Antimicrobial Stewardship Team - Pilot Proposal

Summary

- In 2005, the adult population in the XXX Hospital accounted for 80% of the anti-infective budget.
- Fifteen of the top 20 anti-infective budget items were ID restricted agents.
- Currently, ID fellows provide approximately 11,000 restricted antibiotic approvals annually, of which 9000 approvals are granted for the adult population.

A well-staffed antimicrobial stewardship team at XXX can be a valuable asset, as antibiotic use, antibiotic resistance, and infection control go hand in hand. A comprehensive approach to antibiotic use beyond an approval system relies heavily on Clinical Pharmacy (PharmD) participation to provide approvals, follow up on all patients receiving antibiotics throughout the institution, provide pharmacokinetics dosing services, and perform targeted surveillance. Additional PharmD staffing can help this program achieve its goals:

- Decrease antibiotic costs
- Stabilize antibiotic resistance
- Improve patient safety
- Reduce burden on ID fellows and thereby improve their clinical training

FTEs for 2 additional infectious diseases-trained clinical pharmacists are requested. The activities described below would be gradually phased in over the next 2 years.

Background

Antibiotic resistance is a significant and progressively worsening problem at healthcare facilities around the world. This fact, combined with the lack of new antimicrobial agents in the drug development pipeline, indicates that judicious antimicrobial management is necessary to preserve the antibiotics currently available.

Adverse outcomes result from inappropriate choice, dose, formulation, or duration of antibiotics and include increased cost and antibiotic resistance, along with increased morbidity, mortality, and length of stay. Increased costs associated with antibiotic use are derived from numerous factors, including direct antibiotic drug expenditures and hospital and/or intensive care unit length of stay.

Stabilizing antibiotic resistance requires a multipronged approach including formulary restrictions, education and guidelines, review and feedback, and close surveillance of antibiotic utilization and resistance patterns, with interventions made on a daily basis to optimize antibiotic therapy. Recent literature demonstrates that these activities are most successful with the implementation of multidisciplinary antibiotic stewardship teams involving infectious diseases physicians and infectious diseases-trained clinical pharmacists:

- Carling et al (1999)[1] – Comparison of 14 hospitals showed that only a prospective multidisciplinary intervention program was correlated with a decrease in antibiotic cost.
- Bantar et al (2003)[2] – Multidisciplinary antimicrobial treatment committee led to decreased antibiotic costs (savings >$900,000) and decrease in certain types of antibiotic resistance.
- Gums et al (1999)[3] – Multidisciplinary team led to a decrease in length of stay (by 3.3 days) and in median hospital costs ($2642 per intervention).

Finally, adult ID fellows currently provide approximately 9000 approvals annually, amounting to about 25 approvals each day. These numbers estimate actual approvals and do not reflect rejected requests and phone consultations, which significantly inflate the number of phone calls managed daily. This number has subjectively increased in recent years along with the acuity of the patient population. The need to balance the approval system with fellows' educational needs according to GME requirements places at least one of these processes at a disadvantage on a daily basis. Decreasing the number of hours during which ID fellows are

responsible for antibiotic approvals would allow them to participate more fully in attending rounds and spend more time on their consultative activities.

Current pharmacy staffing levels are limited to direct patient care activities with the ID Consult services and are insufficient to meet the needs of a comprehensive program as outlined in this proposal. A comprehensive program can improve patient safety, stabilize or decrease antibiotic resistance, and provide significant cost savings via the following intervention opportunities:

Proposed Activities

1. ***Antibiotic approvals***

Antibiotic approvals have traditionally been managed by infectious disease fellows at many academic institutions, including XXX. Currently, the adult ID fellows provide approximately 9000 approvals annually (750 approvals each month). However, as this is only one aspect of their training, fellows frequently are limited in time and incentive to carefully consider and respond to each request. In addition, their time constraints limit their ability to be completely familiar with all relevant epidemiology within the hospital that would guide antibiotic decisions.

Under the direction of Dr. Neil Fishman, the Hospital of the University of Pennsylvania developed a multidisciplinary antibiotic management team with clinical pharmacists providing antibiotic approvals. This program has shown that the clinical pharmacists outperformed the infectious diseases fellows on all measures, including appropriateness of antibiotic suggestions and cure rate.[4] The program was also found to be cost-effective, demonstrating annual savings of $300,000 for antibiotic costs, $500,000 for infection-related costs, and >4.25 million in total costs.[5]

2. ***Post-prescribing review/follow-ups***

The antibiotic restriction and approval process is important in reducing the inappropriate use of antibiotics. However, currently this process only affects the initial choice of antibiotic therapy. Post-prescribing review can be important in many ways, including tailoring antibiotics to subsequent microbiology results, changing antibiotics from broad to narrower-spectrum (de-escalation), shortening duration of antibiotic therapy, adjusting antibiotic doses based on drug levels and end-organ function, and converting an antibiotic from an intravenous to oral formulation.

- <u>IV to PO conversions</u>
    - Pharmacists can review the utilization of select newer intravenous antibiotics with excellent oral bioavailability (*e.g.* linezolid and voriconazole) that have not previously been monitored due to resource constraints. This would be an enhancement to our current activities. This includes selected new intravenous agents. This can result in significant cost savings as oral formulations are frequently less costly than intravenous preparations and equally effective if utilized in the appropriate patient populations.
- <u>Antibiotic duration >7 days</u>
    - Duration of antibiotic therapy in the hospital setting is often longer than necessary based on a perceived benefit of longer durations despite clinical improvement early in the course of therapy.[6] Longer durations tend to promote superinfection with organisms that are more resistant.
    - Pharmacists can review all patients who are receiving antibiotics for at least 7 days to assess the possibility for discontinuation. Shortening duration of therapy where feasible can decrease antibiotic drug costs.
- <u>Vancomycin and carbapenem duration >3 days</u>
    - Vancomycin and carbapenems are antibiotics where there is particular concern regarding overuse. Empiric therapy with these agents in severely ill patients is often reasonable initially but can be subsequently discontinued when more microbiological data is available should more susceptible organisms be identified.

    - As above, pharmacists can review these cases and recommend discontinuation where feasible. Broad spectrum antibiotic use can be limited and drug costs decreased by this process.
- Duplicate therapy
    - Patients may unnecessarily receive multiple antibiotics that cover the same organisms. For instance, a patient may be treated with piperacillin/tazobactam + metronidazole for an intra-abdominal infection where the metronidazole is added for a perceived benefit against anaerobic organisms. Treatment with both of these agents is not necessary. Similarly, linezolid may be added to vancomycin therapy to cover vancomycin-resistant gram-positive organisms where the linezolid alone is sufficient in most cases.
    - Pharmacists can review these cases and suggest the discontinuation of one of the duplicate antibiotics.
- Pharmacokinetics service
    - Antibiotics such as vancomycin and aminoglycosides are challenging to dose and require adjustment based on kidney function, weight, and age. Diligence in therapeutic drug monitoring of aminoglycosides is especially important to avoid toxicity and maximize efficacy due to their narrow therapeutic index. Despite maximal educational efforts, therapeutic level monitoring is often performed incorrectly, with levels sent at the wrong time during therapy or relative to drug administration times. Unnecessary costs may accrue due to an increased number of drug levels ordered and potentially increased hospital length of stay due to over- or under-dosing with the antibiotics.
    - Pharmacists are specifically trained in therapeutic drug monitoring and can follow patients receiving aminoglycosides and vancomycin to optimize drug dosing based on the efficient use of drug levels. This can result in more rapid attainment of the "correct dose", thus decreasing the number of serum drug levels sent, maximizing the chance of cure, and minimizing the risk of drug toxicity.
- De-escalation therapy/Streamlining
    - In addition to the above interventions, there are numerous other opportunities for pharmacists to assist in the de-escalation and streamlining of antibiotic therapy. The development of sophisticated computerized surveillance systems can aid in the identification of patients on inappropriately broad or narrow therapy. For example, computerized alerts are being developed at XXX to identify patients whose antibiotic therapy does not "match" the reported microbiologic susceptibilities of the patients' organisms ("bug-drug mismatch alert").
    - Pharmacists would identify patients as described above and suggest a switch to more appropriate antibiotic therapy.

3. ***Surveillance of antibiotic utilization and resistance patterns***

Optimal antibiotic utilization is dependent on a complete and up-to-date understanding of the organisms and resistant patterns that are prevalent in each unit of the hospital.

- Quarterly surveillance
    - Pharmacists can assist in compiling quarterly data on antibiotics utilized in each unit and the most prevalent organisms in those units, along with their susceptibility patterns. Based on these data, the antibiotic management team can provide feedback to each unit with targeted recommendations for antibiotic utilization.
- Targeted surveillance
    - Pharmacists can also perform targeted usage evaluations to identify inappropriate use, opportunities for education, and the need to optimize antibiotic choices or monitoring. This can be helpful when a potential problem in antibiotic resistance or antibiotic utilization in the hospital is recognized (*e.g.* increase in *Acinetobacter* infections and relationship to overuse of imipenem, etc.).

Outcome Measurements

The success of this proposal depends on the regular monitoring and evaluation of the outcomes of interest, namely the impact of these activities on antibiotic use, antibiotic resistance, and cost savings. An annual report will be provided summarizing these outcome measurements.

Intervention	*Potential Cost Savings*	*Clinical and Microbiologic Outcomes*
Antibiotic Approvals		• Improved appropriateness of antibiotic suggestions[5] • Improved infection cure rate[5]
Post-prescribing Review • **IV to PO Conversions** • **Decrease Antibiotic Duration** • **Duplicate Therapy** • **Pharmacokinetics** • **De-escalation/ Streamlining**	**$ 103,000** **$ 242,000**	• Decrease in antibiotic-related adverse drug events • Decrease in median length of stay by up to 3 days[5,7,8] • Decrease in antibiotic resistance[2,9,10]
Surveillance of Antibiotic Resistance and Utilization		• Decrease in inappropriate antibiotic utilization • Decrease in antibiotic resistance
Total potential measurable cost savings	**$ 345,000 ***	
2 Additional FTE's (ID Clinical Pharmacy Specialists)	**$ 180,000 ****	
NET POTENTIAL MEASURABLE COST SAVINGS	**$ 165,000**	

* additional cost savings can be achieved by LOS reductions, safety, resistance, and patient outcomes over time

** excludes benefits

References

1. Carling, P.C., Fung, T. & Coldiron, J.S. Parenteral antibiotic use in acute-care hospitals: A standardized analysis of fourteen institutions. *Clin Infect Dis* **29**, 1189-96 (1999).
2. Bantar, C. et al. A hospital wide intervention program to optimize the quality of antibiotic use: impact on prescribing practice, antibiotic consumption, cost savings, and bacterial resistance. *Clin Infect Dis* **37**, 180-6 (2003).
3. Gums, J.G., Yancey, R.W., Jr., Hamilton, C.A. & Kubilis, P.S. A randomized, prospective study measuring outcomes after antibiotic therapy intervention by a multidisciplinary consult team. *Pharmacotherapy* **19**, 1369-77 (1999).
4. Gross, R. et al. Impact of a hospital-based antimicrobial management program on clinical and economic outcomes. *Clin Infect Dis* **33**, 289-95 (2001).
5. Fishman, N. Antimicrobial stewardship. *Am J Infect Control* **34**, S55-63; discussion S64-73 (2006).
6. File, T.M., Jr. Clinical efficacy of newer agents in short-duration therapy for community-acquired pneumonia. *Clin Infect Dis* **39 Suppl 3**, S159-64 (2004).
7. Fraser, G.L. et al. Antibiotic optimization. An evaluation of patient safety and economic outcomes. *Arch Intern Med* **157**, 1689-94 (1997).
8. Gentry, C.A., Greenfield, R.A., Slater, L.N., Wack, M. & Huycke, M.M. Outcomes of an antimicrobial control program in a teaching hospital. *Am J Health Syst Pharm* **57**, 268-74 (2000).
9. Carling, P., Fung, T., Killion, A., Terrin, N. & Barza, M. Favorable impact of a multidisciplinary antibiotic management program conducted during 7 years. *Infect Control Hosp Epidemiol* **24**, 699-706 (2003).
10. Modjtabai, K., Prato, B.S., Stogsdill, P.B. & Owens, R.C.J. Impact of inpatient prescribing changes on antimicrobial susceptibilities: a five-year longitudinal study [abstr]. in *Programs and abstracts of the 41st annual meeting of the Infectious Diseases Society of America* (Alexandria, VA, 2003).