Common Dermatologic Infections

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Case 1
- 50 year-old male presents with “a very itchy rash” on his hands, wrists, axilla, periumbilical region, and groin

DDx: Pruritic papules
- Papular eczema
- Dermatitis herpetiformis
- Arthropod bites
  - Fleas, bedbugs, mosquitoes, scabies
- Drug reaction
- Prurigo nodularis

What would you do next?
A. Skin biopsy
B. Scabies preparation
C. Empiric topical steroids + antihistamine
D. Empiric topical antifungal
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Clinical course of scabies infection

Burrowing of mite into skin

Hypersensitivity reaction

2-4 weeks

• Tortuous linear papule, 1-10 mm
• Finger webs, feet, breasts, groin
• Asymptomatic at time of infection
• Small round erythematous papules
• Hands, wrists, periumbilical region, groin
• “Itchiest rash ever”
• Typical burden: 10-15 mites


Crusted (Hyperkeratotic) Scabies

Clinical findings

• Thick white plaques with fine scale (“white sand stuck on the skin”)

Risk factors

• Immunosuppression
• Elderly
• Heavy-mite burden

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Image courtesy of Dr. Luis Requena
Transmission

- Close personal contact and fomites
- How easy is it to transmit scabies via fomites?
  - 4/272 non-infected people developed scabies after getting into beds vacated by infected people
  - Scabies can be spread via fomites, but infrequently
  - Crusted scabies exception: easily spread by fomites


Methods to confirm diagnosis

- Skin scraping (Scabies prep)
- Skin biopsy

Boskó G et al. BJD 2001;144:664.

Role of skin scraping

- Method:
  - Identify burrows
  - Apply a 1-2 drop of mineral oil to burrows and slide
  - Scrape burrows with scalpel
  - Rub contents from scalpel onto glass slide
  - Apply cover slip

Uptodate.com

Skin scraping

- Examine slide under low power for mites, eggs, and fecal pellets


Skin scraping

- Frequently, testing is negative since
  - Burrows can be difficult to identify
  - Mite burden usually low
  - Skin biopsy - similar limitations to skin scraping

How to make the diagnosis if tests negative

- Epidemiology (household contacts with similar symptoms)
- Morphology and distribution of clinical lesions
- History of severe pruritus

Treat empirically if high index of clinical suspicion
Treatment

- Antiscabetic therapy
  - Permethrin
  - Ivermectin (systemic)
  - Precipitated sulfur 5-10%
  - Lindane
  - Crotamiton
  - Benzyl benzoate

- Symptomatic treatment
  - Topical steroids and antihistamines

Permethrin

- FDA approved for scabies (> 2 mo age)
- Formulation: 5% topical cream (Elimite)
- Pregnancy category B
- Treatment regimen
  - Apply neck down, leave overnight; repeat in 1-2 wks
- Advantages: Very effective
- Side effects: Burning upon application, dermatitis


Ivermectin

- Advantages: oral and effective
- Side effects:
  - Neurotoxicity, data mixed (caution with elderly)
- Treatment regimen: 200 mcg/kg x 1, repeat 2 wks
- Do not use in children < 5 years (neurtox risk)
- Pregnancy category B
- Avoid in pregnancy


Precipitated sulfur 5-10%

- Safe for infants and pregnant women
- Advantages:
  - Safe with low toxicity
- Side effects:
  - Irritation to skin
  - Malodorous, stains clothing
- Treatment regime
  - Apply 3 successive nights


CDC treatment guidelines

- Permethrin: medication of choice
- Ivermectin: For those who have failed treatment with or cannot tolerate FDA approved medications

http://www.cdc.gov/parasites/scabies/health_professionals/meds.html

Household contacts and fomites

- Treat all family/household members at the same time since patient infectious during incubation time prior to onset of symptoms
- Fomites: wash in hot water and dry in a hot dryer

Additional clinical pearls

- Treatment of crusted scabies
  - Ivermectin plus permethrin, more frequently
- After treatment, symptoms may worsen due to sensitization, not treatment failure
- Rule of thumb at UCSF: if not better in 3-4 weeks, consider an alternative diagnosis


Take home points

- Highest-yield place to detect mite is a burrow, not papule
- Keep crusted scabies in mind older, immunosuppressed
- Scabies preparation often negative
- Scabies prep insensitive so if high clinical suspicion, treat
- Permethrin – first line therapy
- Difficult to transmit via fomites except in crusted scabies

Case 2

- 35 year-old female presents with “round red circles” on her trunk and extremities
- Self-diagnosed as eczema
- Used husband’s eczema medication (topical steroid), but plaques worsened

Image courtesy of Luis Requena, MD

Annular papulosquamous (ring-scaly) eruption: DDx

- Inflammatory
  - Eczema
  - Psoriasis
- Infectious
  - Secondary syphilis
  - Tinea (dermatophytosis)
  - Pityriasis rosea
  - Erythema migrans

- Other
  - Mycosis fungoides
  - Subacute cutaneous lupus erythematosus
  - Erythema annulare centifugum
Eczema  Unknown lesion
Psoriasis  Unknown lesion
Secondary syphilis  Unknown lesion
Tinea  Unknown lesion
Pityriasis rosea  Unknown lesion
Erythema migrans  Unknown lesion
What additional information should you seek?
A. Ask about recent tick bites
B. Take a sexual history
C. Perform a KOH preparation
D. All of the above

KOH prep of our patient

Diagnosis
- Tinea corporis

Tinea
- Superficial fungal infection
- Sites of infection:
  - upper layer of the epidermis
- Causative organisms require keratin for growth

Clinical manifestations
- Circular erythematous scaly papules and plaques
- Central clearing with “advancing border”
- Rarely pruritic
Sites of infection

- Tinea capitis
- Tinea faciei
- Tinea barbae
- Tinea corporis
- Tinea manus/pedis
- Tinea cruris
- Onychomycosis

Atypical manifestations of tinea

- Dermatophytic folliculitis
  - Often after Rx with topical steroids
  - Invasion of hair shaft
  - Absence of scale

Methods to confirm diagnosis: KOH preparation

- Scrape scale onto glass slide
- Apply 1-2 drops of KOH
- Apply cover slip
- If KOH w/o DMSO, gently heat with alcohol lamp or lighter for 2-3 seconds
- Examine under low-power for hyphae


Role of fungal culture?

- Not needed in most cases
- Consider if:
  - KOH negative but high pre-test probability
  - Treatment failure

http://knol.google.com/k/will-johnson/ringworm-tinea-corporis-tinea-faciei/4hmquk6fx4gu/634#

Treatment of tinea

- Limited superficial infection:
  - Topicals recommended
    - Clotrimazole, econazole, oxiconazole
    - Terbinafine
  - Extensive infection, immunocompromised, or failed topicals:
    - Systemic therapy recommended (See Appendix A dosing regimens)
**Additional clinical pearls**

- Empiric treatment of a “rash” with a combination topical steroid/antifungal combination
  - Treatment failure
  - Alteration in clinical appearance, including dermatophytic folliculitis


**Take-home points**

- Papulosquamous differential diagnosis broad
- If it scales, scrape it!!
- Localized disease, treat with topical therapy
- Widespread disease, treat with systemic therapy
- If misdiagnosed as an inflammatory condition and treated with topical steroids, may present in atypical fashion as dermatophytic folliculitis

**Onychomycosis: Laser treatment buzz**

1. PinPointe FootLaser™
2. Noveon®
3. ALA-PDT

- MOA: selectively damage fungi without harming adjacent tissue


**PinPointe FootLaser™**

- FDA cleared as a device for treatment of onychomycosis
- Single treatment
- ~ $1,000
- No articles in Pubmed
- Company website:
  - Clinical evidence submitted to FDA
  - 81% patients had sustained improvement at 12 months

http://pinpointefootlaser.com/

**Noveon®**

- FDA cleared for other indications, not onychomycosis
- n=26

**Treatment vs. Control**

- Unchanged or worse: 23% vs. 55%
- Slight or moderate improvement: 69% vs. 27%
- Marked improvement or cleared: 8% vs. 18%

- Limitations
  - Nail debridement was not controlled for


**Figure 6.** Representative treated case with mild disease at baseline (A) and with, at most, minimal residual disease after 180 days (B).

ALA-PDT

- Case reports
- Nail softened and clipped off prior to treatment

Piraccini BM et al. JAAD 2008;59:575.

What I tell patients

- Cost is high
- Not covered by health insurance
- Two studies available for review, not particularly impressive
- Pursue treatments that have been studied in randomized controlled trial and published in peer reviewed publications

Onychomycosis: standard treatment

- Terbinafine 250 mg PO
  - x 6 weeks for fingernails
  - x 12 weeks for toenails
- Alternative: itraconazole (See Appendix B for dosing regimens)

Case 3

- 55-year old male presents with “red, itchy bumps” on his face, arms, and legs
- He and his wife returned from a weekend vacation to New York City 5 days prior to presentation
- The rash began the day he returned
- Based on news reports he was concerned about bedbugs
- His wife does not have any symptoms

Bedbugs in the news

Image courtesy of Timothy Berger, MD

Bedbugs in the news

http://www.freebedbugadvice.com/bed-bugs-have-gone-mainstream/

DDx: Pruritic papules

- Papular eczema
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How can you confirm the diagnosis of bedbugs at this visit?

A. Bedbugs preparation
B. Identification of bedbugs on the skin on physical examination
C. Skin biopsy
D. There is not one

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Bedbugs: Entomology

- Ectoparasites: “blood meals”
- *Cimex lectularius*
- Primary host: humans
- Fear and avoid light
- Typically feed at night while host sleeps
- After blood meal, leave host and seek areas that are warm and dark, such as mattress seams, cushions, bed frames, etc.
**Bedbugs: Entomology**

- Blood meals take between 5-10 minutes
- Can travel 100 feet, but usually live within 8 feet of hosts
- Lifespan: 6-12 months. Can survive for months without feeding
- Emit a distinctive odor

Joint Statement on Bed Bug Control in the United States from the U.S. Centers for Disease Control and Prevention (CDC) and the U.S. Environmental Protection Agency (EPA)

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**Bedbugs: Why now?**

- Increase in resistance to pesticides
- Increased rates of travel
- Poor understanding of bedbug control
- Lack of effective state and local public health agencies pest control programs

Joint Statement on Bed Bug Control in the United States from the U.S. Centers for Disease Control and Prevention (CDC) and the U.S. Environmental Protection Agency (EPA)

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**Clinical manifestations: cutaneous**

- No reaction seen in ~ 30% of study population
- Lesions: erythematous pruritic papules/nodules, sometimes in linear configuration
- Often on exposed body sites (including face)
- Bites not felt, lesions 1-2 (up to 14) days after bite
- Lesion #: few to numerous
- Clues: Blood spots on linens, skin from molting

Clinical manifestations: other

- Systemic reactions
  - Generalized urticaria
  - Asthma
  - Anaphylaxis
- Psychological impact
  - Anxiety
  - Insomnia
  - Stigma

Goddard et al. JAMA 2009;301:1363.

Bedbugs: Transmission

- “Active dispersal”
  - Bugs crawling to hosts
  - Mechanism by which they can spread to rooms within a building via ventilation ducts
- “Passive dispersal”
  - Transmission by humans in clothes, luggage or furniture
  - Risk factors associated with outbreaks: rapid turnover of residents, overcrowding, etc.


Bedbugs, a vector of infection?

- Bedbugs have been proven to carry 45 pathogens
  - Hepatitis B virus
- No definitive evidence of transmission to host

Delaunay P et al. Bedbugs and Infectious Diseases. CID 2011;52:200

How do you make diagnosis?

1. Clinical suspicion
   - Morphology of clinical lesions
   - Distribution of clinical lesions
   - History of blood spots on clothing
2. Identification of bed bugs
   - Licensed pest control operator
3. Confirm clinical resolution after eradication

Bedbugs management

- Symptomatic therapy
  - Bites do not require treatment
  - If patient uncomfortable:
    - Oral antihistamines
    - Topical mid-potency corticosteroids
- Bedbug eradication

Bedbug eradication

- Integrated approach to control
  - Licensed pest control operator
  - Housing authorities/property managers
  - Federal, state and local public health professions
  - Private citizens

Obstacles to effective control

- Tenants and landlords disagreement
- Pesticide resistance
- Misuse of over-the-counter preparations may promote further resistance


Bed bug common sense

- When sleeping in hotels
  - Check for bed bugs or their feces
    - Examine mattress seams, crack in box springs, headboards, areas behind chipped paint
  - Inspect used sleeping items or clothing


Take home points

- Bedbugs has had a recent insurgence
- Diagnosis is based on clinical suspicion plus identification of bedbugs
- Clinical manifestations vary
- Treatment requires eradication plus symptomatic treatment (if necessary)
- Trained professional often needed

Case 4

- 54 year-old woman with hypertension and acne/roacea developed a prosthetic knee joint infection
  - Initially treated with nafcillin x 4 weeks and then transitioned to trimethoprim and sulfamethoxazole (TMP-SMX)
  - 2.5 weeks after starting TMP-SMX she develops fevers to 39°C

Case 4, cont.

- Three days later, morbilliform rash
- Rash started on the face, neck and upper arms, then spread to the lower extremities
- Periorbital and mid-facial edema
- Diffuse lymphadenopathy involving cervical, axillary and inguinal nodes
Laboratory values
- CBC with differential:
  - WBC: 25
  - Eosinophil count: 3.0 (normal: 0-0.4)
- AST 125; ALT 110
- Blood cultures x 2: negative

The most likely diagnosis is:
A. Sepsis from prosthetic joint infection
B. Simple morbilliform drug eruption
C. Drug-induced hypersensitivity syndrome to Septra
D. Leukemia with cutaneous involvement
E. Drug-induced hypersensitivity syndrome to minocycline

Drug-induced hypersensitivity syndrome (DIHS)
- Potentially life-threatening adverse drug reaction
- Skin rash AND internal organ involvement
- Initially observed in patients on anticonvulsants
- Previously:
  - Phenytoin hypersensitivity syndrome
  - Anti-convulsant hypersensitivity syndrome
  - Drug reaction w/ eosinophilia and systemic symptoms (DRESS)
DIHS: Cutaneous manifestations

- Primary morphology: maculopapular, morbilliform
- Diffuse macular erythema combined with small erythematous papules in a widespread distribution
- Often preceded days of by fevers
- Starts on face and upper body spreads distally
- Peri-ocular and facial edema
- Skin edema → vesicles, bulla, pustules, purpura
- Can progress to erythroderma with mucosal involvement

DIHS: Internal involvement, common

- Hepatic (70-90%):↑AST/ALT, AlkPhos. Liver failure
- Lymphadenopathy (75%) –local or general
- Hematologic system
  - Leukocytosis, up to WBC 50, atypical lymphs
  - Eosinophilia >2.0 (normal 0.0-0.4)
- Renal (11%): renal failure via interstitial nephritis
  - Hematuria/protenuira; eosinophils in urine

DIHS: Internal involvement, less common

- Pulmonary: interstitial pneumonitis, ARDS
- Cardiac: myocarditis
- Neurologic: meningitis, encephalitis
- GI: colitis, intestinal bleeding
- Endocrine: thyroiditis (late)

Histopathology

- Not particularly helpful since findings non-specific includes perivascular and interstitial infiltrate of lymphocytes, histiocytes and eosinophils

Most common agents

- Anticonvulsants (phenytoin, carbamazepine)
- Sulfonamides (sulfamethoxazole, etc.)
- Allopurinol
- Nevirapine
- Abacavir
- Dapsone
- Minocycline

DIHS: Timing

- Usually develops within 2-6 weeks after starting on new medication
- Can start sooner on re-challenge
## Treatment and prognosis

- Discontinue offending medication
- Systemic steroids for internal involvement, usually with starting dose of 1 to 1.5 mg/kg/day
- 10% mortality rate, usually from fulminant hepatitis

## Cutaneous drug reactions

- DIHS
- Simple drug rash
- Life-threatening drug rashes
  - Bullous drug reactions: Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN)
  - Acute generalized exanthematous pustulosis (AGEP)
- Urticaria
- Fixed drug eruption
- Vasculitis
**Simple drug rash**
- Clinical morphology can be nearly identical to DRESS, although face usually not involved
- Usually develop within first 2 weeks of new med
- Often start in the groin/axilla and then generalize within 1-2 days
- No visceral involvement

**Simple morbilliform eruption**

**Bullous drug reactions: SJS/TEN**
- Clinical morphology:
  - Start: erythematous, dusky red or purpuric macules
  - Next: Coalesce to bullae that break easily
    - Asboe-Hansen sign
    - Large sheets of epidermis slough from underlying dermis
- Timing:
  - 7-14 days after medication, sooner if re-exposure
Bullous drug reactions: SJS/TEN

- Definitions arbitrary:
  - SJS < 10 % BSA w/ ≥ 2 mucosal surfaces
  - SJS/TEN overlap 10-30% BSA
  - TEN > 30% BSA

- Histopathology helpful:
  - Lymphocytes along the dermal-epidermal junction
  - Necrotic keratinocytes and full-thickness necrosis
Acute generalized exanthematous pustulosis

- Drug eruption with non-follicular sterile pustules arising within edematous erythema
- Lesions often start on face or intertrigenous zones and quickly disseminate
- Associated with edema of face and hands, purpura, vesicles, bullae, mucous membrane involvement

Prognostic scoring (SCORTEN)

<table>
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<tr>
<th>Prognostic favors</th>
<th>Points</th>
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<tbody>
<tr>
<td>Age &gt; 40 years</td>
<td>1</td>
</tr>
<tr>
<td>Heart rate &gt; 120 bpm</td>
<td>1</td>
</tr>
<tr>
<td>Cancer or heme malignancy</td>
<td>1</td>
</tr>
<tr>
<td>BSA involved on day 1 &gt; 10%</td>
<td>1</td>
</tr>
<tr>
<td>Serum area level (&gt; 10mmol/l)</td>
<td>1</td>
</tr>
<tr>
<td>Serum bicarbonate level (&lt; 20 mmol/l)</td>
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</tr>
<tr>
<td>Serum glucose level (&gt; 14 mmol/l)</td>
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<table>
<thead>
<tr>
<th>SCORTEN</th>
<th>Mortality rate (%)</th>
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<td>0-1</td>
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<td>≥5</td>
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Case 4: Take home points

- Drug chart important
- DIHS has later onset than most other drug reactions
- DIHS involves multiple visceral organs
- Since DIHS clinical morphology can be identical to a simple drug eruption, evaluate for systemic involvement in any drug rash
- Clinical morphology can be helpful in narrowing the type of drug reaction