***no patient handout*

Erythroderma

Synopsis

Erythroderma (also known as exfoliative dermatitis) is typically defined as diffuse redness of the skin affecting more than 90% of the body surface.

The more common causes of erythroderma in adults are **psoriasis**, **atopic dermatitis**, **mycosis fungoides**, **pityriasis rubra pilaris**, and drugs. A number of medications have been reported to cause an exfoliative dermatitis, including but not limited to the following: allopurinol, antibiotics, antiepileptics, calcium channel blockers, opiates, gold, isoniazid, retinoids, lithium, phenothiazine, quinidine, thalidomide, and thiazides. (See also Associated Medications, below.)

Rarer causes of erythroderma include **seborrheic dermatitis**, **contact dermatitis**, **lichen planus**, **dermatomyositis**, **tinea corporis**, **actinic reticuloid**, stasis dermatitis with **autoeczematization**, **crusted scabies**, inherited ichthyoses, and blistering diseases such as **pemphigus foliaceus** and **bullous pemphigoid**. Systemic diseases have also been associated with erythroderma, including systemic lymphoma and solid organ malignancies, as well as **human immunodeficiency virus** (HIV) disease. Around one-third of all erythroderma cases are idiopathic.

Sézary syndrome is a leukemic form of mycosis fungoides in which circulating atypical lymphocytes in the presence of erythroderma form mycosis fungoides.

Erythroderma may develop acutely over days, such as when there is a drug cause, or more slowly over weeks or months, such as in a severe dermatitis or psoriasis. The majority of the skin surface is red, scaly, and usually very pruritic. Systemic manifestations include peripheral edema, which is usually pedal, pretibial, or facial. Increased blood flow and increased fluid loss through the skin can lead to tachycardia and the possibility of developing high-output cardiac failure. The risk of this is higher in acute cases. There are also thermoregulatory imbalances, which produce hyperthermia more frequently, but also hypothermia. Generalized lymphadenopathy is the most common noncutaneous manifestation of drug-induced erythroderma and is seen in approximately half of all patients.

Red Man Syndrome

This is a drug reaction typically caused by parenteral vancomycin. It has also been observed following intraperitoneal and oral use. Signs appear about 5-10 minutes after the start of the rapidly given infusion. The patient complains of generalized burning and itching, and an erythema spreads to involve the face, neck, and upper body. Other symptoms include chills, fever, dizziness, paresthesia around the mouth, chest pain, and dyspnea. There is significant hypotension. The reaction to vancomycin is due to an anaphylactic response mediated by IgE. The erythema usually subsides several hours after completion of treatment. Unlike other erythrodermic drug reactions, exfoliation is usually not present. The most severe reactions occur in patients aged younger than 40, especially children. Treatment with antihistamines relieves the

symptoms, and giving hydroxyzine before the start of a vancomycin infusion lessens the erythema and pruritus.

Pediatric Patient Considerations
While adults are most commonly affected, erythroderma may rarely be seen in neonates and infants. Here, besides atopic dermatitis, psoriasis, and drug eruptions, rare inherited diseases are responsible, such as **Leiner disease**, Omenn disease (severe combined immune deficiency, erythroderma, lymphadenopathy, high IgE levels), **Netherton syndrome**, **bullous congenital ichthyosiform erythroderma**, **non-bullous ichthyosiform erythroderma**, and other inherited ichthyoses (eg, **X-linked**, **lamellar**; see also **harlequin ichthyosis**).

Codes

ICD10CM:
L26 – Exfoliative dermatitis
L27.0 – Generalized skin eruption due to drugs and medicaments taken internally

SNOMEDCT:
238992001 – Drug-induced erythroderma
45454 – Erythroderma

Look For

Shiny, red, scaling skin early in the disease course that extends to involve the entire body surface area. Hair may be shed from the scalp and the rest of the body if the erythema persists for weeks. Nail changes, such as thickening and ridge formation, may also occur.

A drug-induced erythroderma may first appear as a morbilliform or scarlatiniform exanthem. This is first seen in the flexures. Then, the patchy erythema becomes generalized and spreads to involve the entire body. The skin is bright red. Scaling and exfoliation appear 2-6 days later.

Diagnostic Pearls

Over time, continuous scratching causes lichenification and erosions over the erythroderma. Lymphadenopathy may occur if the disease becomes chronic.

The presence of micaceous or silvery scale points to the diagnosis of psoriasis.

Look for further clinical features of specific eruptions to point to diagnosis, such as typical nail changes of psoriasis, palmoplantar involvement in mycosis fungoides, or an orange color to palmoplantar keratoderma in pityriasis rubra pilaris.

Differential Diagnosis & Pitfalls

- **Exanthematous drug eruption**
- **Stevens-Johnson syndrome**
- **Drug hypersensitivity syndrome** (DRESS)
- **Toxic epidermal necrolysis**

- **Acute generalized exanthematous pustulosis**
- **Urticaria**
- **Scarlet fever**
- **Staphylococcal scalded skin syndrome**
- **Toxic shock syndrome**
- **Acute graft-versus-host disease**

Best Tests

This is primarily a clinical diagnosis based on the exam and the history of previous skin disease or use of a preceding causative medication.

Perform a potassium hydroxide (KOH) preparation to rule out tinea corporis.

Perform a skin biopsy to assist with narrowing down the differential diagnosis; however, this may not always be diagnostic as typical disease features may be lost in erythroderma.

Consider performing flow cytometry in cases in which Sézary syndrome is suspected.

A complete blood count and differential may reveal eosinophilia in atopic or contact dermatitis. Perform a blood urea nitrogen (BUN) and creatinine test to assess for any baseline pre-renal failure in acute cases.

For any idiopathic case, perform a full physical examination and consider further studies to rule out malignancy or HIV disease.

Management Pearls

For any acute case of erythroderma, admission to hospital should be undertaken. Aggressive management of the complications of erythroderma (fluid and electrolyte abnormalities, cardiac failure) are important, as temperature dysregulation, fluid loss, and heart failure can become a cause of mortality in patients. Secondary infections and sepsis can occur from breakdown of the skin barrier.

Look closely at the patient's medication list and discontinue any potential culprit drugs immediately.

For cases of Sézary syndrome, consult a hematologist / oncologist to assist with systemic management. For dermatomyositis, rheumatology should be consulted.

Therapy

In the rare situation that erythroderma is caused by tinea corporis, treat with topical and or oral antifungal therapy. (See **Tinea corporis** for further details.)

Otherwise, initially manage the cutaneous inflammation with the use of an emollient cream or a topical steroid and oral antihistamines. These recommendations are for adult patients.

Topical Steroids
Use mid-potency topical steroids as reduced barrier function in erythroderma leads to increased absorption of any topically applied preparations.

Mid-potency topical corticosteroids (class 3-4):

- Triamcinolone cream, ointment – Apply every 12 hours (15, 30, 60, 120, 240 g), or
- Mometasone cream, ointment – Apply every 12 hours (15, 45 g), or
- Fluocinolone cream, ointment – Apply every 12 hours (15, 30, 60 g).

In addition, some experts recommend open wet dressings.

Oral Antihistamines

- Hydroxyzine 25-50 mg 4 times daily or 2-4 mg/kg/day; or cetirizine 10 mg twice daily.

Further treatment should be targeted to the underlying dermatosis. For erythrodermic psoriasis, consider cyclosporine, acitretin, methotrexate, or biologic therapy. For pityriasis rubra pilaris, consider retinoid therapy or methotrexate. For eczemas, dermatomyositis, drug reactions, and idiopathic cases, systemic steroids may be required. Prednisone can be initiated at a dose of 1-2 mg/kg/day.

Red Man Syndrome
Preventive measures include the following:

- Antihistamines should be given prior to vancomycin infusion.
- Dose of vancomycin should be limited to 500 mg.
- Slowly administer vancomycin infusion over a period of 2 hours.

Drug Reaction Data

Below is a list of drugs with literature evidence indicating an adverse association with this diagnosis. The list is continually updated through ongoing research and new medication approvals. Click on Citations to sort by number of citations or click on Medication to sort the medications alphabetically.

Medication	Citations
ACE inhibitor	8
acetaminophen	1
acitretin	2
aldesleukin	1
alitretinoin	1
Alkylating agent	4
all-trans-retinoic acid (ATRA)	2
allopurinol	7
Alpha-adrenergic agonist	1
aminoglycoside	2
aminophylline	6
aminosalicylic acid	1
amiodarone	1

Medication	Citations
amitriptyline	2
amoxicillin	1
ampicillin	1
ampicillin + sulbactam	1
Antiarrhythmic	4
Anticholinergic	1
Anticonvulsant	32
Antidiabetic	2
Antifungal	4
Antigout	7
Antimalarials	4
Antimetabolite	2
Antimycobacterial	9

Medication	Citations
Antineoplastic antibiotic	1
Antineoplastic antimicrotubular	1
arsenic	2
aspirin	2
Atypical antipsychotic	1
aztreonam	2
barbiturate	3
BCR-ABL tyrosine kinase inhibitor	5
benzodiazepine	3
Beta blockers	1
bevacizumab	1
bexarotene	3
boceprevir	1

Medication	Citations
bupropion	2
Calcium channel blocker	5
captopril	5
carbamazepine	20
cefepime	1
cefoxitin	2
celecoxib	1
cephalosporin	3
chlorambucil	2
chloroquine	2
chlorothiazide	1
chlorpromazine	1
chlorpropamide	2

Medication	Citations
cimetidine	2
ciprofloxacin	1
cisplatin	1
clindamycin	2
clofazimine	2
clomipramine	2
clonazepam	1
cobicistat	1
codeine	2
Coumadin	1
daclizumab	1
dalbavancin	1
dapsone	7

Medication	Citations
denileukin diftitox	1
desipramine	2
diazepam	1
diclofenac	1
dicloxacillin	1
didanosine	1
diflunisal	2
diltiazem	3
dipyrone	1
Diuretic	3
docetaxel	1
doxepin	2
doxycycline	1

Medication	Citations
eculizumab	1
efavirenz	1
elvitegravir	1
emtricitabine	1
enalapril	1
ephedrine	1
epoprostenol	2
erlotinib	2
erythromycin	1
erythropoietin	1
escitalopram	1
esomeprazole	1
ethambutol	3

Medication	Citations
ethosuximide	1
etretinate	1
fenbufen	1
fluconazole	2
fluoroquinolone	1
fluoxetine	2
fluvoxamine	2
furosemide	1
gabapentin	1
gemfibrozil	1
Glycopeptides	6
Granulocyte colony-stimulating factor	1
Histamine H2 antagonist	2

Medication	Citations
hydrochlorothiazide	1
hydroxychloroquine	2
imatinib	5
imipramine	3
indinavir	1
Integrase inhibitor	1
interferon	2
isoniazid	3
Isotretinoin	2
ketoconazole	1
lamotrigine	2
lansoprazole	1
leflunomide	1

Medication	Citations
Leprostatic	7
lidocaine	1
linagliptin	1
Lincosamides	2
lisinopril	2
lithium	2
lopinavir	1
macrolide	1
mefloquine	1
mesna	1
methotrexate	1
methyldopa	1
methylphenidate	1

Medication	Citations
metoprolol	1
minocycline	5
mipomersen	1
mirtazapine	2
mitomycin	2
Monoclonal antibody	1
morphine	1
mTOR kinase inhibitor	2
nabumetone	1
neomycin	1
nevirapine	1
nifedipine	2
nitrofurantoin	1

Medication	Citations
non-NRTI antiretroviral	2
nortriptyline	2
NRTI antiretroviral	4
NSAID	9
omeprazole	6
Opioid analgesic	3
oxaliplatin	1
oxcarbazepine	1
pantoprazole	1
paroxetine	1
pazopanib	1
penicillin antibiotic class	7
pentostatin	1

Medication	Citations
phenobarbital	3
phenothiazine	2
phenylbutazone	2
phenytoin	7
piroxicam	1
pomalidomide	1
pralatrexate	1
pregabalin	1
protease inhibitors	2
Proton pump inhibitor	8
protriptyline	2
pseudoephedrine	1
pyrazinamide	2

Medication	Citations
pyrimethamine	1
quetiapine	1
quinidine	2
Retinoid	12
rifampin	3
risperidone	1
romidepsin	1
Salicylates	2
saxagliptin	1
Selective serotonin reuptake inhibitor	4
Serotonin-norepinephrine reuptake inhibitors	2
sertraline	3
sildenafil	1

Medication	Citations
silodosin	1
silver sulfadiazine	1
sirolimus	2
solifenacin	2
sorafenib	3
streptomycin	5
strontium ranelate	1
sulfadoxine + pyrimethamine	1
sulfamethoxazole + trimethoprim	4
sulfonamide	5
sulfonylurea	2
sulindac	1
tadalafil	1

Medication	Citations
tegafur	1
tenofovir	1
terbinafine	1
tetracycline antibiotic class	6
thalidomide	4
Therapeutic gold & gold compounds exposure	2
thiacetazone	3
ticlopidine	1
timolol	1
tobramycin	2
tocainide	1
tocilizumab	1
tolbutamide	1

Medication	Citations
topical tretinoin	1
trazodone	1
Tricyclic antidepressant	3
trimethoprim	1
trimetrexate	1
trimipramine	2
trovafloxacin	1
Typical antipsychotic	1
Tyrosine kinase inhibitor	1
valproate	1
vancomycin	5
venlafaxine	2
verapamil	1

Medication	Citations
yohimbine	1
zidovudine	3
ziprasidone	1
zolpidem	1