Two-Year Surveillance of Antibiotic Resistance in *Streptococcus pneumoniae* in Four African Cities

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Received 29 November 1999/Returned for modification 25 February 2000/Accepted 17 November 2000

Worldwide spread of antibiotic resistance in *Streptococcus pneumoniae* is a major problem. However, data from West and North African countries are scarce. To study the level of resistance and compare the situations in different cities, a prospective study was conducted in Abidjan (Ivory Coast), Casablanca (Morocco), Dakar (Senegal), and Tunis (Tunisia), from 1996 to 1997. The resistances to eight antibiotics of 375 isolates were studied by *E* test, and the results were interpreted using the breakpoints recommended by the National Committee for Clinical Laboratory Standards. Overall, 30.4% of the isolates were nonsusceptible to penicillin G (25.6% were intermediate and 4.8% were resistant). Amoxicillin (96.3% were susceptible) and parenteral third-generation cephalosporins (92.7%) were highly active. Resistance to chloramphenicol was detected in 8.6% of the isolates. High levels of resistance were noted for erythromycin (28%), tetracycline (38.3%), and cotrimoxazole (36.4%). Resistance to rifampin was rare (2.1%). There were significant differences in resistance rates between individual countries. Multiple resistance was more frequent in penicillin-nonsusceptible isolates than in penicillin-susceptible isolates. Recommendations for treatment could be generated from these results in each participating country.

Streptococcus pneumoniae is responsible for a wide variety of infections, resulting in high rates of morbidity and mortality (19). Antibiotic resistance in *Streptococcus pneumoniae* is now a worldwide problem (1) and has reached very high levels in certain countries (11, 15, 30). Penicillin-nonsusceptible isolates are also frequently resistant to other antibiotic classes (1, 9). Levels of penicillin resistance may increase very quickly (4). Furthermore, treatment regimens vary accordingly to penicillin G status and site of infection (13, 16). This situation justifies a continuous surveillance to provide appropriate recommendations for the treatment of pneumococcal infections.

There is a lack of data on antibiotic resistance from West and North Africa. In this study, we report on the levels of resistance to eight antibiotics of *S. pneumoniae* isolated in four African cities: Abidjan (Ivory Coast), Casablanca (Morocco), Dakar (Senegal), and Tunis (Tunisia).

From January 1996 to December 1997, 375 consecutive isolates of *S. pneumoniae* were collected in a prospective study conducted in these African cities as part of the Pan African Link through Microbiology (PALM), whose purpose is to conduct a multicentric surveillance of antibiotic resistance in nine African countries (Algeria, Cameroon, Ivory Coast, Kenya, Malta, Morocco, Nigeria, Senegal, and Tunisia). In all the cities except Abidjan, all the isolates came from one laboratory. Nearly half of the isolates came from cerebral spinal fluid (CSF) or blood (Table 1). The MICs of penicillin G, amoxicillin, erythromycin, rifampin, chloramphenicol, tetracycline, and cotrimoxazole were studied by the *E* test method (AB Biodisk Sweden). The resistance to parenteral third-gen-

eration cephalosporins was studied using cefotaxime or ceftriaxone. *E*-test strips and quality control isolates were provided by the study sponsor (SmithKline Beecham). The susceptibility testing was performed on Mueller-Hinton agar supplemented with 5% sheep or horse blood and incubated for 18 to 24 h at 35°C. MICs were rounded up to the nearest doubling dilution when necessary. Quality control was implemented using *S. pneumoniae* ATCC 49619 according to National Committee for Clinical Laboratory Standards methodology. The breakpoints used for analysis were those recommended by the National Committee for Clinical Laboratory Standards in 1997 (20).

The overall percentages of resistance to penicillin G, erythromycin, tetracycline, and cotrimoxazole were high (Table 2). An important result is that, overall, 30.4% of the 375 isolates were nonsusceptible to penicillin G (penicillin G-nonsusceptible *S. pneumoniae* [PNSSP]), with the interesting feature that most (25.6% of the total) of these PNSSP isolates were in the intermediate range, whereas 4.8% were fully resistant. Amox-

TABLE 1. Origins of the 375 *S. pneumoniae* isolates

Source	No. of isolates				Total	% of all isolates
	Ivory Coast	Morocco	Senegal	Tunisia		
Blood	20	11	12	17	60	16
CSF	31	41	38	15	125	33.3
ENT ^a	77	2	10	10	99	26.4
Pus ^b	9	10	6	4	29	7.7
Respiratory ^c	1	34	15	12	62	16.5
Total	138	98	81	58	375	100

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^a ENT, ear, nose, and throat.

^b Sources of pus were ascitic, arthritis, ocular, and cutaneous fluids.

^c Respiratory sources were sputum, pleural fluid, and bronchial aspirates.

TABLE 2. Overall resistance of 375 isolates of *S. pneumoniae*^a

Antibiotics	% Resistant isolates ^a				
	Ivory Coast (n = 138)	Morocco (n = 98)	Senegal (n = 81)	Tunisia (n = 58)	Total (n = 375)
Penicillin G					
Susceptible	77.5	90.8	38.3	58.6	69.6
Intermediate	18.1	8.2	53.1	34.5	25.6
Resistant	4.3	1	8.6	6.9	4.8
Amoxicillin ^b	3.6	1	3.7	8.6	3.7
Cefotaxime-ceftiraxone ^c	8.8	1	15	3.6	7.3
Chloramphenicol	11	2	14.8	5.2	8.6
Erythromycin	52.6	4.1	11.4	32.8	28
Tetracycline	67.5	12.2	29	34.5	38.3
Rifampin	5.8	0	0	0	2.1
Cotrimoxazole	60.5	14.8	29	19.4	36.4

^a Data include isolates intermediate and resistant to the antibiotic, except for penicillin G.

^b Breakpoints were 0.5 and 2 µg/ml.

^c Breakpoints were 0.5 and 2 µg/ml.

icillin (96.3% were susceptible), parenteral third-generation cephalosporins (92.7%), and rifampin (97.9%) were highly active. Resistance to chloramphenicol was detected in 8.6% of the isolates. These results confirm that antibiotic resistance in *S. pneumoniae* has spread to West and North Africa and correlate with previous reports from Central Africa (21), Egypt (23), Ghana (22), Kenya (24), and Rwanda (3). Nevertheless, for most antibiotics tested, the magnitude of the problem differs from one country to another: for instance, less than 10% of the isolates are penicillin nonsusceptible in Casablanca, whereas this rate exceeds 60% in Dakar. Considerable variations of the antibiotic resistance patterns observed in countries of the same region (1, 25, 27), between regions in the same country (2, 9), or even between hospitals within a region (8) have been reported previously, leading to very different guidelines. The sharp differences observed between countries have been linked to different antibiotic policies: in Germany (26) or Switzerland (32), the favorable situation may be explained by the restricted use of antibiotics. In Nairobi (24), the low rate of resistance to erythromycin may be explained by the fact that this antibiotic was rarely used. On the other hand, resistances to erythromycin in Belgium (31) and to cotrimoxazole in Sweden (14) have been correlated with sustained usage of these antibiotics. This study should be followed by a comparison of the antibiotic policies of the four cities in an attempt to explain the major differences observed.

Since the rates of antibiotic resistance in *S. pneumoniae* vary according to geographic location, time (4, 5), age (3, 9), and site of infection (2, 9), the surveillance must be continuous and the guidelines must be derived from the local epidemiology. Recommendations according to penicillin G status and site of infection have been published: penicillin G, penicillin G or amoxicillin, and amoxicillin have been the recommended treatments for septicemia (13, 16, 28), pneumonia (13, 16), and otitis media (10, 13, 16), respectively.

In this study, resistance to most other antibiotics (amoxicillin, cefotaxime-ceftiraxone, chloramphenicol, erythromycin,

and cotrimoxazole) was more frequent in PNSSP isolates than in susceptible isolates. This finding is well documented (1, 9). Pneumococcal antibiotic resistance is even more worrisome in developing countries because PNSSP strains are often multiresistant and because alternative antibiotics (e.g., third-generation cephalosporins and vancomycin) are expensive. Thus, efforts should focus not only on antibiotic resistance surveillance and guideline formulation but also on appropriate use of antibiotics. Strategies have been proposed, which include restricting access, compliance promotion (7), and reduction in the overprescription and inappropriate use of antibiotics (6).

In the future, more centers from each country and more countries should be involved. Strains should be serotyped to verify that the most frequently encountered resistant serotypes are included in the 23-valent vaccine and in the protein-conjugated vaccine which is being formulated for children under 2 years of age. The knowledge of the serotypes to which the resistant isolates belong would allow an early selection of appropriate treatment as soon as such a strain is detected. For example, for a case of meningitis, the serotype of a culture can be obtained after 24 h of incubation or by immediate detection of pneumococcal antigens in the CSF. The most common resistant serotypes should be compared by molecular biology methods (restriction fragment length polymorphism, random amplified polymorphic DNA, and pulsed-field gel electrophoresis) to detect any clone diffusion and to compare the African clones to those described previously (19).

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