



# **Physician Antibiotic Prescribing Practices and Knowledge in Seven Countries in Latin America and the Caribbean**

**A PAHO/APUA Report**

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## SURVEY HIGHLIGHTS

- A general lack of physician training on antibiotics in Latin America (with 46% of physicians having taken informal courses and only 17.9% having received formal training); what short- or long-term was reported had no significant effect on appropriate antibiotic usage.
- A general lack of antibiotic resistance (ABR) surveillance information, points to a need for more surveillance networks, increased linkages where they exist, and increased dissemination of data. Reference laboratories, likewise, are either lacking and/or physicians are unaware of their existence – 62.9% stated that they do not have access to such a lab.
- There is an urgent need for consumer education as self-medication rates are high in these targeted countries; and availability of written educational materials for consumers on proper compliance with antibiotic treatment is low. Almost 91% of physicians stated that there were no consumer education efforts in their countries that address antibiotic use and abuse and its consequences
- There is a significant need for the collection and dissemination of more local AB resistance data to improve prescribing patterns and patient outcomes. Physicians have little geographically pertinent information available regarding their local disease specific resistance levels. A lack of access to both information on local resistance patterns (only 16% say they have it), and to written information on infectious diseases of local importance and recommended treatments for them (less than 20% say they have this type of information.)
- There is an acute need to raise physician awareness regarding resistance patterns. One third or less of physicians surveyed was aware of resistance patterns for shigella, salmonella & S. pneumoniae. 73.8 % of respondents did not know if the resistance information was applicable to the geographic area where they work.
- There is a general lack of information of physicians to appropriately treat ARI and ADI empirically, with only 57.5% and 33.8% of responders demonstrating such knowledge in each of the 2 cases, respectively
- Respondents prescribed antibiotics as first priority reason ARI/Pneumonia as a first (27%) priority reason. Second (15%) for pharyngo-tonsillitis and third (9%) for UTIs.
- When using antibiotics, physicians reported using Penicillins (PCN, semi synthetic penicillins, beta-lactams) as first option (64%), followed by Cephalosporins (12%) and Quinolones (6%)

## INTRODUCTION

Antibiotic resistance is a complex and serious public health problem, which is increasing at alarming rates worldwide — with Latin America being no exception. Resistant bacteria are highly transmittable and spread rapidly through inadequacies in public health infrastructure and infection control practices. The steady increase in resistant bacteria is compromises the effectiveness of infectious disease therapies and increases their cost. This is of particular concern in developing countries with already limited public health budgets and high rates of infectious diseases. Children are especially vulnerable because of their underdeveloped immune systems and because of frequent use of antibiotics for childhood illnesses.

Resistance develops from a process of natural selection, with the resistant organism passing on its genes through various means. According to a WHO report on infectious diseases, “This process is a natural, unstoppable phenomenon exacerbated by the abuse, overuse and misuse of antimicrobials in the treatment of human illness and in animal husbandry, aquaculture and agriculture. Disease, and therefore resistance, also thrives in conditions of civil unrest, poverty, mass migration and environmental degradation where a large number of people are exposed to infectious diseases with little in the way of the most basic health care. Our challenge is to slow the rate at which resistance develops and spreads (1).”

Antimicrobials are essential to reduce the severity and duration of common illnesses such as acute respiratory infections (ARIs), diarrhea, sexually transmitted diseases, hospital-acquired infections, tuberculosis, malaria and other tropical diseases, as well as to avoid potentially serious complications. Preserving the effectiveness of antimicrobials by using them conservatively will not only save valuable resources, but lives as well.

Only two completely new classes of antimicrobials have been developed since 1970 (streptogramins, such as Synercid®, and oxazolidinones, such as Zyvox®). Other new antimicrobials are variations of existing drugs, and therefore are more vulnerable to resistance. On average, research and development of a single new antimicrobial takes 10-20 years and costs US \$500 million dollars to bring onto the market. However, money spent on research and development of drugs targeted at ARI, diarrheal diseases, malaria and tuberculosis combined was under that minimum amount in 1999 (1).

Globalization has played a large role in bringing resistance and other new challenges to the field. Dr. George Alleyne, PAHO director, stated in a speech in Beijing in September 2000 that, “The prospect for spread of disease among all countries is enormous with this intensity of travel. The movement of people is particularly critical for the emergence of one of the time bombs of public health – the spread of antimicrobial resistance”(2). He further states that antimicrobial resistance typically develops when antibiotics are prescribed in inadequate amounts and/or for a condition that does not warrant their usage, such as for viral infections (2).

Other factors contributing to the development and pervasiveness of antibiotic resistance include: unregulated drug approval, quality control and marketing; lack of patient resources/access to quality health care; patient non-compliance and self-medication; physician misuse of antibiotics; and lack of reliable information sources for physicians such as standard treatment guidelines (STGs) and laboratory facilities to confirm diagnoses.

Counterfeit drugs are problematic, as are quality control deficiencies in pharmaceuticals and pharmaceutical companies. Many countries in Latin America have neither the agencies nor the regulatory mechanisms for approval, quality control and marketing of medicines. Perhaps the single most significant problem in the region is the widespread availability of antibiotics without a prescription. Antibiotics can be purchased from pharmacies, street vendors, convenience stores, outdoor markets, fairs etc. One study, in a country where antibiotic sales are unregulated, showed that healthy children from urban areas carried *Escherichia coli* that were 97% insensitive to ampicillin (3). A survey of drugstore sales of antibiotics in Mexico revealed that only 57% of antibiotic purchases were made with a prescription, and that the person selling the drug gave instructions on its proper use in only 15% of observed transactions (4).

Poverty and lack of health care resources exacerbate the resistance problem in the region. Patients with limited incomes generally cannot afford to see a health care worker or to receive laboratory tests to determine the etiology of the disease (if the tests are available). These patients can sometimes only afford poor quality counterfeit drugs, or a drug course shorter than what would be optimally effective. Counterfeit drugs often contain the wrong ingredient, contain no active ingredient, or contain only weak and inadequate amounts of the active ingredient (1). One study showed that patients who self-medicated were more likely to use an inadequate drug or dose, and to follow treatment for less than five days (5).

Physicians who are overworked, under informed, or feeling other pressures to over prescribe are also contributing to the spread of resistance. Other problems, such as choice of broad-spectrum antibiotics over appropriate narrow spectrum alternatives, or prescribing antibiotics in incorrect doses and/or treatment durations, can occur even when clinical presentations necessitate antibiotic prescription. In a study by Paredes, *et al.*, of 40 physicians in Lima, Peru who were questioned on the proper use of antibiotics to treat diarrhea (6), 36 correctly reported that the majority of diarrheal disease is of viral origin, and antibiotics are not indicated. Yet 35 of these 36 unnecessarily prescribed antibiotics for this condition. Although the physicians were clearly informed of appropriate prescribing practices, other factors – including control of disease, patient demand, patient's family's demands, and practitioner self-confidence - persuaded them to misprescribe. In other cases, inappropriate prescribing has been attributed to insufficient training in infectious diseases and antibiotic treatment, insufficient use of microbiological information, and the difficulty of empiric drug choice (7).

A lack of proper diagnostic facilities and laboratories is another serious issue, so that many physicians must rely on empirical treatment of a disease rather than evidence-based

treatment (1). When available, it is helpful to use bacterial studies in order to confirm diagnosis and make the best treatment decision. Empirical treatment is the norm in most situations in the region; however, it is unclear what information is available to and utilized.

Educational campaigns can effectively reduce antibiotic use, and ultimately, antibiotic resistance rates. An intervention conducted in the United States resulted in a decrease in antibiotic prescribing for bronchitis, from 74% to 48%, compared to a 2% decrease at control/limited intervention sites (8). Dr. Youssef Tawfik cites a successful integrated approach that was carried out in India, Indonesia, and Pakistan (9), combining a Verbal Case Review (VCR) and a tool called Information Sharing, Feedback, Contracting and Ongoing Monitoring (INFECTION). The approach successfully educated practitioners in those countries about standard protocols, and compared their knowledge with actual practices. The results indicate that ongoing monitoring helps to encourage consistent improvement in prescribing practices.

Reviewing the Integrated Management of Childhood Illnesses (IMCI) protocols specifically, J. Tulloch found that health workers in Bolivia increased the frequency of their assessments of children's danger signs from 3% before training to 39% two years after training was initiated. For the same time period, frequency of assessment for all main symptoms increased from 0 to 93%, and for nutritional/feeding status from 28% to 88%(10). These findings also suggest that ongoing monitoring is useful for consistent improvement.

These data suggest that interventions targeted to healthcare workers may be highly effective for minimizing the problem of antibiotic resistance. Such interventions must be tailored to individual groups of caregivers, however, based on their existing knowledge and practices and issues of regional importance. Targeting physicians is one of the most significant components of a comprehensive solution, since doctors, as authorized prescribers of antibiotics, are opinion leaders regarding the best treatment for each clinical case. Individual providers' behavior affects colleagues' practice as well, and also influences public opinion and conduct. For these reasons, the Alliance for the Prudent Use of Antibiotics (APUA) have undertaken this research project in conjunction with the Pan American Health Organization (PAHO) Division of Communicable Diseases, and the IMCI Program, in order to compile information on physicians' knowledge and practices (see appendix A for more information on PAHO/IMCI and APUA).

These data will be used to design appropriate interventions targeted to health care providers. All organizations involved in this project share an interest in improving antibiotic prescription and use patterns in the Americas in order to protect public health and preserve the effectiveness of antibiotics for future generations.

## **METHODS**

### **ANTIBIOTIC USE SURVEY DISTRIBUTION, IMPLEMENTATION AND COLLECTION PROCEDURES**

The survey focused on a cohort of professionals from various countries with the objective of evaluating their knowledge and practices with respect to antibiotic use and bacterial resistance to these medications. In addition, we seek to learn the antibiotic resistance patterns of the more prevalent infectious disease microorganisms that are responsible for high morbidity and mortality in the region, particularly among children.

In-country APUA Chapter Coordinators provided advance publicity of the survey through the news media, key informants and community contacts, and relevant professional or organizational sponsors in the targeted communities; post ads and fliers in newsletters or on bulletin boards of professional associations (i.e. College of Physicians), health centers and hospitals; sent a letter to respondents stating the purpose of survey, its anonymous nature, the benefits or usefulness of the study, what to do or whom to contact if there are questions about the study, the importance of results for the country and patients, and how their participation and time was greatly appreciated.

#### **Choosing a Primary Contact Person/Proctor**

APUA chapter coordinator was responsible at each site where the survey was administered, and who became very familiar with the survey (sections, number of questions, etc.).

#### **Administering the Survey**

Individuals were single handed the survey and asked to return to country coordinator. Estimated total time needed to complete the survey was between 25 to 40 minutes per person.

#### **Timeline**

Surveys were mailed to Boston by each Country Coordinator via pre-paid international courier. The shipment were labeled as having “no commercial value -- containing public health materials only.

Surveys were developed by PAHO/APUA staff and sent to physician study coordinators in Bolivia, the Dominican Republic, Ecuador, El Salvador, - Nicaragua, Paraguay, and Peru. The questions included in the survey were designed to address five general areas:

- I. The demographic characteristics of the responders
- II. The association of levels of formal training in antibiotic use or longer-term infectious disease training with reported antibiotic prescribing patterns

Responders were asked to describe any relevant training they had received that might specifically inform their prescribing patterns. Such training included coursework (defined as 3 days or less) or more long-term formal training (defined as a fellowship or specialty training). Antibiotic prescribing patterns were assessed in two ways.

Firstly, 7 questions asked responders to list situations in which different antibiotics would be justifiably prescribed, and unjustified prescribing patterns were noted.

### **Antibiotic Groupings**

- 1) Penicillins, justified for ARI, skin/soft tissue infections, and ENT infections;
- 2) Cephalosporins, justified for ARI, ENT infections, skin/soft tissue infections;
- 3) Beta-lactams, justified for ARI, sepsis, and gram-negative infections;
- 4) Aminoglycosides, justified for sepsis, gram-negative infections, and UTIs;
- 5) Macrolides, justified for ARI, ENT infections, and STDs;
- 6) Quinolones, justified for UTI, ARI, GI infections; and
- 7) Vancomycin, justified for sepsis, endocarditis, and nosocomial infections, primarily MRSA.

### **Prescribing Practices**

Antibiotic prescribing patterns were also assessed by describing 2 clinical cases of most prevalent infectious diseases in the region, and asking the responder to describe appropriate empiric treatment.

**Clinical case #1**: described a 4 year-old child with a fever of 38°C, cough, wheezing, respiratory frequency of 30, and crepitations (crackling rales) in the left lung. The correct diagnosis of this case is ARI, of probable *H. influenzae* or *S. pneumoniae* etiology; and the correct empirical treatment was defined as penicillin.

**Clinical case #2**: described a 4 year-old girl with a fever of 38°C, and bloody diarrhea. The correct diagnosis of this case was considered to be dysentery of probable *Shigella* etiology; and the correct empirical treatment was defined as TMP-SMX, with fluoroquinolones or 3<sup>rd</sup> generation Cephalosporins also considered appropriate.

I. The association of training and available resources with knowledge of antibiotic resistance patterns of important pathogens.

Responders were asked to report whether or not lab facilities were available for use, and whether or not they received regular information regarding antibiotic resistance patterns. These factors were analyzed with respect to their effect on knowledge of resistance patterns for 3 important pathogens: *S. pneumoniae*, *Salmonella sp.*, and *Shigella sp.* Univariate analysis (Chi-square) indicated potential predictors of that knowledge, and multivariate logistic regression analysis was used to further describe the relationships while controlling for potentially confounding variables.

II. Physician' knowledge regarding Gram-positive and Gram-negative infections, and appropriate treatment.

III. Description responders' patient population and educational materials made available to them.

The countries to which the surveys were sent were selected by PAHO/IMCI (Integrated Management of Childhood Illnesses) Division because the infant mortality rate in many of them is over 40/1,000 newborns. In addition, IMCI protocols are already established in these countries.

One hundred surveys were sent to each contact physician in the participating countries, who then distributed the surveys to respondents at local hospitals. The hospitals were typically in urban areas, not rural, so the results cannot necessarily be generalized to rural areas. The surveys were completed between July 2000 and January 2001. The response rate averaged between 50-60%; however, some countries completed more surveys than initially requested. The Dominican Republic (DR), for example, returned 173 surveys. To account for this discrepancy in our analysis, we randomly chose 51 surveys to represent the Dominican Republic. We received a variable number from each, including: Bolivia (54), Costa Rica (0), the Dominican Republic (173 – we entered 51 into the database), Ecuador (120 – we entered 64 into the database), El Salvador (24), Guatemala (0), Honduras (0), Nicaragua (65), Paraguay (40), and Peru (43). The cities represented are: La Paz (Bolivia); Santo Domingo (Dominican Republic); Quito and Guayaquil (Ecuador); San Salvador, San Miguel (El Salvador); Managua (Nicaragua); Asuncion and Itagua (Paraguay); and Arequipa, Chinchica, Chimbote, Ica, Trujillo and Lima (Peru). The total number of surveys entered into the database is 341.

An SPSS database was created to enter the responses to the questionnaire. See Appendix B for a copy of the survey instrument. A printout of the variables in the database and how the variables are coded can be found in Appendix C. It is entitled “File Information.”

Chi-square analyses were performed on the data to examine the differences and similarities between countries regarding antibiotic resistance. Logistic regression was used to predict the independent effect of certain factors, and 1-way ANOVA to detect significant differences in the continuous variables that produce means for each country. The priority goal was to best describe physicians’ prescribing patterns, and to do so, country-specific frequencies of each response were generated.

## **RESULTS**

### I. General responder demographics:

Of the 341 respondents, 69.7% were male and 30.3% female. The mean number of years in practice was 9.5, with responses ranging from .3 to 53 years. Nearly all of the physicians (99.1%) had completed their internship, 92.7% had completed their residency, and 82.8% a specialization. The top ten medical specializations listed were: internal medicine [63/341], pediatrics [60/341], obstetrics/gynecology [35/341], general surgery [29/341], infectious disease [12/341], other – not specified [12/341], orthopedics [11/341], intensive care [10/341], cardiology [7/341], and neurology [7/341]. Most of the physicians (56%) worked in both the public and private sectors; 30.7% worked exclusively in public facilities and 13.3% exclusively in private clinics. More

specifically, 69.4% worked in public hospitals, 22.3% in private hospitals or medical centers, 6.8% in public health centers, and 1.5% in other settings.

Table 1 indicates the demographics and training background of the responders. Chi-square analysis indicated that responders from Peru and Ecuador were more likely to be male, and less likely to be in a private practice than responders from other countries. Responders from Paraguay were significantly less likely to be employed in an exclusively public practice, and they were significantly more likely to report specialization.

TABLE I. Physician Demographics and Training

	<u>N</u>	<u>Gender</u>		<u>Practice Type</u>			<u>Completed Training</u>			<u>Pediatric</u>		
		<u>n</u>	<u>M (%)</u>	<u>F (%)</u>	<u>n</u>	<u>Public</u>	<u>Private</u>	<u>Both</u>	<u>Internship</u>	<u>Residency</u>	<u>Specialty</u>	<u>Specialty</u>
Bolivia	54	54	70.4	29.6	54	50	7.4	42.6	52/52	38/50	36/47	14/39
DR	51	44	61.4	38.6	51	39.2	25.5	35.3	49/49	46/50	37/45	4/43
Ecuador	64	64	<b>78.1</b>	<b>21.9</b>	64	<b>15.6</b>	34.4	50.0	63/64	61/63	43/63	12/58
El Salvador	24	24	54.2	45.8	24	54.1	4.2	41.7	23/23	19/20	10/13	2/16
Nicaragua	65	65	69.2	38.8	63	38.1	0	61.9	62/62	63/64	40/44	16/56
Paraguay	40	40	55	45	40	<b>2.5</b>	7.5	90.0	36/38	40/40	<b>37/38</b>	7/38
Peru	43	42	<b>88.1</b>	<b>11.9</b>	43	<b>20.9</b>	4.7	74.4	41/41	37/41	38/41	9/38
Total	341	333	69.7	30.3	339	30.7	13.3	56.0	326/329	304/328	241/291	64/288

**Bold**= significantly different frequency distribution  $p < 0.05$  in univariate analyses

Female responders were significantly younger than males (35.3 years vs. 42.6 years, 2-tailed T-test:  $p < 0.001$ ), and had practiced medicine for significantly less time (9.9 years vs. 16 years, 2-tailed T-test:  $p < 0.001$ ).

II. Formal training and its association with responders' antibiotic prescribing patterns

The association of training in antibiotic usage or formal infectious disease training with appropriate prescription of 7 antibiotic classes was determined through calculation of odds ratios (OR). The association of such training with appropriate empiric treatment for the 2 described clinical cases was similarly determined. These data are shown in Table II.

Table II. **Formal training and knowledge of appropriate use of 7 antibiotic classes.**

The frequency of individual responders indicating formal coursework or training in antibiotic usage or infectious disease are indicated below. Knowledge of appropriate indications for prescription of 7 different antibiotics or antibiotic classes is described as the frequency of correct responses to each query, with 3 responses accepted for each category. Odds ratios were calculated to reveal any associations between reported training and knowledge of appropriate indications for each antibiotic category.

	<b>Total Responses</b> (/total possible)	<b>Frequency</b>
<b><u>Training</u></b>		
Antibiotic Coursework	324/341	149/324 (46%)
Formal Training	280/341	50/280 (17.9%)
<b><u>Appropriate Use of:</u></b>		
Penicillins	935/1023	357/935 (38.2%)
Cephalosporins	863/1023	256/863 (29.7%)
B-lactams	653/1023	266/653 (40.7%)
Aminoglycosides	845/1023	347/845 (41.2%)
Macrolides	823/1023	550/823 (66.8%)
Quinolones	789/1023	392/789 (49.7%)
Vancomycin	652/1023	185/652 (28.4%)
<b><u>Appropriate Empiric Treatment of:</u></b>		
Clinical Case 1	341/341	<b>196/341 (57.5%)*</b>
Clinical Case 2	341/341	115/341 (33.8%)

\* Significantly association with infectious disease training, Odds Ratio=0.54, p=0.048

**Bold**= statistically significant association

95% and 82% of responders indicated whether or not formal training had been received, in the form of antibiotic coursework and longer-term formal training, respectively. All responded to the questions regarding the clinical cases presented. A range of responses regarding appropriate uses of the 7 antibiotic classes was received, with a maximum of 3 possible answers from each responder. Knowledge of appropriate indications for each of the 7 classes of antibiotics ranged from 28.4% (for vancomycin) to 66.8% for macrolides

There was no significant association of either short- or long-term formal training in antibiotic usage or infectious disease on the indicated knowledge of appropriate usage of the 7 classes of antibiotics evaluated. There was a negative association between reported formal infectious disease training and appropriate diagnosis and empiric treatment of clinical case #1. Of the 230 responders reporting no formal infectious disease training, 141 (61.3%) indicated appropriate empiric therapy for clinical case#1; while of the 50 responders reporting such training, 23 (46.0%) indicated an appropriate response. This yielded a statistically significant OR of 0.54,  $p=0.048$ .

### III. The association of training and available resources with knowledge of antibiotic resistance patterns of important pathogens

**Table III describes the responses from this section by country.** There were no significant differences among responders from different countries with respect to their receiving information on resistant bacteria (data not shown).

While univariate analysis revealed that responders from Peru reported a higher awareness of the resistance pattern associated with *S. pneumoniae* infection, the slightly, though not significantly higher, rate of formal training on antibiotic usage among Peruvian responders appears to be a confounder of this relationship. In a multivariate logistic regression model examining the independent associations of country of origin and a self-reported history of formal training on antibiotic usage on responders knowledge of antibiotic resistance patterns of *S. pneumoniae*, responders from Peru no longer showed a higher rate of such knowledge. Their higher rate of reported knowledge of *Shigella* resistance patterns remained statistically significant, however, in the multivariate analyses. Responders from the Dominican Republic reported a significantly higher awareness of *S. pneumoniae* resistance patterns that could not be ascribed to prior training (OR=5.0, 95% CI 1.2-21.1), as indicated in the multivariate analysis. These relationships were qualitatively similar when including variables describing regular receipt of information on resistant bacteria specific to the geographic areas in which the responders worked, and the availability of written materials on the most common infectious diseases. Of these two correlated variables ( $p<0.01$ ), only the regular receipt of area-specific resistance information was independently associated with knowledge of *S. pneumoniae* resistance patterns ( $p<0.03$ ), and *Shigella* resistance patterns ( $p<0.01$ ).

We could not envision circumstances in which the responders' gender could directly affect their knowledge of resistance patterns; therefore we did not enter gender into the multivariate model. However, given the gender-associated age differences among the responders, the fact that there were significantly different frequencies of male vs. female responders in certain countries, and the potential for age to affect incorporation of received knowledge, we repeated the above analysis with the addition of age as an independent variable. This model indicated all the same qualitative associations as above, with the additional association of age with knowledge of resistance patterns; each additional year of age increased self-reported knowledge of *S. pneumoniae*, *Salmonella sp.* and *Shigella sp.* resistance patterns.. ( $p<0.04$ ). This effect was independent of



**Table III. Physician Training and Resources, and The Effect on Knowledge of Resistance Patterns**

	<b>Formal AB</b>	<b>Self-Reported Resistance Pattern Awareness</b>			<b>Reference Laboratory</b>
	<b><u>Training</u></b>	<b><u><i>S. pneumoniae</i></u></b>	<b><u><i>Salmonella sp.</i></u></b>	<b><u><i>Shigella sp.</i></u></b>	<b><u>Access</u></b>
Bolivia	10/45	14/36	14/35	11/35	18/50
DR	1/23	17/34*	11/32	7/30	<b>24/45</b>
Ecuador	15/61	19/53	17/51	<b>17/51</b>	28/59
El Salvador	2/22	<b>6/20</b>	<b>3/19</b>	<b>1/18</b>	<b>6/24</b>
Nicaragua	5/61	17/55	8/55	5/55	9/58
Paraguay	8/35	16/33	11/31	10/30	<b>21/37</b>
Peru	9/33	<b>25/38</b>	12/36	<b>15/36*</b>	9/37
<b>Total</b>	<b>50/280</b>	<b>114/269</b>	<b>76/259</b>	<b>66/255</b>	<b>115/310</b>

**Bold**= significantly different frequency distribution p<0.05 in univariate analyses

\*Significantly different distribution in a logistic regression model controlling simultaneously for a history of completing formal training on antibiotic usage.

actually having received formal training, which was significantly associated with self-reported knowledge of each of the three resistance patterns. The reported years of medical practice were significantly correlated with age ( $p < 0.01$ ); as expected, incorporation of this variable into the model revealed similar associations (data not shown).

Overall logistic regression analysis revealed that access to a reference laboratory was a significant predictor of knowledge of Salmonella resistance patterns (OR=3.92) and Shigella (OR=3.5), but not of *S. pneumoniae*.

#### **Section IV. Physician' knowledge regarding Gram-positive and Gram-negative infections, and appropriate treatment.**

Physicians were asked to list first, second and third line choice antibiotic when they were confronted with an infectious disease due by a Gram positive and negative bacteria. Most of respondents (70%) would use appropriately use Penicillin as a first line, followed by Cephalosporin (46%) as the second line option and Cephalosporin (27%) against a Gram + bacteria.

For Gram-negative bacteria, aminoglycosides (48%) was the first line choice followed by cephalosporins as second (28%) and third (28%) line choices.

#### **Section V. Patient characteristics.**

Table IV describes the reported patient characteristics of the responders. Overall, analysis of the association between the availability of patient materials and the % of patients who self-medicated was not statistically significant, although there was a trend toward such a relationship described by responding pediatricians. Responders who did not report a specialty also reported higher numbers of patients who self-medicated. Responders from Bolivia are significantly more likely to have materials on hand for patient education about antibiotic usage. Pediatric specialists are also more likely to have such materials.

Table IV. **Patients characteristics.** Chi-Square analysis was used to analyze frequency differences across countries and across medical specialties.

<u>Country</u>	<u>Self medication</u>				<u>Total</u>	<u>Available patient material</u>		
	<u>&lt; 10%</u>	<u>10-25%</u>	<u>25-50%</u>	<u>&gt; 50%</u>		<u>No</u>	<u>Yes</u>	<u>Total</u>
Bolivia	<b>6 (14%)</b>	20 (48%)	9 (21%)	7 (17%)	42	<b>9 (19%)</b>	<b>39 (81%)</b>	48
DR	<b>9 (19%)</b>	17 (36%)	12 (26%)	9 (19%)	47	27 (55%)	22 (45%)	49
Ecuador	<b>12 (20%)</b>	18 (31%)	14 (24%)	15 (25%)	59	35 (57%)	26 (43%)	61
<b>El Salvador</b>	<b>0</b>	4 (18%)	<b>12 (55%)</b>	<b>6 (27%)</b>	22	14 (61%)	9 (39%)	23
Nicaragua	<b>4 (7%)</b>	22 (37%)	24 (40%)	10 (17%)	60	43 (68%)	20 (32%)	63
Paraguay	7 (19%)	12 (32%)	13 (35%)	5 (14%)	37	19(51%)	18 (49%)	37
<b>Peru</b>	<b>0</b>	<b>18 (44%)</b>	<b>19 (46%)</b>	<b>4 (10%)</b>	<b>41</b>	15 (36%)	27 (64%)	42
<b>Total</b>	<b>38 (12%)</b>	<b>111 (36%)</b>	<b>103 (33%)</b>	<b>56 (18%)</b>	<b>308</b>	<b>162 (50%)</b>	<b>161 (50%)</b>	<b>323</b>
<b>By Physicians' Specialty</b>								
Blank	4 (8%)	<b>9 (19%)</b>	25 (52%)	10 (21%)	48	26 (53%)	23 (47%)	49
Other	25 (12%)	79 (39%)	62 (30%)	39 (19%)	205	117 (54%)	99 (46%)	216
<b>Pediatrics</b>	<b>9 (16%)</b>	<b>23 (42%)</b>	<b>16 (29%)</b>	<b>7 (13%)</b>	<b>55</b>	<b>19 (33%)</b>	<b>39(67%)</b>	58
<b>Total</b>	<b>38 (12%)</b>	<b>111 (36%)</b>	<b>103 (33%)</b>	<b>56 (18%)</b>	<b>308</b>	<b>162 (50%)</b>	<b>161 (50%)</b>	<b>323</b>

**Bold** = statistically significant different frequency of responses in this category.



## CONCLUSIONS

Empirical treatment is the norm in most situations in the region, however, this survey showed inconsistent and unclear knowledge on empiric treatment of the most common illnesses, pointing to a need for wider dissemination not only of Standard Treatment Guidelines, but also of other forms of information which can be used to inform antibiotic prescriptions.

The two case studies given to physicians were chosen represent illnesses that Latin American physicians frequently encounter and that are responsible for a high infant mortality rate. Laboratory information was not available in these cases; the physician needed to determine clinical diagnosis, the probable etiology, and appropriate treatment, based on clinical findings only (physical exam, symptoms and signs). Responses to this question showed a general lack of information that would be necessary in order to appropriately treat these cases empirically, with only 57.5% and 33.8% of responders demonstrating such knowledge in each of the 2 cases, respectively. (Table II).

Interestingly, formal training on antibiotic usage and infectious disease appears to have little effect on appropriate antibiotic prescribing patterns, as indicated by appropriate responses regarding indications for prescription of the 7 different antibiotic classes, and empiric treatment for the 2 clinical cases posed. Indeed, reported formal training significantly decreased the appropriate empiric treatment of clinical case #1 (OR 0.54,  $p=0.048$ ).

Formal training on antibiotic usage does appear to have some effect on the self-reported knowledge of resistance patterns, at least those associated with *S. pneumoniae* and *Shigella sp.* (Table III). However, the differing frequencies of such knowledge according to the responders' country of origin is not wholly explained by the undertaking of such formal training; there appear to be other, unidentified important sources of information to be considered, for which age appears to be a marker. Formal training would probably be most efficiently directed at younger individuals without access to whatever these other sources of information are. One explanation is that older respondents would have benefited from their own experience as well as learning from their colleagues over the years.

The survey revealed a general lack of surveillance information (Table III), pointing to a need for more surveillance networks, or where they exist, increased linkages throughout the region and increased dissemination of data. Reference laboratories, likewise, are either lacking and/or physicians are unaware of their existence – 62.9% stated that they do not have access to such a lab (Table III). Access to a reference laboratory was a significant predictor of knowledge of Salmonella resistance patterns (OR=3.92) and Shigella (OR=3.5), but not of *S. pneumoniae*; therefore, establishment of such facilities would significantly impact physician's access to knowledge regarding local conditions.

Physician's knowledge regarding empiric treatment of Gram-positive and Gram-negative infections indicated that penicillin is most often prescribed for Gram-positive infections

while aminoglycosides are most often prescribed for Gram-negative infections. Most of respondents (70%) would use Penicillin as a first line against gram-positive infections, and, indeed, Penicillin still preserves the power in most of the countries surveyed in Latin America; however, there is a growing concern in infections caused by *S.pneumoniae* where antibiotic resistance is increasing (15). It is also readily available and inexpensive. For Gram-negative bacteria, aminoglycosides was the first line choice for 48% of responders, followed by cephalosporins as second (28%) and third (28%) line choices. Aminoglycosides also preserves the power against most of Gram-negative bacteria; however, resistance is increasing seen in *Enterococcus* spp. Also, a marked difference in antimicrobial activity have been documented in the case of gentamicin were 2% of isolates from outpatients were resistant vs. 8% from hospitalized patients (13). Strains of *Shigella*, *Salmonella*, *Escherichia coli*, and *Klebsiella pneumoniae* collected in the 1960s, 1970s, and 1980s at the Hospital Infantil de Mexico Federico Gomez were tested against ampicillin, chloramphenicol, tetracycline, trimethoprim-sulfamethoxazole, amikacin, gentamicin, and furazolidone. Over the 3-decade period, the resistance of enteropathogens to furazolidone showed the least overall increase. *Klebsiella* susceptibility to the aminoglycosides decreased during the same period (14). The data presented here indicate that increasing attention to the local susceptibility patterns of Gram-negative bacteria in particular is warranted, in order to most appropriately use antibiotics on hand, and prevent the emergence of antibiotic resistance problems in this group of bacteria.

Given the lack of access to both information on local resistance patterns (only 16% say they have it, data not shown), and to written information on infectious diseases of local importance and recommended treatments for them (less than 20% say they have it, data not shown), establishment of surveillance networks and dissemination of their findings appears to be the best solution. Standard treatment guidelines also a need that is not currently being met in the countries taking part in this survey (data not shown), and greater efforts should be made to promote STGs in conjunction with providing local antibiotic susceptibility data.

There is also an urgent need for consumer education as self-medication rates are high in these targeted countries (Table IV); and availability of written educational materials for consumers on proper compliance with antibiotic treatment is low. Almost 91% of physicians stated that there were no consumer education efforts in their countries that address antibiotic use and abuse and its consequences (data not shown). Materials provided by the physicians seem to be of limited utility in preventing self-medication, which may be of a more inappropriate nature than such medication prescribed by the physician.

The data presented here suggest that improve medical school training could substantially affect the ability of new physicians to determine when an antimicrobial is needed, and to understand local resistance patterns, as well as their implications, costs, and other related elements. Also, performing this training with physicians already in practice in order to benefit from their experience and to keep them current on antibiotic resistance developments will have substantial benefit, particularly if targeted to younger practicing

physicians who lack the information support network that appears to benefit older physicians.

Likewise, dissemination of facts about antibiotic resistance among physicians, dentists, community health care workers, veterinarians, and farmers will be of benefit. WHO has established an electronic database of resistance data and surveillance networks. The Antimicrobial Resistance Information Bank (AR InfoBank) provides access to these data to policy-makers and health care professionals. Some countries (Greece, for example) have developed a website “**The Greek System for the Surveillance of Antimicrobial Resistance**”, a national network for continuous monitoring of bacterial antibiotic resistance in the Greek hospitals. Resources like these would be crucial to physicians in Latin America who are not aware of resistance levels in their area, or of the threat of resistance spreading from nearby localities. Potentially, a course could be given to physicians to instruct them on operating WHONET 5, a surveillance software package for Windows for resistance detection and tracking.

The establishment of antibiotic committees within the hospital infection control committees could be responsible for establishing norms for empirical treatment of the most common infectious diseases and for developing treatment guidelines for infections currently present in the community encouraging standardization of care and appropriate antibiotic usage. In addition, this study indicates that educational campaigns aimed at consumers, especially parents, in order to decrease – or eliminate – self-medication with antibiotics will significantly benefit the appropriate use of antibiotics both within and outside of the prescriber-patient relationship.

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