



# The Utility of Tissue Microbiology Studies in Diagnosis and Management of Suspected Dermatological Infection

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**Scholarly Report submitted in partial fulfillment of the MD Degree at Harvard Medical School**

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**Scholarly Report Title:** The Utility of Tissue Microbiology Studies in Diagnosis and Management of Suspected Dermatological Infection

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## Abstract

### **TITLE: The Utility of Tissue Microbiology Studies in Diagnosis and Management of Suspected Dermatological Infection**

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(\* co-first authors)

**Purpose:** Skin tissue microbiology studies are often sent alongside skin biopsies for histology when evaluating patients with suspected skin infections. However, microbiology studies may require a second biopsy and are associated with laboratory time, cost and risk for additional patient discomfort and procedure complication. In this study, we evaluate the frequency in which these studies return positive or influence diagnosis/management in the general dermatology population.

**Methods:** We randomly selected a sample of 150 patients with complete clinical documentation meeting inclusion criteria for whom both pathology and microbiology studies were ordered on skin biopsies by dermatologists at Brigham & Women's Hospital and Massachusetts General Hospital from 2000-2015. Chart review was conducted and each set of microbiology results was defined as a true/false positive/negative based on documented final clinical interpretation. Microbiology sets were categorized based on the positive result interpretation (eg: a hypothetical set with true negative bacterial culture, false positive gram stain, true positive AFB culture, true negative fungal stain and culture would be categorized as a true positive).

**Results:** We found that microbiology studies had a sensitivity of 80.8% (confidence interval: 67.0%-89.9%), specificity of 59.2% (48.8%-68.9%), positive predictive value of 51.2% (40.0%-62.3%), and negative predictive value of 85.3% (74.2%-92.3%) for identifying infection. Microbiology studies altered diagnosis in 48.0% (n=72) of cases and led to management changes in 26.7% (n=40) of cases.

**Conclusions:** We conclude that although microbiology studies have a relatively low yield of true positive results (n=42, 28%), they have high sensitivity and negative predictive value and lead to changes in clinical diagnosis and management. This data serve to guide clinical practice and as the basis for evaluation of the cost-effectiveness of this practice.

**Author Contributions:** Dr(s). Xia and Mostaghimi had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Song, Xia, and Mostaghimi. *Acquisition, analysis, and interpretation of data:* All authors. *Drafting of the manuscript:* Xia, Song, and Mostaghimi. *Critical revision of the manuscript for important intellectual content:* All authors. *Statistical analysis:* Joyce. *Obtained funding:* N/A. *Administrative, technical, or material support:* N/A. *Study supervision:* Mostaghimi. *Conflict of interest disclosures:* None

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**Appendix 1: Article manuscript**

**To the editor:** Skin tissue microbiology studies are often performed alongside skin biopsies for histology in evaluation of suspected infection. Microbiology studies may require another biopsy, with possible patient discomfort, procedure risk, laboratory time and cost.<sup>1,2</sup> Despite the commonality of this practice, data on the utility of tissue microbiology studies are limited. Here we evaluate the yield of skin microbiology studies and how often they influence care in the general dermatology population.

**Methods**

We searched the Partners Healthcare registry for patients for whom both pathology and microbiology studies were ordered on skin biopsies by dermatologists at Brigham & Women's Hospital and Massachusetts General Hospital from 2000-2015. Chart review was conducted for a random sample of 150 patients with complete clinical documentation meeting inclusion criteria. Each set of microbiology results was defined as a true/false positive/negative based on documented final clinical interpretation. We defined false negatives as cases where clinical suspicion overruled negative data, and false positives as showing clinically non-relevant organisms/skin commensals. Microbiology sets were categorized based on the positive result interpretation (eg: a hypothetical set with true negative bacterial culture, false positive gram stain, true positive AFB culture, true negative fungal stain and culture would be categorized as a true positive). The study was approved by the Partners IRB.

**Results**

92% of patients were seen in outpatient dermatology clinics; 43% did not have documented history of immunosuppression (Table 1). Infection was listed among the top differential diagnoses in 70% (n=105) of patients (Table 2). Bacterial culture (n=144, 96%), gram stain 82% (n=123), and fungal culture 82% (n=123) were the most common microbiology studies.

Gram, fungal, and AFB stains were positive in 12.2% (n=15), 0% (n=0), and 1.8% (n=2) of cases, respectively. Bacterial, fungal, and AFB cultures were positive in 50% (n=72), 4.9% (n=6), and 4.6% (n=5) of cases. Microbiology studies were 70.7% (n=106) concordant with dermatopathology results (both suggesting infection, n=21, 14.0%; both without evidence of infection, n=85, 56.7%). The 150 sets of microbiology studies had a sensitivity of 80.8% (confidence interval: 67.0%-89.9%), specificity of 59.2% (8.8%-68.9%), positive predictive value of 51.2% (40.0%-62.3%), and negative predictive value of 85.3% (74.2%-92.3%) for identifying infection.

Microbiology studies altered diagnosis in 48.0% (n=72) of cases (showing no infection when infection was listed among the top differential diagnoses, n=68, 45.3%; demonstrating infection when infection was not listed among the top differential diagnoses, n=4, 2.7%). Upon the return of microbiology results, antimicrobials were started in 22.7% (n=34) of cases, including 27 where infection was listed among the top differential diagnoses but antimicrobials were withheld until return of microbiology data, and in 2 cases where antimicrobials were started based on clinical judgment despite negative microbiology results. Antimicrobials were stopped in 0.7% (n=1) of cases, altered in 2.7% (n=4) of cases, and triage/disposition recommendations were changed in 0.7% (n=1) of cases.

## Discussion

These findings suggest that despite a low yield of true positive results (n=42, 28.0%), microbiology studies have high sensitivity and negative predictive value and lead to changes in clinical management. Our results contrast with those of a prior group, who found a low yield (1/158 true positive)<sup>3</sup> of microbiology studies sent on immunocompromised cancer inpatients, most of whom on antibiotics at time of culture.<sup>3, 4</sup>

Our study is limited by its retrospective nature. Additionally, our sensitivity/specificity calculations are based on sets of microbiology studies as opposed to individual microbiology studies. Despite this, our data suggest that routine tissue microbiology studies influence diagnosis and clinical management with reasonable sensitivity and negative predictive value. Future studies should evaluate which clinical features would enhance the yield/utility of microbiology studies and evaluate the cost-effectiveness of this practice.

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Table 1: Patient demographics and clinical factors

|                                                                   |                  |
|-------------------------------------------------------------------|------------------|
|                                                                   | Overall<br>n=150 |
| Age at time of biopsy, mean (SD)                                  | 56.3 (16.1)      |
| Gender, n (%)                                                     |                  |
| Male                                                              | 52 (34.7)        |
| Female                                                            | 98 (65.3)        |
| Race/ethnicity, n (%)                                             |                  |
| White                                                             | 94 (62.7)        |
| Black                                                             | 20 (13.3)        |
| Hispanic                                                          | 15 (10.0)        |
| Asian                                                             | 4 (2.7)          |
| Other/Unknown                                                     | 17 (11.3)        |
| Setting, n (%)                                                    |                  |
| In-patient dermatology consult                                    | 12 (8.0)         |
| Out-patient dermatology visit                                     | 138 (92.0)       |
| Antimicrobial Therapy at time of Dermatology Encounter,<br>n (%)  |                  |
| Antibiotics                                                       | 40 (26.7)        |
| Anti-yeast or antifungal                                          | 7 (4.7)          |
| Antiviral                                                         | 7 (4.7)          |
| Other                                                             | 1 (0.7)          |
| Medical History/Immunosuppressive factors, n (%)                  |                  |
| Diabetes                                                          | 10 (6.7)         |
| Recurrent skin infections                                         | 8 (5.3)          |
| Autoimmune disease                                                | 41 (27.3)        |
| Hematologic/solid organ malignancy                                | 24 (16.0)        |
| Solid organ transplant/bone marrow transplant                     | 10 (6.7)         |
| On systemic immunosuppression in past 3 months                    | 52 (34.7)        |
| HIV/AIDS                                                          | 8 (5.3)          |
| History of Opportunistic Infections                               | 6 (4.0)          |
| No immunosuppressive factors noted                                | 65 (43.3)        |
| Clinical factors at the time of dermatology encounter             |                  |
| Presence of Fever > 38.0°C on the day of biopsy<br>(n=12*), n (%) | 3 (25.0)         |
| Median WBC (interquartile range) (n=19*)                          | 7.8 (5.4-12.4)   |

\* Patients for whom vitals and laboratory values were available

Table 2: Yield of microbiology studies and their influence on diagnosis and management

|                                                                                             | Overall<br>n=150 |                          |
|---------------------------------------------------------------------------------------------|------------------|--------------------------|
| Infection listed among the top differential diagnoses, n (%)                                |                  |                          |
| Yes                                                                                         | 105 (70.0)       |                          |
| No                                                                                          | 45 (30.0)        |                          |
| Microbiology panels, n (%)                                                                  | Sent, n (%)      | Returned positive, n (%) |
| Gram stain                                                                                  | 123 (82.0)       | 15 (12.2)                |
| Fungal stain                                                                                | 37 (24.7)        | 0 (0.0)                  |
| Acid-Fast Bacilli stain                                                                     | 109 (72.7)       | 2 (1.8)                  |
| Bacterial culture                                                                           | 144 (96.0)       | 72 (50.0)                |
| Fungal culture                                                                              | 123 (82.0)       | 6 (4.9)                  |
| Acid-Fast Bacilli culture                                                                   | 109 (72.7)       | 5 (4.6)                  |
| Concordant microbiology and pathology results, n (%)                                        | 106 (70.7)       |                          |
| Both suggesting infection                                                                   | 21 (14.0)        |                          |
| Both without evidence of infection                                                          | 85 (56.7)        |                          |
| Microbiology results interpretation                                                         |                  |                          |
| True positive, n                                                                            | 42               |                          |
| True negative, n                                                                            | 58               |                          |
| False positive, n                                                                           | 40               |                          |
| False negative, n                                                                           | 10               |                          |
| Sensitivity, % (95% Confidence interval)                                                    | 80.8 (67.0-89.9) |                          |
| Specificity, % (95% Confidence interval)                                                    | 59.2 (48.8-68.9) |                          |
| Positive predictive value, % (95% Confidence interval)                                      | 51.2 (40.0-62.3) |                          |
| Negative predictive value, % (95% Confidence interval)                                      | 85.3 (74.2-92.3) |                          |
| Microbiology results, n (%)                                                                 |                  |                          |
| Change in diagnosis                                                                         |                  |                          |
| Showing absence of infection when infection was listed among the top differential diagnoses | 68 (45.3)        |                          |
| Demonstrating infection when infection was not listed among the top differential diagnoses  | 4 (2.7)          |                          |
| Change in management                                                                        |                  |                          |
| No changes/continue current therapy                                                         | 104 (69.3)       |                          |
| Start new antimicrobial therapy                                                             | 34 (22.7)        |                          |
| Stop current antimicrobial therapy                                                          | 1 (0.7)          |                          |
| Alter current antimicrobial therapy                                                         | 4 (2.7)          |                          |
| Triage or disposition change recommended                                                    | 1 (0.7)          |                          |
| Other                                                                                       | 7 (4.7)          |                          |