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Six-Month Multicenter Study on Invasive Infections Due to *Streptococcus pyogenes* and *Streptococcus dysgalactiae* subsp. *equisimilis* in Argentina

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During a 6-month period, 95 invasive infections due to *Streptococcus pyogenes* and group C or group G *Streptococcus dysgalactiae* subsp. *equisimilis* were recorded from 40 centers of 16 cities in Argentina. We describe here epidemiologic data available for 55 and 19 patients, respectively, associated with invasive infections due to *S. pyogenes* and *S. dysgalactiae* subsp. *equisimilis*. The associated isolates and 58 additional pharyngeal isolates were genotyped and subjected to serologic and/or antibiotic susceptibility testing. Group A streptococcal *emm* type distribution and strain association with toxic shock appeared to differ somewhat from results found within the United States; however, serologic characterization and *sof* sequence typing suggested that *emm* types found in both countries are reflective of shared clonal types.

Streptococcus pyogenes is frequently involved in uncomplicated infections such as pharyngitis and impetigo. However, suppurative and nonsuppurative complications are often sequelae of these mild infections. Additionally, since the 1980s there has been a marked increase in reported invasive group A infections including cases of streptococcal toxic shock syndrome (STSS).

Groups C and G *Streptococcus* have shown a similar pathogenic pattern to *S. pyogenes* (10), and groups C and G streptococci recovered from aboriginal children in Australia were found to elicit myosin cross-reactive antibodies (11). Groups G and C *Streptococcus dysgalactiae* subsp. *equisimilis* express homologs of the M virulence proteins of *S. pyogenes* that are antiphagocytic (7), and some strains contain superantigen genes first characterized in *S. pyogenes* (13, 15). As with *emm* genes of *S. pyogenes*, the groups C and G *S. dysgalactiae* subsp. *equisimilis* homologs are used for sequence-based typing (5, 8, 13), with more than 40 sequence types presently described (available for downloading from http://www.cdc.gov/ncidod/biotech/strep/doc.htm).

Resistance to macrolides, tetracycline (TET), and chloramphenicol (CMP) has been observed among groups A, C, and G β-hemolytic streptococci (17, 22, 23); however, there are few data concerning the epidemiology and antimicrobial susceptibility of invasive β-hemolytic streptococci from Latin American countries. Serotyping and antimicrobial testing of streptococci recovered in Argentina have previously focused on pharyngeal isolates (16, 20, 30), but information concerning recently recovered invasive streptococcal isolates is lacking.

In gram-positive organisms, erythromycin (ERY) resistance is mediated by either target modification or active efflux (17, 29). Target modification may be produced by mutation or by posttranscriptional methylation of adenine molecules in 23S rRNA (4, 29). In streptococci, TET resistance is due to active efflux or ribosomal protection (22), while CMP resistance is mediated by target modification, active efflux, or antibiotic inactivation (23). High-level resistance to aminoglycosides has been described in a few isolates of *S. pyogenes* and groups G and C *S. dysgalactiae* subsp. *equisimilis* (9, 33).

In this study we determined strain distribution, antibiotic resistance, and resistance mechanisms of *S. pyogenes* and groups C and G *S. dysgalactiae* subsp. *equisimilis* isolated in 40 Argentinian centers from invasive infections during a 6-month period.

MATERIALS AND METHODS

Bacterial isolates. All *S. pyogenes*, group C *S. dysgalactiae* subsp. *equisimilis*, or group G *S. dysgalactiae* subsp. *equisimilis* strains isolated from invasive infections during October 1998 to March 1999 in 40 centers of 16 Argentinian cities were

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studied. Pharyngeal isolates obtained in only one center from Buenos Aires were used to compare epidemiological trends.

Only the type distribution of those isolates recovered from patients with sufficient available data (77.9% of the total isolates) was analyzed. Hemolysis was detected on 5% sheep blood Columbia agar. Pyrrolidonyl arylamidase, leucine aminopeptidase, and bacitracin susceptibility tests were performed by using Britania disks (Buenos Aires, Argentina). The observation of chains was performed in gram smears prepared with drops of overnight cultures in thioglycolate broth. Identification and grouping were completed by using the latex agglutination method (Slidex Strepto kit; bio Mérieux, Marcy l'Etoile, France) and the Voges-Proskauer test. Isolates were subjected to surface carbohydrate grouping, T typing, antiopacity factor (AOF) typing, *emm* and *sof* sequence typing, and M serotyping as previously described (2).

***emm* typing.** Identification as group A was confirmed by slide agglutination (Phadebact Streptococcus tests; Boule Diagnostics AB, Huddinge, Sweden) and *emm* typed as described at ww.cdc.gov/ncidod/biotech/strep/protocols.htm. Briefly, this process includes performing two different sets of *emm* amplicon restriction fragment length (RFLP) polymorphism analysis. For one set the frequently cutting restriction enzyme DdeI is used, and for the other set a HincII plus HaeIII double digest is used. Geographically and temporally related isolates sharing identical profiles for both RFLP sets, identical T agglutination profiles, and opacity factor phenotype (or, more reliably, presence or absence of *sof*) (2) are seen to share the same sequence type (3). *S. dysgalactiae* subsp. *equisimilis* isolates were *emm* typed in an identical manner, except that T typing and opacity factor reactions (or *sof* PCR) were not used. In each instance amplicons from two to five individual isolates sharing identical *emm* RFLP and T types were subjected to *emm* sequence analysis as described (3). Sequences with 92% sequence identity over the first 90 bases encoding the deduced processed M protein of the type reference strain were assigned the same *emm* type as described at http://www.cdc.gov/ncidod/biotech/strep/assigning.htm. The *emm* types are designated with either the prefix *emm*, indicating acceptance as an M protein gene from *S. pyogenes* by an international panel, or *st* (sequence types from *S. dysgalactiae* subsp. *equisimilis*). Subtypes were assigned as previously described (19) on the basis of any alterations within the coding region for the predicted 50 N-terminal residues of the processed M protein compared to the Centers for Disease Control and Prevention type reference strains (always designated with 0.0; e.g., *emm1.0*, *emm4.0*, *emm9.0*, etc.) Signal cleavage sites were deduced as previously described (see www.cbs.dtu.dk/services/SignalP/). New subtypes were screened against previously described subtypes in the GenBank database.

Antimicrobial susceptibility tests. Disk diffusion tests were performed by the Bauer and Kirby method according to NCCLS guidelines with 5% sheep blood Mueller-Hinton agar (25). Disks of penicillin (PEN; 10 U), ERY (15 μg), clindamycin (CLI; 2 μg), TET (30 μg), and CMP (30 μg) were from BBL (Cockeysville, Md.). Incubation was performed at 35 ± 1°C during 24 h in normal atmosphere. Blunting of the CLI inhibition zone near the ERY disk indicated an inducible type of resistance to macrolides, lincosamides, and streptogramin B (MLS_B), while no blunting indicated the probability of the efflux-mediated M resistance phenotype (resistance to macrolides) (28). Resistance to both CLI and ERY indicated a constitutive type of MLS_B resistance. Disks of gentamicin (120 μg), streptomycin (300 μg), and kanamycin (120 μg), currently used to detect high-level aminoglycoside resistance in enterococci, were used as a possible screening method for the same kind of resistance in β-hemolytic streptococci (27).

The agar dilution method was used for susceptibility testing of five antibiotics with 5% sheep blood Mueller-Hinton agar plates according to NCCLS guidelines (25). Concentration ranges were as follows: PEN and CRO, 0.007 to 4.0 μg/ml; ERY, CLI, and azithromycin, 0.06 to 128 μg/ml.

Staphylococcus aureus ATCC 29213 and *Enterococcus faecalis* ATCC 29212 were used as reference strains for antimicrobial susceptibility testing.

Genotypic characterization of antimicrobial resistance. Methods used to detect antibiotic resistance genes were recently described (14, 21).

Types of disease. (i) Infections localized in deep tissues, blood, cerebrospinal fluid, or other liquids obtained by puncture, where causative organisms were isolated from otherwise sterile samples, were defined as invasive infections. (ii) Streptococcal toxic shock syndrome (STSS) was defined as an invasive infection due to a β-hemolytic streptococcus in which hypotension and two or more of the following were found: renal impairment, coagulopathy, liver abnormalities, acute respiratory distress syndrome, extensive tissue necrosis, and erythematous rash (31).

Statistical analysis. Six-month mortality and proportion of STSS in children and adults were compared by a Fisher's exact test. Overall differences were considered significant when P was ≤ 0.05 by the use of two-tailed significance levels.

RESULTS

During the 6-month period, 95 invasive infections due to groups A, C, or G β-hemolytic streptococci were recorded (Table 1). Of these, 51 were found in Buenos Aires City and its surroundings (population of approximately 11 million), 12 in Tandil, 9 in Rosario, 6 in Mar del Plata, 6 in Neuquén, 5 in La Plata, 3 in Salta, and 1 each in Bahía Blanca, Córdoba, and Tres Arroyos. No isolates were obtained in Goya or Esquel.

Sixty-eight streptococci were identified as *S. pyogenes*, 1 as group A *S. dysgalactiae* subsp. *equisimilis*, 20 as group G *S. dysgalactiae* subsp. *equisimilis*, and 6 as group C *S. dysgalactiae* subsp. *equisimilis*. Complete epidemiologic data were available for 55 patients associated with *S. pyogenes* etiology and 19 invasive infections due to *S. dysgalactice* subsp. *equisimilis*. Thirty-eight patients were adults (>16 years old), and 36 were children (≤16 years old), including one newborn (<1 month). Seven additional *S. pyogenes* isolates and four additional group G *S. dysgalactiae* subsp. *equisimilis* sterile site isolates from individuals of unknown ages, STSS diagnosis, and outcomes were also characterized. STSS was found in 31.8% of known adult patients and in 9.4% of known children (Table 2). The most frequent predisposing conditions for STSS in adults were diabetes ($n = 10$) and malignancy ($n = 3$). Most of these severe episodes [STSS ($n = 5$) and fatal cases ($n = 4$)] due to all three groups of β-hemolytic streptococcus were clustered in Tandil, a city of 130,000 inhabitants of the Buenos Aires province (Table 2). Twenty percent mortality was found among adults (six *S. pyogenes* and two group G *S. dysgalactiae* subsp. *equisimilis* isolates), three of whom had no identifiable underlying predisposing conditions. For five cases of STSS in adults, diabetes or burns were predisposing factors. Five children (14.3%) suffering invasive *S. pyogenes* (four cases) or group G *S. dysgalactiae* subsp. *equisimilis* (one case) streptococcal disease died, four of them with STSS and one with pneumonia. In these cases, mortality was attributable to the β-hemolytic streptococcal infections.

Fifty-one group A *S. pyogenes*, four group C *S. dysgalactiae* subsp. *equisimilis*, and three group G *S. dysgalactiae* subsp. *equisimilis* pharyngeal streptococcus isolates were used for comparison in *emm* type distribution and in antimicrobial susceptibility.

***S. pyogenes*.** Sixty percent of patients infected with *S. pyogenes* were children (33 of 55) and included a newborn (Table 1). The initial sites of infection were skin and soft tissue (63.6% [21 of 33] of children and 54.5% [12 of 22] of adults), the respiratory tract (9.1% [3 of 33] of children and 9.1%[2 of 22] of adults), gyneco-obstetric (18.2% [4 of 22] of adults), and other or unknown sites (27.3% [9 of 33] of children and 18.2% [4 of 22] of adults).

Most cases (4 of 7) occurring in young females were related to gyneco-obstetric procedures. Mortality due to group A streptococci was 27.3% (6) in adults and 12.1% (4) in children. STSS occurred also more frequently in adults (31.8%) (7) than in children (12.1%) (4).

One fatal infection due to *S. pyogenes* in a child was associated with acute myeloid leukemia and bone marrow transplantation, and another child who died had varicella (Table 2). Fatal cases in two children without underlying diseases in-

TABLE 1. Characteristics of invasive β-hemolytic streptococci isolated in a 6-month period in 40 Argentinian centers

Subtype[a]	No. of adult patients	No. of children	No. of cases with age, STSS, and survival unknown	No. of STSS[b]		No. of deaths[b]		Serologic features[c]	*sof* type[d]
				A	P	A	P		
emm1.0	2	13	1		3		3	T1, M1, OF−	PCR neg
emm3.1	1	1						T3, M3, OF−	PCR neg
emm4.0	1	1 (newborn)	2					T4, M4, AOF4	*sof4*
emm9.0		1						T14, MNT, AOFNT	ND
emm11.0			1					T11/12, MNT, AOF25	*sof25*
emm12.0	3	2		2	1	1	1	T12, M12, OF−	*sof12*
emm18.7	1	1						TNT, M18, OF−	PCR neg
emm22.0	1					1		T11/12, M22, AOF22	*sof22*
emm33.0			1					T3/B, M33, OF−	PCR neg
emm43.5	1			1				TNT, M43, OF−	PCR neg
emm58.0		2						T8/25/1, AOF58	*sof58*
emm66.0	1	1						T12, M66, AOF66	*sof66*
emm75.0	3			1		1		T25/1, M75, AOF75	*sof75*
emm78.0		1						T11/12, MNT, AOF78	*sof78*
emm82.0	2	1		2		2		T5/27/44, MNT, AOFNT	*sof82*
emm83.1		1						T3/13/B, OF−	PCR neg
emm87.0	1	3	1					T28, M87, AOF87	*sof87*
emm89.0		1						T11, M89, AOF89	*sof89*
emm92.0	1	1		1		1		T8/25/1, MNT, AOF92	*sof92*
emm94.0		1						T3/13, MNT, AOFNT	*sof94*
emm123.0			1					T9/3/B, MNT, OF−	PCR neg
Not typed	4	2						ND	ND
stC1400.0	1							NA	NA
stC6979.0	1							NA	NA
stC57.0	1							NA	NA
stC36.3	3							NA	NA
stG6.0	3	1	2	1			1	NA	NA
stG6.1									
stG10.0	2	2						NA	NA
stG480.0	4		1	1		2		NA	NA
stG485.0	1							NA	NA
stG4222.0			1					NA	NA

[a] All *emm* designations represent *S. pyogenes*. *stC* or *stG* designations indicate either group C or group G *S. dysgalactiae* subsp. *equisimilis* except in one instance described in footnote b. Six *S. pyogenes* were not available for typing (Not Typed). For each *emm* type (or *st*) representing two or more isolates, at least two were subjected to *emm* amplicon sequencing, and each singly occurring *emm* type was directly determined through sequence analysis.

[b] A, adult patients; P, pediatric patients. Two sets of each category are provided to accommodate two sets of results of sequencing.

[c] All isolates were T typed and subjected to opacity factor production test (OF). At least the majority of isolates were M serotyped and subjected to anti-opacity factor (AOF) testing. Representative results are shown and no discrepant results were found.

[d] Specific *sof* sequence types are result of sequence typing at least one random isolate within this *emm* type. neg, negative; ND, not done; NA, not available.

[e] One isolate was identified as a group A *Streptococcus dysgalactiae* subsp. *equisimilis*.

volved a severe community-acquired pneumonia and a wound infection in one leg followed by purpura fulminans.

No adult fatalities from invasive disease due to *S. pyogenes* were associated with type *emm1*. Type *emm1* invasive isolates were recovered from only two adult patients (Table 2), neither of whom died or suffered STSS (data not shown). In contrast, 13 of 31 isolates from children were type *emm1*, and 3 of these were associated with fatal infections (Table 2).

S. pyogenes-mediated STSS was a consequence of infections due to types *emm1* ($n = 3$), *emm12* ($n = 4$), *emm82* ($n = 2$), *emm43* ($n = 1$), *emm75* ($n = 1$), and *emm92* ($n = 1$).

Groups C and G *S. dysgalactiae* subsp. *equisimilis*. Patients infected with groups C and G *S. dysgalactiae* subsp. *equisimilis* were mainly adults (5 of 5 and 10 of 13, respectively). One group A *S. dysgalactiae* subsp. *equisimilis* isolate with *emm* type *stG6* and identified by API 20 Strep (bio Mérieux, Marcy l'Etoile, France) was also obtained from an adult patient (6).

The adult age range for *S. dysgalactiae* subsp. *equisimilis* infection was 21 to 86 years. Diabetes was found in four patients infected with group G and in two infected with group C *S. dysgalactiae* subsp. *equisimilis*. There were three toxic shock cases (fully recovered) and one death in a newborn with an early onset neonatal sepsis attributed to group C or group G *S. dysgalactiae* subsp. *equisimilis* infections within the study period. Also, two additional invasive cases among elderly diabetics resulted in death (Table 2). This newborn and two children (7 and 9 years of age) with a postsurgical infected wound and cellulitis, respectively, were the only three pediatric patients infected with *S. dysgalactiae* subsp. *equisimilis*.

Antibiotic susceptibility profiles among β-hemolytic streptococci. All *S. pyogenes* isolates were susceptible in vitro to PEN and CRO (MICs of ≤0.007 μg/ml).

Five Tet^r *S. pyogenes* isolates were found among the 68 tested (7.3%) and were all associated with the presence of the *tet*(M) gene. These included isolates of *emm* subtypes 9.0, 11.0, 41.2, and 43.5. One additional isolate not available for *emm* typing was also Tet^r and contained the *tet*(M) gene. Resistance to TET was common among *S. dysgalactiae* subsp. *equisimilis* isolates (33.3% of group C and 40% of group G) and each Tet^r isolate was PCR positive for the presence of *tet*(M). As a whole

TABLE 2. Features of fatal streptococcal infections and/or STSS cases over a 6-month period in Argentina

Patient group	Parameter[a]								
	Age	Sex	Source	Underlying disease	Shock	Death	Group	*emm* type	City
Adults	71 yrs	F	Blood	Diabetes	Yes	No	A	12	Tandil
	52 yrs	F	Blood	None	Yes	Yes	A	75	Tandil
	70 yrs	F	Blood	Diabetes	Yes	Yes	A	12	Tandil
	59 yrs	M	Blood	Burnt	Yes	Yes	A	82	Tandil
	78 yrs	M	Blood	None	Yes	Yes	A	82	Tandil
	28 yrs	F	Blood	None	Yes	No	A	12	T. A.
	57 yrs	M	Blood	Burnt	NA	Yes	A	92	B. Aires
	28 yrs	F	Blood	None	NA	Yes	A	4	Ezeiza
	61 yrs	M	Blood	COLD	Yes	No	A	43	M. del P.
	72 yrs	F	Blood	Diabetes	Yes	No	C	*stc*36	Tandil
	62 yrs	M	Blood	CRF	Yes	No	G	*stg*6.1	Tandil
	86 yrs	F	Blood	Diabetes	No	Yes	G	*stg*480	Rosario
	62 yrs	M	Blood	Diabetes	No	Yes	G	*stg*480	Lanus
	71 yrs	M	Blood	Diabetes	Yes	No	G	*stg*480	Rosario
Children	6 mos	F	Blood	Varicella	Yes	Yes	A	1	Salta
	6 yrs	F	Blood	Leukemia	Yes	Yes	A	12	B. Aires
	3 yrs	F	Blood	None	Yes	Yes	A	1	B. Aires
	9 mos	M	Blood	None	ND	Yes	A	1	La Plata
	5 yrs	F	Blood	KTS	Yes	No	A	1	B. Aires
	2 days	M	Blood	None	Yes	Yes	G	*stg*6	Tandil

[a] T.A., Tres Arroyos; B. Aires, Buenos Aires; M. del P., Mar del Plata; COLD, chronic obstructive lung disease; CRF, chronic renal failure; KTS, Klipper-Trenaunay syndrome; NA, not available.

40.7% of *S. dysgalactiae* subsp. *equisimilis* isolates were Tet^{r}as previously described (20). Tet^r isolates were found within types *stG10* ($n = 3$), *stG480* ($n = 2$), *stC36* ($n = 1$), *stG6* ($n = 4$), and *stC6979* ($n = 1$).

ERY resistance was observed in three invasive *S. pyogenes* isolates (4.4%) of *emm* subtypes 4.0, 12.0, and 43.5 (data not shown). These isolates had ERY and azithromycin MICs of 2 to 16 and 8 to 16 μg/ml, respectively. They contained the *mef*(A) gene and had CLI MICs of ≤0.125 μg/ml. The single Ery^r *S. dysgalactiae* subsp. *equisimilis* isolate, *emm* subtype *stg6*, was PCR positive for the presence of *ermTR* and showed the inducible MLS resistance phenotype, consistent with previous observations (17).

Only pharyngeal isolates were tested for susceptibility to ERY and CLI by the disk diffusion method. Only *S. pyogenes* showed ERY resistance (23.5%) with an M phenotype (probably efflux). Most of these isolates were *emm12* ($n = 7$). Other Ery^r isolates were *emm1* ($n = 2$) and one each of *emm75*, *emm87*, and *emm77*.

All *S. pyogenes* isolates were susceptible to CMP (disk diffusion zones between 21 and 30 mm). No resistance to CLI, CMP, PEN (MIC at which 90% of strains are inhibited, ≤0.007 μg/ml), and CRO (MIC at which 90% of strains are inhibited, ≤0.007 μg/ml) was detected among *S. dysgalactiae* subsp. *equisimilis* isolates. A highly gentamicin-resistant group C *S. dysgalactiae* subsp. *equisimilis* isolate was found, with the bifunctional AAC(6′)-APH(2″) determinant conferring high-level resistance to important aminoglycosides.

Types *emm2.0*, *emm3.0*, *emm3.2*, *emm6*, *emm77*, *emm102.0*, *stC36.1*, *stG166B.0*, and *stG4831.0* were only found among pharyngeal isolates, while *emm3.1*, *emm9.0*, *emm11.0*, *emm18.7*, *emm22.0*, *emm33.0*, *emm43.5*, *emm58.0*, *emm66.0*, *emm83.1*, *emm87.0*, *emm89.0*, *emm92.0*, *emm123.0*, *stC1400*, *stC36.0*, *stG10.0*, *stG485.0*, and *stG4222.0* were only seen among invasive isolates.

Argentinian invasive *S. pyogenes* isolates generally share the same *emm* subtypes, serologic features, and/or *sof* sequence types as corresponding invasive strains recovered in the United States. Except for a single example of type *emm123*, all of the *emm* types in Table 1 were common types seen among 1,061 consecutively typed invasive *S. pyogenes* isolates recently recovered in the United States (19). Furthermore, all of the subtypes shown in Table 1 except for *emm18.7*, *emm9.0*, and *emm123.0* represented major *emm* sequence subtypes encountered in the U.S. survey. For example 188 of 194 (96.9%) type *emm1* isolates from the U.S. survey were subtype *emm1.0*, and 82 of 108 type *emm3* isolates (75.9%) were subtype *emm3.1*.

With the exception of type *emm11*, serologic and *sof* gene features (PCR positive or negative and specific *sof* sequence type) of all of the group A streptococcus *emm* types are reflective of the majority of isolates of these same *emm* types recovered within the United States (2). While the *sof11*/AOF-11 isolate is most commonly found within type *emm11*, we have also previously encountered the *emm11*/*sof25*/AOF-25 association from an isolate recovered in Hawaii (2). Twelve of the 21 *emm* types comprising 36 of the 54 isolates (66.7%) of known *emm* type (Table 1) are targeted by a 26-valent group A streptococcus vaccine currently undergoing clinical trials that was formulated against *S. pyogenes* in North America (12).

DISCUSSION

This work represents the first national multicenter study in Argentina of invasive infections caused by *S. pyogenes* and *S. dysgalactiae* subsp. *equisimilis* and the first detailed characterization of such strains. An analysis of group B isolates obtained

at the same time by the same centers was recently published (21).

All β-hemolytic streptococci included in this study were susceptible in vitro to PEN, CMP, and CRO. Lower rates of Tet^r were observed in *S. pyogenes* isolates (7.3%) than in *S. dysgalactiae* subsp. *equisimilis* isolates (40.7%). All Tet^r isolates were associated with the presence of the *tet*(M) gene. ERY resistance due to efflux mechanism [*mef*(A) gene] was observed in 4 invasive isolates (5.9%) and in 12 (23.5%) pharyngeal isolates of *S. pyogenes*. The only Ery^r group A *S. dysgalactiae* subsp. *equisimilis* isolate showed an inducible methylase-mediated mechanism (*ermTR* gene). No Ery^r isolates were found among pharyngeal group C or group G *S. dysgalactiae* subsp. *equisimilis* isolates.

Invasive serotypes frequently associated with STSS are M1, M3, M12, and M28 (1), and these four types also comprise the four most common invasive types in the United States and Canada (26, 32). In the United States STSS was associated with types *emm1* and *emm3* (26). We found that the classic invasive type M1 (*emm1*) was associated with invasive disease more often in children than in adults (Table 1). While type *emm3* represented 7.1% of invasive cases in the United States during 1995 to 1999, only two type *emm3.1* invasive isolates (2 of 85, or 2.3%) were found in the present study (26). Type *emm12* was associated with five cases overall, including four invasive STSS cases. These STSS cases included three adults (two fatalities) and one child (fatal outcome) (Table 2). The *emm28* type was not found among invasive isolates in this survey, which is consistent with the absence of this type among a sampling of 55 pharyngeal *S. pyogenes* isolates recovered in Buenos Aires during 1999 and its absence in a 1985 study of invasive isolates recovered in Argentina (16). The *emm87* type appears to be frequent in both invasive and pharyngeal isolates in Argentina (Table 1).

Invasive infections by β-hemolytic streptococci were frequent in Tandil, a city with 130,000 inhabitants. Hospital Santamarina is a 175-bed hospital that receives all cases of severe diseases occurring in the city. A population-based analysis showed a prevalence of 12 cases of streptococcal invasive infections, 8 SSTS cases, and 6 deaths/100,000 population/year. Hospital Pirovano also is the reference center for severe diseases in Tres Arroyos (100 km from Tandil). Comparatively, the rate of either invasive streptococcal infections or STSS was 3.4 cases/100,000 population/year. No deaths due to invasive streptococcal infections were recorded in Tres Arroyos during the 6-month study period.

S. dysgalactiae subsp. *equisimilis* can colonize the throat, skin, and the genitourinary tract. From these sites the organisms frequently invade soft tissue and other deep structures (10). The *S. dysgalactiae* subsp. *equisimilis* invasive isolates described in our study were most frequently recovered from adults. Most isolates of group C *S. dysgalactiae* subsp. *equisimilis* were obtained from blood cultures, but a cutaneous, bone, or respiratory focus was suspected for three blood isolates (data not shown). One group C *S. dysgalactiae* subsp. *equisimilis* isolate was associated with endocarditis and accompanying fever, rash, and shock in a 72-year-old diabetic woman, but appropriate antimicrobial therapy resulted in recovery. Other cases of endocarditis from group C *S. dysgalactiae* subsp. *equisimilis* infection have already been described in the literature (10). Cellulitis, pneumonia, and osteomyelitis due to group C streptococcus (GCS) have also been reported elsewhere, including one case of STSS (18). Another case of endocarditis was found in a 71-year-old diabetic man infected with an *stg480* group G *S. dysgalactiae* subsp. *equisimilis*. As a whole, two cases of endocarditis were observed among 14 patients with bacteremia due to *S. dysgalactiae* subsp. *equisimilis* infection, but no cases of endocarditis were recorded among bacteremic patients infected with *S. pyogenes*.

It should be mentioned that all of the sequence types encountered during this study have also been seen within the United States. The cumulative serologic and genotypic data shown in Table 1 strongly suggest that *S. pyogenes emm* types are representative of the same clonal types in both Argentina and the United States. The data are also suggestive that a multivalent vaccine currently undergoing study (12) could theoretically profoundly impact the incidence of invasive disease due to *S. pyogenes* in Argentina.

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