Winnipeg's tertiary care centres' program for the prevention of antimicrobial resistance

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In Winnipeg, there are two tertiary care teaching centres and five community hospitals. Although the two tertiary care centres are distinct, they share many similarities. The infectious disease consultants at both institutions are members of one section, and, as a result, the concept of 'one program, two sites' prevails. Decision-making and thought processes involved in antimicrobial prescription are generally similar among members of the infectious diseases section with some variations. Because the antibiotic stewardship programs at Winnipeg's tertiary care centres (St Boniface General Hospital and the Health Sciences Centre) are sufficiently similar, they were summarized in the present report and used to illustrate how Winnipeg's tertiary care centres are involved in the prevention of the emergence of antimicrobial resistance.

Although the summary that follows is based on the current situation in Winnipeg, it is important to note that the city's health care system is being restructured. All of the city's hospitals will ultimately report to the Winnipeg Health Authority (WHA), a governing body that will oversee the administration and function of all the hospitals. Currently, the two tertiary care teaching hospitals have separate pharmacy and therapeutics committees, each with a distinct antimicrobial subcommittee; however, after the health care system is restructured, to streamline hospital formularies, the two tertiary care centres will share a joint pharmacy and therapeutics committee and a joint antimicrobial subcommittee. Each institution will continue to review its internal issues independently and report to the joint subcommittee. Under the WHA it is anticipated that the pharmacy and therapeutics committees and an-

timicrobial subcommittees of all city hospitals (community and teaching) will become part of city-wide joint pharmacy and therapeutics committee and antimicrobial subcommittee.

ANTIMICROBIAL STEWARDSHIP

By definition, stewardship is the office or term of duties of a steward, and a steward is one who is entrusted with the management of property, finances or other affairs not his own (1). Thus, an antimicrobial stewardship program should serve as a vehicle for the rational management of antimicrobial use. Discrimination of antimicrobial use has been advocated for prevention of the emergence of antimicrobial-resistant microorganisms (2-4). Various groups have recommended antimicrobial control methods as ways to slow down the emergence of antimicrobial-resistant bacteria (5-7). The goals of the antimicrobial stewardship program at Winnipeg's two tertiary care centres are as follows:

- to provide education regarding proper antimicrobial selection and use;
- to limit inappropriate antimicrobial selection and use;
- to guide the appropriate selection, dosing and duration of empirical/therapeutical antimicrobials;
- to prevent the emergence and spread of antimicrobial-resistant microorganisms;
- to establish a system to monitor, review and regulate antimicrobial use.

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TABLE 1a
Health Sciences Centre (Winnipeg, Manitoba) 1995 antibiogram for Gram-negative bacteria antibiotic susceptibilities

Organism	<i>Haemophilus influenzae</i>	<i>Escherichia coli</i>	<i>Enterobacter aerogenes</i>	<i>Enterobacter cloacae</i>	<i>Klebsiella oxytoca</i>	<i>Klebsiella pneumoniae</i>	<i>Proteus mirabilis</i>	<i>Pseudomonas aeruginosa</i>	<i>Serratia marcescens</i>	<i>Citrobacter freundii</i>	<i>Xanthomonas maltophilia</i>	<i>A. baumannii</i>
Number of isolates	68	3733	134	829	309	1013	387	1841	215	252	207	175
Ampicillin	68	59	25	37	42	23	85	—	—	44	—	—
Amoxicillin/clavulanate	100	94.5-	—	9	96	99	99	—	—	99	—	85
Piperacillin	—	64	81	88	92	79	92	93	99	80	54	82
Cefazolin	—	97	8	5	89	98	98	—	—	14	—	—
Cefoxitin	—	100	—	9	100	98	100	—	69	18	—	9
Cefuroxime	100	99	58	64	97	97	100	—	—	73	—	38
Cefotaxime* ¹	—	100	96	92	100	100	100	71	99	94	27	80.7
Ceftazidime†	—	100	72	91	100	100	100	92	99	81	60	92
Amikacin*	—	100	99	99	99	100	99	97	100	100	17	99
Gentamicin	—	97	99	98	99	99	90	89	100	98	18	87
Tobramycin	—	99	98	98	100	99	91	95	92	97	15	96
Ciprofloxacin†	100	100	98	98	98	99	100	95	93	94	63	81
TMP/SMX	94	76	99	91	94	83	86	17	96	69	95	63
Imipenem*	—	100	100	99	100	100	99	92	99	100	—	100
Nitrofurantoin‡	—	99	—	—	96	71	—	—	—	—	—	—

*Level 1 restricted agent; †Level 2 restricted agent; ‡Nitrofurantoin is a urinary tract agent only. A baum/haem Acinetobacter baumannii/haemolyticus TMP/SMX Trimethoprim/sulfamethoxazole

TABLE 1b
Health Sciences Centre (Winnipeg, Manitoba) 1995 antibiogram for Gram-positive and anaerobic bacteria antibiotic susceptibilities

	<i>Staphylococcus aureus</i>	<i>Staphylococcus epidermidis</i>	<i>Enterococcus faecalis</i>	<i>Enterococcus faecium</i>	Coag neg staphylococci	<i>Bacteroides fragilis</i>	<i>Bacteroides fragilis</i> group
Ampicillin	12	11	100	48	30	—	—
Amoxicillin/clavulanate)	97	46	100	77	66	100	98
Cloxacillin	97	47	—	—	67	—	—
Cefazolin	97	47	—	—	67	—	—
Cefoxitin	—	—	—	—	—	88	81
Ciprofloxacin*	96	75	78	58	81	—	—
Clindamycin	98	65	—	—	77	98	92
Gentamicin	96	57	—	—	79	—	—
Imipenem†	97	45	100	64	66	98	100
Metronidazole	—	—	—	—	—	100	98
TMP/SMX	98	71	—	—	77	—	—
Rifampicin	99	96	69	69	99	—	—
Vancomycin	100	100	100	99	100	—	—

*Level 2 restricted agent; †Level 2 restricted agent. Coag neg Coagulase-negative; TMP/SMX trimethoprim/sulfamethoxazole

TABLE 2

St Boniface General Hospital (Winnipeg, Manitoba) antibiogram, January to December 1996 showing number of times each type of organism was tested with percentage susceptible in parentheses

Organism	<i>Bacteroides fragilis</i>	<i>Haemophilus influenzae</i>	<i>Enterobacter cloacae</i>	<i>Escherichia coli</i>	<i>Klebsiella pneumoniae</i>	<i>Proteus mirabilis</i>	<i>Pseudomonas aeruginosa</i>	<i>Staphylococcus aureus</i>	Coag neg staphylococci	<i>Enterococcus faecalis</i>	<i>Streptococcus pneumoniae</i>
Ampicillin	—	237 (73)	—	1910 (67)	—	209 (79)	—	—	—	190 (100)	—
Cloxacillin	—	—	—	—	—	—	—	1073 (98)	692 (40)	—	—
Penicillin	128 (14)	—	—	—	—	—	—	1073 (14)	692 (8)	—	107 (96)*
Piperacillin	66 (97)	—	273 (72)	1910 (69)	430 (73)	209 (84)	573 (95)	—	—	—	—
Cefazolin	—	—	—	1910 (94)	430 (97)	209 (87)	—	1073 (98)	692 (40)	—	—
Cefoxitin	66 (98)	—	—	566 (98)	189 (95)	75 (99)	—	—	—	—	—
Cefotaxime	—	68 (100)	202 (77)†	566 (100)	189 (100)	75 (99)	—	1073 (98)	692 (39)	—	—
Ceftazidime	—	—	273 (74)†	1910 (100)	430 (100)	209 (100)	573 (93)	—	—	—	—
Gentamicin	—	19 (89)	273 (94)	1910 (96)	430 (99)	209 (92)	573 (84)	1073 (98)	692 (49)	—	—
Tobramycin	—	—	273 (93)	1910 (98)	430 (99)	209 (29)	573 (97)	—	—	—	—
Ciprofloxacin	—	—	273 (95)	1910 (98)	430 (98)	209 (100)	573 (91)	1073 (96)	692 (58)	1062 (57)‡	—
Clindamycin	66 (95)	—	—	—	—	—	—	1073 (96)	692 (56)	—	—
TMP/SMX	—	67 (91)	273 (94)	1910 (84)	430 (95)	209 (82)	—	1068 (99)	692 (67)	—	81 (91)
Erythromycin	—	—	—	—	—	—	—	1073 (88)	692 (33)	—	92 (96)
Tetracycline	—	—	71 (89)	1344 (75)	241 (95)	—	—	1073 (96)	692 (84)	1061 (24)	84 (95)
Imipenem	66 (100)	—	202 (97)	566 (100)	185 (99)	75 (96)	420 (85)	1073 (98)	692 (38)	1061 (98)	—
Nitrofurantoin	—	—	71 (42)	1344 (98)	241 (76)	—	—	88 (100)	178 (100)	568 (95)	—
Chloramphenicol	66 (100)	89 (100)	—	—	—	—	—	—	—	—	114 (99)
Metronidazole	66 (100)	—	—	—	—	—	—	—	—	—	—
Vancomycin	—	—	—	—	—	—	—	1073 (100)	692 (100)	1062 (100)	—
Cefuroxime	—	68 (100)	—	—	—	—	—	—	—	—	—

*For intermediate and high level resistance; †Not recommended due to inducible beta-lactamase; ‡For urinary tract infections only. Coag neg Coagulase negative; TMP/SMX Trimethoprim/sulfamethoxazole

PROGRAM STRUCTURE

The Winnipeg's tertiary care centres' program for the prevention of antimicrobial resistance depends on input from individuals with varied backgrounds. Guidance is sought from infectious disease consultants, the antimicrobial subcommittee, the pharmacy and therapeutics committee, medical microbiologists, clinical pharmacists and the infection control staff. All members contribute so that rational decisions may be made about how to implement an antibiotic stewardship program that will satisfy the goals outlined above.

Infectious disease consultants: Infectious disease consultants provide an integrated summary of what is occurring at the bedside in terms of disease entities, current antimicrobial use and current knowledge from the available scientific literature.

Antimicrobial subcommittee: This committee is composed of infectious disease consultants, medical microbiologists, clinical pharmacists and representatives from the infection control staff. Trends in antimicrobial use are reviewed in relation to antimicrobial resistance trends. Decisions concerning formulary additions or deletions of antimicrobials are considered in terms of their effects.

Infection control unit staff: The infection control unit tracks

the epidemiology of antimicrobial-resistant organisms within the institution and, with the assistance of the microbiology laboratory, detects changing trends in the antimicrobial resistance profiles and undertakes appropriate investigations to determine how and why the trends are occurring. Surveillance for antimicrobial-resistant microorganisms is continuous and can be used to identify problem areas early within the institution. A bimonthly newsletter is produced by the Infection Control Unit staff. In addition to infection prevention, specific efforts are made in the newsletter to heighten awareness about appropriate antimicrobial use.

Medical microbiologists: The medical microbiologist provides important insights into antimicrobial resistance. Trends are tracked and reported to the infection control unit staff, antimicrobial subcommittee, infectious disease consultants and the clinical pharmacists.

Microbiology laboratory: Microorganism antibiogram data are collated from the microbiology laboratories at both tertiary care centres and reproduced in antibiogram cards. Tables 1a, 1b and 2 present data from the most recent antibiogram cards from the Health Sciences Centre and St Boniface General Hospital. These cards are provided as part of the adult

antimicrobial-dosing guidelines at the two institutions. The cards provide a tabular representation to help guide targeted antimicrobial prescribing.

The microbiology laboratory provides selective susceptibility profiles for microorganisms identified on culture. An example of a susceptibility profile is the 'cephalosporin cascade report configuration'. If an organism is susceptible to a first generation cephalosporin, second- or third-generation cephalosporins are not reported in the configuration; however, if the organism is resistant to a first-generation cephalosporin, then the susceptibility profile for the second- and third-generation cephalosporins is reported and suppressed, respectively. If the microorganism is resistant to the second-generation cephalosporin, results of susceptibility testing for the third-generation cephalosporin are reported. Antimicrobial susceptibility profiles for ciprofloxacin, ceftazidime, tobramycin and the carbapenems are usually not reported for enterobacteriaceae; however, the susceptibility reports are available from the microbiology laboratory on request. Through simple measures, the microbiology laboratory is able to emphasize the use of first-line antimicrobials and de-emphasize the use of higher generation antimicrobials, such as ciprofloxacin, vancomycin and ceftazidime, that are best saved for specific indications.

PROGRAM IMPLEMENTATION

Education about proper antimicrobial selection and use:

The Section on Infectious Diseases, Pharmacy Department, Infection Control Unit and Microbiology Laboratory have undertaken extensive campaigns to provide education about proper antimicrobial selection and use. The infection control unit, microbiology laboratory and pharmacy department have circulated educational newsletters. In addition, formal presentations on proper antimicrobial selection and use have been made at medical grand rounds, service rounds and hospital multidisciplinary rounds. 'Bug Day', coordinated by nursing educators in conjunction with the Health Sciences Centre Infection Control Unit, was particularly successful. 'Bug Day' consisted of a series of lectures of broad appeal, targeting areas such as antimicrobial-resistant bacteria, and how to limit their emergence and dissemination.

Limitation of inappropriate antimicrobial selection and use:

In an effort to restrain inappropriate antimicrobial prescription, several measures have been taken. Some antimicrobials have been put on a 'restricted' list. Level 1 restriction requires mandatory consultation with the infectious diseases service. The antimicrobials include ceftazidime, fluconazole, parenteral ciprofloxacin, imipenem/cilastatin, piperacillin/tazobactam, nonformulary antimicrobials and ribavirin. Level 2 restriction means that approval must be sought from the infectious disease service by telephone discussion for the use of cefotaxime, oral ciprofloxacin, acyclovir (parenteral or oral) and oral vancomycin. The agents included on this list are continually re-evaluated as are new agents added to the antimicrobial formulary. The infectious diseases service is also open to discussing the selection of antimicrobials case by case. Sometimes, a formal infectious disease consultation request is made for thorough evaluation of a case.

Surveillance audits: Restricted antimicrobials are surveyed routinely as antimicrobial audits to ensure that specific antimicrobial agents are used for indicated purposes only.

Step down therapy: Whenever possible, empirical antimicrobial choices are reviewed and changes recommended if a more appropriate antimicrobial with a narrower spectrum exists.

POTENTIAL PROGRAM LIMITATIONS

The current system to prevent the emergence of antimicrobial-resistant organisms at Winnipeg's tertiary care centres is multifactorial and multidisciplinary but has limitations. The primary concern is the cost of manpower required to fulfill the antibiotic stewardship program. To implement such a program of ongoing antimicrobial audits, staff education and co-ordination of protocols in conjunction with medical staff at least two additional full time drug utilization pharmacists (\$38,000 per pharmacist per year or \$76,000 per year salary support) would be required. Medical staff have raised concerns about being allowed to prescribe the antimicrobial that they wish for the indication they choose without having to seek approval from the infectious diseases service. Many of these medical staff members also suggest that the current measures are somewhat harsh and are concerned with the never-ending vigilance that the measures demand. The reply that is provided to their concern is that Winnipeg's tertiary care centres remain relatively safe from antimicrobial-resistant organisms (8).

THE FUTURE

Although the current strategy has served Winnipeg's tertiary care centres by limiting the emergence of antimicrobial-resistant bacteria, the challenge to incorporate community hospitals into this network lies ahead. Antimicrobial use in the community hospitals is less restricted, and higher generation antimicrobials are frequently used as first-line therapy.

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