Dermatologic drugs and drug reactions
Vehicles – foam/spray, solution, lotion, cream, ointment

Level of potency all else being equal
foam --solution-->lotion-->cream -->ointment
## Topicals - steroids, low-med-hi

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
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<tbody>
<tr>
<td><strong>Least Potent</strong></td>
<td></td>
</tr>
<tr>
<td>Cetacryl Lotion, 1%</td>
<td>Hydrocortisone</td>
</tr>
<tr>
<td>Cortaid Cream/Spray/Ointment</td>
<td>Hydrocortisone</td>
</tr>
<tr>
<td>Hyamine Cream/Lotion, 1%</td>
<td>Hydrocortisone</td>
</tr>
<tr>
<td>Micort-HC Cream, 2%</td>
<td>Hydrocortisone</td>
</tr>
<tr>
<td>Nutracort Lotion, 1%</td>
<td>Hydrocortisone</td>
</tr>
<tr>
<td>Synacort Cream, 1%</td>
<td>Hydrocortisone</td>
</tr>
<tr>
<td><strong>Lowest Mid-Strength</strong></td>
<td></td>
</tr>
<tr>
<td>Capex Shampoo, 0.01%</td>
<td>Fluocinolone acetonide</td>
</tr>
<tr>
<td>Citric Acid, 0.5%</td>
<td>Fluocinolone acetonide</td>
</tr>
<tr>
<td>Cultivate Cream/Lotion, 0.05%</td>
<td>Fluocinolone acetonide</td>
</tr>
<tr>
<td>Dermokap Cream, 0.1%</td>
<td>Prednicarbale</td>
</tr>
<tr>
<td>DesoWen Lotion, 0.05%</td>
<td>Desoximetasone</td>
</tr>
<tr>
<td>LoVid Cream/Lotion/Ointment/Solution, 0.1%</td>
<td>Hydrocortisone</td>
</tr>
<tr>
<td><strong>Mid-Strength</strong></td>
<td></td>
</tr>
<tr>
<td>Corian Ointment, 0.05%</td>
<td>Flurandrenolide</td>
</tr>
<tr>
<td>Eucerin Cream, 0.1%</td>
<td>Mometasone furoate</td>
</tr>
<tr>
<td>Kenalog Cream/Spray, 0.1%</td>
<td>Triamcinolone acetonide</td>
</tr>
<tr>
<td>Synalar Ointment, 0.03%</td>
<td>Fluocinolone acetonide</td>
</tr>
<tr>
<td>Topican LP Cream, 0.05%</td>
<td>Desoximetasone</td>
</tr>
<tr>
<td>Topican LP Ointment, 0.05%</td>
<td>Desoximetasone</td>
</tr>
<tr>
<td>Westcot Cream, 0.02%</td>
<td>Hydrocortisone valerate</td>
</tr>
<tr>
<td><strong>Superpotent</strong></td>
<td></td>
</tr>
<tr>
<td>Clobex Lotion/Spray/Shampoo, 0.05%</td>
<td>Clobetasol propionate</td>
</tr>
<tr>
<td>Corderon Tape, 4mg/g, cm</td>
<td>Flurandrenolide</td>
</tr>
<tr>
<td>Cormax Cream/Solution, 0.05%</td>
<td>Clobetasol propionate</td>
</tr>
<tr>
<td>Dipropiene Ointment, 0.05%</td>
<td>Beclometasone dipropionate</td>
</tr>
<tr>
<td>Lexette Foam, 0.05%</td>
<td>Halobetasol propionate</td>
</tr>
<tr>
<td>Olux E Foam, 0.05%</td>
<td>Clobetasol propionate</td>
</tr>
<tr>
<td>Olux Foam, 0.05%</td>
<td>Clobetasol propionate</td>
</tr>
<tr>
<td>Pincon Ointment, 0.05%</td>
<td>Diflucortolone methasone</td>
</tr>
<tr>
<td>Pincon E Ointment, 0.05%</td>
<td>Diflucortolone methasone</td>
</tr>
<tr>
<td>Temovate Cream/Ointment/Solution, 0.05%</td>
<td>Clobetasol propionate</td>
</tr>
<tr>
<td>Topican Topical Spray, 0.25%</td>
<td>Desoximetasone</td>
</tr>
<tr>
<td>Ultracort Cream/Ointment, 0.05%</td>
<td>Halobetasol propionate</td>
</tr>
<tr>
<td>Ultracort Lotion, 0.05%</td>
<td>Halobetasol propionate</td>
</tr>
<tr>
<td>Vanos Cream, 0.1%</td>
<td>Flucinolide</td>
</tr>
<tr>
<td><strong>Potent to Superpotent</strong></td>
<td></td>
</tr>
<tr>
<td>Bynhalt Lotion, 0.01%</td>
<td>Halobetasol propionate</td>
</tr>
<tr>
<td>Doubat Lotion, 0.01%/0.045%</td>
<td>Halobetasol propionate/tazarotene</td>
</tr>
</tbody>
</table>
Practical clinical practice

- Low potency – Triamcinolone 0.025% cream (for use on the face or body fold areas)
- Mid potency - Triamcinolone 0.1% cream (for use on the body)
- High Potency – Clobetasol 0.05% cream (for use on thick plaques)
Topical Antibiotics

- Mupirocin 2% ointment – gram positive coverage
- Hibiclens wash (OTC)
- Gentamycin ointment 0.1% – gram negative coverage (think about this any time the wound is below the waist)
Oral steroid

Poison ivy dosing
• Prednisone 40 mg daily in the morning for 7 days, 20 mg daily in the morning for 7 days, 10 mg daily for 7 days

Other steroid considerations:
Steroids will worsen psoriasis so use with extreme caution in psoriasis patients
Topical Steroid Sparing Agents

• Topical calcineurin inhibitors: indication for Atopic dermatitis
  • Tacrolimus ointment, concentrations 0.03%, 0.1%, use twice daily
    • Pediatric dosing 0.03% [2-15 yo]
  • Pimecrolimus cream, concentration 1%, twice daily
    • Pediatric dosing 2 years and older

• Topical PDE4 inhibitors: indication for Atopic dermatitis
  • Crisaborole ointment concentration 2%, twice daily
    • Pediatric dosing 3 months and up
Vitamins

• Topical calcipotriene (vitamin D): indicated for psoriasis
  • **Dosage forms:** OINT: 0.005%; CRM: 0.005%; SOL: 0.005%
  • Pediatric dosing for 12 and up
  • May use while pregnant or breastfeeding

• Urea: indicated for hyperkeratosis
  • **Dosage forms:** GEL: 45%; CRM: 10%, 20%, 39%, 40%, 45%, 47%; LOTION: 10%, 40%, 45%; FOAM: 35%; SOL: 50%
  • Pediatric dosing for 2 and up
  • May use while pregnant or breastfeeding
Vitamins

• Topical retinol: Indications acne and facial aging
  • **Dosage forms:** CRM: 0.025%, 0.05%, 0.1%; GEL: 0.01%, 0.025%, 0.04%, 0.05%, 0.1%
  • Pediatric dosing 10 and up
  • Avoid in pregnancy
Oral antibiotics

• Indications
  • acne, rosacea (papulopustular), folliculitis, hidradenitis suppurativa
  • Doxycycline 100 mg twice daily
  • Minocycline 100 mg twice daily
    • Pediatric ages 8 and up
    • Not safe in pregnancy and breastfeeding
### In office injectables

- ILK for inflamed cyst, acne papule, psoriasis, alopecia areata, lichen planus of the nails
- Intralesional candida or bleomycin for warts

<table>
<thead>
<tr>
<th>Condition</th>
<th>Concentration ILK</th>
<th>Amount injected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acne Pimple</td>
<td>2.5 or 5 mg/cc</td>
<td>.5cc</td>
</tr>
<tr>
<td>Inflamed cyst back</td>
<td>5 or 10 mg/cc</td>
<td>1 cc</td>
</tr>
<tr>
<td>Alopecia areata (Scalp)</td>
<td>10 mg/cc</td>
<td>1 cc per area</td>
</tr>
<tr>
<td>Alopecia areata (eyebrow)</td>
<td>2.5 to 5 mg/cc</td>
<td>0.5cc</td>
</tr>
<tr>
<td>Lichen planus nails</td>
<td>10 mg/cc</td>
<td>Around cuticle</td>
</tr>
</tbody>
</table>
Oral Apremilast

- Indicated for Psoriasis, unlike traditional treatments for psoriasis recent medications target specific parts of immune system pathways selectively.
- Inhibits an enzyme known as phosphodiesterase 4 (PDE4) that controls inflammatory action within cells and effects inflammation.
- 30 mg twice daily dosing, after a 5 day start taper.
- Meant to be taken continuously to maintain improvement.
- Adverse effects: Diarrhea, Nausea, URI, Headache.
- More rare depression, weight decrease.
- Think about using it in combination with phototherapy or topicals.
• What is a biologic?
• It’s ALIVE!
  • Given IV or Injections – biologics are proteins derived from living tissue or cells cultured in a lab
• Dupilumab is the first approved biologic for the treatment of moderate to severe atopic dermatitis in adolescence and adulthood and has led to a significant improvement in the treatment of this chronic disease.
• Body contains interleukins (IL) that fight against viruses/bacteria as part of immune system but in AD these are overactive and they result in chronic inflammation

• Dupilumab blocks IL-4 and IL-13 from binding to their cell receptors limiting overreaction of the immune cascade and limiting inflammatory symptoms of AD
Dupilumab

- Loading dose two injections (600 mg)
- One injection (300 mg) every other week
- Most common adverse reactions: conjunctivitis, injection site reaction, cold sores
- Also note can cause transient elevation in eosinophils so good to have a baseline
- No starting or routine recommended lab testing
Omalizumab for Urticaria

• This is a humanized monoclonal IgG antibody against IgE
• Approved for adults and children 12 and up for urticaria symptomatic on H1 antihistamines
• 150 or 300 mg subcutaneous injections every 4 weeks
• No routine baseline or monitoring labs
• Commonly reported Adverse effects:
  • Headache, tired feeling, joint/muscle pain, rash, injection site reaction, hair loss, URI symptoms, dizziness
Hidradenitis suppurativa (HS)

- Adalimumab has new indication to treat moderate to severe HS in people 12 years of age and older
# Treatment Comparison

<table>
<thead>
<tr>
<th>Biologic Treatments</th>
<th>Indication</th>
<th>Mechanism of Action</th>
<th>Method of Delivery</th>
<th>Dosage and Frequency</th>
<th>Possible Side Effects</th>
<th>Warnings and Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Secukinumab</strong></td>
<td>Psoriasis</td>
<td>Blocks interleukin 17 (IL-17)</td>
<td>Subcutaneous self-injection</td>
<td>Psoriasis and/or psoriatic arthritis: Week 0, 1, 2, 3 and 4, then every four weeks</td>
<td>Cold or flu-like symptoms, Diarrhea, Upper respiratory infection</td>
<td>Serious infection, Tuberculosis (TB) testing before starting, Cosentyx, Inflammatory bowel disease (IBD), Serious allergic reaction</td>
</tr>
<tr>
<td></td>
<td>Psoriatic arthritis (Adults)</td>
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<tr>
<td><strong>Etanercept</strong></td>
<td>Psoriasis</td>
<td>Blocks TNF-alpha</td>
<td>Subcutaneous self-injection</td>
<td>Adult psoriasis: Twice weekly for 3 months, then once weekly, Pediatric psoriasis: Once weekly, Adult psoriatic arthritis: Once weekly</td>
<td>Infection, Injection site reaction</td>
<td>Serious infection, Fungal infection, Nervous system problem, Lymphoma, New or worsening heart failure, Low blood count, Hepatitis B reactivation, Serious allergic reaction, Lupus-like syndrome</td>
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<tr>
<td></td>
<td>(People over 4 yr)</td>
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<tr>
<td><strong>Biosimilar to Etanercept</strong></td>
<td>Psoriasis</td>
<td>Blocks TNF-alpha</td>
<td>Subcutaneous self-injection</td>
<td>Psoriasis and/or psoriatic arthritis: Once every other week</td>
<td>Infection (including upper respiratory and sinus), Injection site reaction, Headache, Rash</td>
<td>Serious infection, Fungal infection, Malignancies, Serious allergic reaction, Hepatitis B reactivation, Nervous system problem, Low blood count, New or worsening heart failure, Lupus-like syndrome</td>
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<td><strong>Adalimumab</strong></td>
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</tbody>
</table>
Drug reactions
Dermatologic Red Flags:

- Rash + fever (infectious vs. inflammatory)
- Mucosal membrane involvement
- Evidence of blistering or desquamation
- Systemic instability: tachycardia, hypotension, renal failure, etc.
- Skin pain out of proportion
- Erythroderma, patient shaking/inability to regulate body temperature
Morbilliform drug
Morbilliform drug

Erythematous macules and papules start on the chest and spread outwards to arms and back and legs, symmetric.

History of new medication started 2-8 weeks previously.

Itching, most patients are afebrile, a low-grade fever may occur in more severe reactions.
Morbilliform drug

- most commonly seen with the use of antibiotics (penicillins and sulfas), allopurinol, phenytoin, barbiturates, chlorpromazine, carbamazepine, gold, d-penicillamine, captopril, naproxen, and piroxicam, but many other drug culprits have been reported, including chemotherapeutic, biologic, and immunotherapeutic (checkpoint inhibitor) agents
Morbilliform drug – work up

- A punch biopsy usually shows nonspecific perivascular mononuclear cells. Eosinophils in the biopsy are suggestive of a drug-induced eruption.

- Liver function tests – Look for elevated alanine transaminase (ALT), although aspartate transaminase (AST) and alkaline phosphatase can also be elevated. Liver function test abnormalities can persist for months despite adequate therapy.

- CBC with differential – Look for the presence of leukocytosis with eosinophilia and atypical lymphocytes.

- Urinalysis and renal function tests – Look for elevated blood urea nitrogen (BUN) and creatinine, proteinuria, and hematuria.
Morbilliform drug – Treatment

• Discontinue the offending agent(s).
• Antihistamines for itching (hydroxyzine 50 mg every 4-6 hours, cetirizine 10-20 mg twice daily, or fexofenadine 180 mg daily).
• Systemic corticosteroids are usually of little benefit. Medium- or high-potency topical steroids (such as betamethasone dipropionate 0.05% cream twice daily or triamcinolone acetonide 0.1% cream twice daily, for up to 14 days) may alleviate pruritus in some patients.
• Note: It may take an additional 7-14 days after stopping the medication before the eruption completely resolves.
DRESS (Drug reaction with eosinophilia and system symptoms)

- a serious multisystem drug reaction
- fever, rash, eosinophilia, and internal organ involvement
- occur between 2-8 weeks after starting a new medication but may develop months later
- Additional clinical findings include pharyngitis, lymphadenopathy, and facial and hand edema, while internal organ involvement most commonly affects the liver and hematologic and renal systems
DRESS (Drug reaction with eosinophilia and systemic symptoms)

Common Inciting Drugs

- Anticonvulsants
  - phenytoin, carbamazepine, phenobarbital, and lamotrigine
- Minocycline, allopurinol, azathioprine, metronidazole, dapsone, antiretroviral agents (e.g., abacavir), clopidogrel, and ticlopidine, sulfonamides, and nonsteroidal anti-inflammatory drugs (NSAIDs)
DRESS (Drug reaction with eosinophilia and systemic symptoms)

- It is important to identify any internal organ involvement.

Laboratory studies:

- Liver function tests – Look for elevated alanine transaminase (ALT), although aspartate transaminase (AST) and alkaline phosphatase can also be elevated. Liver function test abnormalities can persist for months despite adequate therapy.
- CBC with differential – Look for the presence of leukocytosis with eosinophilia and atypical lymphocytes.
- Urinalysis and renal function tests – Look for elevated blood urea nitrogen (BUN) and creatinine, proteinuria, and hematuria.
- Chest x-ray and/or ECG can be ordered if symptoms of cough or chest discomfort are present.
DRESS (Drug reaction with eosinophilia and system symptoms)

• inciting drug must be identified and immediately stopped
• May warrant hospitalization
  • temperature regulation, nutrition, and fluid and electrolyte balance
• Oral rechallenge tests and skin testing may be harmful and are therefore not recommended
• increased risk for becoming hypothyroid. This usually occurs 4-12 weeks after the reaction.
• dose of 1-2 mg/kg prednisone daily, slow taper 4-6 weeks relapses may occur with more rapid tapering
Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)

• Variants of the same condition

• Serious drug reaction of the skin and mucous membranes. Starts with flu-like symptoms, followed by a painful rash that spreads and blisters. Then the top layer of affected skin dies, sheds and begins to heal after several days.

• SJS - Skin detachment < 10% of body surface area (BSA)

• TEN - Detachment > 30% of BSA
Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)

- develops within the first week of antibiotic therapy but up to 2 months after starting an anticonvulsant. For most drugs, the onset is within a few days up to 1 month.

- Before the rash appears, there is usually a prodromal illness of several days duration resembling an upper respiratory tract infection or ‘flu-like illness. Symptoms may include:
  - Fever > 39 C
  - Sore throat, difficulty swallowing
  - Runny nose and cough
  - Sore red eyes, conjunctivitis
  - General aches and pains.

- There is then an abrupt onset of a tender/painful red skin rash starting on the trunk and extending rapidly over hours to days onto the face and limbs (but rarely affecting the scalp, palms or soles). The maximum extent is usually reached by four days.
Sjs/ten Offending medications

• The drugs that most commonly cause SJS/TEN are antibiotics in 40%. Other drugs include:
  • Sulfonamides: cotrimoxazole
  • Beta-lactam: penicillins, cephalosporins
  • Anti-convulsants: lamotrigine, carbamazepine, phenytoin, phenobarbitone
  • Allopurinol
  • Paracetamol/acetaminophen
  • Nevirapine (non-nucleoside reverse transcriptase inhibitor)
  • Nonsteroidal anti-inflammatory drugs (NSAIDs) (oxicam type mainly).
Care of a patient with SJS/TEN requires:

• Cessation of suspected causative drug(s) — the patient is less likely to die, and complications are less if the culprit drug is on or before the day that blisters/erosions appear.

• Hospital admission — preferably immediately to an intensive care and burns unit with specialist nursing care, as this improves survival, reduces infection and shortens hospital stay.

• Consider fluidised air bed.

• Nutritional and fluid replacement (crystalloid) by intravenous and nasogastric routes — reviewed and adjusted daily.

• Temperature maintenance — as body temperature regulation is impaired, the patient should be in a warm room (30–32C).

• Pain relief — as pain can be extreme.

• Sterile handling and reverse isolation procedures.

• Skin care

• Examine daily for the extent of detachment and infection (take swabs for bacterial culture).

• Topical antiseptics can be used (eg, silver nitrate, chlorhexidine [but not silver sulfadiazine as it is a sulfa drug]).

• Dressings such as gauze with petrolatum, non-adherent nanocrystalline-containing silver gauze or biosynthetic skin substitutes such as Biobrane® can reduce pain.

• Avoid using adhesive tapes and unnecessary removal of dead skin; leave the blister roof as a ‘biological dressing’.
Care of a patient with SJS/TEN requires:

- **Eye care**
  - Daily assessment by an ophthalmologist
  - Frequent eye drops/ointments (antiseptics, antibiotic, corticosteroid)

- **Mouth care**
  - Topical oral anaesthetic

- **Genital care**
  - If ulcerated, prevent vaginal adhesions using intravaginal steroid ointment, soft vaginal dilators.

- **Lung care**
  - Consider aerosols, bronchial aspiration, physiotherapy
  - May require intubation and mechanical ventilation if trachea and bronchi are involved

- **Urinary care**
  - Catheter because of genital involvement and immobility
  - Culture urine for bacterial infection

- **General**
  - Psychiatric support for extreme anxiety and emotional lability
  - Physiotherapy to maintain joint movement and reduce the risk of pneumonia
  - Regular assessment for staphylococcal or gram negative infection
  - The appropriate antibiotic should be given if an infection develops; prophylactic antibiotics are not recommended and may even increase the risk of sepsis
  - Consider heparin to prevent thromboembolism (blood clots).
How can SJS/TEN be prevented?

- People who have survived SJS/TEN must be educated to avoid taking the causative drug or structurally related medicines as SJS/TEN may recur. Cross-reactions can occur between:
  - The anticonvulsants carbamazepine, phenytoin, lamotrigine and phenobarbital
  - Beta-lactam antibiotics penicillin, cephalosporin and carbapenem
  - Nonsteroidal anti-inflammatory drugs
  - Sulfonamides: sulfamethoxazole, sulfadiazine, sulfapyridine.
  - In the future, we may be able to predict who is at risk of SJS/TEN using genetic screening.
  - Allopurinol should be prescribed for good indications (eg, gout with hyperuricemia) and commenced at a low dose (100 mg/day), as SJS/TEN is more likely at doses > 200 mg/day.
Fixed drug eruption

- Cutaneous adverse drug reaction that recurs at the same body site each time the individual is re-exposed to the culprit drug
- One or more sharply demarcated, red or violaceous patches that are typically round develop within minutes to hours of exposure to the inciting drug
- may vary from 0.5 to several centimeters in size
- usually asymptomatic, although burning, pain, or pruritus may occur
- Early features, Clinical presentation
- Offending medications
- Management pearls
Fixed drug eruption

• any cutaneous surface may be affected, the oral and anogenital mucosa are most frequently involved

• most commonly solitary, but some individuals may develop multiple patches
Most commonly associated drug classes

- Antibiotics (in particular sulfonamides, trimethoprim, fluoroquinolones, and tetracyclines), NSAIDs (including naproxen, ibuprofen, and celecoxib), and barbiturates.

- Amoxicillin, erythromycin, metronidazole, fluconazole, paracetamol (acetaminophen), cetirizine, hydroxyzine, methylphenidate, oral contraceptives, quinine, and phenolphthalein.

- Biologic agents including ustekinumab, adalimumab, and abatacept have been reported to cause fixed drug eruptions.

- A nonpigmenting variant is seen with pseudoephedrine.
Treatment

- important to consider any medication ingested in the 1- to 2-week period before FDE onset, including over-the-counter medications; health food supplements, such as ginkgo biloba leaf extract and vinpocetine; and prescription medications
- Discontinue the implicated drug
- Avoidance of the causative drug and its related compounds in the future should prevent recurrences. It is important to counsel patients that the secondary pigment alteration may be persistent.
- symptomatic treatment, topical corticosteroids may be used.