

# Dermatology Pearls and News Flash

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# Conflict of interest

- No conflicts to disclose
- I have chosen articles of interest published in the past year



# Educational Objectives

- Review recent dermatology topics of importance to internal medicine
- Understand current guidelines for managing simple abscess
- Be familiar with latest treatment options for hidradenitis suppurativa and atopic dermatitis
- Review recent information about skin cancer prevention option for high risk patients



# Presentation of case

- A 22 year old previously healthy female presents to clinic with a 3 day history of erythema, edema and pain of L thigh
- Exam: fluctuance, erythema, 3 cm nodule L thigh



- **How would you treat this patient?**
- A. Incision and drainage
- B. Treat with oral antibiotics
- C. Incision and drainage followed by oral antibiotics
- Background: recent studies have recommended incision and drainage alone for simple abscess
  - Singer et al. Systemic antibiotics after I+D of simple abscess: meta analysis. Emerg Med J 2013



# Management of simple abscesses

- Talan et al. Trimethoprim-sulfa vs placebo for uncomplicated skin abscess. NEJM 2016
- Randomized controlled trial of 5 US E.D. comparing trimethoprim/sulfa to placebo in patients undergoing I+D
- Outcome: clinical cure of abscess at day 7-14



# Results

- 45.3% cultures positive for MRSA
- Clinical cure 80.5% in T-S group compared to 73.6% in I+D only group (MITP) and 92.9% TS vs 85.7% (PP)
- T-S superior in secondary measures:
  - Lower subsequent surgical drainage
  - Lower skin infections at new sites
  - Lower infections in household members
  - TS had more GI side effects

# Conclusions

- In settings where MRSA is prevalent, T-S treatment resulted in a higher cure rate among patients with a drained abscess compared to placebo
  - Differences are small but significant
  - Only 1 antibiotic studied
  - In both arms, the abscesses subsequently resolved
  - IDSA published guidelines





# Presentation of case

- A 40 year old healthy female presents for treatment of toe nail fungus.
- Previous treatments: Vicks vapor rub, apple cider vinegar and topical clotrimazole without improvement
- Past medical history: hypothyroid, acne
- Medications: thyroid replacement, tretinoin cream



# How would you treat this patient?

- No treatment. Medications too risky
- Oral ketoconazole
- Oral terbinafine
- Topical efinaconazole
- Topical clotrimazole

# Answer

- No treatment. Medications too risky
- Oral ketoconazole
- **Oral terbinafine**
- Topical efinaconazole
- Topical clotrimazole

# Evaluating the need for laboratory testing in the treatment of onychomycosis

- Mikailov et al. Cost effectiveness of confirmatory testing before treatment of onychomycosis JAMA Derm 2016
- Kanzler. Reevaluating the need for laboratory testing in the treatment of onychomycosis JAMA Derm 2016.



# Onychomycosis therapy

- Empirical treatment with terbinafine is more cost effective than confirmatory testing with minimal effect on patient safety
- Confirmatory testing before treatment with efinaconazole 10% is associated with reduced costs

# Onychomycosis treatment

- When onychomycosis is suspected. Treat w/ course of terbinafine
  - If no response, could be saprophyte or yeast (don't respond to terbinafine). Treat with pulse fluconazole 200mg weekly x 3-9 months
  - Cost for terbinafine and fluconazole is low
  - Cost of efinaconazole is high (cure rates 15%). Better to have confirmation of onychomycosis
  - Safety of oral agents is good
    - Significant liver injury is uncommon and most resolve with discontinuation of the drug
    - Need to reconsider need for extensive lab testing for dermatologic drugs like pulse anti fungal therapy, isotretinoin, spironolactone and others



# Presentation of case

- 24 year old male with asthma and seasonal allergies presents to clinic with worsening eczema
- Current treatment: triamcinolone 0.1% ointment, neosporin, loratadine and diphenhydramine as needed
- Prior treatments: clobetasol ointment, pimecrolimus cream, cephalexin, medrol dose pack, prednisone







# How would you treat this patient?

- A. Prednisone taper
- B. Mometasone cream BID
- C. Diphenhydramine and hydrocortisone 1% cream BID
- D. Dupilumab
- E. UVB Phototherapy



# Answer

- A. Prednisone taper
- B. Mometasone cream BID
- C. Diphenhydramine and hydrocortisone 1% cream BID
- D. Dupilumab**
- E. UVB Phototherapy



# The New York Times

- ***New Drug for Severe Eczema is Successful in 2 New Trials***
  - Gina Kolata, Oct 1, 2016
  - “on Saturday the results of 2 large clinical trials of a new drug offered hope to an estimated 1.6million adult Americans with uncontrolled moderate-severe atopic dermatitis...”

# Dupilumab for atopic dermatitis

- Simpson et al. 2 phase 3 trials of dupilumab vs placebo in atopic dermatitis. NEJM 2016
  - Dupilumab monoclonal antibody that binds and inhibits IL-4 and IL-13 (type 2 cytokines)
  - Adults with moderate-severe atopic dermatitis inadequately controlled on topical treatment
  - 1:1:1:1 dupilumab 300mg sq weekly, 300mg sq every other week or placebo, placebo
  - Primary outcome: proportion of patients with IGA of 0 or 1 (clear, almost clear) or reduction of 2 points or more from baseline at week 16

# Results-dupilumab

- Big study: 671 study 1, 708 study 2
- IGA 0/1: 38% dupilumab every 14 days, 37% dupilumab weekly, 10% placebo both arms
  - Significantly more patients in dupilumab arms achieved EASI 75% reduction compared to placebo
  - Reduction in pruritus, decreased anxiety/depression, and improved quality of life
  - Injection reactions and conjunctivitis greater in dupi arms

# How do we treat moderate-severe atopic dermatitis?

- Skin care, emollients, bleach baths, anti itch products, antibiotics
- Topical corticosteroids and calcineurin inhibitors
- Systemic steroids
- Phototherapy
- Immunosuppressive medications:
  - Cyclosporine, methotrexate, mycophenolate, azathioprine
- And soon, dupilumab





# Presentation of case

- 30 year old female presents to clinic with a 5 year history of recurrent draining nodules of the bilateral axillae, inguinal folds, proximal thighs
- Previous treatments: topical clindamycin lotion, I+D, intralesional steroids, trimethoprim/sulfa, doxycycline







# How do you treat this patient?

- A. Excision of all nodules
- B. Refer to another provider
- C. Clindamycin lotion BID
- D. Treat with adalimumab
- E. Minocycline 100mg BID x 10days



# Answer

- A. Excision of all nodules
- B. Refer to another provider
- C. Clindamycin lotion BID
- D. Treat with adalimumab**
- E. Minocycline 100mg BID x 10days

# Adalimumab for hidradenitis suppurativa (HS)

- Kimball et al. 2 phase 3 trials of adalimumab for HS. NEJM 2016
  - Period 1: adalimumab 40mg weekly vs placebo x 12 weeks
  - Period 2: adalimumab 40mg every other week vs adalimumab 40mg weekly x 24 weeks
    - Primary end point: 50% reduction in abscess and inflammatory nodule count and no increase in abscess or draining fistula counts

# Adalimumab and HS: results

- Clinical response at week 12 for adalimumab >placebo (41.8% vs 26%) and (58.9% vs 27.6%)
- Also superior for lesions, pain, Sartorius score
- SAEs were low in both period 1 and period 2
  
- Conclusion: treatment with adalimumab 40mg weekly as compared to placebo resulted in significantly higher clinical response rates in both trials at 12 weeks. Rates of SAEs were similar in study groups



Hidradenitis Suppurativa Treatments by Hurley Stage		
Hurley Stage I and II	Topical, injectable and intralesional	<ul style="list-style-type: none"> <li>• Topical antibiotics (e.g. clindamycin 1%)</li> <li>• Intralesional corticosteroids</li> </ul>
	Oral options	<ul style="list-style-type: none"> <li>• Oral antibiotics</li> <li>• Hormonal therapies</li> <li>• Metformin</li> </ul>
	Surgical and physical options	<ul style="list-style-type: none"> <li>• Less invasive surgical approaches</li> <li>• Laser therapy</li> <li>• Photodynamic therapy</li> </ul>
Hurley Stage II and III	(Includes Stage I to II approaches)	<ul style="list-style-type: none"> <li>• More invasive surgical approaches</li> <li>• Systemic retinoids</li> <li>• Biological treatments</li> </ul>
All Stages	<ul style="list-style-type: none"> <li>• Weight loss</li> <li>• Pain control</li> <li>• Smoking cessation</li> <li>• Zinc supplementation</li> <li>• Antimicrobial wash</li> </ul>	

Also consider infliximab, anakinra

# Case example

- 28 y.o. female with a many year history of recurrent painful oral ulcers
- Multiple ulcers present in mouth nearly every day
  - No genital ulcers





# How would you treat this patient?

- A. Dexamethasone elixir swish and spit
- B. Medrol dose pack
- C. Valacyclovir episodically for flares
- D. Silver nitrate application to lesions
- E. Apremilast
- F. Colchicine



# Answer

- A. Dexamethasone elixir swish and spit
- B. Medrol dose pack
- C. Valacyclovir episodically for flares
- D. Silver nitrate application to lesions
- E. Apremilast**
- F. Colchicine**



# Introduction

- Recurrent aphthous ulcers (RAU), recurrent aphthous stomatitis (RAS)
- Most common oral ulcerative condition
- Shallow, round ulcers with a pseudomembrane and peripheral erythema
- Size varies: 1mm to >10mm
- 5-25% of general population
- More common in females, adults <40yrs, Caucasians

# Systemic conditions associated with aphthous ulcers

- Behcet's disease
- Sweet's syndrome
- Reiter's syndrome
- Inflammatory bowel disease
- HIV infection
- Celiac disease
- Systemic lupus erythematosus
- Cyclic neutropenia

# Diagnostic tests for aphthous ulcers

- Nutritional deficiencies:
  - Iron, ferritin, folate, vitamin B1, B2, B6, B12, zinc
- CBC
- ANA
- HIV
- Total IgA, IgA tissue transglutaminase
- Mucosal biopsy (edge of lesion. Get some epithelium)
- If bullous disease suspected, studies for immunofluorescence
- Endoscopy

Hatemi et al. Apremilast for Behcet's syndrome.  
Phase 2 Placebo controlled Study. NEJM 2015

- 111 patients w/ Behcets received apremilast 30mg BID vs placebo x 12 weeks with an extension phase where all received apremilast
- Primary end point: number of oral ulcers
- Mean number of oral ulcers reduced in apremilast arm
  - Also reduced pain
  - Nausea, vomiting, diarrhea higher in apremilast arm

# Topical Treatment

- **Corticosteroid gels (clobetasol gel)**
  - Other vehicles for oral mucosa available (orabase)
  - Dexamethasone elixir
- **Topical anesthetics**
  - Viscous lidocaine, benzocaine lozenges, Magic mouthwash
- **Antimicrobial agents**
  - Chlorhexadine rinse
  - Topical tetracyclines
- **Topical sucralfate**
  - 5mL 4x/day



# My Treatment strategy

- For minor RAS:
  - topical corticosteroid gel BID +/- topical anesthetic agent
- For major RAS:
  - Colchicine 0.6mg BID along w/ corticosteroid gel and topical anesthetic agent
  - If no response, add/switch to dapsone
  - If no response, consider azathioprine, TNF inhibitor, **apremilast**
  - Also vitamin B12, zinc, omega 3



# High risk skin cancer patients



# Reduction of non-melanoma skin cancer in high-risk patients

- Chen et al. Phase 3 randomized trial of nicotinamide for skin cancer chemoprevention. NEJM 2015
- Nicotinamide 500mg BID vs placebo in high risk patients x 1 year
  - 386 patients with at least 2 skin cancers in previous 5 years
  - Evaluated number of new skin cancers and safety

# Nicotinamide and skin cancer

- At 12 months, rate of new NMSC was lower by 23% in nicotinamide arm (both BCC and SCC)
  - Number of AKs was 11% lower at 3 months, 14% lower at 6 months and 13% lower at 12 months
  - No difference in AE between groups
  - Benefits dissipated when nicotinamide discontinued
  - Compliance with nicotinamide 90% (whereas sunscreen compliance was 50%)

# Select resources

- [HS-Foundation.org](http://HS-Foundation.org)
- [Nationaleczema.org](http://Nationaleczema.org)
- UpToDate Dermatology sections
- [AAD.org](http://AAD.org)
  - basic derm curriculum
  - Clinical guidelines



# References

- Talan et al. Trimethoprim-sulfa vs placebo for uncomplicated skin abscess. NEJM 2016
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- Mikailov et al. Cost effectiveness of confirmatory testing before treatment of onychomycosis JAMA Derm 2016
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- Hatemi et al. Apremilast for Behcets syndrome-phase 2 placebo controlled study. NEJM 2015

