PIDSP Journal 2006 Vol 10 No.1

THE 2005 ANTIMICROBIAL RESISTANCE SURVEILLANCE DATA

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Resistance data for 29,782 isolates were reported and analyzed with an increase of 25% from the number reported in 2004. This was mainly due to the increase in the number of bacterial isolates reported for 2005 from twelve out of the 17 sentinel sites, namely Eastern Visayas Regional Hospital (EVR – 79%), Research Institute for Tropical Medicine (RTM – 63%), Lung Center of the Philippines (LCP – 54%), San Lazaro Hospital (SLH – 52%), Cotabato Regional Hospital and Medical Center (CMC – 36%), Philippine General Hospital (PGH – 35%), Bicol Regional Teaching & Training Hospital (BRT – 29%), Baguio General Hospital (BGH – 25%), Vicente Sotto Memorial Hospital (VSM – 21%), Zamboanga Medical Center (ZMC – 20%), National Kidney & Transplant Institute (NKI – 16%) and Davao Medical Center (DMC – 11%) which all had significantly more isolates in 2005. However, five sentinel sites had decreased number of reported isolates for 2005, namely: Celestino Gallares Memorial Hospital (GMH), Rizal Medical Center (RMC), University of Santo Tomas Hospital (STU), Far Eastern University Hospital (FEU) and Corazon Locsin Memorial Hospital (MMH). The major contributors of antibiotic susceptibility data were the Philippine General Hospital (PGH) 9,824 (33%), National Kidney and Transplant Institute (NKI) 5,331 (18%), DMC 2,369 (8%), Lung Center of the Philippines 1,949 (7%) and STU 1,381 (5%). The rest of the participating hospitals contributed less than 5% of all isolates.

The most common specimen sources were urine and respiratory both of which accounted for 23% of all specimens, blood 20% and wounds 15%. There were only 429 genital tract isolates reported, compared to 478 in 2004. There were 750 CSF isolates compared to 298 in 2004, more stool specimens at 607 in 2005 compared to 482 in 2004. The PGH was the biggest contributor of respiratory (34%), blood (32%), CSF (51%), genital tract (24%) and stool (16%) isolates. NKI was the biggest contributor of urine isolates (36%). BGH, BRT, CMC, EVR, GMH, MMH, SLH and ZMC contributed mainly blood (44% of 1,344 isolates, 39% of 485, 38% of 742, 31% of 694, 39% of 359,
30% of 451, 50% of 698 and 48% of 788 respectively); FEU, NKI, RTM and STU mainly urine (55%% of 1,067, 46% of 5,331, 25% of 515, and 50% of 1,381 respectively); and LCP mainly respiratory (70% of its 1,949 isolates). Some sentinel sites generally had low numbers of respiratory isolates like BGH – 5%, BRT – 3%, CMC – 10%, GMH – 6% and ZMC – 3% which had been observed even during the past years. EVR and RTM had increased their CSF isolates from 0-2 in 2004 to 7 each in 2005, however, BRT, GMH, LCP, MMH and NKI still have 1 to 2 isolates each which were still fewer than expected as in previous years.

Keywords: antimicrobial susceptibility, antimicrobial surveillance

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The distribution of pathogens reported were as follows: *E. coli* –16%, *Klebsiella* – 11%, *Pseudomonas aeruginosa* – 11%, *Enterobacter* – 8%, *Acinetobacter* – 8%, *Staphylococcus aureus* – 7%, coagulase negative Staphylococci – 5% and others. There were 356 isolates of *Moraxella catarrhalis* and 197 isolates of *Neisseria gonorrhea*. The number of *Moraxella* isolates increased from 98 isolates in 2004 to 356 in 2005 while the number of gonococcal isolates decreased by 10% from 257 to only 227 in 2005. LCP contributed 89% of the total isolates of *M. catarrhalis,* DMC 10%, NKI and VSM contributed <1% each. Thirty five percent (35%) of the gonococcal isolates came from the patients of Zamboanga Provincial Hospital (ZPH) followed by BRT (32%), SLH (23%) and Rafael Tumbokon Hospital (RTH) (4%). The other sentinel sites of the gonococcal resistance surveillance RTM and Sucat STD Clinic contributed only six (2.6%) and five (2.2%) isolates each. DMC, NKI, RMC and VSM contributed one isolate each whereas the other gonorrhea surveillance sites, MMH and EVR submitted no *N. gonorrheae* isolates. There were more isolates of *Salmonella typhi* and *Vibrio cholerae* in 2005 at 369 and 217 respectively, compared to 276 and 166 in 2004. The top three contributors of *Salmonella typhi* isolates were SLH 34%, EVR 14% and PGH 12%. The most common nontyphoidal *Salmonella* serotypes identified were *Salmonella* Enteritidis (8 isolates), *Salmonella* choleraesuis var Kunzendorf (6 isolates), *Salmonella ser* Typhimurium (3 isolates) and *Salmonella* Stanley (2 isolates). BRT ranked as the highest contributor of *Vibrio cholerae* at 31%, CMC 15%, VSM 14% and BGH 10%.

There was a 56% increase in the number of *Haemophilus influenzae* isolates submitted at 159 compared to the 102 in 2004. The following hospitals were the main contributors of data for *H. influenzae*: PGH 31%, LCP 20%, DMC and NKI both contributed 15% each. Only a 3% increase in the total number of *Streptococcus pneumoniae* isolates was noted for 2005 at 202 as against the 197 contributed in 2004. The main contributors of data on *S. pneumoniae* were PGH 23%, LCP 13%, and NKI 12%. There were 28 isolates of *Shigella* which were reported by 11 hospitals with PGH 10 isolates (36%), 3 isolates each from EVR, FEU and VSM (11%), 2 isolates each from GMH and NKI (7%) and one each from MMH, RTM, SLH, STU and ZMC.

There was a 23% decrease in the number of gonococcal isolates in 2005 compared to 2004 reported by most sentinel sites especially RTH (69 to 8), Sucat STD Clinic (37 to 5), and RTM (33 to 6). On the other hand, ZPH had the most number of isolates contributed (80), followed by BRT (72). SLH started to submit gonococcal isolates and had 52 isolates as their initial contribution.

1. Enteric pathogens

Resistance rates of all *Salmonella typhi* isolates to ampicillin, chloramphenicol and cotrimoxazole remained low at <1% each as compared to 0.8%, 0.4% and 0.8% in 2004. Among the 228 isolates submitted from Metro Manila, 3 were tested to be resistant to ampicillin and one each to chloramphenicol and contrimoxazole. There were no ceftriaxone nor ciprofloxacin resistant *S. typhi* reported for 2005 as in the past many years.

The resistance rate of *S. typhi* gathered from regional hospitals show that the organism remains to be sensitive to chloramphenicol, cotrimoxazole and ampicillin, where no resistance was observed to the 3 antibiotics. Based on the above epidemiologic information, empiric therapy for suspected uncomplicated typhoid fever could still consist of chloramphenicol, cotrimoxazole, or amoxicillin.

As has been previously observed, nontyphoidal S*almonellae* showed higher

resistance rates to chloramphenicol 14%, ampicillin 29%, cotrimoxazole 28% and ciprofloxacin 4% compared to rates for *S. typhi*. Resistance to ampicillin and cotrimoxazole increased from 27% and 20% respectively in 2004. Although chloramphenicol and ciprofloxacin resistance decreased to 14% and 4% respectively in 2005, the continued presence of ciprofloxacin resistance is of particular concern Five isolates of *Salmonella* choleraesuis var. Kunzendorf, 1 *Salmonella* typhimurium, 1 *Salmonella* Stanley, and 1 *Salmonella* Hissar were confirmed to be nalidixic acid resistant. Of the 8 nalidixic acid resistant isolates, 1 was reported by FEU, 1 by NKI, 3 by SLH, and 3 by UST.

For the first time, reports of nalidixic acid resistant and ciprofloxacin resistant *Shigella* were reported at 19% and 4%, respectively which is a cause for alarm since both antibiotics are considered second line treatment options for this infection. The resistance rate of *Shigella* to cotrimoxazole was 46% which was lower than the figure of 67% in 2004. As no resistance to nalidixic acid had been reported in the past years in the Philippines, its presence indicates a need to look into other alternative antibiotics for treatment of shigellosis. Most of the *Shigella* isolates came from Metro Manila. The rate of nalidixic acid resistance among 10 *Shigella* isolates tested from Metro Manila was 20%.

Resistance rates of *V. cholera* 01 to tetracycline and chloramphenicol were 0.9% and 0.5% respectively which were almost the same as the 2004 figures but resistance rate for cotrimoxazole had a fivefold increase at 16% in contrast with the 2.6% reported in 2004. This increase was mainly due to CMC where 25 out of 32 *V. cholerae* isolates were resistant to cotrimoxazole. There were only 2 tetracycline resistant *V. cholerae*, which came from Metro Manila and CMC at 1 isolate each.

2. ARI pathogens

Among the respiratory and invasive isolates of *Streptococcus pneumoniae,* 11%, 16%, and 4% were resistant to penicillin (as determined by screening with 1 ug oxacillin disk), cotrimoxazole, and chloramphenicol respectively. The extent of resistance to all three drugs was slightly higher than those of 2004 where it was 5% for penicillin and chloramphenicol but lower for cotrimoxazole at 15%. Eleven out of 18 penicillin resistant isolates came from Metro Manila with no isolate confirmed as truly resistant by MIC. Lung Center of the Philippines (LCP) and Rizal Medical Center (RMC) reported the biggest number of penicillin resistant *S. pneumoniae*.

Among the isolates of *Haemophilus influenzae* - 15%, 10%, and 20% of the isolates were resistant to cotrimoxazole, ampicillin and chloramphenicol, respectively. It was higher for chloramphenicol whose resistance rate was only 9% in 2004 but lower for cotrimoxazole whose resistance rate was 36% in 2004. Resistance rate for ampicillin remained the same at 10%.

3. Staphylococci and other Gram positive cocci

Overall MRSA rate significantly increased from 17% in 2004 to 31% in 2005. Results of MICs done by ARSRL on 202 oxacillin-resistant isolates showed that 167 (80%) were truly methicillin-resistant (MRSA).

Resistance rate from Metro Manila increased to 34% in contrast to the 18% seen in 2004. Among the regional sentinel sites, MRSA rates were as follows: GMH (72%), ZMC (50%), EVR (44%), VSM (34%), BRT (31%), BGH (26%), MMH (10%), DMC (3%) and CMC (1%).

Resistance rate of *Staphylococcus epidermidis* to oxacillin, erythromycin and cotrimoxazole increased to 63%, 60% and

44% respectively. There were no vancomycin resistant *Staphylococcus aureus* and *Staphylococcus epidermidis* reported in 2005.

There were 325 and 457 isolates of *Enterococcus faecalis* and *E. faecium*, respectively. Majority of *E. faecalis* (202 isolates) came from NKI while majority of *E. faecium* (418 isolates) came from PGH. Vancomycin and ampicillin resistance among *E. faecalis* and *E. faecium* were 2.2% and 0.7%, respectively for vancomycin and 5% and 12%, respectively for ampicillin.

4. Gram negative bacilli

For *Pseudomonas aeruginosa,* overall resistance to ciprofloxacin decreased to 23% from 27% in 2004, to amikacin 17% from 18% and to cefepime 15% from 17%. Ceftazidime and imipenem resistance rates remain the same as that of 2004 at 16% and 17% respectively. Among aminoglycosides, resistance to amikacin was lowest at 17% in comparison to rates for gentamicin, tobramycin and netilmycin which ranged from 22-27 %. Among the regional hospitals, BRT showed higher resistance rate of *P. aeruginosa* than other sites including Metro Manila to ceftazidime 38%, cefepime 29% and piperacillin/tazobactam 30%.

Many of the Enterobacteriaceae showed high resistance rates to several antibiotics tested but resistance rates of *E. coli* to ampicillin and cotrimoxazole remain fairly the same with that of 2004 at 78% and 67% respectively. It remained to be relatively susceptible to third and fourth generation cephalosporins but exhibited high resistance rates to second generation cephalosporins (i.e. cefuroxime at 20% which increased from 17% in 2004) and beta lactam-beta lactamase inhibitors (i.e. ampicillin-sulbactam at 27% which increased from 25% in 2004).

No significant change was observed in comparing data for *E. coli* among regions. As had been seen in 2004, very high resistance rates existed against cotrimoxazole (range: 39 to 70%), cephalothin (range: 28 to 100%), but were variable for co-amoxiclav (range: 14% in CMC to 44% in ZMC). Other sentinel sites with high resistance rates to co-amoxiclav were BRT (43%), GMH (39%) and DMC (37%). Low resistance rates were generally observed against ceftriaxone (range: 0 to 18%) with significant increase seen in Metro Manila from 5% in 2004 to 12% in 2005.

Generally, resistance rates of *Klebsiella* against a number of antibiotics increased in 2005. There was a high resistance rate (27%) against gentamicin but low for amikacin where the resistance rate was only 13%. High resistance rates were likewise exhibited against first generation cephalosporins like cephalothin (44%) and second generation cephalosporins like cefuroxime (33%) and beta lactam-beta lactamase inhibitors like ampicillin-sulbactam at 38%. There was a higher resistance rate for 2005 against ceftriaxone and cefepime at 23% and 11% respectively as compared to the 2004 rates of 15% and 5%.

The presence of extended spectrum beta lactamases had been confirmed from bacterial isolates of *E. coli* and *Klebsiella* referred by all 17 tertiary care sentinel sites of the ARSP to RTM. NKI had the most number of confirmed ESBL (+) isolates at 68 followed by DMC at 20. Three sentinel sites did not refer isolates, which may possibly be ESBL producers, namely: LCP, RTM, and STU. For instance, LCP had 7 and 9 ceftazidime resistant *E. coli* and *Klebsiella*, respectively. RTM had 1 ceftriaxone and 1 ceftazidime resistant *E, coli* and 2 ceftazidime and 2 ceftriaxone resistant *Klebsiella*. STU had 1 ceftazidime resistant and 1 cefotaxime resistant *E. coli* and 1 ceftazidime resistant *Klebsiella*. There is a need to closely monitor the presence of this enzyme among the *Enterobacteriaceae* in view of the very limited antibiotics (i.e. carbapenems, beta lactam-beta lactamase inhibitors) which can

be utilized for patient therapy in the presence of such enzyme.

Resistance rates of urinary *E. coli* from outpatients versus inpatients showed no significant difference in rates for most antibiotics with a trend towards higher resistance rates for outpatient isolates as was observed in 2004. In isolates obtained from outpatients, least resistance was observed against cefuroxime axetil and nitrofurantoin among oral antibiotics at 20% and 17% respectively. For parenteral antibiotics, amikacin had the least resistance at 6% followed by ceftriaxone at 10% and cefotaxime at 13%.

5. *Neisseria gonorrheae*

Resistance to penicillin and tetracycline increased to 86% and 61% respectively from 2004 rates of 83% and 44%. Ciprofloxacin and ofloxacin resistance however decreased to 49% and 51% respectively from previous rates of 58% and 60%. Only about one percent resistance was observed with spectinomycin and no resistance to ceftriaxone and cefixime. There was only one reported ceftriaxone and cefixime resistant isolate referred from San Lazaro Hospital which turned out to be sensitive to both drugs on MIC.

In 2005, a total 1917 isolates were referred which was 40% higher than the number referred in 2004 which totaled 1,129 isolates.

Recommendations

1. Based on the above-mentioned antimicrobial resistance surveillance data:

    a. Empiric treatment for suspected uncomplicated typhoid fever could still consist of either chloramphenicol or cotrimoxazole or amoxicillin/ampicillin.

    b. The fluoroquinolones and 3rd generation cephalosporins are better treatment options for non-typhoidal Salmonella. However, physicians should be aware of the existence of fluoroquinolone resistant nontyphoidal Salmonella in a small proportion of isolates.

    c. Ciprofloxacin may be considered as the drug of choice for treatment of suspected shigellosis among adult patients while nalidixic acid may still be considered as empiric treatment for the pediatric age group until additional data confirms the persistence of high rates of resistance to this antibiotic. In view of the emerging resistance of *Shigella* to the quinolones, continued surveillance of the resistance pattern of this organism should be pursued with the possibility of considering alternative antimicrobial treatment such as ceftriaxone or azithromycin if the rates continue to rise.

    d. Tetracycline and chloramphenicol remain good treatment options for cholera cases.

    e. Infections secondary to *S. pneumoniae* can be covered with penicillin or chloramphenicol although there is a need to closely monitor the changing trends of resistance among pneumococci especially against penicillin in view of the significant increase in resistance to penicillin. Furthermore, there is a need for sentinel sites to refer all their isolates of S. *pneumoniae* to RITM for determination of minimum inhibitory concentration (MIC), the internationally accepted test for determining the antimicrobial susceptibility of the pneumococcus.

f. Ampicillin is the best antimicrobial option for treating *Hemophilus influenzae* infections in view of the increasing resistance rates of this organism to cotrimoxazole and chloramphenicol. Ampicillin resistance in *H. influenzae* is usually mediated by beta lactamase and would therefore respond to beta lactam-beta lactamase inhibitor combinations, extended spectrum oral cephalosporins and the newer macrolides. Laboratories should therefore screen all isolates of *H. influenzae* for beta lactamases as part of its antimicrobial susceptibility test procedure. Beta lactamase negative ampicillin resistant (BLNAR) *H. influenzae* exist and selection of antibiotics for treatment of these strains should be based on results of antimicrobial susceptibility tests (ASTs)

g. In view of the very significant rise in rates of methicillin/oxacillin resistance among staphylococci in 2005, there may be an indication to shift empiric treatment of suspected staphylococcal infections from oxacillin to vancomycin in areas where MRSA rates exceed 20%. However, in order to ensure prudent use of vancomycin, guidelines for judicial use of vancomycin should be followed. Situations in which use of vancomycin is appropriate include the following: 1) for treatment of serious infections attributable to beta-lactam-resistant gram-positive organisms, 2) for treatment of infections attributable to gram-positive microorganisms in patients with serious allergy to beta-lactam agents, 3) when antimicrobial-associated colitis fails to respond to metronidazole therapy or if it is severe and potentially life threatening, and 4) for prophylaxis for endocarditis after certain procedures in patients at high risk of endocarditis, and 5) for prophylaxis for major surgical procedures involving implantation of prosthetic materials or devices at institutions with a high rate of infections attributable to methicillin-resistant *S. aureus* or methicillin-resistant coagulase-negative staphylococci. Furthermore, the appropriate guidelines to contain spread of such organism should be followed such as the observation of contact precautions. Contact precautions are implemented to prevent the transmission of epidemiologically important microorganisms from an infected or colonized patient through direct contact (touching the patient) or indirect contact (touching contaminated objects or surfaces in the patient's environment). Contact precautions entail the following: 1) placement of patients with such precautions in a private room, although patients infected with the same organism may be placed in the same room when private rooms are not available; 2) observance of barrier precautions to prevent contamination of exposed skin and clothing should be employed such as use gloves when entering patients' room and removing these before leaving it; and 3) wearing of gowns if health care worker anticipates substantial contact of his or her clothing with the patient and removal before leaving patient's room.

h. Hospitals should base their treatment recommendations for the Enterobacteriaceae on their institution's prevailing resistance

patterns as these patterns have been found to be variable from hospital to hospital. There is need to closely monitor the presence of ESBLs from among the Enterobacteriaceae in hospitals in view of the very limited antibiotics (i.e. carbapenems, beta lactam-beta lactamase inhibitors) which can be utilized for patient therapy in the presence of such enzyme. The continued rise in MRSA rates and cases of infection secondary to ESBL may indicate very inadequate implementation of infection control procedures in some hospitals, which the Department of Health (DOH) should look into.

i. Cefixime and ceftriaxone can remain as empiric antibiotics of choice for gonococcal infections.

Acknowledgments

For the year 2005, financial support for the activities of the ARSP were derived mainly from suballotted funds from the Department of Health, the World Health Organization Global Salmonella Surveillance and the National Institute of Infectious Diseases, Japan for their support for the Salmonella Surveillance

Antimicrobial Resistance Rates By DISC DIFFUSION, Department of Health Antimicrobial Resistance Surveillance, Jan- Dec., 2005
Prepared by the Antimicrobial Resistance Surveillance Coordinating Group, Research Institute for Tropical Medicine

ORGANISMS **PERCENT RESISTANCE(NUMBER TESTED)**

	Ampicillin	Chloramphenicol	Ciprofloxacin	Cotrimoxazole	Tetracycline	Nalidixic Acid
A. Enteric Pathogens						
1. *Salmonella typhi*	0.9 (337)	0.3 (326)		0.3 (331)		
2. *Nontyphoidal salmonella*	29 (102)	14 (103)	4 (98)	28 (94)		
3. *Shigella*	74 (19)	43 (21)	4 (24)	46 (22)		19 (16)
4. *Vibrio cholera*		0.5 (209)		16 (162)	0.9 (211)	

	Ampicillin	Cefuroxime	Chloramphenicol	Ciprofloxacin	Co-amoxiclav	Cotrimoxazole	Erythromycin	Penicillin	Amp-sulbactam
B. ARI Pathogens									
1. *Streptococcus pneumoniae*			4 (182)			16 (164)		11 (193)	
2. *Haemophilus influenzae*	10 (145)		20 (143)			15 (146)			
3. *Moraxella catarrhalis*	16 (343)				7 (307)	50 (341)	32 (332)		

	Ampicillin	Benzylpenicillin	Ciprofloxacin	Cotrimoxazole	Erythromycin	Oxacillin	Vancomycin
C. Staphylococci and Enterococci							
1. *Staphylococcus aureus*		96 (1979)	11 (1725)	9 (1587)	14 (1681)	31 (2061)	0 (2041)
2. *Staphylococcus epidermidis*		92 (1577)		44 (1206)	60 (1206)	63 (1622)	0 (1623)
3. *Enterococcus faecalis*	5 (325)						2 (325)

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ORGANISMS **PERCENT RESISTANCE(NUMBER TESTED)**

	Amikacin	Ampicillin	Ampi-Sulbactam	Cefuroxime	Ciprofloxacin	Ceftriaxone	Cephalothin	Gentamicin	Cotrimoxazole	Cefepime	Imipenem
D. Enterobacteriaceae											
1.E. coli	6 (3756)	78 (4057)	27 (3162)	20 (1845)	39 (3651)	10 (3565)	48 (2399)	24 (3970)	67 (3562)	6 (3494)	
2. Klebsiella	13 (2901)		38 (2463)	33 (1215)	30 (2599)	23 (2746)	44 (1142)	27 (2770)		11 (2803)	0.6 (3096)
3. Enterobacter	16 (2092)				21 (1982)	24 (1961)	77 (1119)	30 (2067)		10 (1978)	2 (2277)

	Amikacin	Cefepime	Ceftazidime	Ciprofloxacin	Gentamicin	Imipenem	Netilmicin	Piper-Tazo	Tobramycin
E. Gram negative nonfermentative bacilli									
1. Pseudomonas aeruginosa	17 (2928)	15 (2808)	16 (3005)	23 (2764)	26 (2808)	18 (3057)	17 (1165)	10 (2000)	19 (1387)
2. Acinetobacter	36 (2067)	23 (1967)	29 (2088)	33 (1982)	41 (1972)	17 (2170)	24 (511)	27 (1765)	27 (742)

	Cefixime	Ceftriaxone	Ciprofloxacin	Ofloxacin	Penicillin	Spectinomycin	Tetracycline
F. *Neisseria gonorrheae*	0 (201)	0 (225)	49 (219)	51 (195)	86 (216)	1 (203)	61 (219)