

Clinical Microbiology 2015: Effects of select chemicals on the opportunistic multidrug-resistant bacterial pathogen, *Stenotrophomonas maltophilia* and its bio-film- Joanna S Brooke- DePaul University

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Abstract

Stenotrophomonas maltophilia may be a global human opportunist which is related to infections that include those of the tract, bloodstream, soft tissue and bone, eye, heart and brain. *S. maltophilia* infection is of serious concern in immunocompromised patients and a high death rate has been reported. This bacterium is found in water, washed foods, plant roots and soils and animals. Hospital-acquired and community-acquired infections of *S. maltophilia* have been reported. Antimicrobial resistance surveillance monitoring networks worldwide report a steady rise in the number of drug-resistant strains of *S. maltophilia* recovered from patients. *S. maltophilia* is resistant to a wide range of antimicrobials, including beta-lactams, fluoroquinolones, aminoglycosides, polymyxins, macrolides, carbapenems, tetracyclines, chloramphenicol and trimethoprim-sulfamethoxazole. Intrinsically drug-resistant strains of *S. maltophilia* are recovered from environments outside of the clinical setting. New strategies are needed to prevent/challenge *S. maltophilia* infections. *S. maltophilia* forms biofilms on medical devices and on living tissues. One of the goals of our laboratory is to study the molecular mechanisms used by this pathogen to form biofilms and subsequently identify suitable targets for treatment strategies to prevent/inhibit *S. maltophilia* growth, biofilms, and cell survival. We have observed that *S. maltophilia* is in a position to make biofilms on PVC, polystyrene and glass. We have screened various chemicals and observed that the growth and biofilm formation of *S. maltophilia* can be hindered. We will report on recent studies that examine the consequences of select chemicals on the expansion, biofilm development and survival of *S. maltophilia*.

INTRODUCTION

Clinical microbiologists have long recognized the importance of identifying infectious microbial pathogens as the cause of disease in humans. The emergence of new multiple-drug-resistant (MDR) organisms (MDROs) found in nonclinical environments, the increasing reports of community-acquired infections, and the spread of these pathogens in the clinical setting have all underscored the need to monitor these organisms. The increase in reported cases of MDRO-associated infections has resulted in efforts to examine possible sources of these pathogens, assess the current antimicrobial strategies used

for the treatment of infections, and elucidate the molecular mechanisms used by these pathogens during infection and disease.

Gram-negative bacterial pathogens have received much attention, as they're often MDROs thanks to multidrug resistance pumps, plasmids harboring antibiotic resistance genes, and various gene transfer mechanisms involved within the acquisition of antimicrobial resistance. *Pseudomonas aeruginosa* is an example of such an MDRO that causes respiratory infections in patients, particularly those with CF (CF) or those with chronic lung diseases. *P. aeruginosa* has been reported to survive for months on dry surfaces (180), and it is able to persist and grow in contaminated antimicrobial hand soap containing triclosan, making it a significant issue of concern for hospital staff.

Stenotrophomonas maltophilia is an environmental global emerging Gram-negative MDRO that's most ordinarily related to respiratory infections in humans. It can cause various serious infections in humans. This current review focuses on the strategies used or being developed to treat infections associated with *S. maltophilia*; the cellular and molecular mechanisms important for its survival, persistence, and pathogenesis; and its multiantibiotic resistance and provides a comparison of clinical and environmental *S. maltophilia* isolates.

MICROBIOLOGY

Characteristics of *S. maltophilia*

S. maltophilia is a Gram-negative obligate aerobe that is rod shaped and motile with a few polar flagella. It is able to persist in nutrient-poor aqueous environments. The growth characteristics of *S. maltophilia*. Standard microbiology reference data currently indicate that *S. maltophilia* is an oxidase-negative bacterium. Recent data, however, suggest that some *S. maltophilia* isolates are oxidase positive.

Burdge et al. reported the misidentification of *S. maltophilia* as *Pseudomonas cepacia*. In that study, 3 (9%) of 32 clinical isolates were incorrectly identified as being *P. cepacia* isolates as a result of a delayed reading (3 min instead of within 1 min) of the oxidase test and not holding the tests for DNase

production 72 h prior to observation of the results. The misinterpretation of those tests has clinical importance, as *P. cepacia* is a significant pathogen in CF patients.

S. maltophilia has been coisolated with other microorganisms (e.g., *Pseudomonas aeruginosa*, *Burkholderia* species, *Staphylococcus aureus*, methicillin-resistant *S. aureus*, *Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella* species, *Enterobacter* species, *Enterococcus* species, *Bacteroides* species, *Corynebacterium* species, and *Candida albicans*) in samples recovered from patients. The non-fermenting Gram-negative bacteria *P. aeruginosa*, *A. baumannii*, and *S. maltophilia* are all pathogens of the human tract. The reader is directed to recent publications for further information about the relationship of *S. maltophilia* to *P. aeruginosa* and *A. baumannii*. Selective agar media are designed to enhance the isolation of *S. maltophilia* from polymicrobial cultures.

To improve the isolation of *S. maltophilia* from CF patient sputum samples, VIA medium, containing vancomycin, imipenem, and amphotericin B, was developed. VIA medium consists of a mannitol agar base with a bromthymol blue (BTB) indicator, 5 mg/liter vancomycin, 32 mg/liter imipenem, and 4 mg/liter amphotericin B. A comparison of *S. maltophilia* colony counts recovered from sputum samples on VIA medium with counts on bacitracin (10,000 U/liter) chocolate (BC) medium revealed that VIA medium detected a better ($P < 0.0001$) number of *S. maltophilia*-positive samples than BC medium with an imipenem disk on its surface. VIA medium was particularly useful for the detection of low colony counts (102 to 106 CFU/ml) (77).

Gram-negative selective agar (GNSA) medium was later developed by Moore et al. to detect Gram-negative microflora in CF patient sputa. GNSA medium contains novobiocin (5 mg/liter), cycloheximide (100 mg/liter), amphotericin (2 mg/liter), nisin (48 mg/liter), and crystal violet (2 mg/liter) and detects 6.70×10^3 CFU of *S. maltophilia*/ml sputum. Other Gram-negative organisms recovered from adult CF patients and ready to grow on this selective medium include *P. aeruginosa*, *Burkholderia cepacia*, *E. coli*, and *Alcaligenes xylosoxidans*. This medium is beneficial for high-throughput specimen screening, because it is compatible with semiautomerization

using digital image capture and processing with transilluminant white light.

Culture media are developed to differentiate between the bacterial species present in mixed culture samples (e.g., colony color differences between *S. maltophilia* and *P. aeruginosa* reflect their different metabolic abilities). The production of acid from maltose but not from glucose by *S. maltophilia* has been used to distinguish it from *P. aeruginosa*, as *P. aeruginosa* produces acid from glucose and does not use maltose or lactose to a great extent. Colonies of *S. maltophilia* appear yellow and blue on BTB-containing medium containing maltose and glucose, respectively, in contrast to *P. aeruginosa* colonies, which appear blue on BTB medium containing maltose and yellow green on medium containing glucose. A selective and differential agar medium, SM2i, contains Mueller-Hinton agar supplemented with maltose, dl-methionine, vancomycin, imipenem, amphotericin B, and bromthymol blue. *S. maltophilia* colonies are smooth, round, and green, with a green center with a peripheral lighter green area or a dark green center with a green peripheral area surrounded by a blue-green halo. The colony appearance of *S. maltophilia* is definitely distinguished from those of other Gram-negative bacteria, such as *P. aeruginosa*, which appears white or colored but very often silver, or *E. faecium*, which appears minute and colorless. In one study, this medium was successfully used to recover *S. maltophilia* from water samples and cotton swab samples of cold water taps. Another study using this medium resulted in an increased awareness by health care workers of the importance of strict adherence to hand hygiene measures, the use of point-of-use (POU) water filtration, and regular maintenance of swan-necked faucets with a regimen of descaling, disinfection, and drying.

S. maltophilia could also be related to polymicrobial infections or grow slowly within the host, leading to some difficulty in isolating this bacterium. Various molecular biology techniques have been used to identify different strains of *S. maltophilia*. PCR amplification of the 16S rRNA gene has been used to detect *S. maltophilia* in blood samples of patients undergoing chemotherapy for leukemia or myelodysplastic syndrome. That study suggested that PCR analysis of blood would be useful for cases where the bacterial species grows poorly in blood culture medium.