# *LEPTOTRICHIA* BACTEREMIA: DEFINING WHO GETS INFECTION AND HOW TO OPTIMIZE TREATMENT

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## ABSTRACT

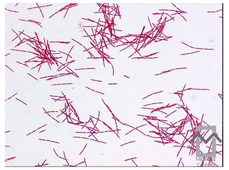
### BACKGROUND
*Leptotrichia* spp. are anaerobic, gram-negative bacilli that are part of the normal oral and intestinal flora. Although traditionally considered non-pathogenic, invasive infections including bacteremia have been observed in immunosuppressed patients, particularly those with neutropenia. There is limited published data to inform best management strategies in those with *Leptotrichia* bloodstream infection (BSI).

### METHODS
All cases of *Leptotrichia* spp. bacteremia between January 2012 and 2022 at our tertiary academic medical center were retrospectively reviewed to determine patient risk factors, clinical outcomes, and antimicrobial susceptibilities. Descriptive statistical methods were used. Antimicrobial susceptibilities were performed using Wadsworth agar dilution.

### RESULTS
26 cases of *Leptotrichia* spp. bacteremia were identified. The mean patient age was 55 years (SD 17), with 9 female patients (35%). All 26 patients were immunocompromised, predominantly due to hematologic malignancy (69%) or hematopoietic stem cell transplant (23%) (HSCT). 25 of 26 patients were actively neutropenic, with a median duration of neutropenia of 21 days (13-26). The most frequent sources of *Leptotrichia* bacteremia were gastrointestinal translocation (60%), followed by catheter-related bloodstream infection (35%). 10 patients had polymicrobial bacteremia (38.5%). The primary antibiotics utilized included metronidazole (42%), piperacillin-tazobactam (27%), and carbapenems (19%). Overall, the mean duration of treatment was 11 days, with a 60-day mortality of 19% (Table 1) and no cases of microbiologic relapse. In the 22 clinical isolates evaluated for susceptibility, *Leptotrichia* spp. were largely susceptible to metronidazole, penicillin, ertapenem, and piperacillin-tazobactam, but uniformly resistant to moxifloxacin.

### CONCLUSIONS
*Leptotrichia* spp. may be a rare cause of bacteremia in neutropenic hosts, particularly those with underlying hematologic malignancies and HSCT. The pathogen has a favorable susceptibility profile to penicillins and carbapenems, but has high degree of resistance to fluoroquinolones, which are frequently used as prophylaxis in neutropenic patients.

## BACKGROUND



### MICROBIOLOGY
- Facultative anaerobic, Gram-negative bacilli [1]
- Challenging to isolate: G variable, filamentous, 16s rRNA sequencing or MALDI-TOF MS necessary
- Common colonizer of oropharyngeal, intestinal, and female genital flora
- 7 species identified to date [2]:

| Species | Common associated clinical infections |
|---|---|
| *L. buccalis* | BSI, chorioamnionitis, periodontitis/gingivitis |
| *L. wadei* | BSI, pulmonary abscess, dental infections/caries |
| *L. trevisanii* | BSI (particularly neutropenic hosts) |
| *L. goodfellowii* | BSI, prosthetic valve IE, vascular graft infection |
| *L. hongkongensis* | BSI, dental infection/caries |
| *L. shahii* | Dental infections/caries |
| *L. hofstadii* | Periodontitis/gingivitis |

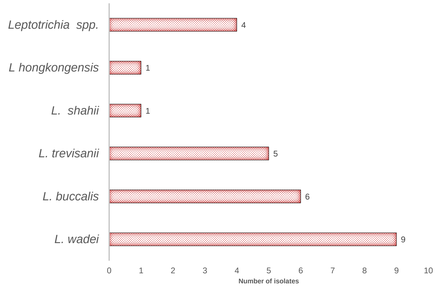
### LEPTOTRICHIA BLOODSTREAM INFECTION (BSI) IS SIGNIFICANT IN IMMUNOCOMPROMISED HOSTS
- BSI noted in hematologic malignancy [3], febrile neutropenia [4], chemotherapy [5].
- Couturier et al, 2012: BSI observed in 11/13 patients with hematopoietic stem cell transplant (HSCT) with neutropenia associated mucositis/enteritis [6].

## METHODS

1. Retrospective review of all cases of Leptotrichia spp. bloodstream isolates submitted to Mayo Clinic Laboratories between 2012 – 2022 to determine:
   - Molecular ID
   - Antimicrobial susceptibility profile (AST) using Wadsworth agar dilution
2. Clinical evaluation of patient risk factors, treatment strategies, outcomes, and susceptibility profile of patients (n=26) treated at Mayo Clinic.

## RESULTS

### FIGURE 1: *Leptotrichia* species identified in clinical isolates




### TABLE 1: Antimicrobial susceptibility profile of *Leptotrichia* spp.

| Antibiotic | Isolates | % susceptible (MIC) | % intermediate (MIC) | % Resistant (MIC) |
|---|---|---|---|---|
| Clindamycin | 22 | 100 (≤2 mcg/mL) | 0 (4 mcg/mL) | 0 (>4 mcg/mL) |
| Metronidazole | 22 | 90.0 (≤8 mcg/mL) | 9.1 (16 mcg/mL) | 0 (>16 mcg/mL) |
| Penicillin | 22 | 100 (≤0.5 mcg/mL) | 0 (1 mcg/mL) | 0 (>1 mcg/mL) |
| Ertapenem | 12 | 100 (≤4 mcg/mL) | 0 (8 mcg/mL) | 0 (>8 mcg/mL) |
| Piperacillin-Tazobactam | 12 | 100 (≤32/4 mcg/mL) | 0 (64/4 mcg/mL) | 0 (>64/4 mcg/mL) |
| **Moxifloxacin** | 10 | 0 (≤2 mcg/mL) | 0 (4 mcg/mL) | 100 (>4 mcg/mL) |

### TABLE 2: Baseline clinical demographics of patients with *Leptotrichia* BSI

| Patient demographics | Patients (n = 26) |
|---|---|
| Age (mean [SD]) (year) | 54.6 (16.6) |
| Sex | |
| Female | 9 (34.6) |
| Male | 17 (65.6) |
| Charleston comorbidity index (median [IQR]) | 5 (4-6) |
| Pitt bacteremia score | |
| 0 | 18 (69.2) |
| 1 | 5 (19.2) |
| 2 | 3 (11.5) |
| Immunocompromising condition | 26 (100) |
| Hematologic malignancy | 18 (69.2) |
| Hematopoietic stem cell transplant | 6 (23.1) |
| Solid organ transplant | 1 (3.8) |
| Pharmacologic immunosuppression | 1 (3.8) |
| Patients with neutropenia | 25 (96.2) |
| Time from severe neutropenia onset to BSI (median [IQR]) (days) | 7 (5-10) |
| Antimicrobial prophylaxis during 30-days preceding BSI | 18 (69.2) |
| Fluoroquinolone | 6 (23.1) |
| Penicillin | 5 (19.2) |
| Trimethoprim/sulfamethoxazole | |
| Duration of hospitalization (mean [range]) (days) | 18.2 (12.2) |
| Need for ICU care | 4 (15.4) |

### TABLE 3: Characteristics and outcomes of *Leptotrichia* BSI management

| Leptotrichia BSI characteristics and outcomes | Patients (n=26) |
|---|---|
| Source of bacteremia | |
| Gastrointestinal source | 15 (57.7) |
| CRBSI | 9 (34.6) |
| Dental or oropharyngeal | 4 (15.4) |
| Respiratory | 1 (3.8) |
| No source identified | 1 (3.8) |
| Presence of polymicrobial bacteremia | 10 (38.5) |
| Antimicrobial susceptibility testing performed | 22 (84.6) |
| Antimicrobial treatment directed at Leptotrichia | |
| Penicillin | 2 (7.7) |
| Aminopenicillin + B-lactamase inhibitor | 2 (7.7) |
| Piperacillin-Tazobactam | 7 (26.9) |
| Carbapenem | 5 (19.2) |
| Fluoroquinolone | 3 (11.5) |
| Metronidazole | 11 (42.3) |
| **Duration of antimicrobial treatment (mean [SD]) (days)** | **11.0 (4.5)** |
| **All-cause mortality*** | **5 (19.2)** |
| **Microbiologic relapse**** | **0** |

**Figure legend:** * All-cause mortality (measured at 60-days post-therapy). ** Microbiologic relapse (defined as BSI with same organism within 90-days)

## TAKE-HOME SUMMARY

*L. wadei, L. buccalis*, and *L. trevisanii* were primary causes of BSI. All species have favorable AST, except for uniform resistance to Moxifloxacin.

All patients with BSI were immunocompromised, with median 7-days from neutropenia to BSI. Majority were on Fluroquinolone prophylaxis.

Sources of BSI were due to mucositis/enterocolitis or vascular catheter infection. BSI was frequently polymicrobial (*S mitis* or anaerobes).

Primary treatment regimens included: Flagyl, Zosyn, or Ertapenem. Mean duration of therapy was 11 days, with no microbiologic relapse.

## DISCUSSION AND CONCLUSION

*Leptotrichia spp.* are a rare, but important cause of BSI in severely neutropenic patients with disrupted mucosal barriers.

*Leptotrichia spp.* are resistant to Fluroquinolones, which form the backbone of prophylactic therapy in hematologic malignancy and HSCT.

Future studies should focus on determining optimal regimens, duration of therapy, and outcomes including attributable mortality.

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