Bedside diagnostics in dermatology

Viral, bacterial, and fungal infections

Karolyn A. Wanat, MD,[a] Arturo R. Dominguez, MD,[b,c] Zachary Carter, BS,[d] Pedro Legua, MD,[e] Beatriz Bustamante, MD,[e,f] and Robert G. Micheletti, MD[g,h]
Iowa City, Iowa; Dallas, Texas; Lima, Peru; and Philadelphia, Pennsylvania

Learning objectives
After completing this learning activity, 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 infectious dermatologic conditions; interpret micrographs to diagnose infectious dermatologic conditions using these bedside 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 infectious dermatologic diseases.

Disclosures
Editors
The editors involved with this CME activity and all content validation/peer reviewers of the journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Authors
The authors involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Planners
The planners involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s). The editorial and education staff involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Viral, bacterial, and fungal infections are frequently encountered in clinical practice, resulting in numerous cutaneous manifestations. Although diagnosis of these infections has changed over time because of technological advancements, such as polymerase chain reaction, bedside diagnostic techniques still play an important role in diagnosis and management, enabling rapid and low-cost diagnosis and implementation of appropriate therapies. This 2-part article will review both common and infrequent uses of bedside diagnostic techniques that dermatologists can incorporate into daily practice. This article examines the utility of bedside tests for the diagnosis of viral, bacterial, and fungal infections. The second article in this series reviews the use of bedside diagnostics for parasitic and noninfectious disorders. (J Am Acad Dermatol 2017;77:197-218.)

Key words: acid-fast; bedside diagnosis; cytology; Gram stain; slit-skin; Ziehl–Neelsen.

Bedside diagnostic tests and exfoliative cytology can yield rapid, reliable results that are especially helpful to confirm or exclude dermatologic diseases. Although other tests (including histopathology, polymerase chain reaction, and culture) play an undeniably important role, dermatologists should be aware of these tests and their potential to help expedite diagnosis in the clinic, on the inpatient wards with complex and critically ill patients, and in resource-limited settings

From the Department of Dermatology, Pathology, and Infectious Diseases,[a] University of Iowa, Iowa City; Departments of Dermatology[b] and Medicine,[c] University of Texas Southwestern, and the University of Texas Southwestern Medical School,[d] Dallas; Instituto de Medicina Tropical "Alexander von Humboldt,"[e] Universidad Peruana Cayetano Heredia and Departamento de Enfermedades Infecciosas, Tropicales y Dermatológicas,[f] Hospital Cayetano Heredia, Lima; and the Departments of Dermatology[g] and Medicine,[h] University of Pennsylvania, Philadelphia.
Funding sources: None.
Conflicts of interest: None declared.

Reprints not available from the authors.
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.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2016.06.034
Date of release: August 2017
Expiration date: August 2020

Abbreviations used:

CBE:	chlorazol black E stain
H&E:	hematoxylin–eosin
HFMD:	hand-foot-mouth disease
HSV:	herpes simplex virus
KOH:	potassium hydroxide
MC:	molluscum contagiosum
PCR:	polymerase chain reaction
SJS:	Stevens–Johnson syndrome
SSSS:	staphylococcal scalded-skin syndrome
TEN:	toxic epidermal necrolysis
VZV:	varicella zoster virus

where other tests are unavailable. The focus of this 2-part continuing medical education series is the use of bedside diagnostic tests for rapid diagnosis of infectious and noninfectious disorders.

VIRAL INFECTIONS

Tzanck smear

Key points

- **Tzanck smear is an inexpensive, rapid, simple, noninvasive technique that is useful for diagnosing viral and bacterial infections and many inflammatory disorders**
- **A variety of stains are commercially available**

The Tzanck smear was initially introduced by Arnault Tzanck in 1947 for the cytologic examination of vesicular lesions to distinguish between blistering disorders.[1] Since that time, multiple uses have been described, including many in dermatology. As with other techniques, the utility of the tool is dependent on the user's experience.

The Tzanck smear is a simple, relatively noninvasive, rapid, inexpensive test that can be performed easily on multiple sites, including the mucosa.[2-5] For herpetic and other lesions, an early vesicular lesion is preferred for highest diagnostic yield.[6] The desired area is cleaned, the overlying crust or vesicle roof is incised and folded back, the base of the lesion is scraped with a no. 15 scalpel, and the contents are smeared thinly onto a glass slide (Supplemental Video 1, available at http://www.jaad.org). Specimens are air-dried and should be stained shortly after preparation to avoid cellular swelling and loss of nuclear detail. Depending on the stain used, fixation occurs either with alcohol (which is often incorporated into stains for self-fixing of the specimen) or heat. Stains used include May-Grunwald-Giemsa, Wright–Giemsa, and various modifications of these. These stains typically contain a combination of methylene blue, eosin, and Azure B.[2-5] Numerous stains are commercially available as kits (for example Quik-Dip [Mercedes Medical, Sarasota, FL], Wright-Giemsa [Sigma-Aldrich, St. Louis, MO], Hemacolor [Millipore Sigma, Billerica, MA], or Diff-Quik [Microptic, Barcelona, Spain]). Different stains result in variable coloring, but the nuclear features are the same. Evaluation of nuclear detail often requires ×20, ×40, or ×100 (oil-immersion) magnification.

Herpetic infections

Key points

- **Tzanck smear is most sensitive and specific when performed on early vesicular or pustular lesions**
- **Tzanck smear cannot differentiate between herpes simplex viruses 1 and 2 and varicella zoster virus**
- **Key cytologic features of herpetic infection include multinucleate keratinocytes, acantholysis, keratinocyte ballooning, and nuclear margination**

Herpes simplex viruses 1 and 2 (HSV1/2) and varicella zoster virus (VZV or HHV3) are exceedingly common viral infections worldwide. The characteristic clinical appearance of grouped vesicles on an erythematous base involving the orolabial or genital mucosa may not require additional confirmatory testing for HSV 1/2. However, atypical presentations can be a source of diagnostic confusion, especially in immunocompromised patients. Rapid confirmation of infection enables earlier treatment, institution of infection control measures, and avoidance of complications.

Several studies have shown that dermatologists can accurately and reliably diagnose herpetic infection using the Tzanck smear after proper training.[7-9] Diagnosis of herpetic infection depends upon visualization of the characteristic cytologic features. These features include "ballooning" of keratinocytes to sizes as great as 80 μm, multinucleation, and acantholysis. Nuclear changes include enlarged nuclei, peripheral margination of chromatin, nuclear molding, and blurry staining with "ground glass" cytoplasm. Cowdry type A bodies, which are intranuclear inclusion bodies surrounded by a subtle clear halo, are characteristic but may be difficult to find[6,10,11] (Fig 1). Tzanck smears cannot distinguish between HSV1/2 and VZV, and they are less sensitive for old or crusted lesions.[6,11,12]

Several published studies have compared Tzanck to other techniques, including viral culture, polymerase chain reaction (PCR), direct fluorescent antibody, biopsy with cytologic examination and immunohistochemical staining, and electron microscopy.[7,8,12-17] Reported sensitivity ranges from