Bedside Diagnosis

PARASITES AND MITES
Parasites and Mites

1. Scabies
2. Demodex
3. Leishmaniasis
4. Onchocerciasis
Question:

How can you increase the yield of your scabies preps?

a) Concentrate attention on “hot spot” areas like the finger webs and wrists
b) Scrape multiple areas and prepare 2-3 slides
c) Perform dermoscopy prior to scraping
d) All of the above
1. Scabies

- *Sarcoptes scabiei var hominis*
- Worldwide distribution
- Transmitted by direct skin-to-skin contact
1. Scabies

• Emperic scabies treatment is common, but confirmation of infestation is useful:
  – To avoid unnecessary treatment
  – To enable appropriate infection control measures and treatment of close contacts and home environment
  – To prevent future diagnostic confusion
1. Scabies

- Despite often severe itching, the total mite burden in an immunocompetent host is 10-15
- Hot spots (high-yield for scraping) include:
  - Web spaces
  - Flexural wrists, elbows, axillae
  - Umbilicus, waistline
  - Glans penis
  - Nipple / areola
Materials and Methods—scabies prep
Slide, 15-blade, mineral oil
Methods

Scabies Prep:
• Dip 15-blade in mineral oil
• Scrape erythematosus papule or burrows vigorously to the point of near bleeding
• Transfer scales to slide
• Scrape several areas or prepare more than one prep to increase yield
• Add another drop of mineral oil, if needed, and apply cover slip
Microscopy

Diagnosis depends on visualization of mites, eggs, feces (scybala)
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Diagnosis depends on visualization of mites, eggs, feces (scybala)
Tips, Pearls, and Variations

• Mineral oil is not always readily available; can use Purell or other alcohol-based cleanser instead

• If there is significant scale, add a drop of KOH to the slide
Question:

How can you safely perform a scabies prep on a child or infant?
**Tips, Pearls, and Variations**

Pediatric-friendly “curette prep”

- 3mm disposable curette instead of 15-blade scalpel
- Scrape lesion with a gentle scooping motion
- Use a cotton-tip applicator to push contents onto slide

Better control and less frightening to children

**The Curette Prep: A Modification of the Traditional Scabies Preparation**

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Tips, Pearls, and Variations

Adhesive tape test:

- Transparent packing tape cut to the size of a slide
- Firmly applied to a lesion for several seconds, then rapidly pulled off
- Transferred to a slide and evaluated
- Sensitivity 68% and specificity 100%
- Negative predictive value 85%

Intern Med 2006;45 (14) 857-859.
Tips, Pearls, and Variations

Dermoscopy:
• Visualization of burrows
• “delta wing sign” indicates the presence of a mite

Test Characteristics

Traditional scabies prep:
- Sensitivity 46%-90%
- Specificity 100%
- Negative predictive value 77%

Adhesive tape test:
- Sensitivity 68%
- Specificity 100%
- Negative predictive value 85%

Dermoscopy:
- Sensitivity 83%-91%
- Specificity 46%-86%
- Negative predictive value 85%
Test Characteristics

- Use of a dermatoscope may make burrows and mites easier to locate
- Increases the yield and efficiency of traditional skin scraping (or tape test)

Table 2. Comparison of diagnostic accuracy between "with dermoscopy" and "without it" (total n = 49)

<table>
<thead>
<tr>
<th>Outcome of skin scraping (n)</th>
<th>With dermoscopy</th>
<th>Without it</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive (%)</td>
<td>41 (84)</td>
<td>23 (47)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Duration of the procedure (sec)</td>
<td>35 ~ 802</td>
<td>195 ~ 1215</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

SD: standard deviation.
Case Example

28yo man with longstanding psoriasis, worsening over 3 months

Started on adalimumab by his dermatologist

Now admitted to the hospital with a new diagnosis of HIV (CD4=17)
Case Example

Which of the following diagnoses is most likely?

a) Psoriasis (in setting of HIV/AIDS)
b) Seborrheic dermatitis (in setting of HIV/AIDS)
c) Drug eruption to HAART
d) Crusted scabies
Crusted (Norwegian) scabies

- Occurs when host immunity fails to control mite proliferation
  - AIDS, leukemia/lymphoma, others
- Hyperinfestation with thousands to millions of mites
- Classically non-pruritic
- Characteristic hyperkeratotic, sand-like scale up to 15mm thick
Crusted (Norwegian) scabies

• Not difficult to demonstrate on scabies prep due to high mite burden

• Issues of test sensitivity are much less pertinent
Crusted (Norwegian) scabies

• Not difficult to demonstrate on scabies prep due to high mite burden

• Issues of test sensitivity are much less pertinent
A crusted rash in a patient with AIDS

Emily Baumrind, BA; Evan Piette, MD; Robert Michelelli, MD

Caked-on, sand-like scale is essentially pathognomonic
Prompt recognition, effective infection control measures essential
Treat repeatedly orally and topically; must demonstrate clearance

Case Example

56yo woman with granulomatosis with polyangiitis (Wegener’s) s/p pulse steroids and rituximab, on maintenance azathioprine

Seen for acute onset of rosacea-like facial eruption with erythematous papules and pustules
Case Example

Tzanck smear of pustule on left cheek shows:

a) Herpes simplex
b) Scabies mite
c) Demodex mite
d) Eosinophilic folliculitis
2. Demodex

- *Demodex folliculorum* and *Demodex brevis*
- Ubiquitous in the pilosebaceous unit
- Associated with eye itching, lid thickening and scaling, madarosis, rosacea
- Prevalence increases with age
2. Demodex

- May proliferate in immunodeficiency states (HIV, post transplant)
- Can mimic folliculitis due to other causes, with inflammatory papules and pustules
- In such cases, topical permethrin and/or oral ivermectin, or oral metronidazole can be used
Materials and Methods—*Demodex*

Scabies prep: slide, 15-blade, mineral oil

OR, Tzanck: slide, 15-blade, Quick-DIP
Case Example

The patient improved rapidly with topical permethrin.
Case Example

22yo man presents with two ulcerated plaques after vacationing in Costa Rica
Question

Based on the clinical presentation, what do you expect to see on Tzanck smear?

a) Round, pigmented, thick-walled structures: “copper pennies”

b) Thick, ribbon-like aseptate hyphae

c) Motile, tapered round worms

d) Intracellular amastigotes referred to as a “swarm of bees”
Methods
Scraping (thick drop method):
• Use a scalpel blade to nick the inflamed border of the lesion
• Distribute drops of the oozing blood onto glass slides
• Allow drop to dry at room temperature without smearing
• Stain using Tzanck
3. Leishmaniasis

- Intracellular infection with *Leishmania* species
- Approximately 12 million cases worldwide
  - Middle East, Central and South America
- Skin lesions occur at sites of inoculation by *Phlebotomus* or *Lutzomyia* sandfly bites
Test Characteristics

Thick drop is the most sensitive light microscopy method (compared to PCR)

- 64% sensitive vs 39% for smear and 44% for punch biopsy (P < 0.005)

Quicker and less invasive than biopsy

No fixation or special processing → advantage in resource-limited setting

Another study calculated sensitivity 77% and specificity 100%

Variations

• Alternatively, a touch prep can be prepared from base of biopsy specimen
• Stained with Tzanck
• More sensitive than biopsy and quicker

• Reportedly 50-70% sensitive

4. Onchocerciasis

- *Onchocerca volvulus*
- Spread by *Simulium* black fly living near fast-flowing water in Africa (99% of cases), Yemen, and Central and South America
- May be diagnosed years after emigration from endemic areas
4. Onchocerciasis

- Second leading infectious cause of blindness in the world (a.k.a. African river blindness)
- Skin disease results in intense pruritus, subcutaneous nodules (onchocercoma)
- Chronic onchodermatitis results in dyspigmentation and loss of skin elasticity (hanging groin)
- Can mimic atopic dermatitis; peripheral eosinophilia common
What is the gold standard for diagnosis of onchocerciasis?

a) Skin biopsy
b) Skin snip
c) Diethylcarbamazine (DEC) patch test
d) Antibody test
Materials and Methods—skin snip

Slide, syringe, scalpel
Methods

Skin Snip:

• Sample normal-appearing, non-lesional skin where microfilariae are present

• Highest-yield sites are the iliac crests, scapulae, and calves
Methods

Skin Snip:

• A syringe is held perpendicular to the skin
• The skin is pierced and lifted
• A scalpel is used to snip off a small piece of skin beneath the needle
• The depth of snip is approximately that of the superficial dermis
Methods

Skin Snip:
- The skin snip is placed on a slide in a drop of normal saline
- Incubation at room temperature for 24 hours allows microfilariae to emerge from the tissue
- The organism can be visualized microscopically without staining
Test Characteristics

Advantages:
• Relatively painless and bloodless
• Few resources required

The gold standard for diagnosis of onchocerciasis
Test Characteristics

Disadvantages:
• Sensitivity can be limited (20-50%) in early or low intensity infection

Six snips (2 each from scapula, iliac crest, calf) provide highest sensitivity

Antibody, antigen, DEC patch, and PCR are sensitive and specific but limited by cost and availability

Bedside Diagnosis

OTHER APPLICATIONS AND CONCLUSIONS
Case Example

Newborn infant brought to emergency department with disseminated vesicular rash
Case Example

Tzanck smear is most consistent with which of the following diagnoses?

a) Disseminated HSV infection
b) Erythema toxicum neonatorum
c) Disseminated candidiasis
d) Transient neonatal pustular melanosis

Courtesy of Dr. Aileen Chang
Erythema Toxicum Neonatorum

Common benign, self-limited eruption seen in 1/3 of full-term newborns

Occurs within a few days of birth

Resolves over several days without therapy

Indian Pediatr. 2010 Sep;47(9):793.
Pustular Dermatoses in the Neonate

- During the neonatal period, the infant is extremely vulnerable to infection; pustules therefore evoke concern
- Simple diagnostic tests can differentiate transient, benign eruptions from serious and life-threatening ones
- Important to rule out infectious causes
Pustular Dermatoses in the Neonate

1. Erythema toxicum neonatorum
2. Transient neonatal pustular melanosis
3. Acropustulosis of infancy
4. Neonatal Acne
5. Incontinentia Pigmenti (vesicular stage)

Compare with:
6. Local or disseminated bacterial infection
7. HSV, VZV, CMV
8. Disseminated candidiasis
9. Scabies
Pustular Dermatoses in the Neonate

- Tzanck is an easy, rapid and sensitive way to diagnose infectious as well as noninfectious pustules (eosinophils, neutrophils)
- Gram stain and KOH may also be indicated

Goal is to spare healthy neonates invasive evaluations, harmful antibiotics, hospitalizations, etc. for benign, transient conditions
Infectious Pustular Eruptions

Bullous Impetigo (gram) → Neutrophils and GPC in clusters

HSV, VZV (Tzanck) → Multinucleation, margination, moulding

Candidiasis (KOH) → Pseudohyphae and spores
Case Example

A 50yo woman presents with bullae and erosions on the skin and oral mucosa.

a) Herpes simplex
b) Bullous impetigo
c) Pemphigus vulgaris
d) Bullous pemphigoid
Pemphigus Vulgaris

Tzanck smear:
- Round acantholytic cells
- Hypertrophic nuclei
- Basophilic cytoplasm with peripheral rim
- Cell adherence
Pemphigus Vulgaris

Tzanck smear:
Chains of white blood cells ("streptocytes")
Pemphigus Vulgaris

Tzanck smear:
Isolated epithelial cells ringed by leukocytes (Sertoli rosette)
Pemphigus Vulgaris

Peripheral fluorescence of isolated acantholytic cells or network-like if grouped
Pemphigus Vulgaris

Particularly useful for early diagnosis of oral erosions, when Bx is less reliable

- 37/40 patients positive by cytomorphology
- All patients positive by immunocytology

Can sample many skin lesions simultaneously and non-invasively

Bullous Pemphigoid

Tzanck smear:
- Nonspecific findings
- No acantholytic cells
- Abundance of eosinophils

Serves mainly to rule out pemphigus
Blistering Diseases

1. Pemphigus vulgaris
2. Bullous pemphigoid
3. Hailey-Hailey
4. Darier
5. Stevens-Johnson syndrome / TEN
Stevens-Johnson Syndrome / TEN

Medical emergency; prompt diagnosis essential

Scrape freshly-denuded area induced by Nikolsky sign

Avoid excess blood and vesicle fluid

Spread cellular material onto slide

Stain per Tzanck protocol
Stevens-Johnson Syndrome / TEN

Differentiate SJS/TEN from Staph Scalded Skin:

SJS/TEN:
Necrotic cuboidal basal keratinocytes with large nuclei, fibroblasts; inflammatory cells present

SSSS:
Acantholytic broad superficial keratinocytes with small nuclei; no inflammatory cells

Arch Dermatol 1975;111:1433-1437.
Alternatively, the blister roof can be submitted for frozen section

Reveals full-thickness epidermal necrosis

Stevens-Johnson Syndrome / TEN
Case Example

A 52yo woman presents with a small, flesh-colored, dome-shaped papule on the right upper cutanesous lip.
Case Example

Tzanck smear of the lesion is shown. Which diagnosis is most likely?

a) Angiofibroma
b) Dermal nevus
c) Sebaceous hyperplasia
d) Basal cell carcinoma
Basal Cell Carcinoma

Common tumor

Sometimes difficult to differentiate from other benign and malignant lesions

High diagnostic reliability of cytology
Basal Cell Carcinoma

Looks just like the biopsy:

- Packed clusters of atypical basal cells
- Uniform large size, strongly basophilic
- May see peripheral palisading
Test Characteristics

Meta-analysis of 8 primary studies:

1261 biopsy-proven BCCs

Cytology was:
• 97% sensitive (only 3% misdiagnosed)
• 86% specific

**Advantages**

Simple, highly reliable

Significant time and cost savings vs biopsy

Diagnostic confirmation at the initial visit

Conservative means of diagnosis for cosmetically sensitive sites, multiple lesions

May be appropriate when planning to treat with non-surgical modality

Methods (cytology for tumors / solid lesions)

Tzanck smear / Wright–Giemsa stain:

- Use scalpel blade to scrape lesion surface
- Generally need to nick the surface of non-ulcerated lesions
- Scrape material onto glass slide
- Fix and stain using Tzanck protocol
- View immediately
Tips and Pearls

• Break skin in non-ulcerated lesions
• Remove slough/scab
• Scrape down to papillary dermis
• Treat keratotic lesions with Vaseline
• Scrape leading edge

**Make sure to get a sufficient sample**

Case Example

48yo man with a pink, scaly plaque on the upper back
Case Example

Tzanck smear shows large, pleomorphic cells with multiple nuclei and vacuolated cytoplasm.

The most likely diagnosis is?

a) Psoriasis
b) Squamous cell carcinoma
c) Eczematous dermatitis
d) Lichenoid seborrheic keratosis
Squamous Cell Carcinoma

Very common

Sometimes difficult to differentiate from other benign and malignant lesions (e.g. psoriasis, etc.)
Test Characteristics

Most reliable for nodular, soft, ulcerated, and non-keratotic lesions (including oral and genital lesions)

Less reliable for keratotic or verrucous lesions
Malignancies, Benign Tumors / Other

- Basal cell carcinoma
- Squamous cell carcinoma
- Paget disease
- Erythroplasia of Queyrat
- Mastocytoma
- Histiocytosis
- Clear cell acanthoma
- Melanomas and Nevi
- Spongiotic dermatitis
- Seborrheic keratosis
- Granulomatous disorders
- And more…
Diagnostic Reliability

Diagnostic reliability of Tzanck for erosive vesiculobullous (k=0.79) and granulomatous (k=0.68) diseases was substantial.

Reliability for tumors (k=0.50) was moderate.

Bedside Diagnosis

CONCLUSION
Logistical considerations—CLIA Certification

• CLIA establishes minimum performance standards for all laboratory testing, quality control
• Certificate of provider-performed procedures
• Certificate of compliance
• Yearly competency tests with regular quality checks
• State dependent:
  – CMS.gov; CDC.gov
• Once approved, can bill for performing bedside tests
Conclusion

• Bedside diagnostic tests such as the Tzanck smear can provide rapid answers to important clinical questions

• These include common and uncommon infectious diseases

• As well as a wide variety of benign and malignant dermatologic conditions
<table>
<thead>
<tr>
<th>Cytologic diagnosis</th>
<th>Diagnostic cytologic findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal cell carcinoma</td>
<td>Clusters of basaloid cells</td>
</tr>
<tr>
<td>Bullous impetigo</td>
<td>Acantholytic cells, cocci, neutrophils</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>Pseudohyphae, spores</td>
</tr>
<tr>
<td>Contact dermatitis</td>
<td>&gt;10 tadpole cells (OM x100)</td>
</tr>
<tr>
<td>Cutaneous leishmaniasis</td>
<td>Leishman–Donovan bodies</td>
</tr>
<tr>
<td>Darier’s disease</td>
<td>Acantholytic cells, corps ronds, grains</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>Hyphae, spores</td>
</tr>
<tr>
<td>Foreign body granuloma</td>
<td>Foreign body giant cells, foreign body</td>
</tr>
<tr>
<td>Granuloma annulare</td>
<td>Palisading granuloma, mucin</td>
</tr>
<tr>
<td>Granulomatous dermatitis</td>
<td>Granuloma formation, Langhans and/or foreign body giant cells</td>
</tr>
<tr>
<td>Happle–Happle disease</td>
<td>Acantholytic cells without positive direct immunofluorescence</td>
</tr>
<tr>
<td>Hand, foot and mouth disease</td>
<td>Keratinocytes with syncyrial nuclei, absence of acantholytic cells</td>
</tr>
<tr>
<td>Herpetic infection</td>
<td>Acantholytic cells, multinucleated giant cells</td>
</tr>
<tr>
<td>Infected eczematous contact dermatitis</td>
<td>&gt;10 tadpole cells (OM x100), cocci or bacilli</td>
</tr>
<tr>
<td>Juvenile xanthogranuloma</td>
<td>Touton giant cells, foamy cells</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Atypical lymphocytes</td>
</tr>
<tr>
<td>Masocytoma</td>
<td>Abundant mast cells</td>
</tr>
<tr>
<td>Melanocytic nevus</td>
<td>Dermal- and epidermal-type nevocell</td>
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<tr>
<td>Melanoma</td>
<td>Atypical nevocell</td>
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<tr>
<td>Metastatic carcinoma</td>
<td>Atypical (non-keratinocytic and non-nevocell) cells</td>
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<tr>
<td>Mycobacterial infection</td>
<td>Acid-fast bacilli</td>
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<td>Pemphigus</td>
<td>Acantholytic cells with positive direct immunofluorescence</td>
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<td>Pemphigus herpetiformis</td>
<td>Acantholytic cells, &gt;10 tadpole cells (OM x100)</td>
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<tr>
<td>Sarcoidosis</td>
<td>Granuloma formation, Langhans, Touton and/or foreign body giant cells</td>
</tr>
<tr>
<td>Scabies</td>
<td>Absence of bacteria, fungi, parasites, necrobiosis materials, mucin</td>
</tr>
<tr>
<td>Scabies</td>
<td>Sarcoptes scabiei</td>
</tr>
<tr>
<td>Sebaceous hyperplasia</td>
<td>Clusters of sebocytes</td>
</tr>
<tr>
<td>Seborrheic keratosis</td>
<td>Hyperkeratosis, horny cysts</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>Cytologic atypia of keratinocytes</td>
</tr>
<tr>
<td>Staphylococcal scalded skin syndrome</td>
<td>Dyskeratotic acantholytic cells (without neutrophils and cocci)</td>
</tr>
</tbody>
</table>

*aBased on Durdu et al. (2011).*

OM, original magnification.
Conclusion

- Bedside tests complement more expensive and time-consuming tests
- Rapid, practical, economical
- Well-tolerated, repeatable, suitable for difficult surfaces like the face, genitals, or mouth
- May be particularly valuable in resource-limited settings, on inpatient wards, and in the clinic
Conclusion

• Each technique is easily performed...but requires some expertise in interpreting
• Dermatologists (with dermpath training) have the knowledge to carry out and interpret these tests
• Like dermoscopy, a useful adjunct to the clinical exam; also like dermoscopy, it has limitations and a learning curve
• When utilized appropriately, these tests provide unique efficiency and operational autonomy
Thank you