A Pharmacist–Physician Antibiotic Support Team

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ABSTRACT
A pharmacist–physician Antibiotic Support Team (AST) was designed and implemented to decrease overall costs and improve patient care by modifying antimicrobial regimens. During the pilot study program (from March to November 2000), 953 interventions were implemented with an overall estimated cost savings of $124,480. A pharmacist–physician team had a significant impact on economic outcomes. As a result, the P&T committee approved several pharmacist-initiated programs.

INTRODUCTION
The rising costs of medications and decreasing reimbursement from payers have led to a search for ways to decrease overall costs and improve patient care. As a result of the prominence of antibiotic resistance that we are encountering today, the need to optimize the use of antimicrobial agents in hospitals has never been greater. This increase in resistance is preceded by the inappropriate use of antibiotics, which can increase the risk of therapeutic failure, superinfection, and drug resistance and can also raise the cost of health care.

Several methods are available to help control inappropriate antimicrobial use and to decrease overall costs, such as formulary restrictions, education programs, and antibiotic-management programs, several of which have been described in the literature. These programs sometimes involve “streamlining,” which might entail discontinuing or narrowing the antibiotic regimen after culture results and susceptibility results are known. However, these streamlining programs have several limitations, including:

- the use of an inappropriate agent during the time period between the initiation of an antimicrobial regimen and the reporting of culture results.
- noncompliance by physicians.
- a lack of physician support.

Other antibiotic-management programs target the control of restricted or nonformulary antimicrobial agents, but these programs do not discourage the inappropriate use of formulary or unrestricted antibiotic agents.

Recognizing the known limitations of a traditional antibiotic-management program, a pharmacist–physician Antibiotic Support Team (AST) was developed and implemented at Akron City Hospital in Akron, Ohio. The Division of Infectious Disease and the Department of Pharmacy joined together in an effort to evaluate the appropriateness of initial intravenous (IV) antibiotic therapy, including empirical therapy. The goals were to improve patient care and to decrease overall costs by modifying the antimicrobial regimens.

SETTING
Summa Health System (SHS) is a 963-bed nonprofit health care delivery network that was created by the 1989 merger of Akron City Hospital and St. Thomas Hospital. A third facility, Cuyahoga Falls General Hospital, has now been added to the system. Notable services include cardiac surgery, kidney transplantation, dialysis, oncology, behavioral health, ophthalmologic surgery, senior health services, level III perinatal care services, and level I trauma services.

Akron City Hospital is a major teaching facility for affiliated medical, pharmacy, and nursing schools. Summa Health System uses a partially restricted antibiotic formulary that is reviewed on an annual basis. Dedicated to quality patient care, community service, and medical education and research, the hospital has had a unique decentralized clinical pharmacy program since 1996.

Pharmacists rotate through patient-care areas, where they enter physician orders, monitor patients, review medical records, and perform general medication-related problem-solving tasks. Having the pharmacist in the patient-care areas allows more interaction with physicians, nurses, and other health care professionals. Several clinical lead pharmacists serve as mentors to the clinical pharmacy staff and routinely participate in various patient-care rounds, from internal medicine to critical care.

Historically, the recommendations of pharmacists to switch patients from IV to oral (PO) agents and to adjust dosages for renal impairment have demonstrated economic and clinical benefits; however, we thought that more aggressive changes—such as discontinuing unnecessary anti-infective agents and choosing alternative, more cost-effective regimens—might have a greater impact. When presented as recommendations from pharmacists, these interventions are sometimes met with resistance from the prescribing physicians. We proposed that an infectious-disease physician, working with the pharmacist, might further increase the acceptance rate for interventions and might improve the use of appropriate anti-infective drugs.

DEVELOPMENT AND IMPLEMENTATION
The Performance Council at Summa Health System is a cooperative effort between the clinical service line and the system. The Performance Council at Summa Health System is a cooperative effort between the clinical service line and the system. The findings in this article were presented at the Midyear Clinical Meeting of the American Society of Health-System Pharmacists (ASHP) in New Orleans, Louisiana, on December 4, 2001, and at the Great Lakes Pharmacy Residency Conference in Indianapolis, Indiana, on April 26, 2002.
tem’s senior administration to improve patient care and reduce costs. It is composed of the physician department chairpersons, vice-presidents representing the various entities that constitute the health system, the system chief executive officer, and a representative of the system board of directors. We chose to present this project to this group because of our dual goals of improving cost-effectiveness and clinical outcomes for patients receiving antibiotic therapy. We hoped that the backing of this group might have a tremendous impact on the success of the project.

We presented the program to the Summa Health System Performance Council in February 2000. An eight-month pilot study of the AST project took place on the Akron City Hospital campus. After eight months, we assessed the effect of the AST and reported the results to the Performance Council.

The AST consisted of an infectious-disease physician and a clinical pharmacist. For this program, three clinical lead pharmacists were relieved of their other responsibilities for two to three months on a rotating basis to work full-time on the AST.

Physicians from the Infectious Disease Division worked with the AST. Several of these physicians were employed by the hospital; those infectious-disease physicians not employed by the hospital who were interested in participating were paid an agreed-upon hourly rate for their participation on the team. The payments originated from the hospital pharmacy budget for the program.

A clinical pharmacist directed the AST every Monday through Friday. Before initiating the AST, the Infectious Disease Division and the Department of Pharmacy developed guidelines for an appropriate empirical choice of an antibiotic for a working diagnosis. The guidelines were distributed to the AST’s clinical lead pharmacist.

Each day, a query was sent through the pharmacy computer system (BDM Systems, Saskatoon, Saskatchewan) to list all patients who had begun IV antimicrobial therapy within 24 hours at Akron City Hospital. The targeted parenteral antimicrobials excluded agents that were restricted to the Infectious Disease Division, such as trovafloxacin mesylate (Trovan®, Pfizer), amphotericin B lipid complex (Abelcet®, Infectious Disease Division, such as trovafloxacin mesylate (Trovan®, Pfizer), amphotericin B lipid complex (Abelcet®, Enzon), aztreonam (Azactam®, Elan), and linezolid (Zyvox™, Pharmacia). These agents were restricted to infectious-disease physicians because of their high cost and their potential for inappropriate use.

We originally intended to continue to monitor patients throughout their hospital stay. The burden of providing a plan of pharmaceutical care for more than 50 new patients per day—while continuing to follow previous patients—proved to be too time-consuming for just one pharmacist. Patients who had been evaluated for appropriate antibiotic use were those admitted to Akron City Hospital from March to November 2000 who had started IV antibiotic therapy within the past 24 hours in the medical-surgical, critical care, oncology, geriatric, and neurology services. The following groups were excluded:

- patients in the obstetrics and gynecology units
- patients in the special care nursery
- patients admitted to the hemodialysis unit
- patients with a one-time prophylactic antibiotic order or who had consulted with an infectious-disease specialist

The pharmacist screened all patients for inappropriate antibiotic use, defined as:

- an empirical choice that failed to meet the criteria according to the established guidelines.
- an improper dosage or frequency.
- an inadequate spectrum of activity for a specified infection.
- administration of an antimicrobial agent for an infection in which the causative microorganism was resistant.

The Cockcroft-Gault equation was used to calculate renal function and to estimate creatinine clearance on the basis of the patient’s serum creatinine level, age, body weight, and sex. The pharmacist also evaluated patients who were receiving IV therapy for an IV-to-PO switch.

Antimicrobial agents that have the same chemical entity, similar area-under-the-curve (AUC) profiles, and high oral bioavailability were considered for a change from IV to oral therapy. When patients did not meet the appropriate criteria as determined by the established guidelines, the pharmacist consulted with the infectious-disease physician. If recommendations were necessary, either the physician or the pharmacist communicated with the attending physician via a note or a telephone call. On the next two days, the pharmacist then reviewed the recommendations for acceptance or rejection.

The ASHP’s CliniTrend for Microsoft Windows was used as the database to track all interventions. Within the subcategories of interventions, drug charges were modified according to actual costs for Summa Health System. The operating costs per patient per day for nursing, pharmacy, housekeeping, overhead, and the dietary area were elicited from the respective departments and entered into the database. The cost savings for each category were calculated according to the following formula:

\[
\text{Cost savings} = \frac{A \times \{[(C + D + E + F + G) \times B] - (I + J + K + L + M) \times H\} + \{N \times O\}}{H}
\]

where:

- \(A\) is the average duration of effect in days,
- \(C, D, E, F, G\) are the costs of the initial treatment,
- \(I, J, K, L, M\) are the costs of the revised treatment,
- \(B\) and \(H\) are the number of doses per day of the initial and revised treatments, respectively.
- \(N\) is the average number of days of reduced length of hospital stay,
- \(O\) is the operating cost of one day in the hospital.

In an IV-to-PO switch program for levofloxacin (Levaquin™, Ortho-McNeil), values for the average duration of effect (1.5 days) and reduced length of stay (LOS) (0.5 days) were entered into the database. These values were based on reported data using similar programs that targeted levofloxacin for community-acquired pneumonia (CAP) and demonstrated reduced usage of IV antibiotics and decreased LOS.\(^{10}\)
Antibiotic Support Team

Results

For the other interventions, we began with the values predefined in the CliniTrend program.

For LOS, with the interventions of initiating IV therapy and changing the antibiotic to obtain better coverage, the values were three days and two days, respectively. We decreased the values for all other interventions to ensure that we did not overestimate the cost savings. The Los at Summa Health System has traditionally been below the national benchmarks. If the change in LOS was unknown and was likely to be minimal, the value was changed to zero.

IV-to-PO Switch Program for Levofloxacin

After the AST study was completed, a case-control evaluation was performed to assess the AST group. The control group included patients from March to November 1999. Patients in each of the groups were selected if they had received initial IV levofloxacin therapy and had a diagnosis of CAP. Baseline criteria are listed in Table 1.

Upon admission, the Patient Outcome Research Team (PORT) score was used to assess the patients with a point system that included:

- demographic data (e.g., age).
- coexisting illnesses (e.g., congestive heart failure and liver, renal, neoplastic, and cerebrovascular disease).
- physical examination findings (e.g., altered mental status, respiratory rate).
- laboratory results (e.g., arterial pH, and pleural effusion).

Patients were stratified into five classes according to severity of disease; those in classes I to III were considered to be at low risk for death or complications, and those in classes IV to V had a higher risk of mortality and complications.

The PORT score was used to determine the severity of illness and to compare CAP patients in the AST and historical control groups. We also repeated the PORT score at the time of the IV-to-PO switch program. The average PORT score was not statistically different for the AST group (at baseline, 97) and control group (at baseline, 87) and at the switch (87 and 79, respectively).

Patient outcomes were designated as follows:

- **Positive response.** Antibiotic therapy was discontinued because a cure took place or because patients were discharged home with a corresponding oral antibiotic to finish the course of therapy.
- **Negative response.** A switch was made to another antibiotic, or treatment failure occurred because of persistence of the infection.
- **Neutral response.** Antibiotic therapy was discontinued for another reason, such as placement of the patient on comfort care only or the absence of infection.

Clinical outcomes, as assessed by patients’ responses to therapy, were positive in 91% of the AST group and in 88% of the historical control group.

In the IV-to-PO switch for the levofloxacin intervention group, 48 patient charts were reviewed retrospectively (26 in the control group and 22 in the AST group). For the average duration of IV therapy, the AST group received fewer days of IV therapy (1.6 days) than the control group did (2.9 days) ($P < .005$). For LOS, the difference between the AST group and the control group was 0.4 days (favoring the AST group; $P = .375$).

**Modifications of IV Therapy: Dose, Duration, and Frequency**

After the AST program was completed, interventions for dose reduction in patients with renal insufficiency were evaluated. Baseline demographics are listed in Table 2.

Patient outcomes were assessed, as described earlier; 87% of patients achieved a positive clinical response. The average duration of therapy with the inappropriate dose before the switch was 1.75 days. The average LOS for these patients was 4.25 days.

**Changing an Antibiotic to Improve Coverage**

A total of 77 interventions were performed to change an antibiotic to obtain better coverage. Of these interventions, 35 (45%) were based on empirical treatment, 27 (35%) on culture reports, and the remainder on culture and susceptibility reports. Some examples are presented in Table 3.

**DISCUSSION**

Inappropriate use of antimicrobial agents can lead to therapeutic failure, superinfection, increased overall drug use.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient Demographics for Switching from Intravenous to Oral Levofloxacin</th>
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<tbody>
<tr>
<td></td>
<td><strong>Historical</strong></td>
</tr>
<tr>
<td><strong>Total No. of patients</strong></td>
<td>26</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>15 (58%)</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>11 (42%)</td>
</tr>
<tr>
<td><strong>Average age</strong></td>
<td>71 (47–94 yrs)</td>
</tr>
<tr>
<td><strong>Medical–surgical</strong></td>
<td>24 (92%)</td>
</tr>
<tr>
<td><strong>Intensive-care unit</strong></td>
<td>1 (4%)</td>
</tr>
<tr>
<td><strong>Regular diet</strong></td>
<td>21 (81%)</td>
</tr>
<tr>
<td><strong>Nursing home</strong></td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Other oral medications</strong></td>
<td>23 (88%)</td>
</tr>
</tbody>
</table>
costs, and the emergence of antimicrobial resistance. The AST has been developed as one option to ensure optimal therapy and to control the escalating costs of antimicrobials. We have demonstrated that pharmacists play an important role as members of the multidisciplinary team in the effort to reduce inappropriate use of these medications.

Historically, pharmacists have participated in antimicrobial management (e.g., antibiotic-streamlining) programs, which modify antimicrobial therapy according to culture and susceptibility findings. However, our program focused on the empirical and early treatment of an infection to minimize the duration of inappropriate usage of antibiotics that generally occurs between the time of initial therapy and the reporting of culture results. Several studies have indicated that appropriate initial antimicrobial therapy is an important predictor of overall mortality.

In a prospective cohort study, Kollef et al. evaluated the relationship between inadequate antimicrobial treatment and hospital mortality for patients requiring admission to an intensive-care unit. In fact, reports in the literature, primarily in patients with pneumonia, indicate a reduced mortality rate associated with appropriate initial antibiotic therapy. Alvarez-Lerma reported a higher mortality rate attributed to inadequate antimicrobial coverage of microorganisms in patients with ventilator-associated pneumonia.

The AST focused primarily on reviewing parenteral antimicrobial agents. The rationale for reviewing only parenteral antimicrobial agents was based on their potentially greater impact, both clinically and economically. Patients in acute-care settings are more likely to be started on IV rather than PO antimicrobials because of the severity of their acute illness. Furthermore, parenteral antimicrobials are generally more expensive than oral antimicrobials. After considering these factors, we thought that targeting parenteral antimicrobials would have a more significant impact.

The AST program incorporated the experience, expertise, and support of infectious-disease physicians. Although compliance was voluntary, we assumed that other physicians would be more likely to accept recommendations for antimicrobial treatment by infectious-disease physicians than recommendations by pharmacists alone. Infectious-disease physicians spent an average of less than 30 minutes per day in consultations regarding the AST patients.

Reductions in cost were associated primarily with decreased usage of the more expensive antibiotics or dosage forms. In the IV-to-PO switch program for levofloxacin, the AST group experienced a significant reduction in the need for IV therapy (1.3 days), in comparison with the historical control group.

Compared with the historical controls, the AST group experienced a reduced LOS of 0.4 days. Although this difference was not statistically significant (probably because of the small sample size), these results are comparable to those of similar programs targeting levofloxacin and CAP. These programs have reported a reduced usage of IV therapy of 1.5 days and a reduced LOS of 0.5 days.

After we evaluated the acquisition data, we found that the purchase history of IV and oral levofloxacin 500 mg confirmed this decrease in IV usage. The percentage of IV levofloxacin usage was 49% during the study and 54% before the implementation of the study (Figure 1).

Several studies have shown that patients with CAP can be safely switched from IV to oral therapy. This conversion would potentially reduce the duration of IV therapy and would minimize LOS without adversely affecting overall outcomes. Baseline demographics in the IV-to-PO levofloxacin groups were similar.

The PORT score is a clinical prediction rule to determine mortality risk, which can be interpreted as an indicator of a patient’s severity of illness. In our analysis, the PORT score was used to show similarities in the severity of illness between the

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Table 2 Demographics of Patients with Renal Insufficiency and Interventions to Change Intravenous Doses

<table>
<thead>
<tr>
<th>Total No. of Patients</th>
<th>15 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>6 (40%)</td>
</tr>
<tr>
<td>Female</td>
<td>9 (60%)</td>
</tr>
<tr>
<td>Average age</td>
<td>76 (48–91 yrs)</td>
</tr>
<tr>
<td>Nursing home</td>
<td>5 patients (33%)</td>
</tr>
<tr>
<td>Community-acquired pneumonia</td>
<td>6 patients (40%)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>5 patients (33%)</td>
</tr>
<tr>
<td>Average white blood cell count</td>
<td>12.4 thou./mm³ (3.6–29.7)</td>
</tr>
<tr>
<td>Average creatinine level</td>
<td>2.4 mg/dl (0.9–6.7)</td>
</tr>
</tbody>
</table>

Table 3 Examples of Changes Recommended for Improved Antibiotic Coverage

Recommendations based on empirical choice
1. Suspected aspiration pneumonia: to broaden antibiotic regimen to include anaerobic pathogens.
2. Suspected perforated abdomen: to broaden coverage from levofloxacin to beta-lactam/beta-lactamase inhibitor.
3. Intra-abdominal abscess: to broaden antibiotic regimen to include anaerobic pathogens.

Recommendations based on cultures
1. Wound infection with *Bacteroides fragilis*: to add anaerobic coverage.
3. Urinary tract infection with enterococcus: to change antibiotic regimen to include enterococcal activity.

Recommendations based on culture and susceptibilities
1. Positive blood culture for methicillin-resistant *Staphylococcus aureus*: to start vancomycin.
2. Urinary tract infection: to change antibiotic regimen according to susceptibilities.
3. Pneumonia: to change antibiotic regimen according to susceptibilities.
control and the AST groups. The average baseline score for the AST group was 97 (class IV), and the average score for the controls was 87 (class III). The percentage of patients with baseline PORT scores above 90 (in classes IV and V) was 64% in the AST group and 42% in the control group.

In patients with a class IV PORT score, the mortality rate was 9.3%; in those with a class III score, it was 0.9%. This finding suggests that overall pneumonia severity of disease for AST patients was potentially higher than that for control patients. However, the mean PORT score did not differ statistically between the two groups. As a consequence, we inferred that the illness of the control group was not more severe than that of the AST group. The AST demonstrated that a substantial cost savings could be obtained by converting from IV to PO therapy without adversely affecting overall patient outcomes.

On the basis of these findings, the P&T committee approved an automatic substitution from IV to PO ciprofloxacin (Cipro®, Bayer), levofloxacin, and fluconazole (Diflucan®, Pfizer) after the study was completed. In this program, pharmacists automatically switched patients who did not need critical care from IV to PO therapy if they met the following criteria:

- The patients had to have been prescribed and had to be tolerating an oral diet (clear liquid diets were excluded).
- The patients had to be taking other oral medications.

This program has been in place since July 2001 and has been well received by the medical staff.

For the intervention of modifying the IV dose, duration, and frequency, the AST quickly adjusted regimens in the patients with renal insufficiency, thereby minimizing the duration of inappropriate dosing. Evans et al. evaluated the impact of a computer-assisted, antibiotic dose-monitoring system in reducing the number of days of excessive dosages and adverse drug events (ADEs) secondary to antibiotic intake. In this study, the dose-monitoring system brought about a reduction in average days of excessive dosage from 4.7 in the pre-intervention group to 2.9 in the intervention group and also decreased the frequency of ADEs associated with excessive dosages.

In our program, the AST patients were switched to the correct regimen at 1.75 days, and 87% had a positive clinical response. Benefits to patients who had initially received underdosed antibiotic therapy were also appreciated.

The P&T committee approved an automatic dosage adjustment according to the renal-function program. Several antimicrobials were selected for this program, such as ampicillin/sulbactam (Unasyn®, Pfizer), cefotaxime (Claforan®, Aventis), cefepime (Maxipime®, Elan), ciprofloxacin, imipenem/cilastatin (Primaxin®, Merck), levofloxacin, and piperacillin/tazobactam (Zosyn®, Wyeth). This program is currently being implemented.

After implementation of the AST, the antibiotic cost per patient discharge decreased by $17.08, although the overall antibiotic budget did not decrease during this time period. The analysis of the impact of the pharmacy budget was complicated by the introduction of antibiotics that were newly approved by the Food and Drug Administration, changes in contract pricing, the arrival of a new infectious-disease physician, and an increased patient census in the hospital.

CONCLUSION

The impact of the AST demonstrated a significant reduction in overall costs to the institution, with a predicted annual cost avoidance of $186,720.41. Overall costs declined, primarily because of the reduced use of certain drug classes, such as IV levofloxacin, and because of shortened hospital stays.

The antibiotic cost per patient discharge decreased by $17.08 after implementation of the AST. After the AST program ended, we recommended prioritizing the following interventions before the Performance Council in April 2001:

- switching from injectable to oral levofloxacin
- alternative IV dosage, frequency, and duration
- changing the antibiotic to obtain better coverage

The AST program led to the following changes:

- an automatic substitution by staff pharmacists from IV to oral levofloxacin, ciprofloxacin, and fluconazole
- an automatic renal dosage adjustment by staff pharmacists
- continuation of the AST project by an infectious-disease clinical lead pharmacist, a position that was approved after the AST program
The effect of these aggressive automatic substitutions will be the subject of future study. We also expect to expand the program to another system hospital (St. Thomas Hospital), to continue patient follow-up throughout the hospital stay, and to review re-admissions to Summa Health System for up to 30 days after discharge.

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REFERENCES