Bedside diagnostics in dermatology

Parasitic and noninfectious diseases

Robert G. Micheletti, MD,[a] Arturo R. Dominguez, MD,[b] and Karolyn A. Wanat, MD[c]
Philadelphia, Pennsylvania; Dallas, Texas; and Iowa City, Iowa

Learning objectives
After completing this learning activity, the participants should be able to describe and perform diagnostic tests that dermatologists can perform at the bedside; select the appropriate bedside technique for diagnosis of specific parasitic and noninfectious dermatologic conditions using these bedsides laboratory techniques; and judge appropriate situations for utilization of bedside laboratory techniques to save time or money in the timely diagnosis and treatment of patients with important parasitic and noninfectious dermatologic diseases.

Disclosures

Editors
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In addition to aiding the diagnosis of viral, bacterial, and fungal diseases, mineral oil preparation, Tzanck smear, and other techniques can be used to diagnose parasitic infections, neonatal pustular dermatoses, blistering diseases, Stevens–Johnson syndrome, and a plethora of other benign and malignant conditions, including granulomatous diseases and tumors. In many cases, these techniques are specific, reliable, and easy to perform and interpret. In others, a certain amount of training and expertise are required. In the proper clinical scenario, these tests are rapid, economical, and compare favorably with other diagnostic methods. (J Am Acad Dermatol 2017;77:221-30.)

Key words: bedside diagnostic tests; mineral oil preparation; parasitic infections; quality improvement; rapid diagnosis; skin snip; Tzanck smear.

PARASITES AND MITES

Scabies

Key points

- **Scabies preparation yield is highest in "hot spot" areas, such as the web spaces, flexural wrists, elbows, axillae, umbilicus, waistline, glans penis, and the nipple/areola**
- **Dermoscopy may allow visualization of burrows and mites (delta wing sign), increasing diagnostic sensitivity independently or in conjunction with scabies preparation**

Sarcoptes scabiei infestation is common throughout the world, with the highest prevalence in India, Brazil, and Central America. It is a disease of low socioeconomic status, poor nutrition, and poor hygiene, transmitted by direct skin-to-skin contact; in some cases, it is transmitted sexually.

Empiric scabies treatment of patients with pruritic dermatoses is common in primary care and dermatology offices, but confirmation of infestation is useful for the following reasons: 1) to avoid unnecessary treatment, 2) to enable appropriate

From the Departments of Dermatology and Medicine,[a] University of Pennsylvania, Philadelphia; Departments of Dermatology and Medicine,[b] University of Texas Southwestern, Dallas; and the Department of Dermatology, Pathology, and Infectious Diseases,[c] University of Iowa, Iowa City.
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Correspondence to: Robert G. Micheletti, MD, Departments of Dermatology and Medicine, Perelman School of Medicine at the University of Pennsylvania, 2 Maloney Bldg, 3400 Spruce St, Philadelphia, PA 19104. E-mail: robert.micheletti@uphs.upenn.edu.
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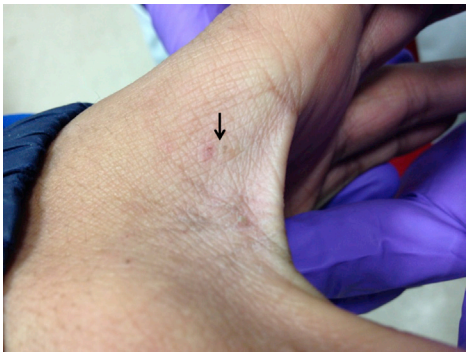

Fig 1. Excoriated papules in the web space between the first and second fingers (*arrow*).

infection control measures and treatment of close contacts and the home environment, and 3) to prevent future diagnostic confusion if symptoms persist. A well-executed scabies preparation can be extremely helpful.

Scabies preparation. Despite often severe itching caused by mite saliva, eggs, and feces, etc, the total mite burden in an immunocompetent host is only 10 to 15. Hot spots that are high-yield for scraping include the web spaces, flexural wrists, elbows, axillae, umbilicus, waistline, glans penis, and the nipple/areola (Fig 1). To perform a scabies preparation, a no. 15 scalpel is dipped in mineral oil to provide a viscous surface to which scale, mites, and debris can adhere. Erythematous papules or burrows in "hot spot" areas should be scraped vigorously, and scale is transferred to a glass slide. Scraping several areas can increase the diagnostic yield. Diagnosis depends on visualization of mites, eggs, or feces (scybala) on microscopic examination (Fig 2). Sensitivity of scabies preparation ranges from 46% to 90%, and the negative predictive value is 77%. Specificity is 100% by definition.[1-3]

Mineral oil is not always readily available, so any viscous substance to which scale adheres may suffice. Purell or another alcohol-based cleanser can work well as a mineral oil substitute. If there is significant scale, as in patients with crusted scabies, it may be useful to add a drop of potassium hydroxide (KOH) to the slide to diminish keratinous debris. A modified, pediatric-friendly "curette prep" using a 3-mm disposable curette instead of a no. 15 scalpel to scrape lesions with a gentle scooping motion may provide better control and be less frightening to children.[4] Transparent adhesive packing tape cut to the size of a slide and firmly applied to "hot spot" areas/lesional skin, then rapidly pulled off and transferred to a slide, can replace scraping where appropriate. Sensitivity is 68% and the negative predictive value 85%, with specificity again 100%.[5]

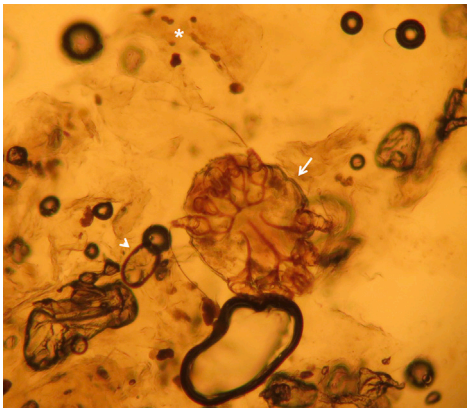

Fig 2. A *Sarcoptes scabiei* mite (*arrow*), ovum (*arrowhead*), and scybala (*asterisk*) visible at high power. (Original magnification: ×400).

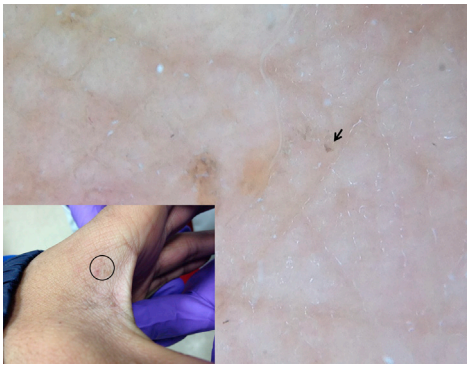

Fig 3. Positive "delta wing sign"; mites appear as small triangles on dermoscopy (*arrow*).

Dermoscopy is a useful adjunctive tool to enable visualization of mites and burrows. On dermoscopy, mites appear as small triangles, the so-called "delta wing sign" (Fig 3).[6] Sensitivity of this method is excellent (83-91%), with a negative predictive value of 85%. Specificity, however, is lower (46-86%), reflecting the potential for false positives. Combining traditional scabies preparation with dermoscopy to locate mites and burrows increases the yield of skin scraping, raising sensitivity from 47% to 84%, while simultaneously decreasing time spent on the procedure.[7]

Demodex

Key points

- ***Demodex* may play a role in rosacea and ocular symptoms, as well as folliculitis in immunocompromised patients**
- **The organism can be demonstrated using scabies preparation or Tzanck smear of an acneiform pustule**

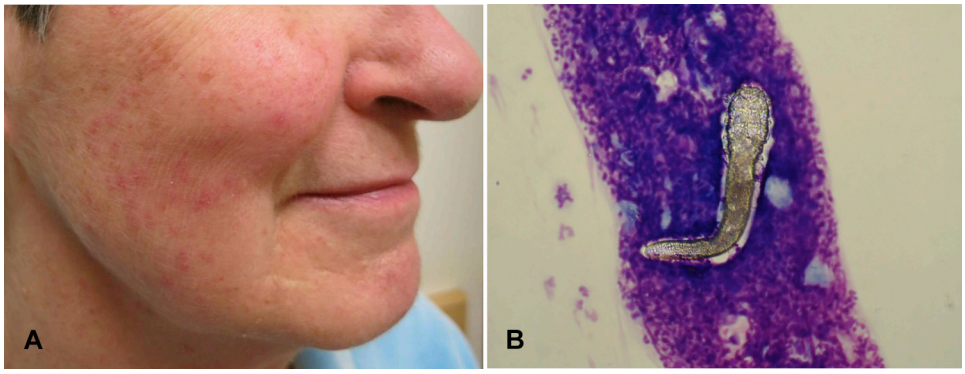

Fig 4. **A**, Patient with granulomatosis with polyangiitis on chronic immunosuppression, seen for acute onset of rosacea-like erythematous papules and pustules. **B**, Tzanck smear of the *Demodex* mite appearing as a negative (unstained) image. (Original magnification: **B**, ×100).

Demodex folliculorum and *Demodex brevis* are ubiquitous organisms living in the pilosebaceous unit which are associated with eye itching, lid thickening and scaling, madarosis, and rosacea. In immunodeficient states (eg, posttransplant patients or patients with HIV), *Demodex* infestation can mimic folliculitis due to other causes (Fig 4, *A*), with inflammatory papules and pustules that respond to therapy with topical permethrin or oral ivermectin.[8,9]

Demodex can be demonstrated using mineral oil scraping (scabies preparation) or Tzanck smear. In both techniques, a no. 15 scalpel is used to scrape a follicular pustule, and the material is spread onto a glass slide. Whether the slide is unstained or stained using Tzanck (Wright–Giemsa stain), the mite appears clear and elongated. If a Tzanck preparation is used, the organism appears as a negative (unstained) image and may be easier to visualize (Fig 4, *B*).[10]

Leishmania

Key points

- **Cutaneous leishmaniasis frequently presents as ulcerated nodules or plaques on exposed areas**
- **The "thick drop method," a modified Tzanck preparation, is the most sensitive light microscopy method for diagnosing cutaneous leishmaniasis**
- **Intracellular amastigotes appear as a "swarm of bees" within parasitized macrophages**

Cutaneous leishmaniasis results from intracellular infection of macrophages by protozoal *Leishmania* species. Cutaneous lesions, which generally present as ulcerated nodules or plaques, occur at sites of inoculation by *Phlebotomus* or *Lutzomyia* sandfly bites. The disease burden is highest in the Middle East and Central and South America.

Thick drop method. Rapid bedside diagnosis of cutaneous leishmaniasis can be confirmed using a modified Tzanck preparation known as the "thick drop method." A no. 15 scalpel is used to nick the inflamed border of the lesion (Fig 5, *A*), and drops of the oozing blood are placed onto a glass slide or slides. The drop(s) of blood are allowed to dry at room temperature without smearing and are then stained using Wright–Giemsa (Tzanck). Intracellular amastigotes (Leishman–Donovan bodies) are readily detected on microscopy as a light blue, round or oval "swarm of bees" (Fig 5, *B*). The thick drop method is the most sensitive light microscopy method, with sensitivity ranging from 64% to 77% compared to 44% for punch biopsy specimens and 39% for scraping and smearing a thin layer of material on a glass slide. Specificity is reported at 100% because of the distinctive appearance of the parasite.[11,12] Alternatively, a touch preparation can be prepared from the base of a biopsy specimen, then stained with Wright–Giemsa. The sensitivity of this method is higher than that of biopsy (50-70% overall), enabling diagnosis in cases where the biopsy was ultimately nondiagnostic.[13] Lastly, these bedside scrapings can be used subsequently for polymerase chain reaction (PCR) testing with high sensitivity and specificity, suggesting a kind of practical, algorithmic approach to the diagnosis of cutaneous leishmaniasis, beginning with the thick drop method.[11] Because no fixation or special processing are required, these methods have distinct advantages in resource-limited settings. While PCR is highly sensitive, it is limited by cost and availability.

Onchocerciasis

Key points

- **Onchocerciasis ("African river blindness") can be intensely pruritic and mimic chronic atopic dermatitis**

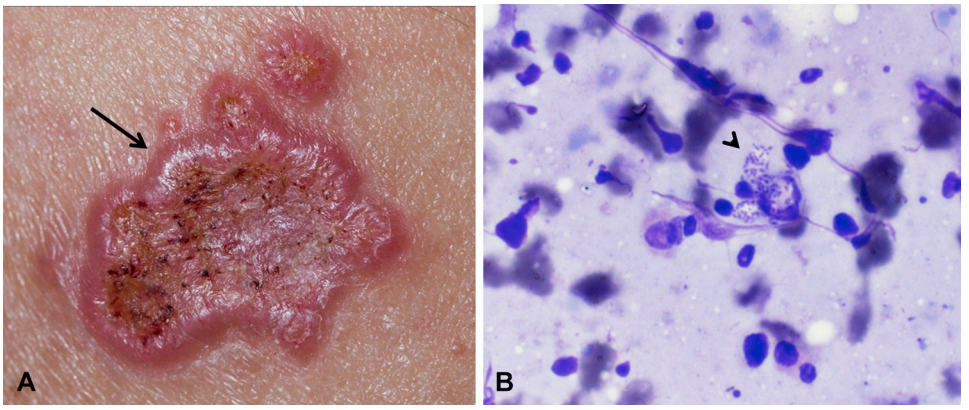

Fig 5. **A**, Cutaneous leishmaniasis: an ulcerated plaque with central atrophy and raised border. In the "thick drop method," a no. 15 scalpel is used to nick the inflamed border (arrow), and drops of blood are placed onto a glass slide to dry. **B**, Intracellular amastigotes (Leishman–Donovan bodies) are readily detected on microscopy as light blue, round or oval "swarm of bees" (arrowhead). (Photograph courtesy of Brian Swick, MD; original magnification: **B**, ×400.)

- **The skin snip is relatively bloodless and painless and is the criterion standard for diagnosis worldwide**

Onchocerciasis is the second leading infectious cause of blindness in the world. Cutaneous involvement (onchodermatitis) results in intense pruritus and dyspigmentation, mimicking atopic dermatitis. Subcutaneous nodules (onchocercoma) and loss of skin elasticity with loose-hanging skin folds (hanging groin) may also result.

Skin snip. The criterion standard of onchocerciasis testing is the skin snip. In this procedure, normal-appearing, nonlesional skin is sampled to look for microfilariae. The highest-yield sites are the iliac crests, the scapulae, and the calves. A syringe with a small needle is held perpendicular to the skin (Fig 6 and Supplemental Video 1, available online at www.jaad.org). The skin is pierced and tented up, and 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. The skin snip is placed on a glass slide in a single drop of normal saline, then incubated at room temperature for 24 hours to allow microfilariae to emerge from the tissue. The organism can then be visualized microscopically with or without staining as an elongated, motile round worm with tapered ends. In settings where the skin snip is performed regularly, specialized tools for sampling may be available.

This method of skin sampling has distinct advantages. It is relatively bloodless and painless, requiring no anesthesia. Few resources (only a syringe, scalpel, slide, and microscope) are required. It is also considered the criterion standard for diagnosis of onchocerciasis worldwide. While the specificity of the skin snip is approximately 100%, sensitivity can be limited (20-50%) in early- or low-intensity infection. A method of taking 6 snips (2 each from the scapulae, iliac crests, and calves) provides the highest diagnostic sensitivity. Antibody and antigen tests, diethylcarbamazine patch test, and PCR are highly sensitive and specific but limited by cost and availability.[14]

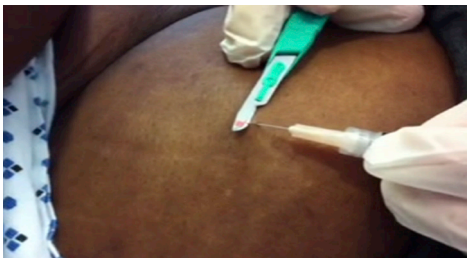

Fig 6. A skin snip for onchocerciasis is performed on normal skin of the iliac crests, scapulae, and calves using a needle and scalpel without anesthesia.

Bedside techniques for the diagnosis of parasitic diseases are summarized in Table I.

DISEASES OF EARLY CHILDHOOD/ PUSTULAR DERMATOSES OF THE NEONATE

Key point

- **Tzanck, Gram stain, or KOH preparation can help distinguish benign neonatal pustular dermatoses from potentially life-threatening disseminated infections**

During the neonatal period, the infant is vulnerable to infection; pustules therefore evoke concern. Simple diagnostic tests have the potential to rule out

Table I. Parasitic diseases

Disease	Technique	Microscopic appearance
Scabies	Mineral oil preparation	Mites, eggs, and scybala
Demodex folliculitis	Mineral oil or Tzanck smear	Elongated, clear mite
Leishmaniasis	"Thick drop method" or touch preparation with Tzanck smear	Intracellular "swarm of bees"
Onchocerciasis	Skin snip	Elongated, motile round worm

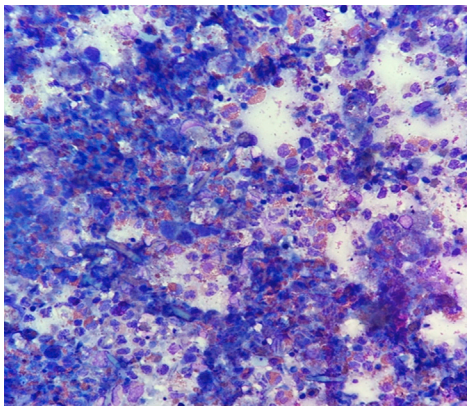

Fig 7. Erythema toxicum neonatorum in a newborn and corresponding Tzanck smear showing numerous eosinophilis. (Photograph courtesy of Aileen Chang, MD; original magnification: ×400.)

or rule in infectious causes, quickly differentiating transient, benign eruptionsm such as erythema toxicum neonatorum (Fig 7) and transient neonatal pustular melanosis from serious and life-threatening ones, such as neonatal herpes simplex or disseminated candida. The Tzanck smear is an easy, rapid, and sensitive way to evaluate pustules in the neonate; Gram stain and KOH/chlorazol black E preparation may also be indicated. Such testing may quickly identify infectious diseases while sparing healthy neonates more invasive evaluations and potentially harmful interventions for benign, transient conditions (Table II).[15]

Blistering diseases

Key points

- **Tzanck smear can enable differentiation of pemphigus vulgaris from various autoimmune and genetic blistering diseases caused by characteristic cytology**
- **Rapid diagnosis of Stevens–Johnson syndrome/toxic epidermal necrolysis and differentiation from staphylococcal scalded-skin syndrome can be achieved using Tzanck or "jelly roll"**

Bedside diagnostic tests can also be used to differentiate various autoimmune and genetic blistering diseases, as well as Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) and staphylococcal scalded-skin syndrome (SSSS). Doing so accurately requires some degree of familiarity with each entity's diagnostic cytologic appearance, but the sampling technique is the same. In each entity, a Tzanck smear is performed by scraping the freshly denuded base of a blister or erosion, then staining per usual protocol (described in the first article in this continuing medical education series).

In pemphigus vulgaris, characteristic findings include round acantholytic cells, hypertrophic nuclei, basophilic cytoplasm with peripheral rim, and cell adherence or clustering. Additional characteristic findings include chains of white blood cells (streptocytes) and isolated epithelial cells surrounded by a ring of leukocytes (Sertoli rosette). Peripheral fluorescence results if direct immunofluorescence is performed (Fig 8). Advantages of this technique, in addition to the rapidity of diagnosis, include a high degree of sensitivity. Multiple samples from different skin lesions can be sampled to increase yield and include lesions at different stages of disease. Oral erosions may be easier to sample using this method, whereas biopsy specimens of oral erosions may be less reliable.[16,17]

In contrast to pemphigus, Tzanck smear of bullous pemphigoid reveals no specific findings beyond an abundance of eosinophils (Fig 9). There are no acantholytic cells. This serves mainly to differentiate bullous pemphigoid from pemphigus vulgaris. Hailey–Hailey disease is characterized by numerous acantholytic cells, large round keratinocytes, hypertrophic, deeply stained nuclei, and deep basophilic staining at the cell periphery. Unlike pemphigus, cells typically do not cluster, and no streptocytes or rosettes are seen (Fig 10).[18] In Darier disease, one sees acantholytic cells as well as corps ronds and grains.[19]

SJS/TEN is a life-threatening emergency in which a prompt diagnosis is critical. The base of a freshly denuded area (or one induced by the Nikolsky sign) is scraped. While avoiding excess blood and vesicle fluid, the cellular material is spread onto a slide and stained per the Tzanck protocol. The presence of necrotic cuboidal basal keratinocytes with large

Table II. Pustular dermatoses in the neonate

Disease	Technique	Microscopic appearance
Erythema toxicum neonatorum	Tzanck smear	Numerous eosinophils
Transient neonatal pustular melanosis	Tzanck or Gram stain	Numerous neutrophils, few eosinophils, and no bacteria
Acropustulosis of infancy	Tzanck or Gram stain	Numerous neutrophils, few eosinophils, and no bacteria
Infantile acne	Tzanck smear	Sebaceous material and *Pityrosporum* yeast
Incontinentia pigmenti	Tzanck or Gram stain	Numerous eosinophils
Bullous impetigo	Gram stain	Neutrophils and GPC in clusters
Herpes simplex virus Varicella zoster virus	Tzanck smear	Multinucleation, margination, and molding of keratinocytes
Candidiasis	KOH preparation	Pseudohyphae and spores

GPC, Gram-positive cocci; *KOH*, potassium hydroxide.

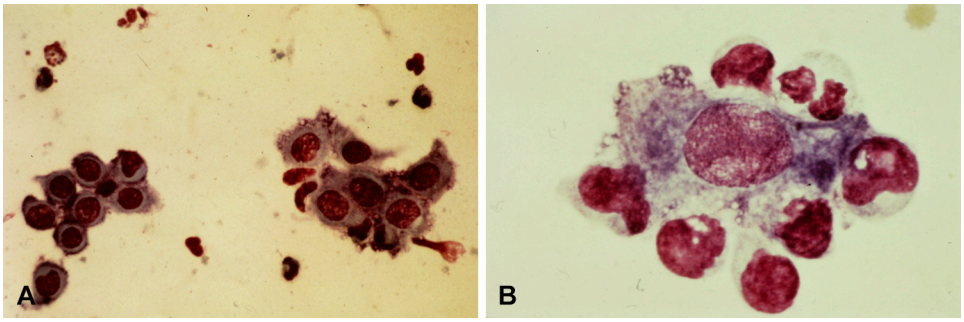

Fig 8. Tzanck smear of pemphigus vulgaris showing (**A**) round, acantholytic keratinocytes with hypertrophic nuclei, basophilic cytoplasm with peripheral rim, and cell adherence/clustering and (**B**) isolated epithelial cells surrounded by a ring of leukocytes (Sertoli rosette). (Photographs courtesy of Amit Pandya, MD.)

nuclei and surrounding inflammatory cells suggests SJS/TEN. By contrast, broad superficial acantholytic keratinocytes with small nuclei and a dearth of inflammatory cells suggests SSSS (Fig 11).[20] Alternatively, the blister roof from a patient with SJS/TEN or SSSS can be submitted on saline-moistened gauze (the so-called "jelly roll") for frozen section processing, revealing full-thickness epidermal necrosis (Fig 12) or intraepidermal necrolysis, respectively (Table III).

Keratinocytic tumors

Key point

- **Exfoliative cytology using Tzanck is a simple, reliable method for diagnosing common skin cancers in the appropriate clinical setting, including basal and squamous cell carcinoma, which have characteristic cytologic appearances**

Exfoliative cytology has widespread use for the diagnosis of cervical cancer. It may also be used for diagnosis of skin tumors in the appropriate setting. Ulcerated lesions can be scraped directly, while the edge of nonulcerated papules or plaques should be nicked with a scalpel before scraping the lesion surface. Removal of slough or scab, pretreatment of keratotic lesions with petroleum jelly, and scraping down to the papillary dermis may all increase the likelihood of getting a sufficient sample and increase the diagnostic yield. Material should be scraped onto a glass slide then stained per the Tzanck protocol and viewed immediately.

Basal cell carcinoma (BCC), which may resemble several benign lesions clinically, looks cytologically much like the familiar histologic appearance on review of the biopsy specimen—packed clusters of atypical, strongly basophilic basaloid cells with uniform large size clump together with peripheral palisading (Fig 13). The diagnostic reliability of cytology for diagnosis of basal cell carcinoma is high. A metaanalysis of 8 primary studies showed that of 1261 biopsy-proven BCCs, cytology was 97% sensitive and 86% specific.[21]

Squamous cell carcinoma (SCC), which can sometimes be difficult to differentiate from other benign and malignant lesions (eg, psoriasis), exhibits pleomorphic isolated cells with hypertrophic, hyperchromic, lobulated or multiple/mitotic nuclei. Cytoplasmic staining may be vacuolated or otherwise unusual (Fig 14). For SCC, Tzanck smear is most reliable for nodular, soft, ulcerated,

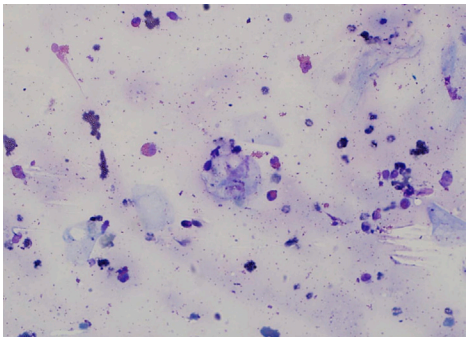

Fig 9. Tzanck smear of bullous pemphigoid reveals no specific findings beyond an abundance of eosinophils. Compare to pemphigus vulgaris shown in Fig 8. (Original magnification: ×400.)

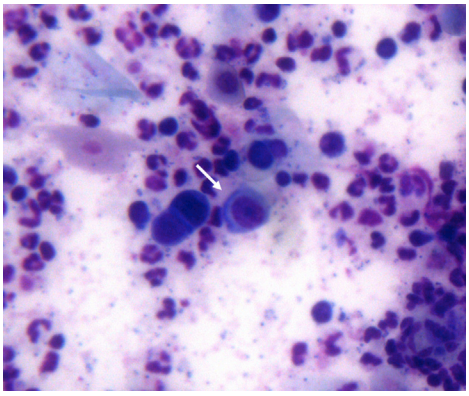

Fig 10. Tzanck smear of Hailey–Hailey disease showing acantholytic cells, large round keratinocytes, hypertrophic nuclei, and peripheral basophilic staining (arrow). Unlike pemphigus vulgaris, cells do not cluster, and no streptocytes or rosettes are seen. (Original magnification: ×400.)

nonkeratotic, and mucosal lesions and is less reliable for keratotic or verrucous lesions with extensive scale.[17]

Tzanck smear for the diagnosis of BCC and SCC is simple and reliable and can represent significant time and cost savings. It allows diagnostic confirmation at the initial visit and may be a more conservative means of diagnosis for cosmetically sensitive sites or multiple lesions. It may be appropriate when planning to treat immediately with destruction or with a nonsurgical modality.[21] However, it should not be considered equivalent to or a replacement for obtaining a biopsy specimen in most circumstances where pathology services are readily available.

OTHER BENIGN AND MALIGNANT TUMORS

Key point

- **Tzanck smear/exfoliative cytology can be used to diagnose a great variety of other benign and malignant cutaneous disorders**

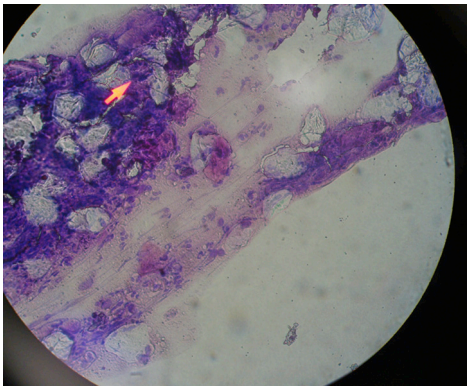

Fig 11. Tzanck smear of staphylococcal scalded-skin syndrome showing broad superficial acantholytic keratinocytes with small nuclei and a dearth of inflammatory cells. (Original magnification: ×400.)

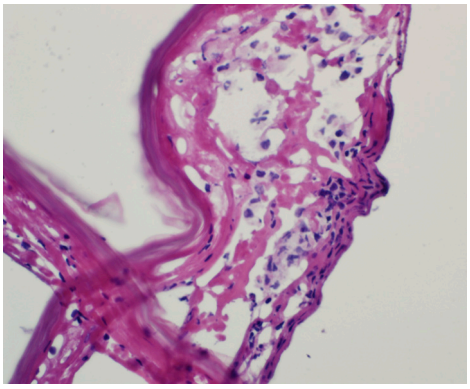

Fig 12. Frozen section processing of the blister roof from a patient with Stevens–Johnson syndrome revealing full-thickness epidermal necrosis. (Original magnification: ×400.)

In addition to BCC and SCC, the Tzanck smear can be used to diagnose a variety of other malignant and benign tumors, granulomatous, and other diseases, including: Paget disease, melanoma,[22] erythroplasia of Queyrat,[18,23] mastocytoma,[24] and histiocytosis[18,23,25]; sarcoidosis, granuloma annulare, necrobiosis lipoidica, foreign body granuloma, and juvenile xanthogranuloma[12]; clear cell acanthoma,[26] spongiotic dermatitis,[19,27] seborrheic keratosis, melanocytic nevus, dermatofibroma, vellus hair cyst, and verruca (Table IV).[22]

The utility of these techniques is limited by the expertise and comfort level of the operator and should not replace formal histology. However, there is evidence to suggest that the diagnostic reliability of the Tzanck smear for these entities can be high. The diagnosis of erosive vesiculobullous and ranulomatous lesions can be made reliably with brief training, showing substantial agreement between experienced and less experienced operators

Table III. Blistering diseases (Tzanck smear)

Disease	Microscopic appearance
Pemphigus vulgaris	Acantholytic cells, hypertrophic nuclei, basophilic cytoplasmic rim; cell adherence, streptocyte, and Sertoli rosette; immunofluorescence
Bullous pemphigoid	Abundant eosinophils; otherwise nonspecific
Hailey–Hailey disease	Acantholytic cells, hypertrophic nuclei, basophilic cytoplasmic rim; no adherence, streptocyte, or rosette; nonfluorescent
Darier disease	Corps ronds and grains (hyaline pink round and ovoid bodies)
HSV and VZV	Multinucleation, molding, and margination of nuclear chromatin
SJS/TEN	Necrotic cuboidal basal keratinocytes, large nuclei, and inflammatory cells
Staphylococcal scalded-skin syndrome	Acantholytic broad superficial keratinocytes, small nuclei, and no inflammation

HSV, Herpes simplex virus; *SJS*, Stevens–Johnson syndrome; *TEN*, toxic epidermal necrolysis; *VZV*, varicella zoster virus.

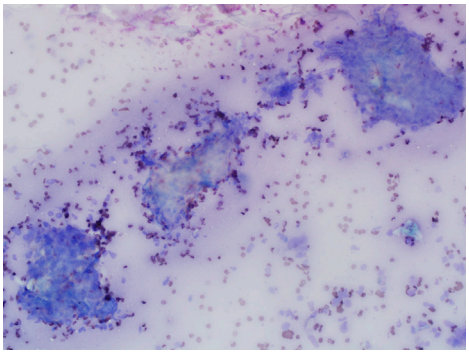

Fig 13. Tzanck smear of basal cell carcinoma showing clusters of atypical, large, basophilic basaloid cells that clump together with peripheral palisading. (Original magnification: ×200.)

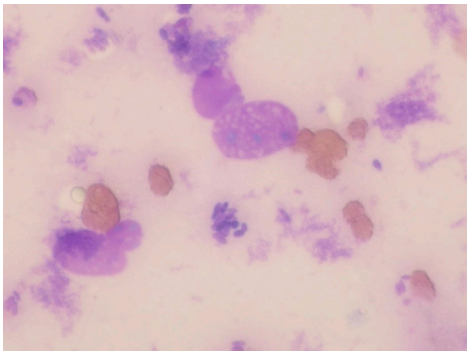

Fig 14. Tzanck smear of squamous cell carcinoma with pleomorphic isolated cells with hypertrophic, hyperchromic, lobulated or multiple/mitotic nuclei and vacuolated cytoplasm. (Original magnification: ×400.)

(κ = 0.79 and 0.68, respectively). The accurate evaluation of tumoral lesions appears to require more experience, showing only moderate agreement (κ = 0.50). When applied to pigmented lesions, the accuracy of the Tzanck smear appears to be similar to that of dermoscopy, with an overall diagnostic accuracy of 90.5%, and superior with respect to differentiating melanocytic from nonmelanocytic pigmented lesions.[22] While not replacing obtaining a biopsy specimen, exfoliative cytology can be a useful adjunct to traditional methods like dermoscopy or biopsy, particularly when pathology services are unavailable (as in resource-limited settings) or when results are needed in a timely fashion.[28]

WET MOUNTS IN THE DIAGNOSIS OF VULVOVAGINAL DISEASES

Key points

- **Pseudohyphae or budding yeast confirm the presence of vaginal candidiasis**
- **The presence of clue cells and absence of lactobacilli can help confirm bacterial vaginosis**

The evaluation of a patient with vulvovaginal diseases often necessitates the use of bedside diagnostics to complement clinical examination. The evaluation of scale, pustules, and vesicles in the vulvar area can be performed using the methods previously discussed. Examination of vaginal secretions, or a "wet mount," may also provide useful information. Wet mount preparations are performed by collecting vaginal secretions with a cotton-tipped applicator from the blades of a speculum, from the secretions pooled within the vagina, or from the vaginal walls. The cotton-tipped applicator is touched or swiped onto a glass slide to create a thin layer of the secretions, followed by application of a drop of normal saline and a coverslip.[29]

The wet mount provides information on the morphology of epithelial cells, inflammatory cells, and the presence of organisms, both colonizing and infectious. The range of normal findings includes mature epithelial cells, which are large, polygonal cells with abundant cytoplasm and small nuclei, and parabasal cells, which are smaller and rounder

Table IV. Malignant and benign tumors and other diseases (Tzanck smear)

Disease	Microscopic appearance
Basal cell carcinoma	Clustered large, atypical, basaloid cells with peripheral palisading
Clear cell acanthoma	Keratinocytes with multiple small cytoplasmic vacuoles
Dermatofibroma	Spindle-shaped fibroblasts
Erythroplasia of Queyrat	Cellular and nuclear polymorphism and enlarged nuclei
Foreign body granuloma	Foreign body giant cells and foreign material
Granuloma annulare	Palisading granulomas and mucin
Histiocytosis	Large pale cells with large reniform nuclei
Juvenile xanthogranuloma	Foamy Touton giant cells
Mastocytoma	Abundant irregularly shaped mast cells; reddish purple granules
Melanocytic nevus	Dermal- and epidermal-type nevoid cells
Melanoma	Atypical nevoid cells; multinucleation, irregular molded nuclei
Paget disease	Large, round cells; microvacuolated cytoplasm; large, eccentric nuclei
Sarcoidosis	Granuloma formation and Langerhans type giant cells
Seborrheic keratosis	Hyperkeratosis and horny cysts
Spongiotic dermatitis (vesicular)	Numerous tadpole cells
Squamous cell carcinoma	Pleomorphic isolated cells with hypertrophic, hyperchromatic, lobulated or multiple/mitotic nuclei and vacuolated cytoplasm
Vellus hair cyst	Numerous vellus hairs within cyst contents

immature epithelial cells with large nuclei. Parabasal cells can be seen in inflamed skin or atrophic, estrogen-deficient vaginal epithelium and represent a disorder in maturation.[29] Lactobacilli, which are small rods of varying lengths that can attach end-on-end to each other, constitute normal bacterial flora in the vagina. Leukocytes in a ratio of 1:1 with epithelial cells also are considered normal. Increased numbers can be seen in infections such as *Trichomonas* or in inflammatory dermatoses.[29-31]

Other abnormal findings can provide a definitive diagnosis. Pseudohyphae, yeast forms, or budding yeast confirm the presence of *Candida* species.[29-31] The presence of clue cells, which are epithelial cells with bacteria adherent to the cell wall so that they appear ragged, together with a lack of lactobacilli, can help confirm the diagnosis of bacterial vaginosis (which is diagnosed on the basis of ≥3 clinical criteria: milky, copious vaginal discharge, pH > 5, positive whiff test, and identification of clue cells).[29-31]

CLINICAL LABORATORY IMPROVEMENT AMENDMENTS CERTIFICATION

Key point

- **Clinical Laboratory Improvement Amendments certification helps ensure minimum performance standards for provider-performed procedures**

The Centers for Medicare and Medicaid Services regulates all human clinical laboratory testing through CLIA. The objective of CLIA is to ensure quality laboratory testing by establishing minimum performance standards and quality control. This jurisdiction extends to provider-performed procedures, such as scabies preparation, KOH preparation, and Tzanck smear (as well as those performed by other specialties, such as wet mount, urinalysis, and arthroscopic fluid analysis, etc). For the purposes of clinical decision making, providers should be certified and compliant by CLIA standards, with regular competency and quality control checks. While certification is not difficult, an understanding of CLIA requirements is necessary.[32] Once certified, standard bedside diagnostic tests are billable. Nonstandard applications of these and other techniques discussed in this manuscript are not among those certified by CLIA.

DISCUSSION

Bedside diagnostic tests can provide rapid answers to important clinical questions, including diagnosis of common and uncommon infectious diseases as well as a wide variety of benign and malignant dermatologic conditions.[28,33] Bedside tests can complement more expensive and time-consuming tests. They are rapid, practical, and economical, well-tolerated, repeatable, and suitable for difficult surfaces like the face, genitals, and mouth. They may be particularly valuable in resource-limited settings, on inpatient wards, and in the clinic.

Each technique is easily performed but requires expertise in interpretation. Dermatologists, with training in surgery and pathology, are well-equipped to carry out and interpret these tests but may need

special training to interpret some of them accurately, such as for cutaneous tumors. Like dermoscopy, and despite their limitations, bedside tests are a useful adjunct to the clinical examination. When used appropriately, these techniques provide unique efficiency and operational autonomy.

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