



ANTIMICROBIAL STEWARDSHIP MANUAL

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A. DEFINITION

Antimicrobial stewardship is an interdisciplinary activity that promotes appropriate selection, dosing, route and duration of antimicrobial therapy to:

- Optimize patient clinical outcomes
- Minimize antibiotic adverse effects / toxicity
- Reduce the selection of certain pathogenic organisms (e.g. *Clostridium difficile*)
- Reduce or stabilize antimicrobial resistance

B. EVIDENCE FOR ANTIMICROBIAL STEWARDSHIP

Antimicrobials are among the most commonly prescribed medications in acute care centers. It is recognized that up to 50% of antimicrobial use is inappropriate resulting in patient adverse effects, *Clostridium difficile* infections, and emergence of resistant organisms (1). All of the above result in increased patient morbidity and mortality, prolonged hospital stays and increased health care costs (1, 2, 3). Antimicrobial Stewardship programs are effective patient safety initiatives designed to optimize safe and effective antimicrobial prescribing and minimize adverse events through multi-pronged strategies. The benefits of antimicrobial stewardship have previously been inferential associating a reduction in antimicrobial use to decreased antimicrobial resistance, adverse drug effects, and *C. difficile* rates. With increased implementation, data is now increasingly available to support attainment of the following goals:

1. Improved Patient Safety

Studies have demonstrated that Stewardship initiatives can limit antibiotic toxicities and unintended consequences of antibiotic therapy such as patient level drug resistance, and *C. difficile* infection, for example:

- prospective audits with intervention and feedback were shown to decrease parenteral broad spectrum antimicrobial use by 22%, despite a 15% increase in patient acuity over a 7 year period, with a corresponding decrease in *C. difficile* and nosocomial drug resistant Enterobacteriaceae infections (4)
- Drug formulary restrictions and pre-authorization requirements have been effective in controlling *C. difficile* nosocomial outbreaks (4, 5, 6).
- A stewardship program including clinical decision pathways resulted in more appropriate dosing of nephrotoxic agents such as gentamicin and vancomycin by at least 20% (7).

Characteristically stewardship results in decreased drug costs, which, while not a prime driver, can allow for stewardship infrastructure development and program support initially.

2. Improved Patient Outcome

Decreased hospital length of stay and re-admission rates are often used as surrogates for patient outcome. One center demonstrated that the implementation of clinical pathways compared with conventional management of community acquired pneumonia resulted in a 1.7 day decrease in the median length of hospital stay, an 18% decrease in the rate of admissions of low-risk patients and 1.7 fewer mean days of intravenous therapy, all without compromising complications, readmission rates or mortality (8). Respiratory tract infections account for 49% of antibiotic prescribing in Intensive Care Units (ICUs); however, 63% of the antibiotics were for clinical suspicion rather than proven infection (9). Singh et al. demonstrated that managing suspected ventilator associated pneumonia (VAP) with a clinical pathway, which entailed empiric ciprofloxacin in patients with CPIS<6 (Clinical Pulmonary Infection Score) and cessation in 72 hours if the CPIS remained <6, resulted in 7 fewer days of antibiotic exposure, 6 fewer days of ICU length of stay and a reduction in antimicrobial resistance from 38% to 14% resulting in early termination of the study (9). One center demonstrated that implementing a prospective audit and feedback program for antimicrobial use was associated with a significant decrease in mean hospital length of stay and mortality without compromising re-admission rates (10).

3. Reduced Antimicrobial Resistance

Reducing antimicrobial resistance is particularly important in this day and age where the emergence of drug resistant organisms is increasing and new antimicrobials approved for use are declining, both of which are limiting our treatment armamentarium. White et al. demonstrated that Infectious Diseases pre-approval of broad-spectrum antimicrobials resulted in increased susceptibility of gram negative bacteria over time to both restricted and non-restricted antimicrobials with no change in time to antibiotic administration (11). Furthermore, upon establishing a comprehensive Antimicrobial Stewardship program, Carney Hospital was able to demonstrate a drastic reduction in the rate of Vancomycin resistant enterococci (VRE), and drug resistant Enterobacteriaceae infections (4).

4. Reduced Healthcare Costs

Antimicrobials account for 30% of the hospital pharmacy budget (1). Health care facilities with comprehensive antimicrobial stewardship programs have demonstrated a 22-35% decrease in antimicrobial use resulting in an annual savings of \$200,000 - \$900,000 thereby justifying the time and resources needed to maintain Antimicrobial Stewardship Programs (2, 4, 10, 11, 12).

C. ANTIMICROBIAL STEWARDSHIP: REQUIRED ORGANIZATION PRACTICES

As of January 2012, Accreditation Canada passed “Antimicrobial Stewardship Required Organizational Practices” for all acute care organizations. Programs will be evaluated for compliance effective January 2014.

Tests for compliance include the following:

Major	The organization implements an antimicrobial stewardship program.
Major	The program includes lines of accountability for implementation.
Major	The program is inter-disciplinary involving pharmacists, infectious diseases physicians, infection control specialists, physicians, microbiology staff, hospital administrators, and information system specialists, as available and appropriate.
Major	The program includes interventions to optimize antimicrobial use that may include audit and feedback, a formulary of targeted antimicrobials and approved indications, education, antimicrobial order forms, guidelines and clinical pathways for antimicrobial utilization, strategies for streamlining or de-escalation of therapy, dose optimization, and parenteral to oral conversion of antimicrobials (where appropriate).
Minor	The organization establishes mechanisms to evaluate the program on an ongoing basis, and shares results with stakeholders in the organization.

D. EDMONTON ZONE ANTIMICROBIAL STEWARDSHIP WORKING GROUP

The Edmonton Zone Antimicrobial Stewardship Working Group functions under the auspices of Quality Assurance and Patient Safety. Alberta Health Services (AHS) and Covenant Health Core members include the following:

- Infectious Diseases Physician(s)
 - Lynora Saxinger, MD (Co-Chair, Provincial Antimicrobial Stewardship Committee; Co-Chair, Edmonton Zone Antimicrobial Stewardship Working Group)
 - Holly Hoang, MD (Medical Director, Antimicrobial Stewardship, Covenant Health)
 - Wendy Sligl, MD (Infectious Diseases, Critical Care)
 - Bonita Lee, MD (Pediatric Infectious Diseases)
- Clinical Pharmacists with Infectious Diseases training
 - Susan Fryters, BScPharm, ACPR (AHS Antimicrobial Utilization/Infectious Diseases Pharmacist)
 - Margaret Gray, BSP (Clinical Practice Lead, AHS/Covenant Health Pharmacy)
- Pharmacists
 - Michael Guirguis, Drug Stewardship pharmacist, Edmonton Zone
 - Sandra Leung, Pharmacy Manager, Continuing Care, Edmonton Zone
- Administrators
 - Donna Daniec (Executive director, AHS Integrated Quality Management; Co-Chair, Edmonton Zone Antimicrobial Stewardship Working Group)
 - Jon Popowich (Vice President, Quality, Covenant Health)
 - Deb vanHaaften (Executive Director, Pharmacy - Edmonton & Area)
 - Gordon Stewart, PharmD (Corporate Director, Pharmacy Services, Covenant Health)
- Clinical Microbiologists
 - Jeff Fuller, PhD, FCCM
 - Jasmine Ahmed-Bentley, MD
- Infection Prevention & Control
 - Uma Chandran, MD (Medical Director, Infection Prevention & Control, RAH/GRH)
 - Janet Barclay (Director, Infection Prevention & Control, Edmonton Zone)
- Representatives from the various medical departments (Internal Medicine, NARP, Surgery, Critical Care, Pediatrics, Seniors Health)

E. PROCESS AND OUTCOME MEASURES

I. ANTIMICROBIAL UTILIZATION DATA

Phase 1:

Each site to have, at minimum, reports showing the amount of drug dispensed from the pharmacy on a quarterly basis by site, program and unit with a display of trends over time measured as:

- Dollars spent on each antibiotic
- Units dispensed

Phase 2:

Standardized measures of antimicrobial consumption are preferred for comparisons across centers, and should be standardized into rates, using hospital denominator data. The denominator data should be derived in the same way between sites of care optimally using the same data used to track nosocomial infections and Antimicrobial Resistant Organisms by Infection Prevention and Control (e.g. DDD/1000 patient days.)

- Defined daily doses (DDDs), as used by the World Health Organization (WHO), is calculated as the total number of grams of an antimicrobial agent used divided by the number of grams in an average adult daily dose. WHO publishes DDD values on <http://www.whocc.no/atcddd/>. DDD is less accurate in pediatrics, across body mass indices, and in populations with renal impairment requiring dose adjustments. Therefore, sites with hemodialysis and pediatrics will not find the conversion as accurate although the intrasite trends will be robust. Direct site to site comparisons would not be expected to be highly useful unless the hospital case mix data are reviewed concurrently. The capability of reporting use in DDDs exists for those sites in Edmonton using the Centricity pharmacy system (all except UAH & RAH).
- Days of Therapy (DOT), as recommended by the Centers for Disease Control and Prevention, is now the preferred measure of antimicrobial use because it is more applicable to different populations and less likely to be affected by different dosing schemes. This would be the eventual goal for all sites, and should be considered as systems upgrade.

II. DELIVERABLES FOR ANTIMICROBIAL UTILIZATION DATA REPORTING

AHS and Covenant inpatient facility antimicrobial utilization / Hospital pharmacy departments have varying information systems and reporting capabilities. Data review and interpretation is a key element of developing stewardship initiatives that target the highest impact interventions. Thus, the following plan identifies imminent, medium and long term reporting requirements to guide IT efforts as they work towards a more standardized reporting system.

Short Term Goals

- 1) All acute care sites should develop the capacity to issue quarterly reports of antimicrobial utilization in expenditures, according to a basic template developed by the Antimicrobial Stewardship Committee (ASC). This should be reported to the Site leadership with analysis and commentary from Antimicrobial Stewardship representatives from that site.
- 2) Site reports should be reviewed by the Zonal Stewardship Working Group or equivalent to help define site based goals and deliverables. Site reports should be collated to a zone wide report (and program based reports if possible) - this should be reviewed by Zone Stewardship Working groups and analyzed with recommendations going to Site and Zone leadership, Pharmacy, and Programs.
- 3) The large academic and tertiary hospital sites should develop the capacity to issue reports in DDDs by April 2013. The data dictionary/spreadsheet could be developed centrally with AHS IT support and shared to reduce workload in converting dollars- to grams to DDDs (WHO defined.)

Medium Term Goals

- 4) All sites develop the capacity to report in DDDs. The core working group membership and the ASC could assist Pharmacy and IT in developing a report template and identifying which data fields are a “must” in the reports.
- 5) Integration of patient demographics in the reporting to get DDDs/1000 pt days per site (admission and discharge day is plus one day) and by admissions (this should be patients admitted to hospital, not admissions to wards) should also be accomplished to have appropriate denominators to look at differing patterns between sites. The demographic information has to be derived from the same source as Infection Prevention and Control (IP&C) numbers to allow concurrent assessment of Antibiotic resistant organisms (ARO) monitoring and *C. difficile* rates.

Longer Term Goals

- 6) Work towards reporting DOTs, with ongoing development of information systems capabilities to support stewardship functions. Sites that have Dialysis programs and Pediatric sites should be first in DOT rollout.
- 7) Integration of antibiogram based resistance data on site and zone basis with utilization data.

III. ANTIMICROBIAL ADVERSE EFFECTS

- Quarterly incidence rates of hospital-acquired *Clostridium difficile* as tabulated by Infection Prevention and Control
- Future development of an antimicrobial adverse event voluntary reporting system which highlights both antimicrobial stewardship and patient safety objectives

IV. ANTIMICROBIAL RESISTANCE RATES

- Antimicrobial resistance pertaining to the following organisms will be examined annually looking for nosocomial resistance pressure which are subject to changes in antibiotic prescribing:
 - *Ps. aeruginosa*
 - *Acinetobacter spp.*
 - Extended spectrum beta-lactamase (ESBL) producing gram negative bacilli
 - *Serratia spp.*

F. ANTIMICROBIAL STEWARDSHIP STRATEGIES AND GUIDANCE DOCUMENTS

I. PROSPECTIVE AUDIT WITH INTERVENTION AND FEEDBACK

Definition and Objectives

Prospective audit with intervention and feedback has been shown to be the most effective method of decreasing inappropriate antibiotic use with the most enduring effects. Audits of antimicrobial use will be conducted on hospital units to gather prescribing data and identify areas for improvement. Collected data will address the following:

- What is the medical indication for the antibiotic?
- According to practice guidelines, was empiric therapy chosen appropriately? In the absence of practice guidelines, appropriateness will be judged by considering the most likely pathogens implicated and whether the antimicrobial provided the most encompassing yet streamlined coverage
- Are antimicrobials streamlined appropriately according to culture results?
- Is the ordered dose and duration of antimicrobial appropriate?
- Was intravenous to oral conversion of therapy performed in a timely manner?

The information will be collected using standardized audit forms (**Appendix 1**). A copy of the form will remain in the chart for the attending service and a copy will be retained for data collection. Attempts will be made to provide feedback to the attending team in person.

Ultimately, the data collected from these audits will be used to identify salient stewardship opportunities that require immediate attention, and to identify needed educational topics for future rounds/educational sessions.

The Audit Process

The frequency and method of performing audits will be site-dependent. Smaller sites may be amenable to more frequent and comprehensive prospective audits whereas this may not be feasible for the larger sites. What follows are examples of auditing processes that can be selected according to site size and priority.

- Routine Audit
 - On a bi-monthly basis, the team will perform an audit of selected hospital inpatient units such that all units are audited over a 12 month span. All patients on the chosen unit will be included if they are on an antimicrobial.
 - This method is suitable for smaller sites that have the ability to canvas all units. Benefits include capturing comprehensive site-wide data that can be used to further target stewardship strategies.
- Audit by Medication
 - All admitted patients at the site are audited if they are on an antibiotic chosen by the Committee to be of interest.
 - This method is useful for investigating prescribing of an antibiotic that is being used in excess (e.g. If the rate of meropenem prescribing doubled, a meropenem audit can be performed to determine if use is appropriate).
- Audit by Diagnosis or Procedure
 - All admitted patients with a chosen admitting infectious diagnosis or receiving a specified procedure are audited.
 - Useful to determine if patients with a specific condition are receiving appropriate antibiotics (e.g. do all patients diagnosed with viral meningitis have their antibacterials discontinued in a timely manner?)

- Audit by Ward
 - All patients on one inpatient ward are audited to better understand the prescribing practices of this one ward (multiple wards can be targeted as necessary).
 - This technique is useful if one ward is prescribing higher numbers of antimicrobials compared to others or if a unit is experiencing an outbreak.

II. FORMULARY RESTRICTION AND PREAUTHORIZATION

Formulary Restriction

In an attempt to provide homogeneity and ease of use across the various Edmonton zone acute care centers, antimicrobial restriction and pre-authorization procedures will remain in line with the Alberta Health Services Formulary, as determined by the Drugs and Therapeutics Committee and its subcommittee, the Antimicrobial Stewardship Committee. The Edmonton zone ASWG, will convene on a regular basis to provide input on the drug formulary antimicrobial selections with the following objectives:

- Identify redundant antimicrobials and enact therapeutic interchanges as necessary
- Identify those antimicrobials that can be replaced by a more effective or safe alternative thereby allowing for therapeutic interchanges (**Appendix 2**) that benefit patient care

Refer to the following website for access to the provincial drug formulary:

http://intraweb01.albertahealthservices.ca/pharmacy/ahs_formulary/criteria_of_use_report.aspx

Refer to **Appendix 2** for a summary of the Therapeutic changes and refer to the following website for a comprehensive list of Therapeutic Interchanges, which is updated on a regular basis: <http://intraweb01.albertahealthservices.ca/pharmacy/documents/formulary/TI.pdf>

Pre-authorization

Currently, the antimicrobials requiring preauthorization in our sites include: Linezolid, Daptomycin, Imipenem, Meropenem, Ertapenem, and Tigecycline

- The rationale for preauthorization of certain antimicrobials is to allow pharmacy based data collection for antimicrobials that are any or all of :
 1. Novel, therefore should be used carefully to reduce development of resistance
 2. Very broad spectrum, and thus diagnostic indications should be tracked for patient safety and resistance concerns

3. Subject to new transmissible resistance mechanisms which require monitoring in conjunction with utilization data.
- Prescribers will be required to complete a *preauthorization form* (**Appendix 3**) for review prior to continued dispensing from pharmacy.
 - Completion of a Preauthorization Form will not be required prior to the initial antibiotic dose, to facilitate patient care, but it must be processed by the end of the next day.
 - Preauthorization Form data should be collated and reported biannually to pharmacy and medical site leads, and department and division heads. Completion rate (per care unit), audit of adherence to guidelines, and follow up actions in discrepancies should be documented.

III. EDUCATION

Continued education pertaining to antimicrobial stewardship will take place at the various sites in the following formats as deemed appropriate:

- Infectious Diseases Stewardship physicians and Pharmacists will participate in regular Medicine Grand Rounds and Pharmacy Rounds, to cover topical infectious diseases cases with concurrent antimicrobial stewardship instruction.
- Medical students and residents regularly suggest a need for more antibiotic teaching. Dedicated Stewardship Teams will co-create a repository of antibiotic modules for training, which can be implemented within local training infrastructure.
- Direct education to prescribing clinicians will be provided by clinical Infectious Diseases pharmacists or physicians during prospective audit and feedback sessions
- Recurring issues pertaining to un-optimized antimicrobial prescribing identified during the prospective audit will be collated and used to provide directed educational seminars.
- Infectious Diseases physicians are on call 24/7 (in Edmonton Zone, weekend coverage is centered at the RAH and UAH) and is available to offer phone consultation regarding antimicrobial prescribing in specific cases at sites without in person coverage.
- The Bugs and Drugs guidelines for commonly managed Infectious Diseases will be summarized in PQR (Pocket Quick Reference) cards (refer to section IV. Practice guideline and clinical pathway dissemination) as an adjunct to the full reference tool.
- The Antimicrobial Stewardship manual will be updated on a regular basis to include accomplished, ongoing or new Antimicrobial Stewardship objectives. It will remain on AHS and Covenant Health websites for staff accessibility.

IV. PRACTICE GUIDELINES

Clinical practice guidelines are developed at increasing frequency. Clinicians often cannot stay up to date in a timely manner due to volume. Furthermore, these guidelines do not account for local antibiograms and drug formularies. In response to these concerns, the following have been developed:

- Bugs & Drugs is an AHS wide (and national) antimicrobial reference that provides recommendations for appropriate antibiotic use based on literature review, expert consultation and local antibiogram characteristics.
- Practice guidelines for the following common infections have been summarized into PQR (Pocket Quick Reference) cards for quick reference (**Appendix 4**):
 - Urinary tract infections
 - Pneumonia (community acquired, hospital acquired, ventilator associated, aspiration)
 - Skin and soft tissue infections

V. CLINICAL PATHWAYS

Clinical pathways targeting high yield antimicrobial stewardship opportunities will be developed to rationalize and optimize antimicrobial use for the following scenarios:

- Pre-operative antimicrobial prophylaxis (in progress)
- Antimicrobial selection in the setting of drug allergies (in progress)
- Intravenous antibiotic to oral conversion (in progress)
- C. difficile treatment (in progress)

VI. STREAMLINING AND SHORTENING DURATION OF THERAPY

Streamlining/de-escalation of broad spectrum antimicrobials will be facilitated by the following means:

- Continued efforts with the Microbiology Laboratory to ensure rapid reporting of susceptibility allowing for efficient narrowing of antimicrobials
- Clinical pharmacists rounding with the attending team will capitalize on opportunities for antimicrobial streamlining according to culture results

- During prospective audit and feedback rounds, opportunities for streamlining antimicrobials will be brought to the attention of the attending team
- A “ Three Day Check” quality indicator (as has been started in Calgary Zone) should be trialed in Edmonton Zone, with documentation of a pharmacy review on the third day of antibiotic therapy. Rollout should be accompanied by 1) Interactive, case based educational rounds for participating pharmacists 2) Documentation of the review findings and recommendations and 3) Documentation of recommendation uptake
- In therapy of certain infections, duration of therapy is well established by data. Targeted reviews of duration of prescribing for a rota of conditions, such as CAP, HAP and VAP offer opportunity to look at guideline concordance and offer academic detailing education for relevant care units.

VII. DOSE OPTIMIZATION

Optimization of antimicrobial dosing specific to patient characteristics (body mass, renal function, hepatic function), microbiology, site of infection and antimicrobial pharmacokinetics, and pharmacodynamics is an essential aspect of improving patient outcome, minimizing adverse effects, and reducing the development of drug resistance. To this end, pharmacists will continue to make recommendations during team rounds regarding how best to optimize drug administration in the following manner:

- Review and adjust medications for renal function as appropriate
- Order and follow therapeutic drug monitoring and adjust antibiotic dosages accordingly
- Enforce therapeutic interchanges to ensure use of formulary drugs and optimal dosing
- Implement automatic stop orders on antimicrobials in the absence of clinical justification for continued therapy

VIII. PARENTERAL TO ORAL CONVERSION OF THERAPY

Table 1 lists those antimicrobials that, due to excellent oral bioavailability, should be administered orally in the presence of a functioning gastrointestinal tract as there is no benefit to using the intravenous formulation. See Bugs & Drugs 2012 page 83 for complete list.

Parenteral to oral conversions for common infectious syndromes are part of the Therapeutic Interchange program but local adaptation and an education kit to reinforce IV to PO conversion will be developed.

Table 1. Antimicrobials with Enhanced Oral Bioavailability

These antimicrobials are equally effective when given orally in the presence of an intact gastrointestinal tract

ANTIMICROBIAL	IV FORMULATION	ORAL FORMULATION
Quinolones		
Ciprofloxacin	400 mg Q12H	500-750 mg BID
Levofloxacin	750 mg daily	750 mg daily
Moxifloxacin	400 mg daily	400 mg daily
Macrolides		
Azithromycin	500 mg daily	500 mg PO once then 250 mg daily x 4 days
Other		
Doxycycline	100 mg Q12H	100 mg BID
Linezolid	600 mg Q12H	600 mg BID
Clindamycin	600 mg Q8H	300 – 450 mg QID
TMP SMX	160 – 240 mg TMP Q6, 8 , or12H	1 DS tab Q12H
Metronidazole	500 mg Q12H	500 mg BID
Anti-fungals		
Fluconazole	400 mg daily	400 mg daily
Voriconazole	4 mg/kg Q12H	200 mg Q12H

Refer to Bugs & Drugs 2012 pages 72-75 for renal dosing and 76-79 for hepatic dosing.

IX. STEWARDSHIP RELEVANT MICROBIOLOGY LABORATORY PRACTICES

Antimicrobial Susceptibility Reporting

The Antimicrobial Stewardship Teams will remain connected to Clinical Microbiology laboratories, to provide clinical context for decisions around susceptibility reporting. Antimicrobial susceptibility testing has been harmonized amongst AHS microbiology laboratories and is in compliance with the most current Clinical and Laboratory Standards Institute (CLSI) recommendations. Reported antimicrobial susceptibilities will include the most targeted and effective antimicrobials for the given organism and corresponding infection site and correspond to the formulary wherever possible. Second line options will only be reported upon physician consultation with a Microbiologist to encourage appropriate use (e.g. rifampin for *S. aureus* is not reported routinely as monotherapy results in resistance development).

Resistance Monitoring and Local Antibigrams

The Provincial Laboratory and Dynalife Diagnostics continue to monitor local resistance rates for commonly isolated pathogens, including multi-drug resistant (MDR) organisms. A local antibiogram presenting more commonly encountered pathogens and local susceptibility rates will be distributed annually. For a the full detailed antibiograms, refer to the following websites:

- Dynalife Diagnostics (Royal Alexandra Hospital, Grey Nuns Hospital, Misericordia, Community Hospitals and Clinics):

<http://dynamifedx.com/HealthProfessionals/LabInformation/Antibiograms/tabid/1317/Default.aspx>

- Provincial Laboratory (University of Alberta Hospital):

<http://www.albertahealthservices.ca/3294.asp>

www.antibiogram.ca

G. ANNUAL REPORTS

Annual reports will be updated as they become available.

REFERENCES

1. John JF, Fishman NO. Programmatic role of the infectious diseases physician in controlling antimicrobial costs in the hospital. *Clin Infect Dis* 1997;24:471-85.
2. Dellit TH, Owens RC, McGowan JE et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for developing an institutional program to enhance antimicrobial stewardship. *CID* 2007;47:159.
3. Marr JJ, Moffet HL, Kunin CM. Guidelines for improving the use of antimicrobial agents in hospitals: a statement by the Infectious Diseases Society of America. *J Infect Dis* 1988;157:869-76.
4. 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* 2003;24:2699-2706.
5. Debast SB, Yaessen N, Choudry A et al. Successful combat of an outbreak due to *Clostridium difficile* PCR ribotype 027 and recognition of specific risk factors. *Clin Microbiol Infect* 2009;15:427-434.
6. Valiquette L, Benoit C, Garant MP et al. Impact of a reduction in the use of high-risk antibiotics on the course of an epidemic of a *Clostridium difficile*-associated disease caused by the hypervirulent NAP1/027 strain. *Clin Infect Dis* 2007;45:S112-21.
7. Roberts GW, Farmer CJ, Cheney PC et al. Clinical decision support implemented with academic detailing improves prescribing of key renally cleared drugs in the hospital setting. *J Am Med Inform Assoc* 2010;17:308-312.
8. Marrie TJ, Lau CY, Wheeler SL et al. A controlled trial of a critical pathway for treatment of community-acquired pneumonia. *JAMA* 2000;283:749-55.
9. Singh N, Rogers P, Atwood CW et al. Short-course empiric antibiotic therapy for patients with pulmonary infiltrates in the intensive care unit. *Am J Respir Crit Care Med* 2000;162:505-11.
10. Gentry CA, Greenfield RA, Slater LN et al. Outcomes of an antimicrobial control program in a teaching hospital. *Am J Health Syst Pharm* 2000;57:268-74.
11. White AC, Atmar RL, Wilson J et al. Effects of requiring prior authorization for selected antimicrobials: expenditures, susceptibilities, and clinical outcomes. *Clin Infect Dis* 1997;25:230-9.
12. Fishman N. Antimicrobial stewardship. *Am J Med* 2006;119:S52-S61.

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Appendix 1: Standardized Audit Form

 <p>Antimicrobial Audit Form</p>	Patient Name:	
	Hospital Number-Case:	
	Personal Health Number:	

Site:	Unit:	Antibiotic Allergies:
<input type="checkbox"/> University of Alberta Hospital (UAH)	<input type="checkbox"/> Medicine (unit ____)	Abx: _____
<input type="checkbox"/> Royal Alexandra Hospital (RAH)	<input type="checkbox"/> General Surgery (unit ____)	Nature of reaction (if known):
<input type="checkbox"/> Misericordia Community Hospital (MCH)	<input type="checkbox"/> Critical Care (unit ____)	
<input type="checkbox"/> Grey Nuns Community Hospital (GNCH)	Ht _____ cm Wt _____ kg	

Diagnosis for which antimicrobial agent is being used: documented inferred from chart

Date of Admission (dd/mm/yy):

ANTIBIOTIC THERAPY

List each antibiotic course only once.

A. Previous (within the last two weeks) Antibiotic(s), including outpatient therapy if known:

Antibiotic	Dose/Route Frequency	Start Date (mmm dd)	Stop Date (mmm dd)	# of Doses Received	Ordered by:		
					Att. Service	ID consult	Other

B. Empiric (pre-C&S report) Antibiotic(s) (must include ≥ 1 of targeted antibiotics):

Antibiotic	Dose/Route Frequency	Start Date (mmm dd)	Stop Date (mmm dd)	# of Doses Received	Ordered by:		
					Att. Service	ID consult	Other

C. Definitive (post-C&S report) Antibiotic(s) (if changed from B):

Antibiotic	Dose/Route Frequency	Start Date (mmm dd)	Stop Date (mmm dd)	# of Doses Received	Ordered by:		
					Att. Service	ID consult	Other

Comments on clinical diagnosis/treatment:

Instructions for Completing Antimicrobial Audit Form

Hospital Number-Case - include case number

Personal Health Number - this is the Alberta Healthcare number. Also called ULI (unique lifetime identifier) on some addressograph labels and usually ends in AB.

Antibiotic Allergies - include only antibiotic allergies and include the nature of the reaction if known or documented in chart or computer, e.g. rash, anaphylaxis, hives, urticaria, trouble breathing, etc.

Diagnosis for which antimicrobial agent is being used - include type/site of infection and whether this information was documented on the chart or you inferred the diagnosis from the information in the chart.

ANTIBIOTIC THERAPY

- List each antibiotic course only once unless dose, route or frequency changes.
 - If the antibiotic was ordered by either the attending medical staff or by ID consult, put a check mark in that column. If neither of these, fill in the name of the prescriber or program who ordered the antibiotic under Other.
- A. Previous Antibiotic(s) - list each antibiotic course of therapy that the patient received in the previous two weeks. Include outpatient therapy if known/documented.
 - B. Empiric Antibiotic(s) - list each empiric antibiotic course of therapy. Empiric is defined as anti biotic therapy prescribed before the culture & susceptibility (C&S) results are known. Empiric therapy must include at least one of the targeted antibiotics.
 - C. Definitive Antibiotic(s) - list each antibiotic course of therapy prescribed after the culture & susceptibility results are known (post-C&S report) if changed from the antibiotic therapy listed in Table B.
- If additional targeted antibiotics are ordered for the same patient for:
 - o the same diagnosis - use the same audit form. A separate evaluation form will be used for each targeted antibiotic.
 - o a different diagnosis/infection - use a new audit form.

MICROBIOLOGY

Specimen Source - list where the culture was taken from or type of fluid, e.g. sputum, blood, superficial skin, abscess, peritoneal fluid, etc

Gram stain results - list # of WBC and RBC as well as morphology of organism, e.g. 4⁺ WBC, 3⁺ RBC, 3+ GNB (morphology suggestive of anaerobes)

Organism(s) - list all organisms cultured, one organism per row so susceptibilities can be listed separately

Antibiotic Susceptibilities - list all antibiotics reported as susceptible (S), intermediate (I), or resistant (R), e.g. S - amp/cefaz/cipro/nitrofurantoin/TMP-SMX

I - cephalothin/tobra

R - gent

If abbreviations are used define them at least once per form. If needed use overleaf for more culture information.

MONITORING

Baseline - date for baseline values is the day the targeted antibiotic was started, **or the closest day to that date.**

Maximum - record the highest value seen over the course of antibiotic therapy. Include the date this peak value was observed.

End of therapy or audit - record the value seen at the end of antibiotic therapy, or the last day of the audit if that occurs first. Include the date.

Clcr - use the following formulae to calculate creatinine clearance (Clcr):

$$\text{IBW (females)} = 45.5\text{kg} + (2.3 \times \text{inches} > 5 \text{ feet})^*$$

$$\text{IBW (males)} = 50\text{kg} + (2.3 \times \text{inches} > 5 \text{ feet})^*$$

$$\text{Clcr (females)} = \frac{(140 - \text{age}) \times \text{IBW}^{**}}{\text{Scr } (\mu\text{mol/L})}$$

$$\text{Clcr (males)} = \text{Clcr (female)} \times 1.2$$

*or (0.92 x cm > 150cm)

** If ABW < IBW, use ABW in Clcr calculations

If obese (ABW > 20% above IBW), use dosing weight (DW)

$$\text{DW} = 0.4 (\text{ABW} - \text{IBW}) + \text{IBW}$$

Appendix 2: Summary of Therapeutic Interchanges

THERAPEUTIC INTERCHANGES (TI)

For the most updated list of TIs, please refer to

<http://intraweb01.albertahealthservices.ca/pharmacy/documents/formulary/TI.pdf>

Interchanges for Medications not on Formulary

<u>ORIGINAL ORDER</u>	<u>THERAPEUTIC INTERCHANGE</u>
Cefaclor 250 mg PO TID (capsules)	Cefuroxime axetil 250 mg PO BID (tablets)
Cefaclor 500 mg PO TID (capsules)	Cefuroxime axetil 500 mg PO BID (tablets)
Cefadroxil PO BID	Cephalexin 500 mg PO QID
Cefprozil PO BID or TID in adults	Cefuroxime axetil tablets PO BID at same dose in adults
Lincomycin IV	Clindamycin 600 mg IV q8h
Moxifloxacin 400 mg IV/PO daily in polymicrobial infections a) non-gastrointestinal infections (eg. skin and soft tissue) b) gastrointestinal infections	a) Levofloxacin 500 mg IV/PO daily + Metronidazole 500 mg IV/PO bid (same route unless patient can tolerate oral/NG intake then change to oral/NG*) *For levofloxacin, tube feeds should be held for 2 hours before and after dose b) Ciprofloxacin 500 mg IV/PO bid + Metronidazole 500 mg IV/PO bid (same route unless patient can tolerate oral/NG intake then change to oral/NG**) **For ciprofloxacin, tube feeds should be held 1 hour prior and 2 hours following dose
Moxifloxacin 400 mg IV/PO daily in pneumonias a) Pneumonias without risk factors for anaerobic infection b) Aspiration pneumonia AND patient at risk of anaerobic infection Risk factors for anaerobic infection: poor oral hygiene, severe periodontal disease, putrid sputum	a) Levofloxacin 750 mg IV/PO daily (same route unless patient can tolerate oral/NG intake then change to oral/NG*) b) Levofloxacin 750 mg IV/PO daily (same route unless patient can tolerate oral/NG intake then change to oral/NG*) + Metronidazole 500 mg IV/PO bid (same route unless patient can tolerate oral/NG intake then change to oral/NG) * Tube feeds should be held 2 hours before and after dose
Norfloxacin 400 mg PO bid	Ciprofloxacin 500 mg PO bid

Dosing/Dosing Interval Interchanges

<u>ORIGINAL ORDER</u>	<u>THERAPEUTIC INTERCHANGE</u>
Amoxicillin q6h or QID	Amoxicillin q8h TID
Amoxicillin-clavulanate 250 mg PO TID in adults	Amoxicillin-clavulanate 500 mg PO BID
Amoxicillin-clavulanate 500 mg PO TID in adults	Amoxicillin-clavulanate 875 mg PO BID
Ampicillin PO q6h or QID	Amoxicillin PO q8h or TID (excluding shigellosis)
Azithromycin 600 mg PO	Azithromycin 500 mg (2 x 250 mg)
Cefazolin IV q6h	Cefazolin IV q8h at same dose
Cefuroxime doses of >750mg IV or intervals more frequent than q8h	Cefuroxime 750 mg IV q8h maximum in adults; 1.5g IV q8h maximum in pediatrics
Ciprofloxacin 500 mg IV dose	Ciprofloxacin 400 mg IV dose

Dosing/Dosing Interval Interchanges Continued

ORIGINAL ORDER	THERAPEUTIC INTERCHANGE
Clarithromycin (Biaxin®) 500 mg PO BID in adults	Clarithromycin extended release (Biaxin® XL) 1000 mg (2 x 500 mg XL tabs) PO once daily with food
Clindamycin IV greater than 600 mg per dose	Clindamycin IV 600 mg, excluding obstetrics and gynecology patients
Clindamycin IV q6h	Clindamycin IV q8h at same dose
Clindamycin PO greater than 450 mg per dose	Clindamycin PO 300 mg qid. For treatment of osteomyelitis or PJP, change to 450 mg PO qid. For other indications, prescriber can increase to 450 mg PO qid.
Erythromycin enteric coated 333mg PO tid	Erythromycin enteric coated base 250 mg PO qid
Levofloxacin 500 mg IV/PO daily for pneumonia in adults	Levofloxacin 750 mg IV/PO daily (In CAP, the recommended duration of treatment is 5 days)
Meropenem 1-2g IV q6-8h in adults	Meropenem 500 mg IV q6h in adults* Exceptions: cystic fibrosis, CNS infections, ophthalmologic infections (consider dose increase to 2g IV q8h) *Dose adjustments required for renal failure
Metronidazole IV q6-8h	Metronidazole IV q12h Exceptions: subdural empyema, brain abscess, or C. difficile where dosing should be q8h
Vancomycin PO doses of greater than 125 mg qid (when used for severe C. difficile infection*) *Severe CDI is defined as WBC>15, creatinine >1.5x, hypotension or shock or documented/impending toxic megacolon	Vancomycin 125 mg PO qid

IV to PO Interchanges

ORIGINAL ORDER	THERAPEUTIC INTERCHANGE
Ciprofloxacin 200 mg IV q12h where patient is on enteral feeds or oral/NG medications	Ciprofloxacin 500 mg PO (or via tube) q12h (q24h if CrCl<30ml/min). Tube feeds should be stopped for 1 hour prior to and 2 hours following dose with 30ml NS flush before. And after each dose.
Ciprofloxacin 400 mg IV q12h where patient is on enteral feeds or oral/NG medications	Ciprofloxacin 750 mg PO (or via tube*) q12h (q24h if CrCl<30 ml/min). *Tube feeds should be stopped for 1 hour prior to and 2 hours following dose with 30ml NS flush before.
Clindamycin IV where patient is on enteral feeds or oral/NG medications	Clindamycin 300 mg PO qid, excluding obstetrics patients. For treatment of osteomyelitis or PJP, change to 450 mg PO qid
Levofloxacin IV daily where patient can tolerate oral/NG intake	Levofloxacin PO daily (same dose/frequency) Tube feeds should be held 2 hours before and after dose
Metronidazole IV where patient is on enteral feeds or oral/NG medications	Metronidazole PO at same dose/frequency Exception: Toxic megacolon where IV should be continued

Drug Formulation Interchange

<u>ORIGINAL ORDER</u>	<u>THERAPEUTIC INTERCHANGE</u>
Amoxicillin chew tab	Amoxicillin oral suspension at same dosage
Erythromycin oral liquid	Erythromycin estolate suspension, equivalent dose
Erythromycin oral solid, eg. erythromycin base tablets	Erythromycin enteric coated base solid dose formulation (250 mg EC capsul) at equal dose
Itraconazole oral capsules	Itraconazole oral solution at same dose and frequency while in hospital
Nitrofurantoin macrocrystal formulation eg. MacroDantin capsules, Tevanitrofurantoin capsules	Nitrofurantoin (60% microcrystal/40% macrocrystal) tablets (AAPharma)
Nitrofurantoin monohydrate/macrocrystal formulation Eg. MacroBID capsules 100 mg PO bid	Nitrofurantoin (60% microcrystal/40% macrocrystal) tablets (AAPharma) 50 mg PO qid
Vancomycin oral doses (capsules)	Vancomycin parenteral solution given orally at same dosage

Other Therapeutic Interchanges

<u>ORIGINAL ORDER</u>	<u>THERAPEUTIC INTERCHANGE</u>
Cefotaxime 1-2g IV q8-12h (in adult patients)	Ceftriaxone 1-2g IV q12-24h
Cefotaxime in pediatric patients > 3 months	Ceftriaxone 50-100 mg/kg/dose IV q12-24h
Cefoxitin 1-2g at any dosing interval in adult patients	Cefazolin 1-2g IV q8h PLUS / MINUS metronidazole 500 mg q12h
Ciprofloxacin IV + Metronidazole IV pre-op for surgical prophylaxis in patients with metronidazole or cephalosporin allergy or severe penicillin allergy	Clindamycin 600 mg IV + Gentamicin 1.5 mg/kg IV pre-op x 1 dose (adults) Clindamycin 15 mg/kg (max 600 mg) IV pre-op + Gentamicin 2 mg/kg (based on ABW) IV pre-op x 1 dose (pediatrics)
Erythromycin IV in adults	Azithromycin 500 mg IV daily. Exceptions: Obstetrics, or if prescribed for gastroparesis
Erythromycin IV in pediatrics	Azithromycin 10mg/kg IV daily (maximum 500 mg daily). Exceptions: Neonates (<1 month old) or when prescribed for gastroparesis

Other Therapeutic Interchanges Continued

<u>ORIGINAL ORDER</u>	<u>THERAPEUTIC INTERCHANGE</u>
Ketoconazole oral	Fluconazole oral tabs at equivalent dosage depending on indication for use
Vancomycin PO at any dose if does not meet clinical guidelines for severe C. difficile infection (CDI)* *Severe CDI is defined as WBC>15, creatinine >1.5x, hypotension or shock or documented/impending toxic megacolon	Metronidazole 500 mg PO tid

Appendix 3: Antibiotic Preauthorization Form and Anti-fungal form

Antibiotic Preauthorization Form:

<http://www.intranet2.capitalhealth.ca/pharmacy/Forms/CH0125UAHantibioticformforrestrictedNFantibioticsPYXIS.pdf>

(currently being updated)

Anti-fungal Preauthorization Form:

http://www.intranet2.capitalhealth.ca/pharmacy/Forms/CH_1057_antifungal_therapy_request_current.pdf

Appendix 4: Pocket Guidelines

In progress