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Patterns of antimicrobial use and antimicrobial resistance among healthy children in Bolivia

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Summary

OBJECTIVE To determine the incidence of antimicrobial-resistant, nonpathogenic *Escherichia coli* among healthy children aged 6–72 months in Camiri town and a rural village, Javillo, in south-eastern Bolivia.
METHOD A community-based survey: stool samples were obtained from 296 healthy children selected by modified cluster sampling in Camiri and all 25 eligible children in Javillo. *E. coli* isolates were tested for antimicrobial susceptibility according to the standard disc diffusion method. By a questionnaire survey of 12 pharmacies and by using simulated patients, we investigated the antimicrobial availability and the usage patterns in Camiri town.
RESULTS In Camiri, over 90%, and in Javillo over 70% of children carried *E. coli* resistant to ampicillin, trimethoprim-sulphamethoxazole (TMP/SMX) or tetracycline. Overall, 63% of children carried *E. coli* with multiple resistance to ampicillin, TMP/SMX, tetracycline and chloramphenicol. In the simulated patients study, antimicrobials were dispensed inappropriately for 92% of adults and 40% of children with watery diarrhoea, and were under-prescribed for males with urethral discharge (67%) or females with fever and dysuria (58%). The dose and/or duration of antimicrobials dispensed was almost always too low.
CONCLUSION Our study showed a disturbingly high prevalence of carriage of nonpathogenic *E. coli* resistant to antimicrobials. The prevalence of resistance to ampicillin and TMP/SMX was higher than that previously reported in developing countries. The existence of a large reservoir of resistance genes in healthy individuals in developing countries represents a threat to the success of antimicrobial therapy throughout the world. Programmes to improve rational and effective drug use in developing countries are urgently needed.

keywords antimicrobial resistance, antimicrobial use, *Escherichia coli*, developing countries, Bolivia

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Introduction

Antimicrobials represent one of the major interventions to reduce mortality in developing countries, and in many such countries they account for the single largest group of drugs purchased (Col & O'Connor 1987). Resistance to antimicrobials is a worldwide problem which may be particularly serious in developing countries, where alternative antimicrobials are often not available or too expensive (O'Brien 1992). The commensal flora of the gut are considered the most important reservoir for antimicrobial resistance genes in both the community and hospital environments (Levy *et al*. 1988; Lester *et al*. 1990). This pool of resistance genes is significant because these genes can be transferred from commensal to pathogenic organisms (Tauxe *et al*. 1989). It is therefore important to investigate the carriage of resistance genes in healthy individuals (Lester *et al*. 1990; Bartoloni *et al*. 1990; Amyes *et al*. 1992; Ismaeel 1993). Inappropriate use of antimicrobials is considered to be one of the main factors responsible for the high prevalence of bacterial resistance in developing countries (Cash 1996), and misuse of antimicrobials is a widespread problem (Kunin *et al*. 1987, 1993; Schorling *et al*. 1991; Misago & Fonseca 1991).

In this paper, we present a study of patterns of antimicrobial availability and use in Camiri town, Bolivia,

and a community-based study of carriage of antimicrobial resistance among nonpathogenic *Escherichia coli* isolates collected from healthy children aged 6–72 months in Camiri and in a nearby rural village, Javillo. These study sites were chosen because a study in 1987 had shown that no *Staphylococcus aureus* and coagulase-negative staphylococcal strains obtained from Javillo residents were resistant to penicillin and only 10% to tetracycline, in marked contrast to the 50% and 53% resistance, respectively, in Camiri (Bartoloni *et al*. 1990). Javillo's isolated setting and the community's lack of antimicrobial usage at that time was thought to have maintained a high level of susceptibility to these agents. We used a selective screening method employed in earlier studies to detect resistant bacteria in stool samples (Datta 1969; Lester *et al*. 1990).

Methods

Study setting

The study was conducted in 1992 in Cordillera province, Santa Cruz department, in south-eastern Bolivia. Camiri is a town of about 28000 inhabitants situated in the foothills of the Andes. It has three main hospitals, the District Hospital (DH) (92 beds) run by the Bolivian Ministry of Health, and two private hospitals, the Hospital de la Caja Nacional de Salud (CNS) (20 beds), and the Hospital de la Caja Petrolera (CP) (47 beds) belonging to the Bolivian National Petroleum Agency (YPFB). In addition, there are five minor private hospitals and 12 private pharmacies. Javillo is a very small community of an ethnically homogeneous group of about 100 Guaraní Indians isolated in the jungle north-east of Camiri, at an altitude of about 1500 m. Villagers live in huts with no sanitary or hygienic facilities. Due to recent structural changes in Bolivia's health services, this community now receives regular visits from physicians.

Antimicrobial availability and usage patterns

A checklist was sent via the District Pharmacy and Laboratory Inspectorate to each of the pharmacies in Camiri, and 10 of 12 returned information on antimicrobials stocked and quantities dispensed monthly. Similar data were obtained by distributing a record to hospital administrators of the three main hospitals, two of which sell drugs through their pharmacy. For each hospital, we also collected data on the annual expenditure for all drugs and for antimicrobials.

We used simulated patients with mock illnesses to examine the current pattern of antimicrobial use by pharmacy personnel (hospital pharmacies were not included since these only dispense drugs after a physician's prescription). Six Bolivian field staff were trained to present to pharmacy personnel with the following complaints: acute watery diarrhoea without fever in (a) a 6-month old child and (b) an adult; fever with sore throat in an 8-year-old child; low grade fever and rhinorrhoea in a 2-year-old child; fever and acute dysuria in an adult female; purulent urethral discharge in an adult male. Each field worker simulated only one complaint and visited each pharmacy; standard answers were provided to anticipated questions. Field workers completed a written

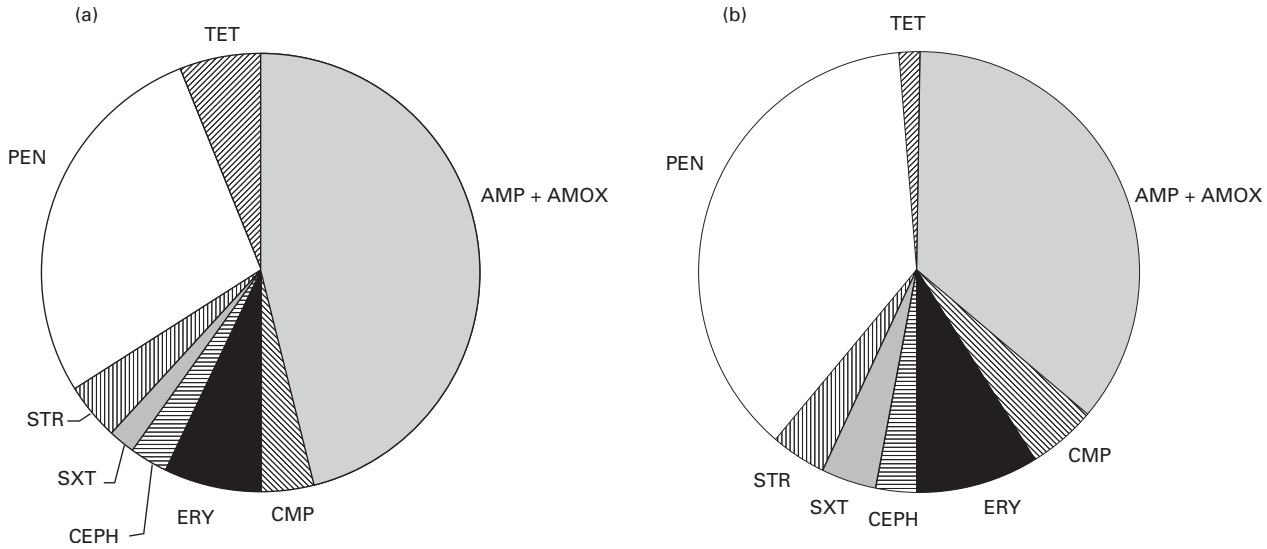

Figure 1. Relative quantities of the most frequent antimicrobials utilized (a) from the Camiri pharmacies and (b) the Camiri hospitals. □ PEN, benzylpenicillin; ▨ TET, tetracycline; ▢ AMP + AMOX, ampicillin + amoxicillin; ▥ STR, streptomycin; ▩ SXT, trimethoprim-sulphamethoxazole; ▤ CEPH, 1st generation cephalosporins; ■ ERY, erythromycin; ▧ CMP, cloramphenicol.

record of the name and quantity of medications dispensed and any advice given by pharmacy personnel.

Antimicrobial resistance patterns

A community survey of healthy children in Camiri was conducted using modified cluster sampling. COOPAGAL (Cooperativa Agua y Alcantarillado), an important water supplier, provided detailed maps outlining the distribution of households in the city's six administrative sectors. The six areas were divided into 30 clusters, each containing approximately the same number of households. Interviewers began at a random household in every cluster and proceeded in a clockwise direction until 10 households with healthy children between the ages of 6 and 72 months had been enrolled in the study in each cluster. If more than one child in the target age group was present, the youngest child was chosen, unless a member of the household had been hospitalised in the previous 4 months, in which case all children were included. Children were eligible if they did not have gastrointestinal symptoms at the day of interview, and had no personal history of hospitalization, antimicrobial therapy, or travel outside the country in the last 4 months. In Javillo, all eligible resident children between 6 and 72 months of age were invited to participate in the study.

At each participating household, a questionnaire was administered to obtain information on the family size, previous drug therapy, and hospitalization of family members, and the child's history of antimicrobial use (verified by examining remaining pills/containers/prescriptions if available), travel, and place of birth. With parental consent, stool samples were obtained from the children by rectal swab.

Specimen collection and susceptibility testing

Rectal swabs were transferred in a cold box to the laboratory of the Camiri District Hospital within one to four hours in Amies transport medium (Trans-cul Laboratory, Milan, Italy) and plated onto MacConkey Agar (Unipath, Milan, Italy). Antimicrobial-containing discs (Sensi-disc, BBL, Becton Dickson Microbiology System, Cockeysville, MD, USA) with the following potencies were then applied to the MacConkey plates: Ampicillin 10 μg; Chloramphenicol 30 μg; Gentamicin 10 μg; Nalidixic acid 30 μg; Nitrofurantoin 300 μg; Cephalothin 30 μg; Trimethoprim-sulphamethoxazole 1.25–23.75 μg; Amikacin 30 μg; Cefotaxime 30 μg; Tetracycline 30 μg; Ciprofloxacin 5 μg; Piperacillin 100 μg. After overnight incubation at 37 °C, a pool of five colonies whose morphology resembled that of *E. coli* and fell within the zones of inhibition of each antibiotic tested were selected, preserved in cystin trypticase agar tubes (Unipath, Milan, Italy) at 4 °C and transported in a refrigerated box to Florence, Italy. Samples yielding nonconfluent colonies were not included in the study. At the laboratory in Florence, isolates were plated onto blood agar (Unipath, Milan, Italy) and incubated for 24 h at 37 °C. Bacteria were identified using the Analytical Profile System (API System, S.A., France). Strains not identified as *E. coli* were excluded from the study. All *E. coli* strains were tested for antimicrobial susceptibility according to the standard disc diffusion method using Mueller-Hinton medium (Unipath, Milan, Italy). Strains for which zone diameters indicated intermediate resistance were classified as susceptible.

Data analysis

Data were entered into EPI-INFO 6.0 (Center for Disease Control, Atlanta, GA, USA), checked and descriptive analyses were performed. Confidence intervals were calculated using the Csample option in EPI-INFO, to account for the cluster sampling design. Further analyses were conducted using STATA 4.0 (College Station, TX, USA). Differences in the proportion of resistant strains to each antimicrobial were examined using the χ^2-test, and odds ratios were calculated to identify variables significantly associated with resistance to a particular antimicrobial. Adjusted estimates of the odds ratios were obtained by stratified (Mantel-Haenzsel) analysis. Statistical differences in the mean number of antimicrobials to which *E. coli* strains were resistant were determined by the *F*-test and Students *t*-test for equal and unequal means.

Results

Antimicrobial availability and usage patterns

All private pharmacies stocked ampicillin, amoxycillin, penicillin and erythromycin, all but one stocked first-generation cephalosporins, chloramphenicol and tetracycline; most stocked isoxazolilpenicillin and gentamicin; half had trimethroprim-sulphamethoxazole (TMP/SMX), lincomycin and rifampicin; and a minority stocked amikacin, streptomycin and doxycycline. Ciprofloxacin, one of the latest fluorinated 4-quinolones, was stocked by two private pharmacies. The figure shows the relative quantities of the most frequent antimicrobials dispensed by the 10 private pharmacies from which data were obtained, and those utilized in the three Camiri hospitals. Broad-spectrum penicillins and benzylpenicillin were the most commonly used antimicrobials; erythromycin, cloramphenicol, first-generation cephalosporin, TMP/SMX, tetracyclines, and streptomycin were also frequently used. Dispensing patterns were generally similar in the hospitals, but first generation cephalosporins, some aminoglycosides (amikacin, netilmicin)

and monobactams (aztreonam) were only used at the district hospital. For the hospitals, antimicrobials represented an average of 40% (34% at the CP, 43% at the CNS, and 51% at the DH) of the total pharmaceutical budget (data not shown).

In the simulated patients study, information was obtained from 12 pharmacies for 4 mock illnesses, from 11 for one and from 10 for another, because one or two pharmacies were closed at the time of the visit on two occasions. Table 1 shows the results of the management of the mock illnesses. Six pharmacies (8.7% of total consultations) did not dispense drugs for at least one of the conditions without a medical prescription. Antimicrobials were dispensed in 68% of simulations; the quantity dispensed varied according to the 'patient's' ability to pay. Antimicrobials were dispensed for 92% of adults and 40% of children with watery diarrhoea, with a maximum of two day's supply; 60% of pharmacies also gave antidiarrhoeals to children while none gave oral rehydration salts. Tetracycline was the most commonly dispensed antimicrobial in adults with diarrhoea and in one case it was given to a six-month old child. For coryza in a 2-year-old child, only 2 pharmacies dispensed antimicrobials (TMP/SMX syrup). For the three mock illnesses for which antimicrobial therapy is indicated, they were dispensed to 91% of children with a sore throat and fever (usually ampicillin/amoxycillin), two thirds of males with urethral discharge (the other third were advised to consult a physician), but only 58% of women with fever and dysuria (42% dispensed only phenazopyridine, a urinary analgesic with no antibacterial activity, while 25% advised the woman to consult a physician). The recommended duration of therapy for women with fever and dysuria ranged from 1 to 5 days, but in all cases a maximum of four tablets was dispensed.

Information on antimicrobial use was also obtained from the community survey. In Camiri, 296 children and in Javillo, 25 children were enrolled; the mean age was 35 months in Camiri and 41 months in Javillo. Mean family size was 6.3 in Camiri and 6.8 in Javillo. Approximately half the children in Camiri and 68% in Javillo were male; 15% and 4%, respectively, had a history of previous travel outside the community. Fifty-eight percent of the children from Camiri and 64% from Javillo were said to have received an antimicrobial more than four months prior to the study ($P = 0.6$). Of the 188 study children who had previously received antimicrobials, the most common reasons were: tonsillitis (29%), other respiratory infections (22%), diarrhoea (19%), and amoebiasis (4%). Ampicillin/amoxycillin (50%) were the most frequently used antimicrobials, but penicillin (28%) was also common. Antimicrobials had been recommended by a hospital physician (67% Camiri, 94% Javillo) or a private physician (23% and 6%) in almost all cases. Most children obtained their medication through a hospital chemist (63% Camiri, 93% Javillo) or pharmacy (31% Camiri, 6% Javillo); only 9 children obtained drugs from the market.

Antimicrobial resistance

Rectal specimens growing *E. coli* in Bolivia were obtained from a total of 321 children. A further 7 specimens failed to grow any bacteria and 30 did not grow *E. coli*; these children were excluded from the study. Bacteria from 25 children failed to regrow in Italy, and there were some cases where a particular colony growth within the inhibition zone of the antimicrobial-containing disc did not regrow. The latter were excluded only from analyses of that particular antimicrobial agent. Table 2 shows the frequency of

Table 1 Antimicrobials dispensed by pharmacy personnel in Camiri for simulated patients

Clinical syndrome	Acute diarrhoea (6-month-old) ($n = 10$)	Acute diarrhoea (adult) ($n = 12$)	Low grade fever + rhinorrhoea (2 years old) ($n = 12$)	Fever + sore throat (8 years old) ($n = 11$)	Fever + acute dysuria (young woman) ($n = 12$)	Purulent urethral discharge (adult male) ($n = 12$)
% of pharmacies requiring medical prescription	10	0	0	9	0	33
% dispensing systemic antimicrobials	40	92	24	91	58	67
Antimicrobials dispensed (number of simulations)	Sulphoguanide (2) Furazolidone (1) Tetracycline (1)	Tetracycline (6) Sulphathiazol (4) Neomycin (2) Streptomycin (2) Furazolidone (1)	TMP/SMX (2)	Ampicillin/ amoxicillin (8) TMP/SMX (2)	Pipemidic acid (3) Sulphametizol (1) Nitrofurantoin (1) Norfloxacin (1) Nalidixic acid (1)	Ciprofloxacin (3) TMP/SMX (2) Benzathine penicillin (2) Dicloxacillin (1) Procaine penicillin (1) Spectinomycin (1)

Table 2 Prevalence of antimicrobial resistance of *E. coli* strains isolated from children in Camiri and Javillo, Bolivia, by disc diffusion

	Percentage of strains testing resistant	
	Camiri (95% CI)	Javillo
Amikacin	0	0
Ampicillin	97 (95–99)[a]	87[a]
Cefotaxime	0	0
Cephalothin	10 (6–14)	25
Chloramphenicol	69 (64–74)	57
Ciprofloxacin	0	0
Trimethoprim -sulphamethoxazole	94 (91–97)[b]	71[b]
Gentamicin	5 (2–8)	0.6
Nalidixic acid	4 (2–6)	0.6
Nitrofurantoin	5 (2–8)	0
Piperacillin	54 (49–60)[c]	33[c]
Tetracycline	92 (89–95)	80

[a]$P < 0.05$, [b]$P < 0.01$, [c]$P < 0.05$

resistance to each of the antimicrobial agents. The prevalence of resistance to the commonly dispensed antimicrobials in Camiri was very high: 97% to ampicillin; 94% to TMP/SMX, and 92% to tetracycline. Resistance was also high to chloramphenicol (69%) and piperacillin (54%, plus another 90 intermediate resistant strains). The prevalence of resistance to other antimicrobials was much lower. In Javillo, resistance was also frequently found to commonly used antimicrobials, although the prevalence was significantly lower than that in Camiri for ampicillin, TMP/SMX and piperacillin.

Most faecal samples in strains from both communities contained more than one resistance determinant in the same strain. In total 99% of strains which could be tested for all 12 antimicrobials (97% of all 296 samples) showed resistance to more than one drug. The most frequently occurring patterns were ampicillin, TMP/SMX, tetracycline, chloramphenicol and piperacillin (40%); the first four of these drugs (23%); and ampicillin, TMP/SMX and tetracycline (12%). Six other patterns which occurred in $> 1\%$ of the samples involved at least one of these five antimicrobials, and 2% of coresistance patterns involved cephalothin or gentamicin. The mean number of antimicrobials to which an *E. coli* strain was resistant by disc diffusion was 4.3 (s.d. = 1.6) in Camiri and 3.3 (s.d. = 1.7) in Javillo ($P < 0.01$). Younger children carried strains resistant to more antimicrobial agents than older children. On linear regression analysis, the mean number of antimicrobials to which children were resistant decreased by 0.18 (95% CI −0.27, −0.09) for each one-year increase in age.

There was no association between the mean number of antimicrobials to which strains were resistant and sex, previous antimicrobial therapy, household size, or hospitalization or drug therapy of another household member. There was a tendency for children born at home who were less than 13 months old at the time of the study to be resistant to fewer antimicrobials than those born in hospital (4.2 *vs*. 4.8, $P = 0.058$). Resistance to ampicillin, chloramphenicol, TMP/SMX and piperacillin decreased significantly with age; with a nonsignificant decrease for tetracycline. Table 3 shows results of univariate and Mantel-Haenszel stratified analyses for other variables found to be significantly associated with resistance to the main antimicrobials. Resistance to TMP/SMX and piperacillin remained significantly higher in Camiri than Javillo after controlling for age. The only other factor associated with resistance to any antimicrobial was a history of hospitalization of a household member in the previous 4 months; this was significantly associated with increased resistance to piperacillin but not other antimicrobials (odds ratio adjusted for age and locality: 3.2, 95% CI 1.3–7.5). Because of this association, we repeated all the above analyses including only the youngest child in each house (since the original sample had more than one child per household only in those in which a member had been hospitalised). The results were virtually unchanged, hence we have presented results for the whole sample. There was no difference in prevalence of antimicrobial resistance in children with or without a history of antimicrobial therapy more than 4 months previously, or according to use of

Table 3 Risk factors for resistance to certain antimicrobials on univariate analysis

Variable	Antimicrobial	Crude Odds Ratio	Adjusted for	Adjusted Odds Ratio	95% CI	*P*-value
Locality of residence	Ampicillin	4.6	age	4.0	0.77–21.0	0.075
	TMP/SMX	6.1	age	6.1	1.70–27.6	0.001
	Piperacillin	3.8	age	3.8	1.00–10.1	0.038
Hospitalization	Piperacillin	2.83	locality + age	3.2	1.3–7.5	0.004

antimicrobials by another family member in the last 4 months (data not shown).

Discussion

This study documents several problems associated with the use of antimicrobials, including inappropriate and ineffective regimes dispensed at pharmacies, widespread use of antimicrobials in young children even in a remote rural area of Bolivia, and widespread carriage of resistant commensal gut bacteria in urban and rural areas. Over two-thirds of the private pharmacies in Camiri dispensed antimicrobials without a medical prescription. Antimicrobials were dispensed inappropriately to 'simulated patients' with conditions that did not warrant this therapy.

Over 90% of adults with watery diarrhoea were given antimicrobials, particularly tetracycline, and 4 of 10 pharmacies gave antimicrobials for a 6-month old child with diarrhoea (one of these gave tetracycline, which is contra-indicated in children). This inappropriate treatment was compounded by liberal dispensing of antimotility drugs and absence of use of oral rehydration therapy, and indicates the urgent need to include the private sector in national diarrhoeal disease control programs. Antimicrobials were dispensed by most pharmacies for two of the three conditions that warranted them, but only 58% of women with fever and dysuria received antimicrobials. The type, dose, and duration of antimicrobials dispensed, however, were rarely correct. More expensive antimicrobials were dispensed instead of cheaper alternatives which could have been more effective since they require only a single dose, e.g. ampicillin or amoxicillin instead of benzathine-penicillin for a child with fever and sore throat and dicloxacillin or TMP/SMX instead of procaine penicillin for purulent urethral discharge (the advantages of oral rather than parenteral therapy in such instances need to be balanced against the likely compliance with the full course of therapy). Whether prescribed appropriately or inappropriately, the quantity of antimicrobials dispensed was almost always too small and could contribute to the selection of resistant strains. Other studies of pharmacies in developing countries have also shown that small quantities of drugs are commonly purchased (Thamlikitkul 1988; Lansang *et al*. 1990; Ismaeel 1993). In developing countries it is often difficult to diagnose infectious diseases correctly without reliable laboratory services, hence physicians feel compelled to prescribe antimicrobials. Although patients expect to receive drugs, they often cannot afford the cost of a full course of treatment (Kunin 1993).

The ready availability of antimicrobials at pharmacies was mirrored by the high utilization of antimicrobials by children in the community survey, even in the remote rural community of Javillo. The most common reason for antimicrobial use in children was upper respiratory tract infection, followed by diarrhoea. In the survey, most families stated that antimicrobials had been purchased at the advice of a physician, though approximately one-third of families in Camiri had obtained the antimicrobial from a pharmacist. Our study did not evaluate prescribing habits of physicians, but other studies have shown that the majority of antimicrobial agents prescribed for hospitalised and ambulatory patients were inappropriate (Stein *et al*. 1984; Islam 1985).

We found a very high rate of antimicrobial resistance in the nonpathogenic *E. coli* of young children in urban and rural areas. The disc-screening method used (plating the rectal swab on MacConkey agar and applying an antibiotic-containing disc on the agar surface proved to be a valid method to detect resistant *E. coli* (Datta 1969; Lester *et al*. 1990). We studied children who had no history of antimicrobial therapy in the last four months. A previous study showed such children to have similar rates of resistance as those who never received antimicrobials and thus represent the healthy members of a community (Lester *et al*. 1990). In Camiri, over 90%, and in Javillo, over 70%, of children carried *E. coli* resistant to ampicillin, TMP/SMX or tetracycline. This represents a marked increase in antimicrobial resistance in Javillo; in 1987, this village was considered almost entirely free of resistance genes (Bartoloni *et al*. 1990). The more recent institution of regular visits by hospital physicians to Javillo appears to have resulted in increased utilization of antimicrobials. Although the use of antimicrobials in young children was equal in Javillo and Camiri, the prevalence of resistance to ampicillin, TMP/SMX and piperacillin was still significantly lower in Javillo, which may reflect the more recent introduction of antimicrobial resistant genes. The prevalence of resistance to both ampicillin and TMP/SMX found in this study is higher than that previously reported in other developing countries. Reports from Chile, Honduras, Costa Rica, Brazil, and Thailand have reported 38–50% prevalence of resistance to TMP/SMX (Murray *et al*. 1985). Our findings for ampicillin resistance are as high or higher than those reported from India, Venezuela, and China, which have previously documented some of the highest frequencies of antimicrobial resistant commensal bacteria within a healthy developing country population (Lester *et al*. 1990; Amyes *et al*. 1992). The apparently high frequency of resistance to piperacillin suggests that resistance to piperacillin is acquired through a common resistance mechanism, perhaps with ampicillin (Gould 1994). The low frequency of resistance to gentamicin, nalidixic acid, nitrofurantoin, amikacin, cefotaxime, and ciprofloxacin probably reflects lower general usage of these drugs in this region.

The widespread prevalence of multiple resistance in this population is especially noteworthy, as it indicates that the resistance genes are carried on plasmid DNA, and because it serves as an important predictor of treatment failure in communities where susceptibility testing is unavailable (Datta 1971; Levy 1986). Although our study was not designed to determine an association between antimicrobial use and resistance, it is of note that the most frequent resistance pattern in the population included four commonly dispensed antimicrobials: ampicillin, tetracycline, trimethoprim-sulphamethoxazole, and chloramphenicol. The frequency of multiple resistance to these four drugs (40%) was double that in a study of children with diarrhoea in the Sudan (Shears *et al*. 1987). The use of chloramphenicol and/or tetracycline has been considered an important risk factor for multiple resistance in *E. coli* (Akiba *et al*. 1960). The correlation between carriage of resistant colonizing bacteria and resistance of infecting bacteria has previously been documented (Akiba *et al*. 1960; Tauxe *et al*. 1989; Lester *et al*. 1990; Amyes *et al*. 1992). In Bolivia this is supported by data from the same district which showed that most children with diarrhoeal disease carried *E. coli* resistant to ampicillin and TMP/SMX (Ise *et al*. 1994). The high prevalence of resistance in our study thus raises doubts about the efficacy of standard treatment regimes for treatment of the sick child that include TMP/SMX and ampicillin**, and** further evaluation of those regimes is indicated (WHO/UNICEF 1986; WHO 1989).

Carriage of resistant nonpathogenic *E. coli* was significantly associated with younger age, which may reflect both the increased use of antimicrobials in both communities in recent years (Bartoloni *et al*. 1990) and the higher incidence of infections, leading to more frequent use of antimicrobials in younger children (Grant 1993). There was a suggestion that hospitals may contribute to community spread of resistant genes, since piperacillin resistance was significantly associated with recent hospitalization of another family member, and infants who had been born in hospital tended to be resistant to more antimicrobials than those born at home (Rosenberg 1995). Spread of resistant genes within a community may be facilitated by environmental conditions such as crowding, poor sanitation, or contaminated food; investigation of the contribution of such factors was beyond the scope of this study. The high prevalence of antimicrobial resistance and the widespread poor practice in pharmacies, with inappropriate use of antimicrobials for those who do not need them and ineffective treatment regimens for those who do, highlights the magnitude of this public health problem. Enhanced surveillance of resistance in developing countries is needed. Additionally, studies to investigate the correlation between antimicrobial usage and resistance (Arason *et al*. 1996) should be conducted in developing countries. Urgent measures are needed to implement effective drug policies in developing countries, and to develop programs which include the private sector (Ronsmans *et al*. 1996). Such programs should investigate how to change community attitudes in order to reduce the demand for antimicrobials.

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