Stenotrophomonas maltophilia: Changing Spectrum of a Serious Bacterial Pathogen in Patients with Cancer

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Stenotrophomonas maltophilia colonization/infection in patients with cancer has significantly increased over the past 2 decades. Patients with prolonged neutropenia, exposure to broad-spectrum antibiotics, and those requiring mechanical ventilation have higher risk of infection. These micro-organisms are intrinsically resistant to carbapenems, and exposure to these agents has been linked to selection of S. maltophilia. Recently, these infections are being documented in patients without traditional risk factors. The spectrum of infection includes bacteremia, catheter-related infection, pneumonia, complicated biliary and urinary tract infection, and skin and skin-structure infection. Trimethoprim-sulfamethoxazole is the therapeutic agent of choice, but resistance is increasingly being reported. Susceptibility to alternative agents is unpredictable. Combination therapy and alternative routes of drug administration, such as aerosolized aminoglycoside, might be necessary. New insights into the mechanisms of drug resistance might lead to identification of new target sites. Agents that improve outer-membrane permeability and broad-spectrum β-lactamase inhibitors may favorably impact difficult-to-treat (i.e., multidrug resistant) S. maltophilia infections.

Patients with cancer, particularly those with profound and prolonged neutropenia, continue to be at risk for serious infection [1, 2]. In most cancer centers, gram-positive bacteria are isolated more frequently than are gram-negative bacilli (GMB) [3]. Despite a decrease in the frequency of gram-negative infections, the proportion caused by nonfermentative GNB (NF-GNB) such as Stenotrophomonas maltophilia has increased [4–6]. Furthermore, a substantial number of cases of S. maltophilia bacteremia in patients with cancer are associated with high bacterial load [2], which may represent increasing severity of infection [7]. This review will focus on the emergence of S. maltophilia as a serious pathogen in patients with cancer.

RISK FACTORS AND EPIDEMIOLOGY

Since the 1980s, S. maltophilia has been increasingly isolated from immunosuppressed as well as immunocompetent patients [6]. Most infection occurs (1) after an extended stay in critical care units; (2) following prolonged (>7 days) mechanical ventilation [8]; (3) in patients with tracheostomy [9]; and (4) in patients with exposure to broad-spectrum antimicrobial agents, such as the carbapenems, extended-spectrum cephalosporins, and fluoroquinolones [6, 8, 9]. These organisms are intrinsically resistant to carbapenems, and exposure to these agents may perpetuate overgrowth and facilitate subsequent superinfection more so than other agents [10]. Additional risk factors include (1) chemotherapy-induced neutropenia (absolute neutrophil count, <500 cells/μL); (2) leukemia or refractory lymphoma [11, 12]; (3) orointestinal mucosal damage after chemotherapy, radiation, or graft-versus-host disease [13]; and (4) diarrhea [14]. Persistent or recurrent infection has been associated with infected foreign bodies [11]. Infection of the urinary or hepatobiliary tract is seen in select groups of patients, including (1) those with obstruction due to tumor mass, (2) those who have experienced fibrosis caused by radiation therapy or surgery, (3) those with other structural abnormalities, and (4) those who have undergone instrumentation [15, 16]. S. maltophilia infection is being seen in patients with cancer who do not have the aforementioned risk factors, and some of these infections are community acquired [17].

Susceptibility surveillance studies conducted at The M. D. Anderson Cancer Center (Houston) have clearly demonstrated the increasing frequency of S. maltophilia infection (table 1).
The increased bacterial load associated with *S. maltophilia* and *P. aeruginosa* (table 2) [2]. The indicators for poor outcome in patients with cancer [12–14]. Other institutions have also reported an increase in the proportion of *S. maltophilia* to the fifth most common. These studies were conducted in 1986–2002 and document an increase in the proportion of *S. maltophilia* from 2% of all GNB isolated in 1986 to 7% in 2002. During this time period, *S. maltophilia* increased from being the ninth most common gram-negative isolate to the fifth most common. Other institutions have also reported an increase in *S. maltophilia* infection in patients with cancer [12–14].

Furthermore, at our institution, moderate-to-high–grade bacteremia ranged from 39% in 1998 to 42% in 2004 [2]. A significant (13%) increase in moderate-to-high–grade *S. maltophilia* bloodstream infection occurred, in contrast to a slight (3%) decrease in similar infection due to *Pseudomonas aeruginosa* (table 2) [2]. The increased bacterial load associated with *S. maltophilia* bacteremia may reflect increasing severity of these infections [2, 7].

Recovery of *S. maltophilia* does not always indicate the presence of an infection. Skin and gastrointestinal colonization are important sources of *S. maltophilia* infection. Intestinal colonization may occur after fluoroquinolone prophylaxis. In a surveillance study, *S. maltophilia* colonization was identified in 10% of hospitalized neutropenic patients [20]. However, none of these patients developed invasive *Stenotrophomonas* infection during a 6-month follow-up period [20].

*Stenotrophomonas* respiratory-tract colonization may occur in the following situations: (1) prolonged stay in critical care units; (2) prolonged exposure to antibiotics, including fourth-generation cephalosporins and carbapenems; and (3) in patients with tracheostomy [8, 21]. In patients who develop *Stenotrophomonas* pneumonia, respiratory-tract colonization often precedes infection.

### CLINICAL MANIFESTATIONS

Although the epidemiology of *S. maltophilia* appears to be changing, the majority of infections are still encountered in patients with risk factors as outlined above. Salient features of *S. maltophilia* infections are outlined in table 3 and are discussed below.

### CATHETER-RELATED BACTEREMIA

Most *S. maltophilia* bacteremias in patients with cancer are associated with infected in-dwelling intravascular devices [22, 25]. These infections may be seen in patients without traditional risk factors [22, 25]. Polymicrobial infections are common in this setting [22, 25]. Catheter-related –*S. maltophilia* bacteremia responds well to removal of the infected catheter and appropriate antibiotic therapy. In nearly one-third of patients, infection may relapse after prolonged latency [26]. Relapse may be significantly reduced by early (<72 h) catheter removal [27].

### NON–CATHETER-RELATED BACTEREMIA

Non-CR *S. maltophilia* bacteremia is a serious infection and is associated with a high rate of treatment failure and infection-associated deaths [22, 28]. Patients often have severe and prolonged (>10 days) neutropenia, and, in most patients (>70%), the primary site of infection is pneumonia [29, 34] or soft tissue [35, 36]. These infections occur in patients after prolonged hospitalization (>3 weeks), often while receiving antineoplastic therapy and broad-spectrum antibiotic therapy [14, 29, 34, 35]. The indicators for poor outcome in patients with cancer with *S. maltophilia* non–catheter-related bacteremia include prolonged (>10 days) neutropenia, bacteremic pneumonia, shock syndrome, thrombocytopenia, and inappropriate initial antimicrobial therapy [29, 34, 35].

In neutropenic patients, multiple-strain *S. maltophilia* bacteremia may occur [36]. Genetically and morphologically distinct strains may have different virulence and antimicrobial susceptibility profiles, which may have an impact on choice and outcome of therapy.

### Table 1. Gram-negative bacilli isolated from patients with cancer at MDACC during survey periods, 1986–2002, documenting increasing isolation rates of *Stenotrophomonas maltophilia*.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-negative isolates, no.</td>
<td>851</td>
<td>679</td>
<td>758</td>
<td>903</td>
<td></td>
</tr>
<tr>
<td><em>S. maltophilia</em>b isolates, no. (%)</td>
<td>22 (2)</td>
<td>23 (3)</td>
<td>45 (6)</td>
<td>61 (7)</td>
<td></td>
</tr>
</tbody>
</table>

**NOTE.** Data are from [18–22]. MDACC, The M. D. Anderson Cancer Center, University of Texas.

a 20% were isolated from blood culture samples, 37% from urine, 19% from respiratory, and 24% from samples obtained from other body sites.

b *S. maltophilia* increased from the ninth-most commonly isolated gram-negative rod in 1986 to the fifth-most common in 2002 (P = .001).

### Table 2. Bacterial load among gram-negative bacilli isolated from patients with cancer at MDACC, 1998–2004, documenting increased association of *Stenotrophomonas maltophilia* with moderate-to-high–grade bacteremia.

<table>
<thead>
<tr>
<th>Blood culture isolates associated with moderate-to-high bacterial loada</th>
<th>No. (%) of isolates</th>
<th>1998</th>
<th>2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-negative isolates</td>
<td>111 (39)b</td>
<td>78 (42)c</td>
<td></td>
</tr>
<tr>
<td><em>S. maltophilia</em> isolates</td>
<td>4 (4)</td>
<td>13 (17)</td>
<td></td>
</tr>
<tr>
<td><em>P. aeruginosa</em> isolates</td>
<td>14 (13)</td>
<td>8 (10)</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter isolates</td>
<td>7 (6)</td>
<td>8 (10)</td>
<td></td>
</tr>
</tbody>
</table>

**NOTE.** *S. maltophilia* and acinetobacter high-grade bacteremia increased 47% in 2004, from 19% in 1998, whereas *Pseudomonas aeruginosa* high-grade bacteremia incidence in 1998 and 2004 was comparable (29% vs. 23%); the increase in high-grade bacteremia that was due to non-*Pseudomonas* non-fermentative gram-negative bacteria was significant (P <.05). Data are from [2]. GNB, gram-negative bacilli; MDACC, The M. D. Anderson Cancer Center, University of Texas.

a Moderate and high bacterial loads were evaluated by standard quantitative culture methods, defined as 101–500 cfu/mL and >500 cfu/mL, respectively.

b Of 284 total GNB.

c Of 186 total GNB.

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Table 3. Clinical manifestations and common sites of infection associated with *Stenotrophomonas maltophilia* in patients with cancer.

<table>
<thead>
<tr>
<th>Manifestation/sites</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonization</td>
<td>Various sites, such as the respiratory tract, skin, and gastrointestinal tract</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>Often catheter related</td>
</tr>
<tr>
<td>Septic thrombophlebitis</td>
<td>Septic emboli not uncommon, although, for patients with cancer and severe thrombocytopenia, ultrasonography may not be sensitive, and correct diagnosis requires venography</td>
</tr>
<tr>
<td>Respiratory and urinary tract infections</td>
<td>Usually in patients with foreign body or structural abnormalities</td>
</tr>
<tr>
<td>Skin and skin-structure infections</td>
<td>Indistinguishable from other causes; deep-tissue involvement, including pyomyositis, may occur</td>
</tr>
<tr>
<td>Other less common <em>S. maltophilia</em> infections, including meningitis, mastoiditis, conjunctivitis, epididymitis, and hepatobiliary infections</td>
<td>Seen in patients with obstruction and in the presence of a foreign device</td>
</tr>
<tr>
<td>Disseminated infection</td>
<td>Often with multiorgan involvement and multisystem failure</td>
</tr>
</tbody>
</table>

**NOTE.** Data are from [14–19, 25–33].

*S. maltophilia* sepsis syndrome has also been noted in patients with severe and prolonged (>3 weeks) mucositis [14] and/or necrotizing gingivitis [37] that presents with pain unresponsive to narcotic analgesic, extensive oral ulceration and/or necrosis, bleeding, and pseudomembrane formation. Life-threatening viridans streptococcal sepsis is a well-recognized complication in this group [38]. *S. maltophilia* should also be considered when starting empirical therapy for ill-appearing febrile neutropenic patients with extensive oro-intestinal mucositis.

**ENDOCARDITIS**

Endocarditis due to *S. maltophilia* is rare in patients with cancer. Most patients who develop endocarditis have an identifiable risk factor, such as (1) recent heart-valve replacement, (2) surgery for correction of congenital heart disease, and (3) history of injection drug use [39, 40]. Infected catheters are an uncommon cause of *S. maltophilia* endocarditis [39]. The aortic valve is a common site for native valve infection. Over 70% of patients who have endocarditis develop complications such as septic embolism, and myocardial abscess. Early removal of infected prosthetic heart sepsis is critical. Despite appropriate therapy, mortality is high (36%–39%) [39, 40]. *S. maltophilia* endocarditis should be suspected in neutropenic patients with fever and persistent or recurrent catheter-related *S. maltophilia* bacteremia. In febrile neutropenic patients receiving broad-spectrum antibiotics, culture-negative endocarditis may occur, and antimicrobial therapy for *S. maltophilia* infection should be considered [41].

**SKIN AND SKIN-STRUCTURE INFECTION**

Neutropenic patients with leukemia may develop hematogenous *S. maltophilia* skin infection [30, 31]. Lesions are either localized or involve various body sites, including extremities. Initially, lesions are tender and are annular in shape, with a violaceous center. The violaceous center subsequently undergoes necrosis, and the lesions resemble ecthyma gangrenosum.

Other conditions that resemble *S. maltophilia* skin infection include pyoderma gangrenosum, leukemia cutis, vasculitis, and disseminated infections caused by *Pseudomonas* species, *Fusarium* species, *Candida* species, and rapidly growing mycobacteria. We suggest early diagnostic skin biopsy, even in patients with known *S. maltophilia* infection, because multiple opportunistic infections can coexist, especially in patients with cancer and severe and prolonged neutropenia, and in stem cell–transplant recipients receiving treatment with high-dose corticosteroids. In patients with *S. maltophilia* cellulitis, deep-tissue involvement such as bacterial pyomyositis [42] needs to be considered. Patients with pyomyositis require surgical debridement in addition to antimicrobial therapy.

**PULMONARY INFECTION**

*S. maltophilia* pneumonia is seen most often in patients with cancer who require prolonged mechanical ventilation. It is also seen in patients with leukemia, most of whom are neutropenic when they develop pneumonia. The infection is often preceded by respiratory-tract colonization with *S. maltophilia* [43, 44]. Infection is often accompanied by a paucity of acute inflammatory response. Focal lung necrosis and hemorrhage are frequent histologic features of *S. maltophilia* pneumonia [43]. Lobular or lobar consolidation is common, whereas pleural effusions are uncommon, and cavitary lesions are seldom seen. Radiographic features of lung infection in immunosuppressed patients with cancer must be interpreted with caution, because other bacteria—including *Nocardia* species, opportunistic fungi, and viral pneumonitis—may coexist in patients with *S. maltophilia* pneumonia. Postviral bacterial superinfection due to NF-GNB, such as *Pseudomonas* species, has been described. In patients with cancer, *S. maltophilia* superinfection may occur.
in the severely immunosuppressed patients with prolonged neutropenia, or stem cell transplant recipients with graft-versus-host disease [45]. We recommend that, for high-risk patients with cancer who present with postviral secondary lung infection, non-*Pseudomonas* NF-GNB be considered during selection of empirical therapy. Necrotizing *S. maltophilia* pneumonia is a serious complication, and despite appropriate therapy, many patients may die because of progressive infection [38] or pulmonary hemorrhage [46]. The infection-associated deaths in patients with cancer with *S. maltophilia* lung infection is high (≥50%) [43, 44]. Patients with bacteremic pneumonia, refractory neutropenia, sepsis syndrome, and delayed appropriate antimicrobial therapy have higher probability of poor outcome.

The presence of obstructive lung cancer creates a milieu for various pathogens, including *S. maltophilia*, especially in those patients with chemotherapy-induced neutropenia or exposure to broad-spectrum antibiotics [43, 44]. Presence of bronchial obstruction is another indicator of poor outcome.

Recently, we reported *S. maltophilia* pneumonia in patients with cancer who had no known traditional risk factors [17]. The disease spectrum was significantly different in these patients, because fewer patients were exposed to carbapenems, had hematologic malignancy, or had nosocomial pneumonia. Bacteremic pneumonia was also less common in these patients than in patients with cancer who had traditional risk factors for *S. maltophilia* pneumonia [17]. Nearly one-third of patients with community-acquired *S. maltophilia* were treated with oral antibiotics and did not need hospitalization. However, among patients who were hospitalized, nearly 30% required critical care unit stay, and duration of critical care unit stay was comparable to patients with *S. maltophilia* pneumonia with traditional risk factors. The overall outcome was similar in both groups, and only stay in critical unit predicted poor outcome [17].

**MENINGITIS**

*S. maltophilia* meningitis is rare, and as with other site-specific (urinary or biliary tract) infections in immunosuppressed patients with cancer, recent history of instrumentation is often present. Gram-negative bacterial meningitis is a known complication after neurosurgical procedures. In patients with meningeval carcinomatosis and who do not respond to empirical broad-spectrum antibiotic therapy, *S. maltophilia* meningitis may be considered for patients who have recently undergone a neurosurgical procedure [32].

**TREATMENT CONSIDERATIONS**

**Antimicrobial resistance.** Trimethoprim-sulfamethoxazole (TMP-SMX) has the most potent and reliable in vitro activity against *S. maltophilia* [33, 47–51]. Early reports documented >98% susceptibility of *S. maltophilia* isolates to TMP-SMX; however, increasing resistance rates (30%–40%) to this agent are being reported [52]. The mechanism(s) of resistance to TMP-SMX is not well understood. Plasmid-mediated resistance due to the presence of the sulI gene has been described for 3 clones that had elevated MICs for TMP-SMX [53]. Outer-membrane impermeability makes *S. maltophilia* intrinsically less susceptible to β-lactam antibiotics; <5% of β-lactam antimicrobials penetrate *Stenotrophomonas*. [54]. Several β-lactams have been reported to have variable activity (40%–70%) against *S. maltophilia*, including the cephalosporins ceftazidime and cefepime and β-lactam/β-lactamase inhibitor combination agents, such as ticarcillin-clavulanate and piperacillin-tazobactam [55–57]. The addition of aztreonam to ticarcillin-clavulanate enhances the in vitro activity compared with ticarcillin-clavulanate alone [57]. β-Lactam resistance is due to inducible β-lactamases types L 1 and L 2. Type L 1 metallo-β-lactamase is capable of hydrolyzing almost all β-lactam classes and is not inhibited by clavulanic acid. It, however, does not hydrolyze aztreonam [58]. In contrast, type L 2 serine-β-lactamase hydrolyzes aztreonam and is inhibited by clavulanic acid and other β-lactamase inhibitors [59, 60].

The aminoglycosides have poor activity against *S. maltophilia*. Several mechanisms of aminoglycoside resistance have been described, including outer-membrane changes, target modification, aminoglycoside-modifying enzymes, and efflux-mediated mechanisms.

Efflux-pump mechanisms conferring multidrug resistance have been identified as an important resistance mechanism among *S. maltophilia* isolates [61, 62]. A novel multidrug efflux pump, SmeDEF, has recently been cloned and characterized. It is expressed in ~33% of isolates and results in increased MICs of several antimicrobial agents (i.e., tetracycline, erythromycin, cloramphenicol, norfloxacin, and ofloxacin) [61]. The quinolones have variable in vitro activity against *S. maltophilia*, and newer quinolones, such as moxifloxacin, are superior to older ones, such as ofloxacin and ciprofloxacin [4, 52]. Mutational resistance to quinolones is either target-site mutation in DNA gyrase or via derepression of outer-membrane efflux pumps [62].

Minocycline and the novel glycycline tigecycline are active against *S. maltophilia*, and susceptibility rates of >87% to tigecycline were recently reported [63, 64]. Clinical experience with this agent is scarce. Colistin and polymyxin B have in vitro activity against most clinical isolates of MDR *Pseudomonas* species, whereas these agents show limited activity against most isolates of *S. maltophilia* [65]. Chloramphenicol may also be active against some *S. maltophilia* isolates. In vitro studies evaluating synergy of various drug combinations against strains of *S. maltophilia* have been published [66]. Synergy or improved killing of bacteria has been demonstrated for combinations such
as colistin plus rifampin, colistin plus TMP-SMX, and quinolones plus β-lactams. Some studies have also demonstrated synergy between TMP-SMX and ticarcillin-clavulanate [66]. These data suggest that combination antibiotic therapy for S. maltophilia infection may be superior to monotherapy.

In vitro susceptibility testing for S. maltophilia remains problematic. The accuracy of various methods and the correlation between the different methods and outcome have been questioned, with discrepancies being reported between various methods [67, 68]. Interpretation of in vitro results after 48 h of incubation, instead of 16–18 h, has also been recommended [53]. This highlights the need for developing more-reliable and -accurate methods for in vitro testing.

**Antimicrobial therapy.** TMP-SMX is still considered the drug of choice for the treatment of S. maltophilia infection, despite increasing resistance (table 4). Some authors have even recommended desensitization in patients who have serious S. maltophilia infection and are intolerant to sulfa drugs [69]. The dose of TMP-SMX is similar to that used to treat *Pneumocystis jiroveci* pneumonia (≥15 mg/kg/day), especially for patients with disseminated infection [51]. Alternative agents, such as β-lactams (ticarcillin-clavulanate and ceftazidime), fluoroquinolones (ciprofloxacin), minocycline, and chloramphenicol, have been used with variable success and most often in combination regimens. The newer fluoroquinolones, such as moxifloxacin, appear to be more active than older agents, such as ciprofloxacin, because they inhibit many ciprofloxacin-resistant strains [71]. This differential activity might be clinically important, because nearly one-half of S. maltophilia blood culture isolates from neutropenic patients [72], and a substantial proportion of isolates obtained from lower respiratory samples are resistant to ciprofloxacin [73]. Although clinical data are scant and the emergence of quinolone resistance is a concern, we consider moxifloxacin to be the preferred quinolone, and we recommend its use in combination with other agents to which the organisms are susceptible, particularly in patients intolerant of TMP-SMX.

The role of combination therapy remains unclear. Several authors prefer combination regimens for the treatment of serious S. maltophilia infection, particularly in individuals immunocompromised because of the bacteriostatic mode of action of most agents and the potential for the development of resistance during monotherapy [56]. Strategies for salvage therapy of MDR *P. aeruginosa* infection include combining agents that individually have limited activity against the organism [74–76]. Similar strategies might be useful for the treatment of S. maltophilia infection. The efficacy of various combinations—such as quinolones, β-lactam, aminoglycosides, and glycyccyclines—with each other or TMP-SMX is unknown and needs clinical evaluation. Additionally, aztreonam has been shown to be an effective β-lactamase inhibitor for *P. aeruginosa*–derived metallo-β-lactamases [77]. Aztreonams capacity to preserve the activity of β-lactams such as ticarcillin-clavulanate and ceftazidime needs to be studied, particularly in infection due to refractory MDR S. maltophilia. At our institution, the efficacy of inhaled aminoglycoside plus systemic antibiotic combination therapy in patients with cancer who have GNB ventilator-associated pneumonia appears promising and is tolerated without serious adverse events [78].

**Future treatment consideration.** Agents that may help to overcome resistance to antibiotics include inhibitors of bacterial β-lactamases. Clavulanate in combination with ticarcillin is an effective combination against *Pseudomonas* species; however, its ability to inhibit increasingly refractory chromosomal β-lactamase produced by MDR-NF-GNB is limited. Investigational agents (e.g., BRL42715 [79]) and broad-spectrum inhibitors (e.g., cephems, sulfones, and oxapenems) may provide effective β-lactamase inhibition for less-responsive β-lactamases targets [80].

Agents that increase outer-membrane permeability may improve therapeutic efficacy of antibiotics. Recombinant peptides have been shown to increase outer-membrane permeability for lysozyme and certain antimicrobial agents [81]. These recombinant hybrid peptides may abrogate the central mechanism of intrinsic bacterial drug resistance and perhaps restitute antimicrobial activity of the currently available drugs.

The results for oral and nasal vaccination against *Pseudomonas* and *Burkholderia* species appear promising [82, 83]. Vaccination may be an alternative approach to reducing colonization and infection due to *Stenotrophomonas* infection. Another interesting approach in promoting the host’s immune defenses against gram-negative bacterial infection includes recombinant antimicrobial peptides that constitute an important

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**Table 4. In vitro activity of antimicrobial agents against *Stenotrophomonas maltophilia* isolated from patients with cancer.**

<table>
<thead>
<tr>
<th>Antimicrobial(s) tested</th>
<th>MIC&lt;sub&gt;50&lt;/sub&gt;–MIC&lt;sub&gt;90&lt;/sub&gt;, μg/mL</th>
<th>Isolates susceptible to antimicrobial tested, % range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>64–512</td>
<td>2–32</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>64–512</td>
<td>6</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>8–256</td>
<td>15–24</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>512–512</td>
<td>0</td>
</tr>
<tr>
<td>Colistin</td>
<td>16–128</td>
<td>26</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>2–32</td>
<td>16–61</td>
</tr>
<tr>
<td>Imipenem</td>
<td>128–256</td>
<td>0–2</td>
</tr>
<tr>
<td>Minocycline&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1–4</td>
<td>97</td>
</tr>
<tr>
<td>Polymyxin B</td>
<td>8–64</td>
<td>35</td>
</tr>
<tr>
<td>Ticarcillin-clavulanate</td>
<td>16–128</td>
<td>43–58</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>0.25–4.75</td>
<td>75–98</td>
</tr>
</tbody>
</table>

**NOTE.** Data are from [49, 50, 69, 70].

<sup>a</sup> S. maltophilia isolated mostly from immunocompetent patients have shown >90% susceptibility to tigecycline.
acellular innate immune response. β-Defensins are bactericidal against most disease-associated strains of gram-negative and gram-positive bacteria; however, these agents probably need to be delivered intranasally or via aerosolized route, because the presence of human serum neutralizes their microbicidal effect [84]. Further research is needed in evaluation of clinical implications of these novel therapeutic interventions.

*S. maltophilia* has been shown to increase local inflammatory response in the respiratory tract in recent ex vivo and animal experiments [85]. Macrophage-derived TNF-α plays a central role in promoting this immunostimulatory response [85]. Targeted cytokine neutralization or focal, transient TNF-α suppression may provide important alternatives for disease modification in the respiratory tract.

**SUMMARY**

*S. maltophilia* is associated with a wide spectrum of diseases and substantial morbidity/mortality in immunosuppressed patients with cancer. Selection pressure created by exposure to broad-spectrum agents, particularly the carbapenems, is an important risk factor [70, 86]. Serious *S. maltophilia* infection is being encountered in patients with cancer who do not have traditional risk factors [17, 87]. Antimicrobial resistance is on the rise. Newer target sites for drug therapy are being identified as our understanding of the complex mechanisms of drug resistance and hosts immune/inflammatory response increases [80, 81, 84, 85].

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