infections.

Polysporin and Neosporin are appropriate to **treat** skin infections.
**Topical antibacterial agents**

- Non-prescription agents (prophylaxis only)
  - Bacitracin
    - Gram positive coverage only
  - Neomycin – gram – and some gram +
  - Polymixin B – gram - organisms
  - Gentamicin
    - Gram negative coverage only
  - Mupirocin*
    - Only one with proven efficacy
  - Gramicidin – gram positive only
  - Retapamulin – *Strep pyogenes and MSSA*

**Derm pharm summary slide**

- Transdermal is for systemic absorption while topical therapy is for local absorption only
- For topical therapy, dosage form is important
- Try non pharmacologic measures first
- Risk of topical ADRs vary significantly with TCS potency and site of application
- Topical CNIs, while not first line, can be safe if used in small amounts for short duration

**Patient Case**

BB, an 8 YO WF, and her mother come into your pharmacy. Mom reports a 2 week history of eczema on her daughter’s legs. She wishes to try some “complementary alternative medicine” for the eczema.

What would you recommend?
Complimentary alternative medicine (CAM) for dermatologic conditions

Introduction
- 35-69% of patients with skin disease have used CAM
- Dermatologic conditions that prompt patients to seek CAM treatment:
  - Atopic dermatitis (AD)/eczema
  - Psoriasis
  - Burns/sunburns/skin damage
  - Acne
  - Wound healing
  - Skin cancer

Probiotics
- Lactobacillii and bifidobacteria species
- Used to prevent: eczema, recurrent wheezing, allergic urticaria, asthma, and food allergies
- Mechanism: Alters gut microbial composition
- Conflicting evidence but AAP says it may delay onset of atopic dermatitis
- A 2002 study by Rautava et al showed decreased risk of AD decreased
- Taylor et al in 2007 showed early probiotic supplementation:
  - Did NOT reduce risk of atopic dermatitis in infants at high risk
  - Was associated with increased allergen sensitization

The Environmental Illness Resource: http://www.ei-resource.org/treatment-options/treatment-information/probiotics-and-prebiotics/
Natural Standard: http://naturalstandard.com/
Tea Tree Oil

- From leaves of Australian Melaleuca Alternifolia tree
- Used for hundreds of years by the aboriginal people
- MOA: the oil has antimicrobial activity against Propionibacterium acnes and Staphylococcus epidermidis
- Common uses: acne, athlete's foot, cold sores, dandruff, lice, nail fungus, skin lesions, and wounds
  - One study failed to demonstrate benefit for AD


---

Tea Tree Oil adverse effects

- Adult topical use considered safe
- Poisonings may cause:
  - drowsiness
  - disorientation
  - rash
  - ataxia
- Skin irritation or contact dermatitis possible due to ingredient, 1,8-cineole
- Oxidized form thought to increase allergies
- Not recommended for use during pregnancy, breastfeeding, and children
- Available as oil, ointment, cream, lotion and soap


---

Wintergreen

- Plant native to Eastern United States
- Historically used by Native Americans as analgesic
- MOA: contains methyl salicylate which is anti-inflammatory
- Uses: HA, gout, arthritis, fever, sciatica, asthma
- ADRs: acid-base disturbances, emesis, increase PT/INR, pulmonary edema, spontaneous pneumothorax, tachypnea, tinnitus
- Drug interactions: warfarin

**Evening Primrose Oil**
- “Evening” blossoms
- Plant grows in North America, Europe, and parts of the Southern hemisphere
- Consists of gamma-linolenic acid, an essential fatty acid for growth, as well as linoleic acid & Vitamin E
- MOA: GLA decreases production on inflammatory markers
- Common uses: eczema
  - Failed to demonstrate benefit for AD in one study
- Oil put into capsules following removal from seeds of evening primrose

**Evening Primrose Oil Precautions**
- AEs: Well tolerated; Mild GI upset and headache possible
- Use caution in patients with bleeding disorders and/or anticoagulation therapy, diabetic and elderly patients, and patients with abnormal blood pressure
- CI: seizure disorders, schizophrenia, anticonvulsant use, active bleeding, and pregnancy
- Di: anticoagulants/antiplatelet agents, phenothiazines

**Aloe Vera**
- Depicted as “plant of immortality” on stone carvings made 6,000 years ago in Egypt
- Active ingredients: anthraquinone, salicylic acid
- MOA: Antibacterial properties, keratolytic
- Common uses: burns, sunburns, skin rash, dandruff, and psoriasis vulgaris
- Topical use: gel or cream
- Internal use: capsules, tablets, powder, tincture, or extract
Aloe Vera concerns

- ADRs: cathartic, melanosis coli, electrolyte abnormalities (hypokalemia), nephritis, eczema/dermatitis, red urine, seizures
- Topical form may delay wound healing
- Caution in diabetes, renal insufficiency, cardiac disease, electrolyte abnormalities, and liver dysfunction
- CI: ileus, bowel obstruction, appendicitis
- DLs: antiarrhythmics, diuretics, digoxin, glyburide, topical hydrocortisone

Topical form may delay wound healing
Caution in diabetes, renal insufficiency, cardiac disease, electrolyte abnormalities, and liver dysfunction

Capsaicin

- Active component of chili peppers
- MOA: leads to depletion of substance P
  - Substance P involved in pathogenesis of psoriasis
- Commonly used for pain; studies indicate benefit in psoriasis
- Availability: $10.99 for 1.5 oz of 0.5% cream at Walgreens

AEs:
- Topical use associated with short term burning
- Internal ingestion can lead to adverse hematological, gastrointestinal, and respiratory effects
- Mothers’ ingestion of cayenne can develop erythematous dermatitis in breastfeeding infants
- DLs: salicylic acid, ACE inhibitors, and theophylline


Capsaicin concerns

- AE:
  - Topical use associated with short term burning
  - Internal ingestion can lead to adverse hematological, gastrointestinal, and respiratory effects
  - Mothers’ ingestion of cayenne can develop erythematous dermatitis in breastfeeding infants
  - DLs: salicylic acid, ACE inhibitors, and theophylline
Dong Quai (or Quay)

- Active ingredient: psoralens
- Decreases epidermal DNA synthesis when Dong Quai is ingested along with UVA exposure
- ADRs: anorexia, bloating, diarrhea, elevated PT/INR, fever, gynecomastia, hemorrhage, photodermatitis, photosensitivity, potentiate response to radiation therapy, vertigo
- DI: anticoagulants and oral contraceptives

Chamomile

- From Greek word meaning “ground apple”
- Ancient Egyptian cold remedy
- Anti-inflammatory activity mediated by inhibition of lipoxygenase and leukotriene B4 (LTB4) formation
- Antibacterial activity against Staphylococcus and Candida
- The flavonoids, quercetin and apigenin, are also active compounds of the flower

Uses:
- Oral – nasal inflammation, allergic rhinitis, fibromyalgia, ADHD, insomnia, GI inflammation
- Topical – hemorrhoids, pressure ulcers, AD, chemotherapy-induced oral mucositis
- Allergic reactions are possible in people with ragweed and chrysanthemum allergies
- ADRs: increased PT, aPTT, INR
- DI: anticoagulants, antiplatelets, sedatives
Balneotherapy
(From the Latin words balneus, or bath)
- Bathing in therapeutic water stimulates circulation, accelerates cell activity, and dilates tissues and vessels
- Mechanical, thermal, and chemical effects
- See increased success due to salinity of water and natural UV exposure
- (balneophototherapy)


Balneotherapy now...
- Thermal springs in Turkey or seawater
- Sulfur waters beneficial in combination with UVB
- Uses: psoriasis, acne vulgaris, atopic dermatitis
  - Kusatsu hot springs in Japan was shown to decrease Staph aureus on skin
- CI: acute infection, active tuberculosis, poorly controlled arterial hypertension, cardiac arrhythmias, and neoplastic diseases


The Blue Lagoon
- Geothermal spa in Iceland
- Regimen: 3 times daily rubbing of silica mud on skin while bathing in special lagoon reserved for patients only
- UVA/UVB light therapy administered simultaneously

**Kangal Hot Springs: Ichthyotherapy**

- In Turkey; MOA unknown
- 2 types of fish: “Strikers” and “lickers”
  - “Striking” and “licking” skin surface may clear psoriatic scales & facilitate penetration of natural UV light
  - Predominantly attack affected sites of skin

---

**The Kangal Hot Springs**

- Waters high in selenium
  - Additional benefit in psoriasis
- Selenium plasma levels low in patients with severe psoriasis
  - Potential reasons:
    - Misbalanced selenium status
    - Decreased antioxidant defense mechanisms

---

**Climatotherapy**

- Natural resources used for healing component
  - Air, temperature, humidity, barometric pressure, water, and light
- Ancient Greeks and Romans widely used sea water as therapeutic agent for:
  - Tuberculosis, psoriasis, and rheumatism
**The Dead Sea**

- One of the world’s first health spas dating back to the time of the Bible’s King Herod.
- Lowest point on earth and highest salt concentration in any natural body of water.
- Comprised of KCl, MgCl₂, CaCl₂, and NaCl.
- Shift in spectrum balance of UV radiation.
- Useful when:
  - Classical phototherapy is not possible.
  - Involvement of the joints (PsA).
  - H/O successful previous stay at the Dead Sea.
  - H/O no success w/other treatments.

**Dead Sea salts**

- Lavender Dead Sea Salts used in eczema & psoriasis to naturally heal the skin, have been used in the Middle East for thousands of years.
- Used in secret preparations and ointments by priests of ancient Egypt.
- Available in crystals, shampoos/conditioners, body mud, scrubs, creams/lotions, body washes, etc.

**Climatotherapy and Elevation**

- High mountain climatotherapy (1560-2018 m) reported to improve psoriasis.
- Use for: dermatoses and allergic diseases such as atopic dermatitis, eczema, psoriasis, T-cell lymphoma, and bronchial asthma.

---

What if travel not possible?

- Treatment in U.S.:
  - Great Pagosa Hot Springs – Colorado
  - Warm mineral springs – Florida
  - Mavena Derm Clinics – Chicago
  - “Tomesa” therapy uses 10% dead sea salt solution
    - Chicago clinic uses 15% concentration

Phototherapy

- Exposure of skin to ultraviolet light
  - UVB rays penetrate skin and slow growth of affected skin cells
  - UVA rays not effective unless used with psoralen (PUVA)
- Sunlight exposure
- Useful in refractory AD, psoriasis

Patient Case

EF is a 5 YO AAM who has had atopic dermatitis for the majority of his life. He is currently using topical hydrocortisone.

EF’s mom heard that sometimes lifestyle changes can help reduce AD symptoms and flares.

What supplements or food may benefit EF?
Sight and Life organization distributes 500 million vitamin A capsules every year to Africa and Latin America in an effort to reduce child mortality rates.

Found in dairy products, fish, and darkly colored fruits and vegetables.

Common Uses: topically for acne and skin damage caused by the sun.

Short term effects: nausea, headache, fatigue, loss of appetite, dizziness, dry skin, desquamation, and cerebral edema.

Long term effects: dry, itchy, scaling, and/or cracking skin, dry lips, anorexia, psychiatric changes, cerebral edema, bone and joint pain, osteoporosis, and hip fracture.

Severe toxicity: eye damage, high calcium levels, and liver damage.

Use caution in patients:
- who smoke and drink alcohol - increased risk for lung cancer and cardiovascular disease
- have liver disease and/or alcohol consumption - increased risk for hepatotoxicity
- taking with antineoplastic agents, tetracyclines, and anticoagulants
- who are children or infants - increased risk for respiratory infection

Available in soft gels, tablets, capsules, and creams.
**Vitamin D**
- Found in Carlson’s lemon flavored cod liver oil
- Shown to increase wound healing
- Used to reduce amount of excess skin cells
  - Experts recommend twice daily administration
  - Topical vitamin D analog (calcipotriene) preferred
- Dis: 3A4 substrates, diltiazem, verapamil


---

**Omega 3**
- Found in fish and plant oils
- Uses: acne vulgaris, psoriasis, atopic dermatitis, systemic lupus erythematosus, and skin cancer
- ADRs: N/constipation/loose stools, decreased nutrient absorption, increase in the luteal phase of the menstrual cycle, flattenence, fishy aftertaste, hemorrhage, hypervitaminosis of vitamins A and D
- Lab interactions: decreased TGs, increased LDL, increased bleeding time
- Dis: anticoagulants and antiplatelet agents including warfarin


---

**Omega 3 availability**
- LA: oils of safflower, grape seed, poppy seed, sunflower, hemp, corn, wheat germ, cottonseed, and soybean
- ALA: green leafy vegetables, flax seed, walnuts, soybean, and canola oils
- Conflicting studies
  - No effect vs. topical effect vs. oral effect

Other active ingredients used in CAM...

- Licorice active ingredient: Glycyrrhizin
- Hogwort active ingredient: Furanocoumarins (psoralens)
- Burdock active ingredient: polyacetylene sesquiterpene lactone
- Figwort, licorice, foxglove, and burdock are thought to relieve psoriasis by reducing inflammation, modulating cytokine production, or inhibiting angiogenesis
- Honey – new promising evidence

Miscellaneous

- Shown to help in atopic dermatitis:
  - topical application of rice bran, licorice gel
  - grapefruit seed extract, vitamin b12
- Psoriasis therapy:
  - Curcumin (from tumeric root)
  - Neem Tree bark (*Azadirachta indica*) (Both of above are in *Ayurveda*)
  - Oatmeal, baking soda, Epsom salts
  - Vinegar, cooking oils, shortening...
- St Johns wort cream
  - Evaluated for treatment of bruising, abrasions, burns, bug bites, neuralgia, inflammation, and muscle pain

Traditional chinese medicine

- Topical *indigo* naturalis:
  - One study showed an 81% improvement in psoriasis for 12 weeks
  - Inexpensive but turns skin blue
- "Phototherapeutic" chinese herbs
  - *Radix angelicae dahuricae and pubescentis*
    shown to prevent damage
  - Green tea extract can do same
- Zemaphyte – 10 herbs
  - Reduced erythema and surface damage in AD
### Alternative therapies

- **Biofeedback**
  - Useful in syndromes with autonomic focus, such as Raynauds
- **Cognitive behavioral therapy**
  - Helps with “dysfunctional thought patterns that result in skin damage”
- **Hypnosis**
  - Targets emotional triggers
- **Acupuncture**


### Which of the following are benefits of breastfeeding?

A. improved immunity for child
B. increased calorie expenditure for mom, possible weight reduction
C. decreased risk of infections for child
D. decreased incidence of atopic dermatitis
E. increased hours of sleep for father

### Breastfeeding

- Prolonged breastfeeding or later intro to solid foods may help in patients at high risk for AD or with a +FH.
- AAP says that exclusive BF for 1st 4-6 months ↓ incidence of AD up to 2 yrs.
  - BF beyond that time didn’t seem to lead to added benefit.
  - Same AAP statement says no evidence that delaying solid food helps either
- 2011 study in eczema showed BF offered no protection EXCEPT in severe cases

**Diet Alterations**

- Alcohol can increase histamine causing increased allergic symptoms
- Decrease intake of:
  - Gluten
  - Dairy
  - Red meat
  - Dyes
  - Preservatives
- Can try Kosher or vegan diet
- Delay introduction of solid feeds in infants

**None of these are of proven benefit...**
(Except in food associated allergies)

---

**Wet Dressings**

---

**What NOT to use...**

- Zinc and gamma linoleic acid FAILED to demonstrate benefit for AD in one study
- Ayurveda – a TCM that can contain arsenic and mercury

- Anything that:
  - worsens the condition
  - causes intolerable effects
  - leads to drug interactions
  - causes any other unwanted effects!
See you on the next cruise!