ABSTRACT

Background
Studies indicate that elderly patients are often inappropriately treated with antimicrobials for asymptomatic bacteriuria (ASB). Interprofessional education may help improve the assessment and management of ASB.

Methods
Retrospective chart audits were conducted on two cohorts of positive urine cultures (n = 201) obtained from a geriatric acute care unit to determine the incidence of treated ASB. The first cohort (n = 101) was analyzed from January to July 2017. Education was provided to unit staff (e.g., nurses, physicians, pharmacists) in Fall 2017. The second cohort (n = 100) was analyzed from January to July 2018. Descriptive statistics were used to summarize and compare the results from the cohorts.

Results
152 patients (n = 201 positive urine cultures) were reviewed: 74% (159) of positive urine cultures were ASB and 21% (42) were urinary tract infections. The incidence of treated ASB was 15% (30) and untreated ASB was 65% (129). The incidence of UTI, treated ASB, and untreated ASB were not significantly different between the two cohorts examined.

Conclusion
The implementation of education did not result in lasting changes in ASB management. Our study suggests that future systemic solutions are necessary to reduce the incidence of treated ASB in the geriatric population.

Key words: asymptomatic bacteriuria, urinary tract infection, urine culture, antibiotic, education, acute care, hospital, geriatric, elderly

INTRODUCTION

Asymptomatic bacteriuria (ASB) is a common condition affecting hospitalized geriatric patients. ASB is defined as the presence of bacteria in the urine (> 100 million CFU/L) in the absence of typical urinary tract infection (UTI) symptoms. (1-3) In order for ASB to be clinically diagnosed, two clean-catch voided urine specimens must be obtained in females, while one specimen is required for males or catheter-acquired samples. (1) Females are more likely to experience ASB due to the anatomy of the female urinary tract, where the shorter length of the urethra allows bacteria to access the bladder easier. (4) Epidemiological trends show that ASB becomes more prevalent with increasing age and is uncommon in healthy young individuals. (1,5) Over 20% of healthy women over the age of 80 and 6–15% of men over the age of 75 living in the community have ASB. (1,5-6) Additionally, the incidence of ASB is greater in patients living in long-term care facilities, ranging from 25–50% of women and 15–40% of men. (1,7)

Careful analysis of positive urine cultures in the context of clinical signs and symptoms of UTI is important to prevent unnecessary antimicrobial treatment. Various studies have examined the benefits and harms of treating ASB. Although treatment was more likely to eradicate the bacteria, no benefit on morbidity or mortality was identified. (8-12) Additionally, treating ASB was associated with increased risk of reinfection, bacterial resistance, and adverse effects from antibiotic therapy. (8)

Currently, guidelines recommend that ASB should not be routinely treated with antimicrobial agents, and treatment should be reserved for special populations only (pregnancy, patients with urological interventions, or patients with kidney transplant within the last three months). (1) Elderly patients are more likely to have comorbid conditions (cognitive impairment, chronic incontinence, chronic kidney disease, indwelling foley catheterization) that confound the typical
assessment of urinary symptoms. Despite evidence against treatment and the IDSA recommendations, studies have shown that elderly patients are still treated inappropriately for ASB. (13-15) Our study was based on the Vancouver Coastal Health (VCH) Antimicrobial Stewardship (AMS) UTI Algorithm, which determines the clinical diagnosis of a UTI when a patient exhibits a fever > 37.8°C and one sign/symptom or 2 symptoms in the absence of fever (i.e., acute dysuria, new or marked increase in incontinence/urgency/frequency/urinary retention, suprapubic pain, gross hematuria, tenderness of the prostate or epididymis). (16) These symptoms were used to distinguish if a patient had a UTI or ASB in this study.

Given the evidence against antibiotic treatment for ASB, the prevention of treated ASB and proper management of positive urine cultures are a priority for hospital antimicrobial stewardship programs. Education and implementation of treatment algorithms are strategies to help reduce rates of inappropriate antimicrobial treatment. There is limited literature that examines the extent of benefit from education strategies or the most efficient way to implement new practice guidelines. The purpose of this study was to examine the current practice on the Acute Care for Elders (ACE) unit at Vancouver General Hospital regarding the assessment and management of positive urine cultures. Our primary aim was to determine whether education directed toward staff would help reduce rates of treated ASB. In addition, the goal of the chart audits was to identify the incidence of ASB and UTI, proportion of treated ASB cases, empiric antibiotics used, and the types of microorganisms and resistance present.

METHODS
Setting
Vancouver General Hospital (VGH) located in Vancouver, British Columbia, is a large quaternary care centre in Canada. This study involved patients admitted to the Acute Care for Elders (ACE) unit, primarily consisting of adults aged 65 and over.

Design
The study and chart audits followed a retrospective observational design. The methodology was reviewed by the local ethics review board prior to the start of the retrospective review. The first 100 positive urine cultures from each audit period (January to July 2017 and January to July 2018) were separated by a four-month education period, where the AMS algorithm and education was reviewed with unit staff (nurses, care aides, allied health and medical trainees). A UTI assessment and management algorithm developed by the AMS program at Vancouver Coastal Health, in addition to the data collected from the first cohort of patients, were used to frame the content of the education sessions. Nursing education was provided to staff in group sessions biweekly for one month by a nurse educator affiliated with the research team. The medical team education (including physicians, residents, medical students, and other allied health) was provided by a clinical pharmacist specialist affiliated with the research team. Education for the medical team was provided at the start of each medical trainee rotation block every four weeks for four months. Each educational session was approximately 20 minutes long, consisting of a presentation and open discussion of the AMS UTI algorithm and data from the 2017 cohort. Paper copies of the educational material were placed in key traffic areas on the ward for staff to access. Adults aged 70 years of age or older admitted to the ACE unit at VGH and having at least one positive urine culture were included in this study. Patients undergoing transurethral resection of the prostate or any other urologic procedure were excluded, since guidelines recommend routine antibiotic treatment for ASB in these populations.

Chart Review Procedure
The Medical Microbiology program was used to identify the first 100 positive urine cultures from the ACE unit at VGH between January to July 2017 and January to July 2018. A total of 88 patients (2017 cohort) and 64 patients (2018 cohort) were identified, which yielded 201 positive urine cultures available for retrospective chart review. Using a computerized charting program, each positive urine culture was assessed for the amount of bacteria present, type of organism cultured, and presence of antibiotic resistance. Each urine culture was cross-referenced with the patient’s medical record for positive symptoms of a UTI, which were used to distinguish presence of UTI or ASB in this study (refer to data collection form, Appendix A). A community acquired infection was defined as the diagnosis of UTI made within five days of hospital admission. A hospital acquired infection was defined as the diagnosis of UTI greater than five days after hospital admission (i.e., symptom onset and urinalysis completed greater than five days after date of hospital admission). Any positive urine culture where the patient did not exhibit typical urinary symptoms of a UTI was classified as ASB, regardless of bacterial count or number of urine specimens collected. Baseline characteristics including coinfection and presence of immunocompromising conditions or concurrent immunosuppressive therapies were collected. Coinfection was defined as the presence of an infection other than a UTI (e.g., pneumonia, cellulitis, osteomyelitis). Immunocompromised patients were defined as those with active immunocompromising conditions or with ongoing immunosuppressive therapies (e.g., post-transplant, chemotherapy/cancer, high-dose prednisone therapy, methotrexate therapy). The type of specimens cultured in the urine samples, resistance patterns, and antimicrobial agents used for empiric treatment were recorded from the computerized charting program.

Statistical Methods
Descriptive statistics were used to describe the primary and secondary outcomes before and after the implementation of the education program. Data were summarized using proportions and percentages for all nominal and dichotomous variables. An alpha-level of 0.05 was used to determine the statistical significance of the p value calculated for the
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RESULTS
A total of 152 patient charts were reviewed (2017 cohort: 88 patients; 2018 cohort: 64 patients), yielding 201 positive urine cultures (2017 cohort: 101 cultures; 2018 cohort: 100 cultures) (Figure 1). Baseline patient characteristics are presented in Table 1.

Data analysis was performed using IBM SPSS version 17.0.2 software and Microsoft Excel 2017.

Comparison of 2017 and 2018 Cohorts Following Educational Intervention

The incidence of ASB (79%) and UTI (21%) was the same for both 2017 and 2018 cohorts (Figure 2). The proportion of treated ASB was 15% compared to 23% in the 2017 and 2018 cohorts, respectively ($p$ value = .29). These findings were not statistically significant, indicating that the educational interventions implemented prior to the 2018 cohort did not result in any clinical benefits for the assessment and management of ASB.

FIGURE 1. Flow diagram of analysis strategy and incidence of ASB/UTI (data were analyzed based on the categories of combined overall positive urine cultures, treated ASB, and UTI, as defined by protocol definitions)

FIGURE 2. Incidence of ASB* and UTI separated by cohort (2017 vs. 2018)

TABLE 1.
Baseline patient characteristics

| Characteristic          | 2017 Cohort (n = 101) | 2018 Cohort (n = 100) | Total Sample (n = 201) |
|-------------------------|-----------------------|-----------------------|------------------------|
| Age (mean)              | 78.6 yrs              | 80.7 yrs              | 79.6 yrs               |
| Sex (% male)            | 35.6                  | 36.6                  | 36.1                   |
| Total # of patients     | 88                    | 64                    | 152                    |
| Total # of positive UCx | 101                   | 100                   | 201                    |

Untreated ASB was defined as patients with a positive urine culture who did not fulfill criteria for a diagnosis of a UTI and did not receive antimicrobial treatment. Treated ASB was defined as patients with a positive urine culture who did not fulfill criteria for a diagnosis of a UTI and received antimicrobial treatment. UTI was defined as patients with a positive urine culture who fulfilled criteria for a diagnosis of UTI based on the AMS UTI algorithm.

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Overall Incidence of ASB and UTI
The incidence of ASB was 80% (159/201) of all positive urine cultures assessed (Figure 2), 20% (42/201) of the positive urine cultures collected were defined as UTI. Overall, 80% (34/42) of UTI cases were hospital-acquired and 19% (8/42) were community acquired.

Overall Incidence of Treated and Untreated ASB
81% (129/159) of ASB cases were untreated and 19% (30/159) of ASB cases were treated with an antimicrobial agent (Figure 2). Of treated ASB cases, 40% (12/30) of patients did not have a co-infection present and were not immunocompromised (Figure 3). In comparison, 23% (7/30) of treated ASB cases had a co-infection present, 17% (5/30) were immunocompromised patients, and 20% (6/30) had both co-infection present and were immunocompromised patients (Figure 3).

Specimens Cultured and Resistance Patterns
The most common microorganism cultured from cases that received antibiotic therapy was *E. coli* (40%) (Figure 4). Other gram-negative organisms such as *Klebsiella pneumoniae* and *Proteus mirabilis* were cultured in 8% and 6% of positive urine cultures that received treatment, respectively (Figure 4). *Enterococcus faecalis* was the most prevalent gram-positive organism cultured (6%). Mixed organism cultures (≥ 2 organisms with bacterial amount < 100 million CFU/L) comprised 12% of the positive urine cultures that received treatment.

Of the more resistant organisms, extended spectrum beta-lactamase–producing organisms comprised of 6% and *Pseudomonas aeruginosa* was cultured in 4% of positive urine cultures that received treatment. Overall, 36% of the cultures evaluated for antimicrobial sensitivity were pansensitive, with no bacterial resistance identified from the cultured specimens. Most microorganisms cultured and evaluated for antibiotic sensitivity were resistant to ampicillin/amoxicillin (47%). Other notable antibiotic resistance patterns included 27% ciprofloxacin resistance, 22% nitrofurantoin resistance, 21% amoxicillin-clavulanate resistance, and 14% trimethoprim/sulfamethoxazole resistance.

Empiric Antibiotic Treatment
The most common antibiotic regimens prescribed for empiric therapy included ciprofloxacin (22%), piperacillin-tazobactam (20%), ceftriaxone (16%), and amoxicillin-clavulanate (15%). Ciprofloxacin as empiric therapy decreased from 33% to 11% from the 2017 to 2018 cohorts. Alternatively, amoxicillin-clavulanate empiric therapy increased from 7% to 23% from the 2017 to 2018 cohorts.

DISCUSSION
According to current guidelines, treatment for ASB is not recommended for most cases in the geriatric population. In our assessment of the ACE ward at VGH, 19% of total ASB cases received antimicrobial treatment. As described previously in the literature, treating ASB is associated with increased risk of reinfection, bacterial resistance, and adverse effects from antibiotic therapy. Despite the educational interventions in this study, the incidence of treated ASB did not decrease from the 2017 to 2018 cohorts. Special consideration should be taken regarding treated ASB in the geriatric population, as UTI is a clinical diagnosis and it is difficult to evaluate elderly

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**FIGURE 3.** Incidence of treated ASB in immunocompromised patients and/or with co-infection present

**FIGURE 4.** Types of microorganisms cultured from patients who received antimicrobial treatment
patients with respect to UTI symptoms. Elderly patients may present with a non-classical presentation of UTI (i.e., confusion, dementia, urinary incontinence, lethargy, falls), which may obscure the clinical assessment by the interprofessional care team. Furthermore, some patients may have difficulty verbalizing or communicating their symptoms to the healthcare team, as these non-classical symptoms may affect their cognition and mental status. Discrepancies in communication may result in difficult documentation for the health-care team when recording their findings in the patient’s chart. Since elderly patients are considered at greater risk for complications of UTIs due to their age and multiple comorbidities, physicians may be more likely to prescribe antibiotics for patients with positive urine cultures, even in the absence of typical UTI signs or symptoms. These considerations likely explain the high prevalence of treated ASB in this study and the literature. These data indicate there is a potential to improve the assessment and management of positive urine cultures in the geriatric population.

The culture and sensitivity data collected were consistent with previously published studies, as *E. coli* was the most prevalent microorganism from positive urine cultures that received treatment (40%). Other gram-negative bacilli such as *K. pneumoniae* and *P. mirabilis* were also identified as expected. Of the gram-positive organisms, the most prevalent organism was *E. faecalis* (6%). The incidence of resistance to antimicrobial agents should be considered during empiric antibiotic selection. Specifically, nitrofurantoin (22% resistance) and SMX-TMP (14% resistance) suggests that, for empiric acute uncomplicated cystitis, using these agents would confer an appropriate empiric selection 78% and 86% of the time, respectively. Empiric ciprofloxacin therapy was prescribed 22% of the time; however, ciprofloxacin resistance was identified in 27% of the organisms cultured. Use of broad-spectrum antibiotics for empiric therapy, such as ciprofloxacin and piperacillin-tazobactam, should be minimized whenever possible to prevent increasing resistance. Fluoroquinolone resistance has been associated with increased risk of multi-drug resistant organisms and resistant strains of *Pseudomonas*. The frequent usage of piperacillin-tazobactam (20%) as empiric therapy may indicate that the sample population had particularly severe infections present or poor clinical status requiring broad-spectrum antibiotics. Improved selection of appropriate empiric antibiotics for treating patients may be an important consideration going forward with the education and initiatives to improve care on this ward.

There are several limitations of this study which may have affected the incidence of ASB identified. A major limitation was the presence and classification of ASB versus UTI was based on retrospective chart review, where a lack of documentation may have caused symptoms of UTI to be missed. Thus, patients with a true UTI could have been classified as a patient with ASB if their chart documentation did not indicate the typical symptoms of UTI. This would cause our study to overestimate the proportion of ASB cases, as well as the incidence of treated ASB. In addition, due to our strict criteria for only classifying patients with typical symptoms of UTI as having a true infection, differences between data collectors in the 2017 and 2018 cohorts may have resulted in less consistency between classification of positive urine cultures between the two cohorts. The atypical presentation of UTIs in the elderly should also be considered, as geriatric patients may present with non-cardinal signs and symptoms of infection including confusion or lethargy. These atypical symptoms were not considered adequate justifications for a UTI diagnosis or antimicrobial treatment for the purposes of this study. Another limitation is that only the first 100 positive urine cultures from January to July in 2017 and 2018 were assessed. Finally, multiple positive urine cultures from the same patient were assessed as separate cases, where the patient’s clinical presentation at that time determined whether the patient was classified to have ASB or UTI. Using multiple urine cultures from a single patient may have created bias towards culturing certain microorganisms or the use of empiric antibiotic treatments. Some patients may have developed concurrent co-infections or were immunocompromised, which could have further provided justification for prescribers to treat ASB. Another consideration includes patients who were approaching end-of-life care, where antibiotic treatment may have been a last effort to help improve the patient’s clinical status. For example, 12 patients in the 2018 cohort approached end-of-life care due to clinical deterioration and three of these patients received treatment for ASB in this study. Other patient factors, such as allergies or concurrent drug therapies, were not considered during the analysis of empiric antibiotic selection.

Future priorities for research should focus on interventions that can produce sustainable systemic improvements in the assessment and management of ASB in the geriatric population. Institution-wide educational methods which encompass interdisciplinary involvement may improve the overall management of positive urine cultures, as each specialty focuses on different aspects along the management pathway. For example, nursing-specific education may include improving staff understanding of the indications for sending urine samples for urinalysis. While physicians and pharmacists may have targeted education focusing on the assessment of correlating both clinical and microbiological findings in defining infection versus other alternative non-infectious causes. More robust educational methods, such as structured work-shops or module training which involve a greater number of educational hours over longer durations of time, may be required for sustainable changes in practice. Implementing required training sessions and frequent recertification training may help provide long-lasting changes. Additionally, the implementation of protocol-specific forms such as pre-printed orders, which require documentation of clinical findings, may help standardize management of positive urine cultures and prevent unnecessary ASB treatment. Given the high rates of ASB and concern for antibiotic resistance, care should be taken in the clinical assessment of older persons. If antimicrobial therapy is warranted, it should be tailored based on urinalysis and the clinical course of the patient.
CONCLUSION

Geriatric patients are at risk for inappropriate antimicrobial treatment for ASB, which may partially be due to the difficult clinical assessment of elderly patients. Even in the absence of typical UTI signs or symptoms, patients with co-infections or who are immunocompromised may receive antibiotic treatment for ASB due to their potential higher risk for complications. The educational strategies implemented in this study were unsuccessful in generating lasting changes in the management of ASB in geriatric patients on this Acute Care for Elders ward. Given the high rate of ASB and concern for antibiotic resistance, antimicrobial treatment should be reassessed frequently and tailored based on urinalysis results and the patient’s clinical course. Future systemic solutions, such as institution-wide targeted interdisciplinary education and implementation of protocol-specific forms with required documentation of clinical findings relating to UTI, may be potential approaches for reducing the incidence of treated ASB in the geriatric population.

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CONFLICT OF INTEREST DISCLOSURES

The authors declare that no conflicts of interest exist.

APPENDICES

Appendix A. Education on ASB Management in the Elderly—Data Collection Form.

| MRN:                        | Is this UTI “community acquired” (on admission)? |
|-----------------------------|-----------------------------------------------|
| Age:                        | ☐ YES ☐ NO (diagnosed within 5 days of hospital stay) |
| Gender:                     | ☐ YES ☐ NO “Hospital Acquired” (in hospital > 5 days prior to symptoms / urinalysis)? |
| Sample number in database:  | Empiric antibiotic ordered:                  |
|                             | PO step-down agent:                         |
|                             | # days before PO step down:                |
|                             | UTI confirmed by Lab test:                  |
|                             | ☐ C&S                                       |
|                             | ☐ Urinalysis (U/A)                          |
| U/A:                        |                                          |
| Leukocytes:                 | ☐ + ve ☐ - ve                               |
| Nitrites:                   | ☐ + ve ☐ ve                                 |
| Presence of co-infection?   | ☐ YES ☐ NO                                  |
| If yes, describe type of infection: |                              |
| Presence of indwelling catheter (>48 hours or removed in the last 48 hours)? | ☐ YES ☐ NO |
| Resident of Long-Term Care facility? | ☐ YES ☐ NO |

*Foul smelling, cloudy urine (is not a symptom of UTI)
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