Hospital Dermatology: Pearls and Pitfalls

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Disclosures

• Relevant Financial Relationships
  – None

• Off Label Usage
  – Yes
Role of Dermatology Hospitalist

Hospitalist

Inpatient Dermatology
- Lymphoma, Autoimmune
- bullous disorders, Ulcers,
- PG, Calciphylaxis, Vasculitis,
- CTD, Erythroderma,
- Generalized dermatitis,
- Hypersensitivity reactions,
- Cellulitis, Psoriasis

Outpatient - Hospital based
- Goeckerman,
- Phototherapy

Consult Service
- Pediatrics/Neonatal medicine, Drug eruptions, GVHD,
- Dermatitis, Lesions,
- Vasculitis/vasculopathy,
- Autoimmune diseases,
- Infection, Ulcers
What is Hospital Dermatology?

• Long-standing unique tradition at Mayo, a tertiary care center with a large referral service

• We preserved and improved on the quality of care rendered our patients with difficult skin diseases in our hospital program

• Hospital core group
  – Clinical Division
    • MDP Davis, R El Azhary, D Wetter, M McEvoy, J Sartori
  – Laboratory Division
    • AG Bridges, MC Camilleri
Pearls and Pitfalls of Hospital Dermatology

Goals of this lecture

- Review clinical and histopathological presentations, differential diagnosis, evaluation and management of major categories of dermatologic diseases in hospitalized patients
"HELP!"
Red and Scaly All Over
Erythroderma

- Psoriasis
- Pityriasis rubra pilaris
- Dermatitis
- Drug eruption
- Lymphoma
- Infection
- Autoimmune bullous disorder
“I itch and nothing helps!!”
Pearl: Atypical presentations of bullous pemphigoid

- 20% non-bullous
- Eczematous, dyshidrosiform, urticarial, erythrodermic, nodular, lichenoid, or targetoid
- Include evaluation for autoimmune bullous disorders in erythroderma and pruritus work-up
Pruritus

- Xerosis
- Dermatitis
- Hypersensitivity reaction
- Dermatophytosis
- Folliculitis
- Scabies
- Autoimmune bullous disease
- Liver disease
- Renal disease
- Thyroid disease
- Anemia
- Lymphoproliferative disorders
I think it’s a drug eruption. Now what do I do?

"Nothing to worry about, Mr. Jenkins, some people do have a mild reaction to the flu shot!"
Drug Eruptions

Simple
- No systemic symptoms
  - Morbilliform
  - Urticarial

Complex
- Systemic involvement
  - Life threatening
  - Drug hypersensitivity reaction
  - Stevens-Johnson syndrome (SJS)
  - Toxic epidermal necrolysis (TEN)

Other
Drug Reactions

3 things you need to know

1. Type of drug reaction
2. Statistics
   - What drugs are most likely to cause that type of reaction?
3. Timing
   - How long after the drug was started did the reaction begin?
# Drug Timeline

<table>
<thead>
<tr>
<th>Reaction Type</th>
<th>Drug</th>
<th>% Rxn for Drug</th>
<th>DATES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morbilliform</td>
<td>ASA</td>
<td>x x x x x x x x x x x x x x</td>
<td></td>
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<tr>
<td>Urticarial</td>
<td>Colace</td>
<td>x x x x x x x x</td>
<td></td>
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<tr>
<td>Fixed Drug</td>
<td>Bactrim</td>
<td>x x x x x x</td>
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<tr>
<td>Erythroderma</td>
<td>Tetracycline</td>
<td>x x x x x x</td>
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<tr>
<td>EM</td>
<td>PCN</td>
<td>x x x x x x x x</td>
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<tr>
<td>SJS</td>
<td>Vancomycin</td>
<td>x x x x x x</td>
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<tr>
<td>TEN</td>
<td>HCTZ</td>
<td>x x x x x x x x</td>
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<tr>
<td>AGEP</td>
<td>Dilantin</td>
<td>x x x x x x x x</td>
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<tr>
<td>DRESS</td>
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<tr>
<td>Vasculitis</td>
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<td>• LCV</td>
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<td>• HSP</td>
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<td>• Other</td>
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<tr>
<td>Lupus-like</td>
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<tr>
<td>Blistering</td>
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<tr>
<td>• Pemphigus</td>
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<td>• LABD</td>
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<tr>
<td>• PseudoPCT</td>
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<tr>
<td>Pseudolymphoma</td>
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<tr>
<td>Cytotoxic</td>
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<tr>
<td>OTHER</td>
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</tr>
</tbody>
</table>

[http://www.drugeruptiondata.com](http://www.drugeruptiondata.com)

**UserName** = Mayo1

**Password** = Physicians

MR = Many Reports
R = Reported
NR = Not Reported
Clinical Pearls

- Drug eruptions are extremely common
- Tend to be generalized
- Maculopapular/morbilliform most common
- Best intervention: Stop the offending drug
- How to spot the culprit?
  - Drug started within days to a week prior to rash
  - Can be difficult!
  - Tip: can generally exclude all drugs started after onset of rash!
- Drug eruptions can continue for 1-2 weeks even after stopping culprit drug
TEN

• Most severe presentation in spectrum which includes EM & SJS
• Generalized erythema, purpura & flaccid bullae
• Widespread epidermal detachment >10% of BSA
• Extensive mucous membrane involvement
• No target lesions
TEN/SJS

- Drug-related
- Extracutaneous involvement
  - Fever
  - Leukopenia
    - Poor prognostic factor
  - Involvement of GI, renal & respiratory mucosa
TEN/SJS

- Drug-related
  - Sulfonamides
    - Slow acetylator phenotype
  - Anticonvulsants
    - Dilantin, phenobarbital, carbamazepine, lamotrigine
  - Penicillin derivatives
  - NSAIDS
  - Allopurinol
• Target lesions
• Generalized erythema or purpura
• <10% epidermal detachment
SJS

- Extensive ulceration of oral, genital, &/or ocular mucous membranes ($\geq 2$ surfaces)
TEN/SJS Bottom Line (Personal View)

- TEN/SJS are both associated with high mortality rates (up to 25%) from sepsis and multiorgan failure
- Require intensive supportive management in ICU/Burn unit
- Discontinue the causative drug or treat underlying infection
  - Mycoplasma in 25% of pediatric patients with SJS
- Bulk of evidence
  - Supports use of intravenous immunoglobulin
    - 0.5-1gm/kg/d X 4 d
    - IVIG blocks Fas mediated apoptosis in vitro and arrests development of TEN in vivo
  - Does not support use of systemic corticosteroids
DRESS Syndrome

Drug Reaction with Eosinophilia and Systemic Symptoms
DRESS Syndrome

• AKA:
  • Anticonvulsant Hypersensitivity Syndrome
  • Drug-induced Pseudolymphoma
  • Drug-induced Hypersensitivity Syndrome
  • Hypersensitivity syndrome
  • Drug-induced Delayed Multiorgan Hypersensitivity Syndrome
DRESS Syndrome

• Severe, idiosyncratic drug reaction
• Commonly implicated drugs: anticonvulsants, sulfonamides, allopurinol, NSAIDS, azithromycin, azathioprine, and anti-retrovirals
• Most cases present after delay of 2-8 weeks, but onset has been reported from 3-105 days after drug initiation
  – Time to abnormally metabolize the drug leading to toxic drug metabolites
• Reactivation of HHV-6 has been observed
Clinical Features of DRESS

- Fever, leukocytosis, eosinophilia
- Huge variability in presentation
  - Each class of drug causes a slightly different clinical picture
- Facial edema mimicking angioedema
- Generalized eruption: erythematous edematous papules, vesicles, bullae, pustules, purpura, target lesions and erythroderma
Clinical Features of DRESS

- Lymphadenopathy
- Myositis
- Liver function test abnormalities
- May result in severe hepatocellular or cholestatic damage, necessitating transplant
  - 10% mortality typically from liver failure
- Variable lung, kidney, heart, thyroid involvement
Treatment of DRESS

• Withdrawal of offending medication
• Avoid cross-reacting medications
• High-dose systemic systemic steroids
  – 1.5-2 mg/kg tapering dose over 1-3 months
• LFTs should be followed until resolved
• Supportive care
• ICU/Burn unit care is not required
Miscellaneous Drug Eruptions You Should Know About

• Acute generalized exanthematous pustulosis (AGEP)
• Linear IgA bullous dermatosis (LABD)
• Symmetric drug-related intertriginous and flexural exanthema (SDRIFE)
• TNF-alpha antagonist-induced lupus-like drug eruption/syndrome (TAILS)
Acute Generalized Exanthematous Pustulosis (AGEP)

- Also known as a pustular drug eruption
- Fever and leukocytosis with neutrophilia and eosinophilia are often present
- Many implicated drugs: macrolide & beta-lactam antibiotics, cephalosporins, tetracyclines, vancomycin, sulfonamides, carbamazepine, allopurinol, furosemide, antifungals, calcium channel blockers, ACE inhibitors, acetaminophen
- Sudden onset 2-5 days after drug started
- Begins on the face and intertriginous areas
- Disseminates in a few hours
Treatment of AGEP

- Discontinuation of drug
- Topical care
- Eruption usually resolves rapidly in 3-5 days with desquamation
- May be due to a specific T-cell reaction
- Neutrophils may be recruited by local cytokines
Drug-induced LABD

• Various clinical presentations
• Vesiculobullous eruption on trunk/extremities
  – Herpetiform or rosette-like bullae
• Morbilliform, urticarial
• Can resemble DH, BP, CP, PV, LP, EM, or TEN
• 40% with mucosal involvement
Drug-induced LABD

- Drug-induced
  - Vancomycin – most common drug
  - Others: Penicillins, cephalosporins, captopril, trimethoprim/sulfamethoxazole, phenytoin, furosemide, glyburide, diclofenac
- Onset: 3-14 days after exposure
- Target Ag - BPAg2 (BP180)
Drug-induced LABD
Treatment
• Removal of the offending agent
• Dapsone, Sulfapyridine, Corticosteroids
Symmetric Drug-Related Intertriginous and Flexural Exanthema (SDRIFE)

- Diagnostic criteria
  - Exposure to systemic drug predominantly aminopenicillins and B-lactams at first or repeated dose (contact allergens excluded)
  - Erythema of the gluteal/perineal area
  - Involvement of at least one other intertriginous/flexural localization
  - Symmetry of the affected areas
  - Absence of systemic symptoms and signs
TNF-alpha Inhibitors

• Using more of these agents to treat chronic inflammatory diseases
  • RA, AS, psoriasis, PsA, and IBD

• Infliximab
  • Chimeric monoclonal Ab (IV)

• Etanercept
  • Recombinant TNF-alpha soluble receptor fused to the Fc fragment of IgG2 (SC)

• Adalimumab
  • Recombinant human IgG1 monoclonal Ab (SC)

• Golimumab
  • Human IgG1 monoclonal Ab (SC)

• Certolizumab
  • Recombinant humanized monoclonal Ab Fab fragment (SC)
TAILS

• Incidence 0.2-0.4%
  • Difficult to establish
  • Based on post-marketing studies
• As use of these agents increases, incidence of cutaneous reactions will increase
• Most cases caused by the agents that have been more widely used
• Onset: <1 month – 4 years
• Diagnostic and therapeutic challenge
TAILS: Pathogenesis

• TNF-alpha inhibitor leads to production of autoantibodies
  • Disruption in cytokine balance
    • Suppression in production of Th1 cytokines, driving the immune response to Th2 cytokine production
  • Interference with apoptosis by decreasing CD44 expression
• Inhibition of cytotoxic T-cells
Drug-induced autoimmunity

• Patients treated with TNF-alpha inhibitors develop antibodies found in patients with SLE (ANA, ds-DNA, ENA) in the absence of clinical features of SLE

• Not an indication to stop drug
Drug-induced autoimmunity

Use of these agents may trigger or unmask SLE in some patients
TNF-alpha Inhibitor Induced SLE: Diagnosis

- In the setting of ongoing treatment with TNF-alpha inhibitor
- No prior history of SLE
- Cutaneous findings of SLE
  - Malar rash, photosensitive rash, mucosal ulcers, alopecia
- Systemic findings of SLE
  - Constitutional symptoms – fever, malaise, weight loss
  - Arthralgias, arthritis
- + Serology – ANA, ds-DNA
- Low complement
- Negative anti-histone antibodies
- Resolution of symptoms when drug is discontinued
TNF-alpha Inhibitor Induced SLE: Management

• Stop the drug
• Resolution of symptoms in 3 weeks to 6 months
• Patients may require systemic therapy
  • Corticosteroids and steroid sparing immunosuppressive agents (methotrexate, azathioprine, mycophenolate mofetil)
Cutaneous Reactions to TNF-alpha Inhibitors

- Injection site reaction
- Urticaria
- Cellulitis
- Psoriasiform dermatitis
- Granulomatous dermatitis
- LE-like syndrome

- Vasculitis
- Alopecia areata
- Erythema nodosum
- SJS
- Morphea
Pitfall

• Not considering other diseases associated with mucosal lesions, blisters, and sloughing when evaluating a patient for possible SJS/TEN
YOU’VE GOT THE WORST CASE OF WHATEVER THIS IS, I’VE EVER SEEN.
Disseminated Zoster Pearls

• Definition
  – > 20 lesions outside of 2 contiguous dermatomes
• At risk group
  – Elderly, immunosuppressed
• Viscera can be affected
• Hutchinson’s sign – Call ophthalmology
• Contact and Droplet isolation
• Treatment
  – IV Acyclovir until lesions healed over or clear
Cutaneous adverse effects of targeted therapies

• Epidermal growth factor (EGFR) inhibitors
  – Papulopustular eruption in a seborrheic distribution
    • Most common cutaneous side effect
    • Dose-dependent
    • 1-2 weeks after therapy
  – Pruritus, xerosis
  – Paronychia
  – Mucositis
  – Pattern or cicatricial alopecia
Pearl

• Dermatologists need to be familiar with the skin-related toxicities associated with targeted therapies
Disseminated Histoplasmosis

• **Histoplasma capsulatum**
  – Grows in soil which contains bird and bat feces
  – Endemic in Mississippi and Ohio river basins; Central and South America; Southern Europe; Africa; South and Southeast Asia

• **Hematogenous dissemination in patients with suppressed immune systems**
Disseminated Histoplasmosis

- Patients may present with ill-defined symptoms
  - Fevers, weight loss
- Up to 20% may present in septic shock and multisystem organ failure
- Variable clinical presentation
  - Papules & nodules with necrosis & hyperkeratosis; ulcers; bullous EM-like; erysipelas-like; petechiae/purpura; acneiform & folliculopustular papules; vesicles, herpetiform; exfoliative, nummular or psoriasiform dermatitis; morbilliform eruption
- Gold standard for diagnosis
  - Tissue cultures
Pearls

• Infection MUST be excluded in an immunocompromised patient!!!

• Recently described phenomenon of immune reconstitution syndrome
  – In the setting of disseminated histoplasmosis in patients who have been on a biologic agent or had reduced cellular immunity
  – Patients do well clinically and have therapeutic itraconazole levels with decrease in histoplasma urine antigens
  – Develop new skin or LN lesions with negative cultures but organisms still present on biopsy
  – Tx with prednisone taper and continue itraconazole
Staphylococcal Scalded Skin Syndrome (SSSS)

• Common in infants and children
• Secondary to extracutaneous S. aureus, phage grp II, infection
  – Produce exfoliative toxins, bind to dsg 1 leading to acantholysis of the upper epidermis
• Fever, irritability, purulent rhinorrhea and conjunctivitis, painful, tender skin
  – Periorificial edema and scale crusts
  – Confluent erythema, superficial erosions and flaccid bullae, esp. in intertriginous sites
Treatment

- Throat culture positive for MSSA
- IV antibiotics
  - Vancomycin (per ID) – stopped after 5 days,
    Clindamycin 80 mg IV q8h and Oxacillin 300 mg IV q6h
- Plastibase ointment
- Zinc oxide ointment to groin and neck
- Mupirocin ointment to nares and severe areas
Eczema Coxsackium

- Enterovirus PCR swabs from both tongue and skin positive
- HSV/VZV PCR swab negative
- Bacterial swab culture grew 2+ Staph aureus
- After 30 hrs of wet dressings, he had 75% improvement
Eczema Coxsackium

- Coxsackievirus A6 infection
- Widespread vesiculobullous exanthem favoring the perioral area, trunk and areas of previous dermatitis or injury as well as classic sites of hand, foot and mouth disease
- Young children
- Summer and Fall
- Spread via fecal-oral and respiratory routes
Anticipating and preventing infection in patients treated with immunosuppressive medications for dermatologic indications: A dermatologist’s checklist

Julia S. Lehman, MD, David A. Wetter, MD, Mark D. P. Davis, MD, Rokea A. el-Azhary, MD, PhD, Lawrence E. Gibson, MD, and Amer N. Kalaaji MD

Rochester, Minnesota

Infection and Infection Prevention in Patients Treated with Immunosuppressive Medications for Autoimmune Bullous Disorders

Julia S. Lehman MD, Dédée F. Murrell MA, BMBCh, FAAD, MD, FACD, Michael J. Camilleri MD and Amer N. Kalaaji MD

Infection and Infection Prevention in Patients Treated with Immunosuppressive Medications for Autoimmune Bullous Disorders, 2011-10-01Z, Volume 29, Issue 4, Pages 591-598, Copyright © 2011 Elsevier Inc.
Table I. Infection prevention checklist for dermatologists when caring for patients with immune-mediated dermatoses requiring iatrogenic immunosuppression

<table>
<thead>
<tr>
<th>Screen patient for infectious risk factors</th>
<th>Consider laboratory screening and/or chest radiography for patients with pertinent risk factors (specific tests to consider in parentheses):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Immunosuppressive medications</td>
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<tr>
<td></td>
<td>Comorbid immunosuppressing illnesses (such as diabetes mellitus, organ transplantation, cancer requiring chemotherapy, hematologic malignancy, HIV, chronic kidney disease requiring dialysis, history of liver failure, and autoimmune diseases requiring immunosuppression)</td>
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<td>History of blood transfusion</td>
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<td>History of high-risk sexual activity</td>
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<td>History of travel to remote or rural areas, or areas with endemic disease</td>
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<td>History of positive PPD test or exposure to tuberculosis</td>
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<td></td>
<td>Nutritional deficiency or malabsorption</td>
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<tr>
<td></td>
<td>Hepatitis B (HBsAg, anti-HBc, IgM anti-HBc, anti-HBs)</td>
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<td>Hepatitis C (HCV enzyme immunoassay)</td>
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<td>HIV (HIV ELISA)</td>
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<td>Strongyloides (stool ova and parasites; Strongyloides ELISA)</td>
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<td></td>
<td>Tuberculosis (PPD tests; interferon-gamma release assay; chest radiograph, including patients with a positive PPD test from previous Bacillus Calmette–Guérin vaccination)</td>
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<tr>
<td></td>
<td>Systemic fungal infections, such as cryptococcosis, histoplasmosis, coccidioidomycosis, blastomycosis, and paracoccidioidomycosis (serum and/or urine studies; chest radiograph)</td>
</tr>
<tr>
<td></td>
<td>Consider pneumocystis pneumonia prophylaxis, particularly in patients of advanced age, multiple medical comorbidities (especially pulmonary), in whom prolonged or intense immunosuppressive therapy is anticipated</td>
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<tr>
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<td>Ensure that the patient’s immunization schedule is up to date; according to the latest recommendations:</td>
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<tr>
<td></td>
<td>Seasonal influenza vaccination (non-live vaccine available; live vaccine to be avoided after immunosuppressive therapies have been begun)</td>
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<tr>
<td></td>
<td>Pneumococcus vaccination (non-live vaccine)</td>
</tr>
<tr>
<td></td>
<td>Herpes zoster vaccination (live vaccine; to be given ≥ 30 days before initiation of immunosuppressive therapies; to be avoided after immunosuppressive therapies have been begun)</td>
</tr>
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<td></td>
<td>Tetanus/diphtheria vaccination (non-live vaccine)</td>
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<td></td>
<td>Educate patients regarding:</td>
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<td></td>
<td>Importance of hand washing</td>
</tr>
<tr>
<td></td>
<td>Avoidance of high-risk infectious exposures where possible (ie, crowded areas, farms, compost, nursing homes, and day cares)</td>
</tr>
<tr>
<td></td>
<td>Early signs and symptoms of infections (such as pneumonia, urinary tract infection, influenza, herpes zoster, etc.)</td>
</tr>
<tr>
<td></td>
<td>Assess possibility of—and treat patients for—impetiginization and colonization (particularly herpes simplex virus, Candida, and Staphylococcus) at each clinical encounter</td>
</tr>
</tbody>
</table>
Inactivated vaccines are safe; effectiveness might be lower.
If vaccination within 2 wks of therapy or while on therapy, should revaccinate (at least 3 months post-therapy if immunity restored).
Live vaccines should be administered ≥ 4 wks prior to therapy.

### General Recommendations on Immunization

**Recommendations of the Advisory Committee on Immunization Practices (ACIP)**

<table>
<thead>
<tr>
<th>YES</th>
<th>MAYBE</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza (inactivated) yearly</td>
<td>Meningococcal</td>
<td>Varicella</td>
</tr>
<tr>
<td>Tdap once, Td booster every 10 years</td>
<td>Hepatitis A</td>
<td>Zoster</td>
</tr>
<tr>
<td>Pneumococcal (PCV13 or PPSV23)</td>
<td>Hepatitis B</td>
<td>MMR</td>
</tr>
<tr>
<td>HPV, if &lt; 26 y/o</td>
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</tbody>
</table>

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- **Influenza (inactivated)** yearly
- **Meningococcal**
- **Varicella**
- **Hepatitis A**
- **Zoster**
- **Hepatitis B**
- **MMR**
- **HPV, if < 26 y/o**
Anticipated treatment: Prednisone ≥20mg/day OR prednisone + cytotoxic agent (e.g. methotrexate, cyclophosphamide)/TNF-alpha inhibitor?

Yes

No

Defer PJP prophylaxis

Estimated Duration of Immunosuppressive Therapy

≥ 4 weeks or unknown

Evaluate for:
- Advanced age
- Preexisting T- or B-cell immunodeficiency
- Human immunodeficiency virus positive status
- Comorbid interstitial pulmonary fibrosis
- Prior organ transplant
- Comorbid hematologic malignancy
- Depressed CD 4 count (<250/microliter)
- Lymphopenia (total lymphocyte count <800/microliter)

Risk factors present

Consider PJP prophylaxis during treatment

No risk factors present

< 4 weeks

Defer PJP prophylaxis

Reassess the need for continuation of immunosuppressive medications

Treatment prolongation is required
The Patient has Purpura!
### Purpura Definitions

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Histologic</th>
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</thead>
<tbody>
<tr>
<td>Erythema</td>
<td>Inflammation of blood vessel walls</td>
</tr>
<tr>
<td>Purpura</td>
<td>RBC extravasation</td>
</tr>
<tr>
<td>Subepidermal vesicles/bullae, ulcers</td>
<td>Necrosis, occlusion and destruction of blood vessel walls</td>
</tr>
</tbody>
</table>

- **Nonpalpable and palpable purpura**
  - *Petechiae – purpuric macules*
  - *Ecchymoses – purpuric patches*
Purpura Definitions

Retiform purpura – livedo reticularis (lace-like) or racemosa (net-like)
Purpura – Etiopathogenesis guides the differential diagnosis

- Immunologic or Allergic
- Infectious or Septic
- Occlusive
- Bleeding diathesis thrombocytopenia
Immunologic or Allergic

Palpable purpura LCV and its Variants

- HSP or IgA vasculitis
- Mixed cryoglobulinemia Types II and III

ANCA-associated vasculitis

- Urticarial vasculitis
LCV - Etiology

Vasculitis is a clinical sign
Ask what underlies the diagnosis

• Idiopathic (45-55%)
• Infection (15-20%)
• Inflammatory diseases/Systemic diseases (15-20%)
  – Connective tissue diseases: Lupus erythematosus, rheumatoid arthritis, Sjögren’s syndrome
• Drugs (10-15%)
  – PCN, sulfas, PTU, allopurinol, thiazides
• Malignancy (<5%)
Evaluation

• **Possible causes & extent of involvement**
  – H & P, hemoccult, CBC, UA, ESR, CRP, ANA, ENA, ANCA, complement studies, RF, SPEP, TSH, cryoproteins, hepatitis serologies, thrombophilia workup, pan cx, CXR

• **Skin biopsies**
  – 1 – 2 day old lesion for routine histology
  – < 24 hour old macule for DIF
  – Do not biopsy ulcers
LVC
Clinical Variants

- Palpable purpura
- Henoch-Schönlein purpura (HSP) or IgA
- Mixed cryoglobulinemia (types II & III)
- Urticarial vasculitis
HSP, Types II & III cryoglobulinemia, ACNA-associated vasculitis

Clinical Features

- Similar to LCV
- Involvement above waist
HSP, Types II & III cryoglobulinemia, ACNA-associated vasculitis

Clinical Features

- Larger lesions with figurate, retiform, or stellate shapes
HSP

- **Histologic Findings**
  - Similar to LCV

- **Immunofluorescence Findings**
  - IgA in blood vessel walls in the superficial dermis in >90%
Clinical Pearl
When to treat?

• If mild and nonprogressive
  – Many do not treat
  – Supportive tx, compression
• If painful, severe or rapidly progressive
  – Treat!
    • Associated with systemic disease
    • Associated with ulcerations
Pitfall

- Treating the ulcer as something other than vasculitis
Clinical Pearl

• Purpura fulminans
  – Due to DIC
  – Induced by meningococcemia

• Emergency!
  – No more than 30 minutes should elapse before the administration of appropriate antibiotics
  – Treat empirically, don’t wait for the results of tests
Pearl

- Purpura fulminans? Identify cause of DIC, manage cause
  - Think meningococcus or other underlying infection
- Medical emergency requiring intensive supportive management in an ICU
- Dermatologists can be valuable in guiding appropriate diagnosis and management
- **Pitfall:** Thinking this is LCV and starting systemic corticosteroids
- Purpura fulminans with **symmetrical peripheral gangrene** is an ominous clinical presentation affecting all age groups
  - Outcome: Death/Amputation
Occlusive

Intraluminal

- Thrombosis Embolism
- Coagulation disorders Fibrin
- Cryoprotein- Type I cryoglobulinemia

Vessel Wall

- Degos’ disease or malignant atrophic papulosis
- Livedoid vasculopathy
Occlusive Vasculitis
Intraluminal
Coagulation Disorder - Fibrin

- DIC/purpura fulminans
- Coumadin necrosis
- Heparin necrosis
- Protein C deficiency
- Protein S deficiency

- Antithrombin III deficiency
- Antiphospholipid antibody syndrome
- Mutation in factor V Leiden
- G20210A mutation in prothrombin gene
Infectious or Septic Vasculitis

Pathogenesis

• Direct infection of blood vessel wall

• Interaction of the host immune response with microorganism in the blood vessel wall
Infectious Vasculitis
Clinical Variants

• Ecthyma gangrenosum (*Pseudomonas*)
• Gonococcemia (*Neisseria gonorrhoeae*)
• Bacterial endocarditis
• Rocky Mountain Spotted Fever (*Rickettsia rickettsii*)
• Fungal sepsis (Candida, Aspergillus)
Infectious Vasculitis
Histologic Features

• Involvement of deeper vessels
• Prominent thrombosis
• Usually cell-poor infiltrate
• Organisms may be visualized in & around blood vessel walls in acute but not chronic septic vasculitis
Clinical Pearls

• Calciphylaxis is multifactorial and usually fatal
• The prognosis is dismal
• 1-year survival: 46%
• 2-year survival: 20%
Clinical Pearls

• Under-recognized syndrome
  – Occurs in 4% of hemodialysis patients
  – Non uremic cases associated with
    • Warfarin therapy, CTD, hematologic malignancies, DM, primary hyperparathyroidism, vitamin D deficiency, protein C and S deficiency, factor V Leiden deficiency, Crohn disease, and liver disease

• No clearly effective treatments
Calciphylaxis treatment strategies

- Correct calcium-phosphate balance
  - Sodium thiosulfate
  - Cinacalcet
  - Low calcium dialysate

- Improve tissue perfusion & oxygenation
  - TPA
  - Hyperbaric oxygen
  - Avoid warfarin for anticoagulation

- Wound Care
  - Debridement
  - Surgical
  - Whirlpool
  - Maggot

- Pain control
  - Palliative care

- Multidisciplinary approach
- Mechanism - Thrombotic tissue ischemia; Must address the clot & prevent more
Occlusive

Intraluminal

Thrombosis
Embolism

Coagulation
disorders Fibrin

Cryoprotein- Type I
cryoglobulinemia

Calciphylaxis
Hydrophilic Polymer Coating

• Purpose:
  – Decrease friction
  – Reduce arterial spasm & pain
  – Reduce thrombosis

• Must be meticulously cleaned and moistened in order to avoid drying out and becoming tacky

• Not to be used for initial vascular access, because passage through entry needles can shear off the hydrophilic coating
“Clinical sequelae ranged from undetectable (no symptoms) to renal failure, myocardial infarction, pulmonary infarction, stroke, ongoing gangrene, and/or death occurring within days to weeks of suspected embolization of foreign material.”
NEW YORK – Coating on endovascular devices is associated with embolization and microvascular occlusion leading to purpura or livedo racemosa, according to a new report.

Dr. Alina Bridges, of the Department of Dermatology at Mayo Clinic in Rochester, Minnesota, said by email that the study was conducted “to make clinicians and pathologists aware of this underrecognized phenomenon of iatrogenic hydrophilic polymer gel embolization that can involve the skin and present with purpura.”

The phenomenon “has distinctive microscopic morphology and potential for internal organ involvement,” she added.

Endovascular devices commonly are coated with hydrophilic polymer gels to improve maneuverability and prevent vasospasm. However, there are reports of the coating embolizing, resulting in severe reactions such as stroke, pulmonary infarction, and death.

Dr. Bridges and colleagues presented a case study of eight patients with livedo racemosa and purpura after an endovascular procedure. The patients had punch biopsies obtained with hematoxylin-eosin-stained sections.
Pearls:
Hydrophilic Polymer Gel Emboli

• Can embolize to the skin and cause microvascular occlusion presenting as purpura, livedo racemosa, livedo reticularis, hemorrhagic panniculitis, or ulceration
• Recent interventional procedure
• Treatment is supportive
• Lesions gradually improve
• Be aware of internal organ involvement of emboli
Yikes!
The flesh eating ulcer
Discussion

Pyoderma Gangrenosum

• There are many weird causes of ulcerations
• Weirdest of all: pyoderma gangrenosum
• Clues in this patient:
  – Irregular, violaceous undermined border
  – Pathergy (triggered by trauma, surgical debridement, and attempts to graft)
Clinical Pearls

• Pyoderma gangrenosum can occur anywhere on body including the breasts

• Characteristic clinical presentation
  – Rapidly progressive ulcerative process
  – Begins as a small pustule which breaks down forming an ulcer
  – Satellite papules may appear at the border, break down, and then fuse with the central ulcer
  – Fully developed: painful, undermined ulcer with blue/purple border
  – Heals with atrophic scar
Associated conditions

- 50% have no underlying cause

Associations (50%)
  - IBD - Most common (1.5%-5% of IBD patients get PG)
  - RA, seronegative arthritis (>1/3 PG pts have arthritis
  - Hematologic abnormalities
Bottom Line with PG

• Diagnosis of exclusion

• BUT! It’s important to do our best since treating a patient for PG when they DON’T have it with steroids and/or immunosuppression has it’s own set of associated risks, and can certainly aggravate the actual condition
Common diseases misdiagnosed as PG

- Vascular occlusive disease
- Chronic venous disease
- Vasculitis
- Neoplasm
- Exogenous tissue injury/Factitial Disease
- Spider bite
- Infection
Lessons learned

• Pyoderma gangrenosum can be underdiagnosed
• Pyoderma gangrenosum can be overdiagnosed
Cellulitis Mimics

"I'LL HAVE TO THINK ABOUT THIS...I DON'T WANT TO MAKE A RASH DECISION!"
Clinical Pearl

- Venous insufficiency, stasis dermatitis, & lipodermatosclerosis and contact dermatitis may be misdiagnosed as cellulitis
- Cellulitis is not bilateral
Contact Dermatitis

• Itch (no pain)
• Patient is non-toxic
• Erythema and edema can be severe
• Look for sharp cutoff
• Treat with topical steroids
• Patch test
In summary, pearls and pitfalls in hospital dermatology

- Erythroderma
- Pruritus
- Drugs – Simple, Complex, Misc
- Infection and infection prevention
- Purpura
- Neutrophilic dermatoses – PG
- Cellulitis mimics
Thank you!

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Comments/questions?