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Challenges in the Control of Gonorrhea in South America and the Caribbean: Monitoring the Development of Resistance to Antibiotics

JO-ANNE R. DILLON, PHD,*† MARTHA RUBEN, MD, PHD,* HUI LI, MSC,* GRACIELA BORTHAGARAY, MSC,‡ CAROLINA MÁRQUEZ, PHD,‡ SUSANA FIORITO, MD,§ PATRICIA GALARZA, MSC,§ JOSÉ LUIS PORTILLA, MSC,‖ LILIA LEÓN, BSC,¶ CLARA INÉS AGUDELO, BSC,** OLGA MARINA SANABRIA, BSC,** AURORA MALDONADO, RT, BSC,†† AND PARIMI PRABHAKAR, MD‡‡

Objective: **The objective of this study was to ascertain the antimicrobial susceptibility of *Neisseria gonorrhoeae* isolates from 6 South American and 13 Caribbean countries participating in the Gonococcal Antimicrobial Surveillance Program (GASP) from 1990 to 1999.**

Study: **A GASP network of laboratories was launched in the Americas and the Caribbean during the 1990s. Standardized methods and interpretative criteria were established for the isolation of *N. gonorrhoeae*, strain identification, and determination, and quality control of antimicrobial susceptibility.**

Results: **Two countries (Argentina and Uruguay) maintained continuous surveillance during the study period. Some countries gathered data periodically and several others were unable to initiate antimicrobial surveillance as a result of lack of resources. The percentage of penicillin-resistant *N. gonorrhoeae* isolated in the region over the decade varied considerably (1.0–11.9% carried chromosomal resistance and 17.9–38.8% produced β-lactamase) with an overall trend to declining numbers of penicillin-resistant isolates. For tetracycline, 7.4% to 36.3% carried chromosomal resistance, whereas 12.0% to 27.4% carried plasmid-mediated resistance. There were no reports of ciprofloxacin-resistant isolates, although *N. gonorrhoeae* with decreased susceptibility to ciprofloxacin and azithromycin as well as spectinomycin-resistant isolates were identified in some countries.**

*From the *Gonococcal Antimicrobial Surveillance Program (GASP) in the Americas and the Caribbean; the †Centre for Research in Biopharmaceuticals and Biotechnology, University of Ottawa, Ottawa, Canada; ‡Universidad de la Republica, Montevideo, Uruguay; §Instituto Nacional de Microbiología, Buenos Aires, Argentina; ‖Instituto Nacional de Salud, Lima, Peru; ¶Instituto Nacional de Higiene "Rafael Rangel," Caracas, Venezuela; **Instituto Nacional de Salud, Bogotá, Colombia; ††Instituto de Salud Publica, Santiago, Chile; and the ‡‡Caribbean Epidemiology Centre, CAREC, Port of Spain, Trinidad and Tobago*

A MAJOR TENET OF GONOCOCCAL control programs holds that infections with *Neisseria gonorrhoeae* can be cured with antibiotics. Nevertheless, *N. gonorrhoeae* isolates have shown incredible adaptability, eventually developing either single or multiple resistances to agents used for therapy. As a result, traditional, inexpensive drugs such as penicillin and tetracycline are no longer effective, whereas resistance to newly introduced antimicrobial agents is continuously developing.[1–3] The antimicrobials currently recommended by the World Health Organization (WHO) and other agencies for the treatment of gonorrhea include fluoroquinolones, third-generation cephalosporins, spectinomycin, and azithromycin.[4] Nevertheless, resistance to all or some of these drugs has been identified in many countries.[5–11] The prevalence of resistant *N. gonorrhoeae* isolates, however, is still poorly recognized in many regions and, consequently, ineffective drugs such as penicillin and tetracycline are still being used to treat gonococcal infections.[12,13]

The Gonococcal Antimicrobial Surveillance Program (GASP) was created in the early 1990s to monitor the prevalence of antibiotic-resistant *N. gonorrhoeae* isolates globally and to ensure that effective antimicrobials were recommended for treating gonococcal infections.[10,14,15] The WHO originally proposed the creation of 6 GASP centres, one for each WHO region[14]; however, only 2 regions were able to establish functional GASP programs.[15] The tasks for each GASP Coordinating Centre included: 1) the development of appropriate laboratory-based training programs in each region; 2) the recommendation of standardized methods and the provision of reference strains; 3) the establishment of international proficiency and quality assurance programs; and 4) the facilitation of information and data-sharing between network participants in each region.[15]

This article summarizes the activities of the GASP Coordinating Centre for the Americas and the Caribbean between 1990 and 1999 and reports on the antimicrobial susceptibility of *N. gonorrhoeae* isolates in 6 South American countries and in countries reporting to the Caribbean Epidemiology Centre (CAREC). Our findings, demonstrating high percentages of penicillin- and tetracycline-resistant isolates, as well as isolates with reduced susceptibility to fluoroquinolones, azithromycin, and spectinomycin, underscore the need for sustained antimicrobial surveillance programs in the region. The significant limitations and constraints to the establishment and maintenance of such surveillance programs are discussed.

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Correspondence: Jo-Anne R. Dillon, PhD, College of Arts and Science, University of Saskatchewan, 9 Campus Drive, c/o Arts Room 226, Saskatoon, SK, Canada S7N 5A5. E-mail: j.dillon@usask.ca.

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Materials and Methods

GASP Participants in the Americas and Caribbean

A total of 130 laboratories that could potentially participate in the GASP network for the Americas and the Caribbean were initially identified in the early 1990s in 43 countries: 3 in North America, 10 in South America, and 30 countries in Central America and the Caribbean region. The laboratory capability of each country was self-evaluated using a questionnaire provided by the coordinating centre in Ottawa. Through various discussions and group meetings, standard methods and interpretative criteria to be used for the transportation and/or culture of the specimens, gonococcal identification, and antimicrobial susceptibility testing methods were agreed on.[16,17] Different options for isolation and strain identification were used based on the availability of reagents and equipment in each country. Network members were encouraged to participate in a number of international or regional proficiency testing programs, as well as individual or workshop-based laboratory training. Courses for training trainers were held at the GASP Centre in Ottawa in 1994 and 1997 and at CAREC in 1995.

Two countries, the United States and Canada, maintain well-established gonococcal surveillance networks that have been operating for several decades. GASP results from these countries are not included in this communication, because they have been published elsewhere.[18,19] Other countries participating in the GASP for the Americas and the Caribbean can be divided into 3 groups: 1) countries that regularly reported their results to the GASP Centre–Ottawa during the period covered by this study (1990–1999). This includes Argentina, which had an established national laboratory-based antimicrobial surveillance network, and Uruguay. Argentina expanded its network in 1996 after holding a national workshop. A 2-day conference was held in Uruguay in 1996 to discuss the GASP network, review national data, and to establish national laboratory guidelines. 2) Countries that periodically reported surveillance data to the GASP Centre–Ottawa included: Venezuela, Colombia, Peru, and Chile. Twenty-one countries in the Caribbean region are members of a regional network and report local results to CAREC, which is located in Trinidad and Tobago. However, data collection, over the period, from most of these countries was sporadic. 3) A third group of countries expressed an interest in developing the infrastructure needed to participate in the GASP program but could not do so during the period in question. Some countries, like Brazil, held several national meetings to establish a national surveillance program. During this period, a number of groups published local data.[20] In addition, some countries (e.g., Cuba[13]) published GASP-independent studies and others (e.g., Bolivia, Costa Rica, Honduras) reported retrospective data, using such methods as disk diffusion assays, or published their results elsewhere (e.g., Nicaragua,[21] Honduras,[22] Panama,[23] El Salvador,[24] and Mexico[25,26]). Therefore, these data are not included in this publication.

Isolate Identification and Antimicrobial Susceptibility Determination

Clinical samples were collected in the various countries according to local procedures. Initial growth on Thayer Martin or an equivalent medium and presumptive identifications based on Gram stain, colony morphology, carbohydrate use, and oxidase testing were carried out locally.[16] Occasionally, some countries sent isolates to the GASP Coordinating Centre in Ottawa for confirmation of identity and susceptibility testing. All countries performing antimicrobial susceptibility testing participated in the international quality control program established by the GASP Centre–Ottawa to ensure data comparability. In most circumstances, the antimicrobials used were locally produced. The procedures and interpretative criteria followed were those recommended by the National Committee for Clinical Laboratory Standards (NCCLS).[17] The discrimination between plasmid-mediated (PPNG) and chromosomally mediated (CMPR) resistance to penicillin was based on β-lactamase testing with nitrocefin.[27] For tetracycline-resistant isolates, on the other hand, Argentina and Uruguay performed TetM determinations,[28] whereas other countries presumptively identified plasmid-carrying isolates (TRNG) based on minimum inhibitory concentration (MIC) values of $\geq$16.0 μg/mL.[17] Most isolates with tetracycline MICs $\geq$2.0 μg/mL were confirmed by the GASP Centre–Ottawa for the presence of a *tetM* determinant (see subsequently). Chromosomally resistant isolates were defined as having an MIC to penicillin of $\geq$2.0 μg/mL and to tetracycline of $\geq$2.0 μg/mL to 8.0 μg/mL (classified as CMPR for penicillin resistance and CMTR for tetracycline resistance) and that were not classified as PPNG or TRNG.

Only a few countries performed either regular or periodic MIC testing to spectinomycin, ciprofloxacin, ceftriaxone, and azithromycin. Isolates with MICs of $\geq$1.0 μg/mL to ciprofloxacin were considered resistant, whereas intermediate susceptibility was defined as an MIC of 0.12 to 0.5 μg/mL.[17] MICs of $\geq$128.0 μg/mL to spectinomycin indicated chromosomal resistance, although several countries only tested up to concentrations of 32 μg/mL.[17] Isolates were considered as being susceptible to ceftriaxone if their MICs were $\leq$0.25 μg/mL, whereas MICs $\geq$0.25 were interpreted as having reduced susceptibility.[17] Concentrations of $\geq$1.0 μg/mL were used to define resistance to azithromycin, and MICs of 0.25 to 0.5 μg/mL were considered as having decreased susceptibility to this antibiotic.[12,17,20]

Isolates tested at the GASP Coordinating Centre in Ottawa were tested for β-lactamase production and their MICs to various antimicrobial agents were also determined. Plasmid profile analysis and *tetM* typing by polymerase chain reaction was used to confirm the presence of plasmid-mediated resistance to penicillin and/or tetracycline.[20]

Quality Control Program

The GASP Coordinating Centre for the Americas and the Caribbean implemented an international quality control program to standardize the interpretation of MIC results obtained for *N. gonorrhoeae* isolates (Abstracts of the 11th Pathogenic Neisseria Conference; November 1–6, 1998, Nice, France). Six centers, including the GASP–Ottawa Centre, participated in the first panel of the program in 1997; 6 countries participated in 1998 and 10 in 1999. These included the Centers for Disease Control and Prevention (CDC), Laboratory Centre for Disease Control (LCDC, Canada), CAREC (Trinidad), Instituto de Salud Publica (Chile), Universidad de la Republica (Uruguay), Instituto Nacional de Microbiologia (Argentina), Instituto Nacional de Higiene "Rafael Rangel" (Venezuela), Instituto Nacional de Salud (Colombia), "Pedro Kouri" Institute of Tropical Medicine (Cuba), and Instituto Nacional de Salud (Peru). The aim of the program was to include all participating GASP countries and to achieve 90% overall agreement between results. This program was suspended in 2000 as a result of lack of sustained funding.

Participating centers tested a panel of 5 isolates randomly selected from a set of well-characterized gonococcal isolates and reported their results and interpretations to the GASP Coordinating Centre, Ottawa. MICs were determined by the agar dilution method as recommended by the National Committee for Clinical Laboratory Standards.[17] Antimicrobial agents were obtained locally. Participants tested 5 antimicrobials: penicillin, tetracycline, spectinomycin, ciprofloxacin, and ceftriaxone; and Argentina,

TABLE 1. Number of *Neisseria Gonorrhoeae* Isolates Tested in 6 South American Countries for Antimicrobial Susceptibility (1990–1999)

	No. Isolates Tested in										
Country	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	Total No (%).
Argentina	15	10	46	62	40	101	134	110	260	297	1075 (38.3)
Uruguay	13	48	52	59	42	32	38	35	21	36	376 (13.4)
Peru						16		34	49	81	180 (6.4)
Venezuela	176	165	173	60	23	14	63	73	51		798 (28.4)
Chile*					65	61	66				192 (6.8)
Colombia			28	21	19	34	12	22	28	21	185 (6.6)
Total	204	223	299	202	189	258	313	274	409	435	2806

*Chile reported results to the GASP Centre–Ottawa between 1994 and 1996. However, this country has an ongoing surveillance program.

Uruguay, Peru, and Venezuela also tested azithromycin. All MIC data received from the quality control-participating centers were entered into a spreadsheet database, and the final analysis of the data was performed in Ottawa using the Statistical Analysis System (version 6.11; SAS Institute Inc., Cary, NC). Ideally, results were considered to be comparable if participating laboratories had >90% agreement (i.e., within a 2-fold dilution) in MIC values for the strains tested. In the majority of panels tested, this number was achieved by participating laboratories indicating that MIC results submitted to the GASP Centre–Ottawa were comparable.

Results

Between 1990 and 1999, 2806 *N. gonorrhoeae* isolates were reported from 6 South American countries (Table 1). Argentina and Uruguay performed antimicrobial susceptibility tests over the entire period and collected 38.3% (n = 1075) and 13.4% (n = 376) of isolates tested, respectively. Venezuela reported results between 1990 and 1998 and tested 28.4% (n = 798) of isolates tested, whereas between 1992 and 1999, Colombia tested 6.6% (n = 185) of the isolates reported in the current study. Peru collected data in 1995 and between 1997 and 1999 (6.4% of isolates reported in this study), whereas Chile reported results in 1994, 1995, and 1996 (6.8% of isolates tested; Table 1).

Between 1990 and 1997, countries reporting to CAREC (Table 2) tested 4528 *N. gonorrhoeae* isolates for penicillinase production (n = 32 Antigua, 232 Bahamas, 79 Barbados, 251 Belize, 26 Bermuda, 195 Cayman Islands, 20 Dominica, 42 Grenada, 77 Guyana, 93 St. Lucia, 272 St. Vincent, 2960 Suriname, 249 Trinidad and Tobago).

TABLE 2. Reported Penicillinase-Producing *Neisseria Gonorrhoeae* (PPNG) in Some CAREC Countries, 1990–1999

Country	Year	Isolates	PPNG (%)
Antigua	1994–1995	32	28 (87.50)
Bahamas	1994–1997	232	102 (43.97)
Barbados	1994–1997	79	27 (34.18)
Belize	1995–1997	251	143 (56.97)
Bermuda	1996	26	2 (7.69)
Cayman Islands	1994–1997	195	63 (32.31)
Dominica	1990	20	12 (60.0)
Grenada	1994	42	3 (7.14)
Guyana	1993–1994	77	51 (66.23)
St. Lucia	1990, 1994–1997	93	3 (3.23)
St. Vincent	1990, 1995–1997	272	57 (20.96)
Suriname	1994–1997	2960	1924 (65.0)
Trinidad	1992, 1995	249	30 (12.05)
Total No.		4528	2445 (54.0)

Penicillin Susceptibility

The total burden of penicillin-resistant isolates (i.e., PPNG and CMPR) reported from South American countries varied between 48.5% (98 of 202 tested) in 1993 and 25.3% (110 of 435) of isolates tested in 1999 with an overall trend to decreasing percentages of isolates that were penicillin-resistant over the decade (Fig. 1). Overall, high percentages of plasmid-mediated (17.9–38.8%; Fig. 2) and chromosomally mediated (1.0–11.9%; Fig. 3) resistance to penicillin were noted in South American countries, although the percentages of resistant isolates varied by country and by year. Between 1990 and 1998, PPNG represented more than 28% of all isolates tested overall for antimicrobial susceptibility (Fig. 2) falling to17.9% in 1999. In Uruguay, more than 40% of *N. gonorrhoeae* isolated between 1990 and 1997 were PPNG, (>60% in 1990, 1992, 1996, and 1997; 23.8% in 1998; and 30.6% in 1999). Similarly, PPNG in Colombia comprised more than 50% of isolates tested between 1992 and 1994 and more than 28% after 1995. Argentina, Venezuela, Peru, and Chile reported PPNG percentages of between 17.4% and 42.9% for the years studied, except for Argentina in 1990 (13.3% of 15 isolates) and Peru in 1999 (4.9% of 180 isolates).

In the countries reporting to CAREC (Table 2), 54.0% (2445 of 4528) of all isolates tested were PPNG. PPNG were reported for multiple years from Suriname (65.0%), Belize (57.0%), Bahamas (44.0%), Cayman Islands (32.3%), Barbados (34.2%), St. Vincent (21.0%), Trinidad (12.1%), Bermuda in 1996 (7.7%), Grenada in 1994 (7.1%), and St. Lucia (3.2%). In those countries reporting several years of β-lactamase testing, a slight decline in the overall percentage of PPNG isolates was generally noted (data not shown).

In 6 South American countries, isolates with chromosomal resistance to penicillin (CMPR; Fig. 3) ranged from 1% in 1990 to a high of 11.9% of isolates tested in 1993. The peak percentages of CMPR isolates were noted between 1993 and 1995. After 1993 (Fig. 3, overall percentage), between 4.2% and 8% of the isolates carried chromosomal resistance to penicillin. The percentage of CMPR in Argentina ranged from 0% to 29% (Fig. 3) with an average percentage of 7.9% over the period tested. Uruguay reported between 0% and 9.5% CMPR isolates during this period (Fig. 3). Venezuela reported CMPR percentages of 1.2% and 2.3% between 1990 and 1992, but this number increased later, surpassing 14% in 1995. Peru did not report the isolation of *N. gonorrhoeae* at the beginning of this study; but in 1998 and 1999, 28.6% and 18.5% of 49 and 81 isolates, respectively, were CMPR. In Colombia, CMPR were not isolated in 1992, 1995, 1997, and 1998, and single isolates were reported in the remaining years (Fig. 3). Chile reported CMPR isolates in 1994 (3.1%) and 1996 (1.5%).

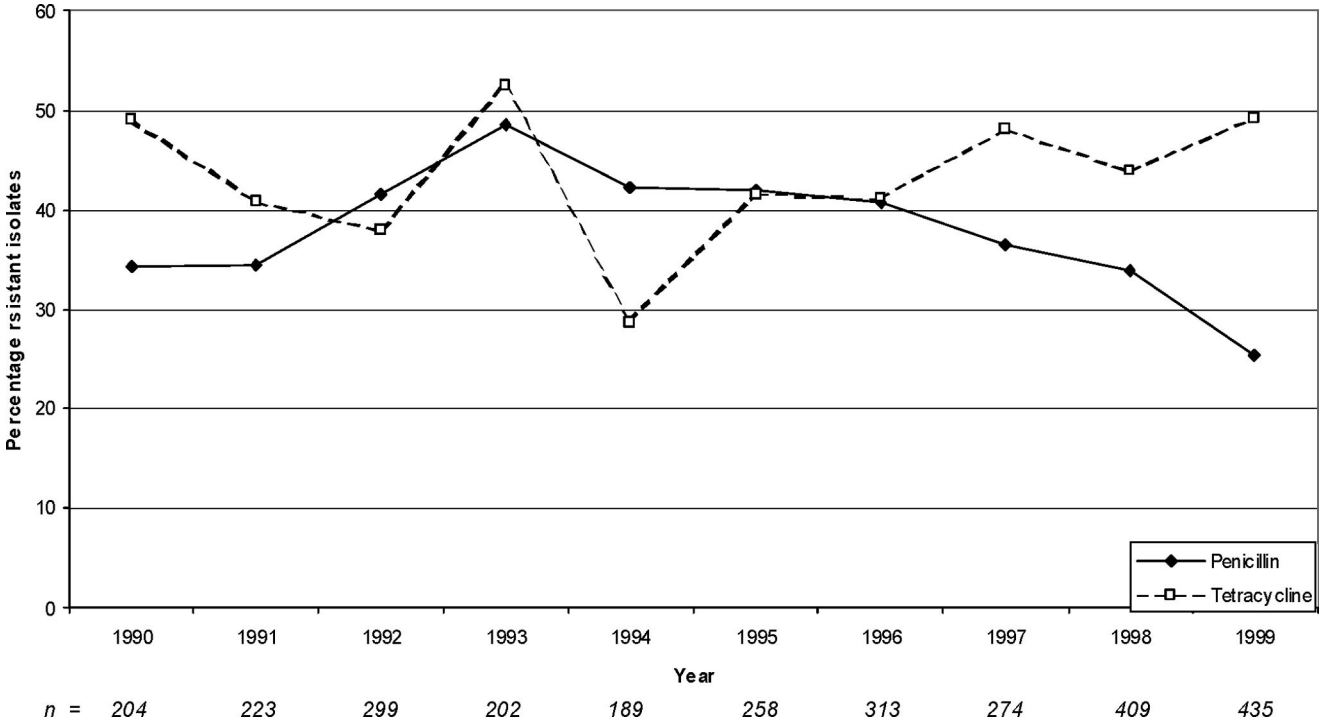

Fig. 1. Trends in penicillin and tetracycline resistance in South America, 1990–1999. Each point represents the percentage of isolates reported by 6 South American countries (Argentina, Chile, Colombia, Peru, Venezuela, and Uruguay) that were either penicillin- (PPNG and CMPR) or tetracycline- (TRNG and CMTR) resistant each year. n indicates total number of isolates reported by all countries in a year.

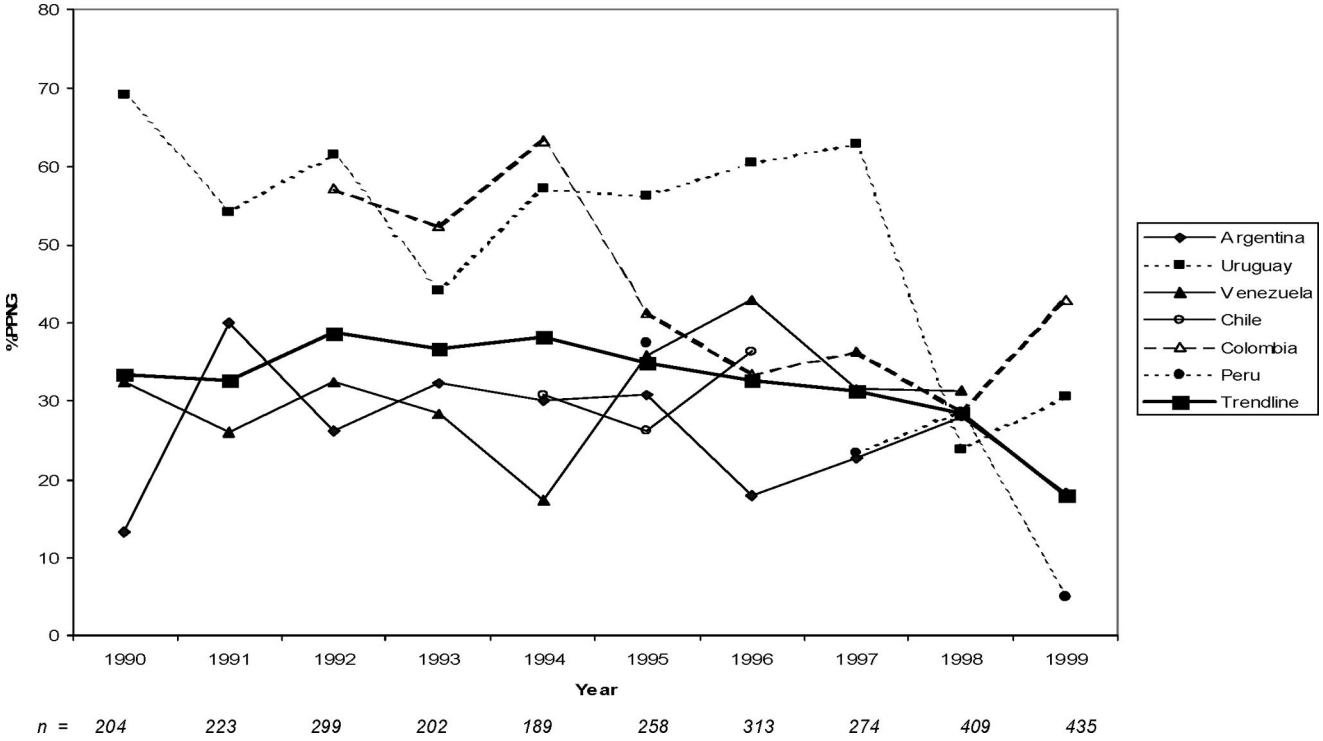

Fig. 2. Isolation of penicillinase-producing *Neisseria gonorrhoeae* (PPNG) in 6 South American countries, 1990–1999: Each point represents the percentage of PPNG isolates reported by a country. n indicates total number of isolates reported by all countries per year. The trend line is the percentage of n that was PPNG.

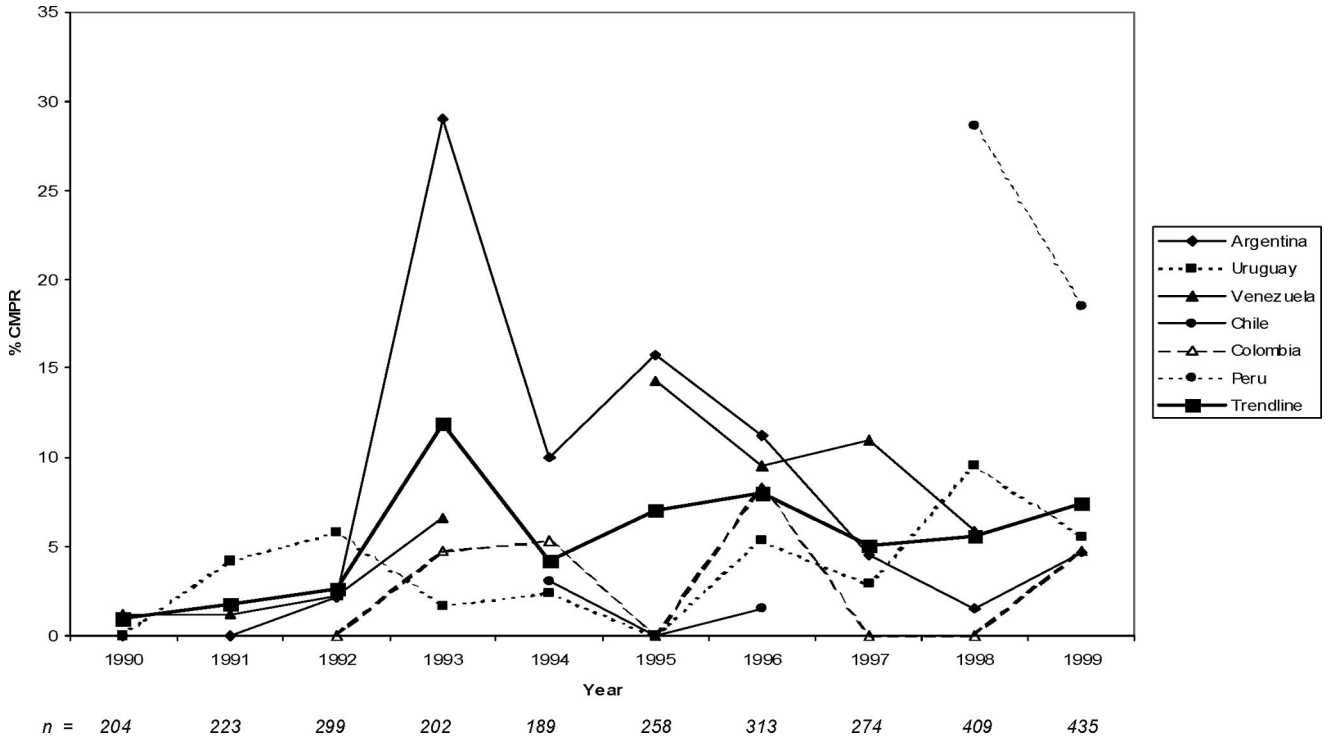

Fig. 3. Isolation of chromosomally mediated resistant *Neisseria gonorrhoeae* (CMPR) in 6 South American countries, 1990–1999: Each point represents the percentage of isolates reported by a country that were CMPR. n indicates total number of isolates reported by all countries per year. The trend line is the percentage of n that was CMPR.

Tetracycline Susceptibility

The total burden of resistance, both chromosomal- and plasmid-mediated, to tetracycline in countries reporting from South America ranged from 28.6% (1994) to 52.5% (1993) of isolates tested, with an average percentage of tetracycline-resistant isolates of 43.4% over the decade (Fig. 1). Reported percentages of TRNG in Argentina, Chile, Columbia, Peru, Uruguay, and Venezuela ranged between12.7% of isolates tested in 1990 to 27.4% in 1997 (Fig. 4). From 1993 to1997, more than 40% of isolates tested in Venezuela were TRNG (in 1998, 33.33% were TRNG). In Colombia, the percentage of TRNG isolated was between 57.1% and 89.5% with an average isolation percentage of 77.1% over the period tested (Fig. 4). Chile submitted results from 1994 to 1996 and reported an increase in TRNG isolations from 10.8% of 65 isolates tested in 1994 to 31.8% of 66 isolates in 1996. Peru reported that 18.4% and 43.2% of isolates tested were TRNG in 1998 and 1999, respectively. The percentage of TRNG isolated in Argentina was either 0% (1990–1992) or ranged from of 1.6% (1993) to 20.9% (1997) with an average percentage of 7.1% TRNG isolated over the period (Fig. 5). In Uruguay, TRNG isolations ranged from 0% (1993) to 13.9% (1999).

Between 7.4% (n = 14; 1994) and 36.3% (n = 74; 1990) of isolates tested from South America were reported as having chromosomal resistance to tetracycline (CMTR; Fig. 5) with the average percentage over the decade being 23.5%. In Uruguay, the percentage of CMTR isolates ranged from 7.7% in 1990 to 36.1% in 1999 (Fig. 5). In Argentina, the percentages of CMTR varied from a low of 10% in 1994 to a high of 54.8% in 1993 and 42.7% in 1997 (Fig. 5). Venezuela reported percentages CMTR ranging from 4.4% (1994) to 38.6% (1990). In Colombia, CMTR isolations ranged from 0% (1994 and 1997) to a high of 16.7% of isolates tested in 1996. For Peru, data for 1998 and 1999 are available, and percentages of isolation of CMTR were 42.9% and 19.8% of 49 and 81 isolates tested, respectively.

Susceptibility to Other Antimicrobial Agents

The countries that tested gonococcal susceptibility to ciprofloxacin or lomefloxacin, ceftriaxone, azithromycin, or spectinomycin are listed in Table 3. No isolates were reported to have MICs >0.25 μg/mL to ceftriaxone (Argentina, Uruguay, and Peru). Overall, 31 isolates (from Argentina, Uruguay, and Venezuela) demonstrated MICs to ciprofloxacin (lomefloxacin was tested in Venezuela) of ≥0.06 μg/mL (2 isolates in Venezuela had a MIC ≥1 μg/mL in 1995 and in 1997 Uruguay reported 2 isolates with MICs of ≥2 μg/mL). A total of 70 isolates from Columbia and Venezuela were reported as having MICs >32.0 μg/mL to spectinomycin; most of those isolates were subsequently retested and were classified as being resistant (≥128.0 μg/mL) to spectinomycin. Uruguay and Venezuela reported 159 isolates with MICs to azithromycin of either ≥0.125 or ≥0.25 μg/mL.

Discussion

Although epidemic infectious diseases resulting in high morbidity and/or mortality trigger public health responses and the immediate allocation of human and economic resources to solve the crisis,[29,30] endemic infections frequently remain unattended within communities.[31] This is an important issue for pathogens such as *N. gonorrhoeae,* which have the potential to develop resistance to multiple antibiotics used for treatment and, in the case of plasmid-mediated resistance, to spread this resistance between strains.[8–10,32,33,34]

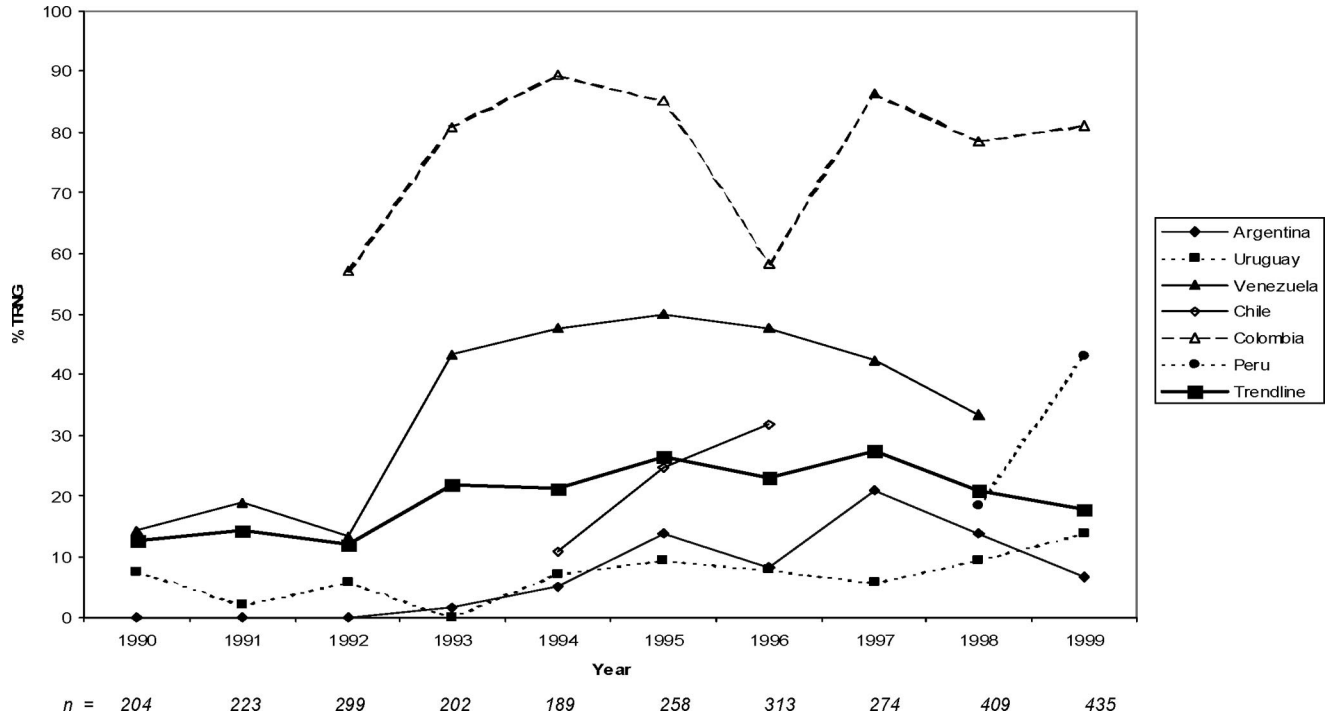

Fig. 4. Isolation of tetracycline-resistant *Neisseria gonorrhoeae* (TRNG) in 6 South American countries, 1990–1999: Each point represents the percentage of isolates reported by a country that were TRNG. n indicates total number of isolates reported by all countries per year. The trend line is the percentage of n that was TRNG.

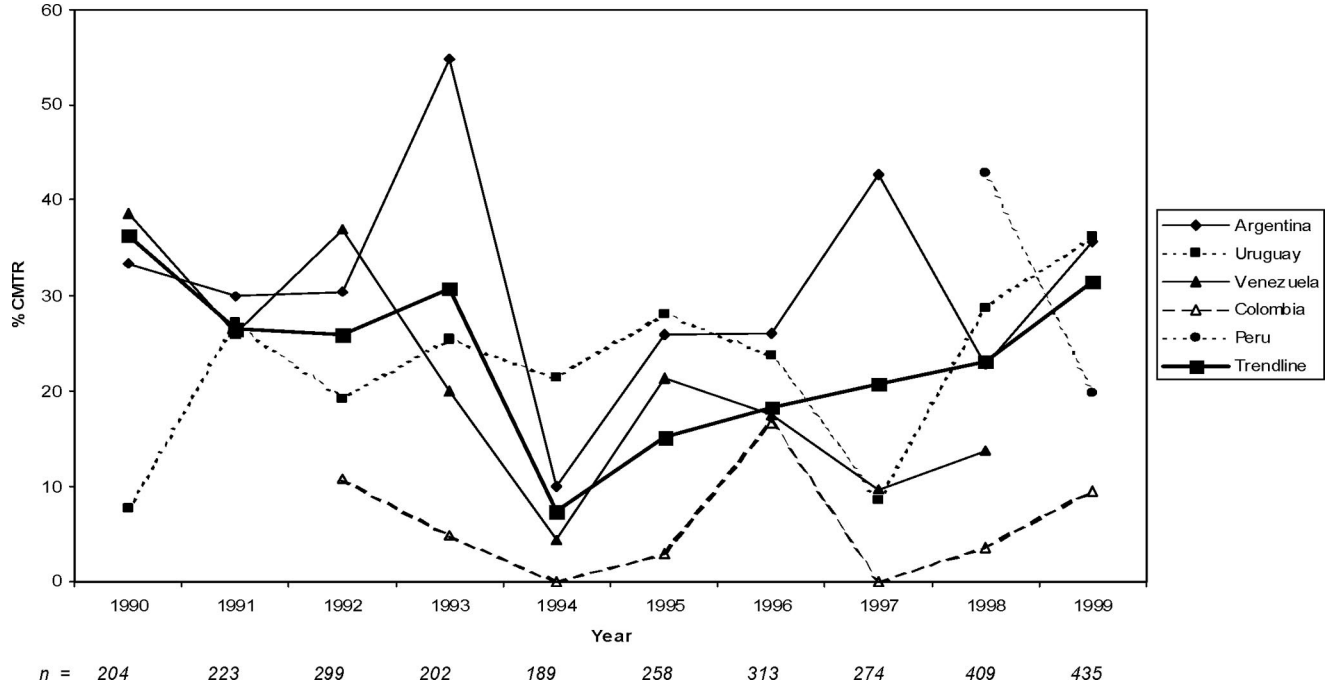

Fig. 5. Isolation of chromosomally mediated resistant *Neisseria gonorrhoeae* (CMTR) in 6 South American countries, 1990–1999: Each point represents the percentage of isolates reported by a country that were CMTR. n indicates total number of isolates reported by all countries per year. The trend line is the percentage of n that was CMTR.

TABLE 3. Isolates Reported With Reduced Susceptibility to Spectinomycin, Azithromycin, Ciprofloxacin, or Ceftriaxone

Country	Years Tested	Years Resistance Detected	No. Isolates Tested	Spectinomycin* MIC >32.00 n (%)	Azithromycin MIC ≥0.125–0.25 n (%)	Ciprofloxacin† MIC ≥0.06 n (%)	Ceftriaxone MIC ≥0.25 n (%)
Argentina	1990–1999	1996	134	0		1	0
Uruguay‡	1990–1999	1991	48	0	ND	7 (14.6)	0
		1992	52	0	ND	3 (5.8)	0
		1993	58	0	ND	3 (5.2)	0
		1995	32	0	27 (84.4)	1	0
		1996	41	0	30 (73)	0	0
		1997	54	0	33 (61)	2 (4)§	0
		1998	46	0	27 (59)	0	0
		1999	31	0	21 (68)	0	0
Colombia	1994–1996	1994	19	3 (15.8)	ND	ND	ND
Peru	1998–1999	1998	49	0	0	0	0
		1999	81	0	0	0	0
Venezuela	1990–1998	1990	176	4 (2.3)	ND	ND	ND
		1991	165	8 (4.8)	ND	ND	ND
		1992	173	6 (3.5)	ND	ND	ND
		1993	60	20 (33.3)	1 (1.7)	0	0
		1994	23	5 (21.7)	0	0	0
		1995	14	1 (7.1)	3 (21.4)	2 (14.3)§	0
		1996	63	19 (30.2)	4 (6.3)	5 (7.9)	0
		1997	73	4 (11.4)	7 (9.6)	4 (5.5)	0
		1998	51	0	6 (11.8)	3 (5.9)	0
Total No			1,443	70	159	31	0

*Many of these isolates were retested locally and found to have MICs ≥128 μg/mL.
†Lomefloxacin tested in Venezuela.
‡It should be noted that updated data from Uruguay for 1996–1999 were provided after retrospective testing. Therefore, in a few cases, some total numbers may not reflect the numbers reported in Table 1.
§Two isolates tested in Uruguay in 1997 had a MIC of: 2 μg/mL and 2 isolates in Venezuela in 1995 had MICs 1 μg/mL.
MIC indicates minimum inhibitory concentration; ND = not determined.

More than 62 million cases of gonorrhea occur annually.[11] An increase in the incidence of gonorrhea cases has been reported in several developed countries, whereas many developing countries maintain high rates.[34–36] This finding is particularly unfortunate because lesions caused by *N. gonorrhoeae* predispose for other genital infections, including the human immunodeficiency virus (HIV).[37–39] *N. gonorrhoeae* causes both symptomatic and asymptomatic infections of the genital tract, as well as extragenital infections. The spectrum of clinical presentations is very wide, sometimes overlapping those of other sexually transmitted diseases, particularly *Chlamydia trachomatis*.[34] Although it is difficult to diagnose gonorrhea based on clinical symptoms, syndromic diagnosis is the recommended method in many resource-limited regions.[4,40] To make matters worse, antibiotics are sometimes prescribed empirically based on presumption of efficacy, and these decisions are often driven by the local availability of antimicrobial agents.[34,41]

This article summarizes the antimicrobial susceptibility of *N. gonorrhoeae* reported during the 1990s to the GASP Coordinating Centre for the Americas and the Caribbean by countries in South America and by Caribbean countries reporting to CAREC. Considerable heterogeneity in the frequency and extent of reporting by the different countries was experienced over this period; nevertheless, changes in the susceptibility of *N. gonorrhoeae* to different antimicrobials were detected. A high percentage of isolates with plasmid-mediated and chromosomally mediated resistance to penicillin were identified throughout the period in all countries, although the total burden of penicillin resistance declined in the late 1990s, probably related to changes made in treatment guidelines. Guidelines in several countries were updated to recommend effective antibiotics over the period of this study, reflecting the impact of even modest surveillance programs such as the GASP on national public health policies.

Resistance to tetracycline was mainly chromosomal in the early 1990s, but the number of TRNG isolates reported increased after 1992. The percentage of TRNG rose to 42% and above in Venezuela between 1993 and 1998 and above 50% in Colombia between 1992 and 1999. Such high values are similar to percentages reported by other countries in the region: Guyana (77.1% in 1992),[12] Cuba (64% of isolates between 1995 and 1998),[13] and Brazil (76.5% in 1998).[20] In Bolivia, resistance to tetracycline ranged between 30% and 73% of *N. gonorrhoeae* isolated during this period (1992–1999), and resistance to penicillin was present in 38% to 65% of isolates (F. Tinajeros, personal communication).

The therapies currently recommended for gonorrhea include fluoroquinolones, third-generation cephalosporins, azithromycin, and spectinomycin.[4,42–44] However, *N. gonorrhoeae* resistant to spectinomycin was detected in Venezuela and Colombia, and isolates with reduced susceptibility or resistance to fluoroquinolones were reported from Uruguay and Venezuela. During the period of this study, resistance to ciprofloxacin was reported in different parts of the world.[3,32,34] The low prevalence of ciprofloxacin-resistant isolates observed in this study may reflect the high cost and therefore low use of this antibiotic in South America. Venezuela and Uruguay[33] as well as Guyana and St. Vincent,[12] Cuba,[13] and Brazil[20] also reported the isolation of *N. gonorrhoeae* with decreased susceptibility or resistance to azithromycin, an antibiotic prescribed in these countries for the simultaneous treatment of *N. gonorrhoeae* and *Chlamydia trachomatis* infections. All isolates in Bolivia were susceptible to ceftriaxone and to ciprofloxa-

cin (F. Tinajeros, personal communication). None of the countries reporting to GASP isolated *N. gonorrhoeae* resistant to third-generation cephalosporins during the 1990s.

Two other countries in the Americas, Canada and the United States, also reported an increase in the prevalence of antibiotic-resistant *N. gonorrhoeae* during the 1990s.[45–47] In 1998, 29.4% of all isolates (1384 of 4712) collected in 28 centres participating in the Gonococcal Isolate Surveillance Project (GISP), in the United States, were resistant to penicillin, tetracycline, or both; this percentage was similar to previous years dating from 1988.[45] Also in 1998, 1% of gonococcal isolates exhibited decreased susceptibility or resistance to ciprofloxacin and a few isolates were resistant to spectinomycin.[45] Additionally, several centers reporting to GISP described an increase in MIC values to cephalosporins.[45] In Canada, TRNG isolations peaked in 1994[48]; CMRNG represented 19.2% of isolates tested between 1994 and 1999 (12.9% of these isolates were also erythromycin-resistant), whereas 2.3% and 0.8% were ciprofloxacin- and azithromycin-resistant, respectively.[46,47]

In comparison, results available from the Western Pacific Region, the only other area with an operational GASP center, also showed variation in reporting between the countries (17–20 countries) and an increase in resistance to most antimicrobials.[49] Widespread penicillin and tetracycline resistance was reported either chromosomally or plasmid-mediated.[49] Quinolone-resistant gonococci were first detected in the West Pacific Region in 1992, and in the following years, an increase in the number of centers reporting isolates with reduced susceptibility or resistance was noted.[2,49]

Since its creation in the early 1990s, the GASP program in the Americas and Caribbean has been affected by fluctuations in public interest and funding. Cutbacks in local and international funding and in technical support had a negative influence on participation in the program. At the time the program was interrupted, several countries were still developing the infrastructure required to conduct this surveillance.

Better management of *N. gonorrhoeae* infections remains a tenet of good public health policy. To be effective, the control of gonorrhea should be completed at the community level, and surveillance programs should be integrated into broader national and international public health programs as a public health priority.

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