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Initial antibiotic therapy for lower respiratory tract infection in the community: a European survey

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Initial antibiotic therapy for lower respiratory tract infection in the community: a European survey. G.J. Huchon, G. Gialdroni-Grassi, P. Léophonte, F. Manresa, T. Schaberg, M. Woodhead. ©ERS Journals Ltd 1996.

ABSTRACT: A survey of first-line antibiotic prescription in community-acquired lower respiratory tract infection (LRTI) by general practitioners (GP) was carried out simultaneously, using the same methodology in France, Germany, Italy, Spain and the UK.

Data were obtained from 2,056 patients and 605 GPs. There was no antibiotic prescription in 17% of all LRTIs and 13% of community-acquired pneumonia (CAP) in the five countries taken together; and in 32% of all LRTIs and in 23% of CAP in Germany. Of patients with acute bronchitis, exacerbation of chronic bronchitis and viral lower respiratory tract infection, 87, 92 and 71% received antibiotics, respectively. The most frequent prescriptions were penicillins in France and the UK, third-generation cephalosporin in Italy, tetracycline in Germany and macrolide in Spain. The daily dosage of aminopenicillin prescribed was: 41% <1.5 g; 49% ≥1.5 g and <3 g; and 10% ≥3 g. In Italy, 53% of all antibiotics were injected in all LRTIs, and 71% in CAP; in contrast, antibiotic injection was lower than 2% both in the UK and Germany, with an average of 14% in the five countries combined.

We conclude that there are variations in antibiotic prescription by GPs in Western Europe; differences are likely to be multifactorial, but could, in part, be explained by differences in health systems and sources of information available to GPs.

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Lower respiratory tract infections (LRTIs) are usually initially managed by general practitioners (GPs). LRTIs are frequent and include community-acquired pneumonia (CAP), exacerbation of chronic bronchitis (ECB), acute bronchitis (AB) and viral lower respiratory tract infection (VRTI). LRTIs are a major health care and economic problem due to their high morbidity and CAP mortality rates and, to the direct and indirect costs that their management generates [1–6]. Antibiotic prescription for LRTI remains controversial. On the one hand, CAP is usually of bacterial origin, is associated with a high morbidity and mortality, and needs to be rapidly treated with an antibiotic. This should preferably be active against *streptococcus pneumoniae*, which is responsible for at least 20% of all CAPs in out-patients and for a high mortality [1]. On the other hand, in a case of LRTI, it is quite difficult to exclude the diagnosis of CAP in out-patients, leading to antibiotic overprescription for self-limiting illnesses, which in turn may cause increased resistance of bacteria to antibiotics [7]. Because LRTI is one of the major reasons for antibiotic treatment and because changes in antibiotic resistance patterns are a threat to the effective treatment of CAP, there is increasing concern about antibiotic prescription in the community. In this context, the pattern of prescription remains largely unknown and, therefore, there is a definite need for a better knowledge of current antibiotic prescription for respiratory infection in the community.

To better understand how patients with LRTI are managed in the community by GPs, we designed and carried out a survey in five Western European countries during the winter of 1993–1994; here, we report the results of the study regarding first-line antibiotic treatment.

Methods

Design of the survey

The study was performed between December 8, 1993, and January 24, 1994, in five European countries: France, Germany, Italy, Spain and the UK. A representative sample of GPs was selected in each participating country by the method of quotas. Each GP was questioned about the last 3 or 4 adult patients examined for community-acquired LRTI, *i.e.* CAP (bronchopneumonia, pneumonia), acute bronchitis (AB), exacerbation of chronic bronchitis (ECB), and viral lower respiratory tract infection (VRTI) - *i.e.* flu or flu syndrome with symptoms and signs of LRTI - which includes influenza. These clinical diagnoses were based on the GP's judgement. Their validity was not assessed, since it is what the GP

thinks that matters. Factors related to the attachment of each of these diagnostic labels are to be the subject of a forthcoming paper. A preliminary study (unpublished) had shown a less frequent prescription of antibiotics in Germany and in the UK; therefore physicians were asked about the last four patients in these two countries and the last three patients in France, Italy and Spain. The survey itself was performed by a poll institute and its subsidiaries (Sofres).

Data collection

The questionnaire was first written in English and translated into French, German, Italian and Spanish; the questionnaires were then translated back to English to ensure coherence of translation. It was designed to obtain data both on GPs and the 3 or 4 patients about whom they reported. Data on GPs, such as age, sex, time elapsed since qualification, characteristics of practice, and sources of knowledge on antibiotics, were collected. Data on each patient included anthropometric details, information on associated chronic diseases, clinical presentation, investigations, presumptive diagnosis, and antibiotic prescriptions.

Statistical analysis

Results are expressed as percentages or means±SD. Percentages have been compared by two-way and multiway frequency analysis, by testing a hierarchical log-linear model to the cell frequencies [8]. Means have been compared by Student's t-test when analysis of variance (ANOVA) had shown a significant difference between groups. A difference was considered as significant if p-value was less than 0.05 [9]. Calculations have been made using BMDP statistical software [10].

Results

Six hundred and five physicians (France 123; Germany 121; Italy 120; Spain 121; and the UK 120) were interviewed, and the medical history of 2,056 patients older than 18 yrs was obtained. Characteristics of GPs and patients, broken down by country, are reported in tables 1 and 2, respectively. There were differences among GPs in age ($p<0.0001$), time since qualification ($p<0.0001$) and gender ($p=0.0022$) between countries. GPs reported their sources of knowledge on antibiotics as shown in table 3. Age ($p<0.0001$), gender ($p<0.0001$), residence in an institution ($p=0.0169$), employment ($p<0.0001$), smoking ($p<0.0001$) and associated chronic disease ($p<0.0001$) rates in patients differed between countries. GP's diagnosis, and rates of recourse to complementary investigations (chest radiographs, white blood cell count and/or microbiological sputum examination) and to hospitalization in the various countries are presented in table 4. AB or VRTI were more frequent than CAP or ECB ($p<0.0001$); diagnosis rates differed between the five countries ($p<0.0001$).

Table 5 shows the rate of nonprescription of antibiotic at the first consultation, broken down by country and diagnosis ($p<0.0001$). Figure 1 shows the antibiotic categories

Table 1. – General practitioner characteristics

Country	Age yrs	Time since qualification yrs	M/F
France	43±8	14±9	3.7
Germany	50±10	21±10	4.0
Italy	46±9	19±10	12.3
Spain	45±11	19±11	3.9
UK	43±9	18±9	2.9
All	45±10	18±10	4.3

M/F: male to female ratio.

Table 2. – Patient characteristics

Country	Age	M/F	Employed	Resident in institution	Current smoker	Chronic disease
	yrs		%	%	%	%
France	51±21	1.1	43±3	4.3±1.1	27±2	44±3
Germany	48±19	1.0	58±2	3.7±0.9	34±2	38±2
Italy	54±20	1.3	39±3	1.4±0.6	34±3	53±3
Spain	51±19	1.6	53±3	3.6±1.0	40±3	38±3
UK	55±21	0.8	32±2	5.6±1.0	27±2	48±2

Values are presented as mean±SD. M/F: male to female ratio.

Table 3. – General practitioner sources of information

	Medical school	Medical journals	Post-graduate teaching	Pharmaceutical companies	National guidelines
	%	%	%	%	%
France	11	60	37	45	3
Germany	63	30	47	64	25
Italy	9	85	41	81	24
Spain	1	55	4	43	4
UK	35	52	38	39	28
All	24	56	33	54	17

Table 4. – General practitioner diagnosis, recourse to complementary investigations and hospitalizations

	n	CAP %	AB %	ECB %	VRTI %	Invest %	Hosp %
France	369	17	26	15	43	21	5
Germany	484	18	39	13	30	43	3
Italy	360	18	28	30	24	24	3
Spain	363	19	33	20	28	36	3
UK	480	18	36	21	25	18	9
All	2056	18	33	19	29	29	5

CAP: community-acquired pneumonia; AB: acute bronchitis; ECB: exacerbation of chronic bronchitis; VRTI: viral lower respiratory tract infection; Invest: investigations; Hosp: hospitalizations.

Table 5. – No antibiotic prescription

	CAP %	AB %	ECB %	VRTI %	All %
France	8	7	5	20	13
Germany	23	31	26	41	32
Italy	3	6	4	28	10
Spain	7	6	1	39	14
UK	16	8	6	19	12
All	13	14	8	29	17

For definitions see legend to table 4.

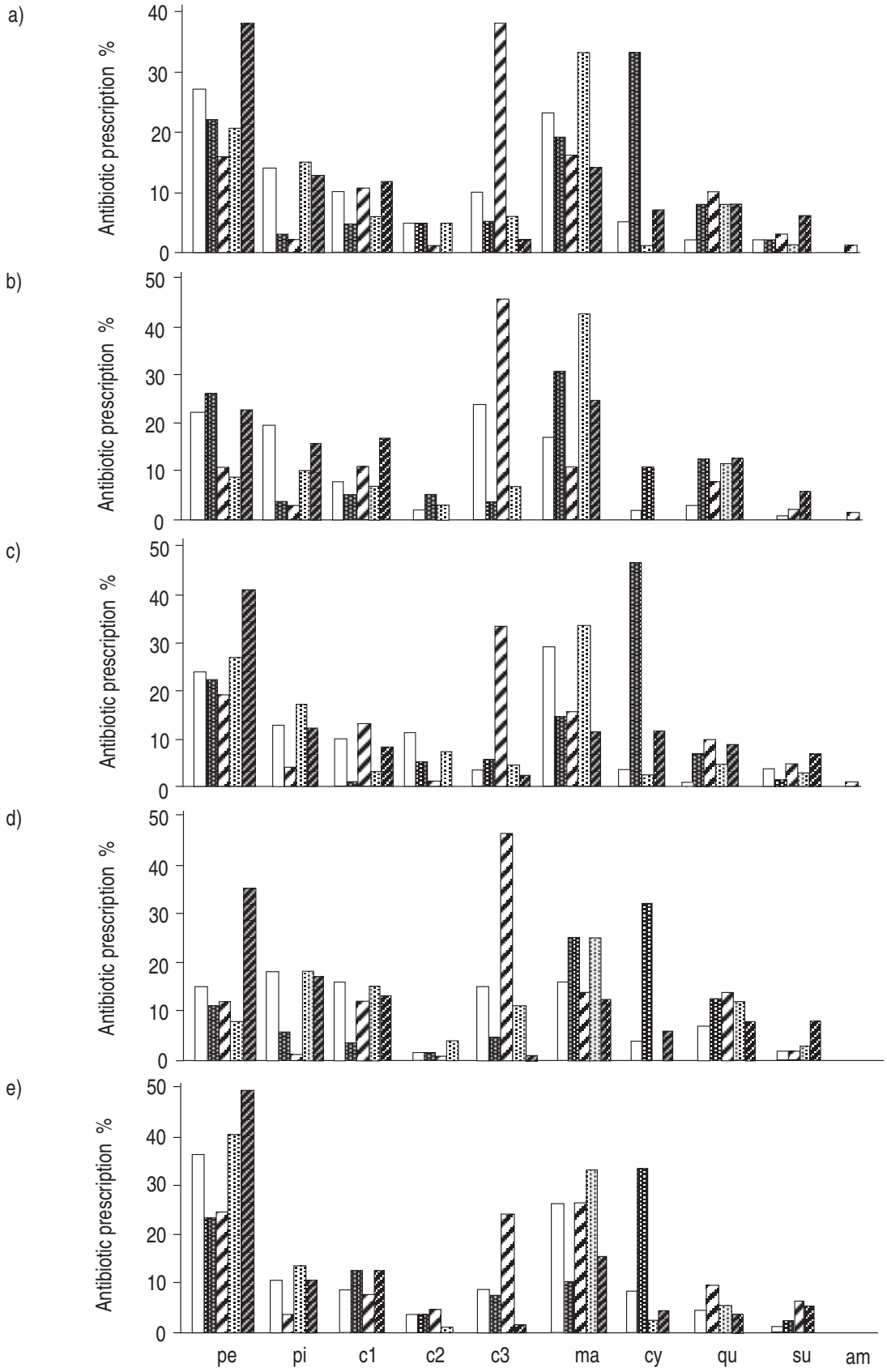

Fig. 1. – Antibiotic prescription in: a) all lower respiratory tract infections; b) community-acquired pneumonia; c) acute bronchitis; d) exacerbation of chronic bronchitis; e) viral lower respiratory tract infection. ☐ : France; ▩ : Germany; ▨ : Italy; ⁝⁝ : Spain; ▨ : UK. pe: penicillin; pi: aminopenicillins and betalactamase inhibitor; c1: cephalosporin first generation; c2: cephalosporin second generation; c3: cephalosporin third generation; ma: macrolide; cy: tetracycline; qu: quinolone; su: sulphonamide; am: aminoglycoside.

Table 6. – Duration of antibiotic treatments

	Duration of treatment days				
	CAP	AB	ECB	VRTI	All
France	9.2±3.0	8.0±1.5	9.0±2.4	7.8±1.9	8.3±2.2
Germany	9.3±4.8	8.2±3.1	8.6±2.6	8.3±2.5	8.6±3.4
Italy	7.4±3.4	6.3±2.3	6.7±2.1	5.9±2.1	6.6±2.5
Spain	9.8±3.3	8.1±3.1	8.9±3.3	7.7±2.9	8.6±3.2
UK	6.4±1.6	6.7±5.5	6.8±2.8	6.1±1.5	6.5±3.8
All	8.4±3.6	7.5±3.7	7.7±2.8	7.2±2.4	7.6±3.2

Values are presented as mean±SD. For definitions see legend to table 4.

Table 7. – Route of administration of antibiotics

	Injected %				
	CAP	AB	ECB	VRTI	All
France	17	7	22	4	10
Germany	6	0	0	0	1.2
Italy	71	47	58	37	53
Spain	15	5	11	3	8
UK	0	0	1.2	0	0.2
All	21	9.9	22	7	14

For definitions see legend to table 4.

prescribed for all and each kind of LRTI in each country; there are significant differences between LRTIs ($p<0.0001$) and between countries ($p<0.0001$). Table 6 indicates the duration of antibiotic treatment and table 7 the route of administration. In the 610 patients receiving aminopenicillin for LRTI, the daily dosage was: 41% <1.5 g; 49% ≥1.5 g and <3 g; and 10% ≥3 g. Figure 2 shows the dosages of aminopenicillin prescribed in the 95 patients with CAP, 224 with AB, 103 with ECB and 188 with VRTI ($p<0.001$). Aminopenicillin daily dosages in CAP were: 48% <1.5 g·day^{-1} in Germany and 74% in the UK; 33% ≥3 g·day^{-1} in Italy and 30% in Germany.

Discussion

This is the first study to have investigated the prescribing of antibiotic simultaneously in a number of European countries using a standardized methodology. The study found large differences in the management of out-patients with LRTI by GPs within the five Western European countries. Among prescribed antibiotics, aminopenicillin, with or without betalactamase inhibitor, was most frequently prescribed, whatever the diagnosis. However, there were some national peculiarities, with preferential prescription of penicillins in France and the UK, third-generation cephalosporin in Italy, tetracycline in Germany and macrolide in Spain. The daily dosage of aminopenicillin was: 41% <1.5 g; and only 10% >3 g. The absence of antibiotic prescription reached 32% in all LRTIs and 23% in CAP in Germany, averaging 13% in all LRTIs and 13% in CAP in the five countries. However, of patients with AB, ECB and VRTI 87, 92 and 71% received antibiotics, respectively. In Italy, 53% of antibiotics were injected in LRTIs and 71% in CAP; in contrast, antibiotic injection was lower than 2% in the UK and Germany, with an average of 14% in the five countries.

Various methodological matters should be discussed. It was not one of the study's objectives to evaluate the diagnostic abilities of GPs with regard to the four clinical groups, CAP, AB, ECB and VRTI, but rather to provide information on the way that GPs made a particular diagnosis and prescribed antibiotics in routine practice. It was, indeed, likely that some diagnoses may have been incorrect; but we were unable to assess this. Again, the objective of the study was only to provide data on diagnostic and therapeutic strategies in the community.

Differences in the medical population in the five countries were not very prominent; German physicians were older and French physicians younger. There were also differences in sex ratio among the physicians, but always with a large majority of males, particularly in Italy, where the overall male to female ratio was 4.3 times. Despite their differences, the participating GPs were representative of the medical populations of the five countries.

There were also differences between patients within countries, in terms of age, sex, residence in an institution, employment, tobacco smoking and associated chronic diseases. Average age ranged 48–55 yrs. The sex ratio was of the same magnitude, except for Spain where the number of males was higher. Current tobacco smoking was higher in Spain (40%) and lower in the UK (27%)

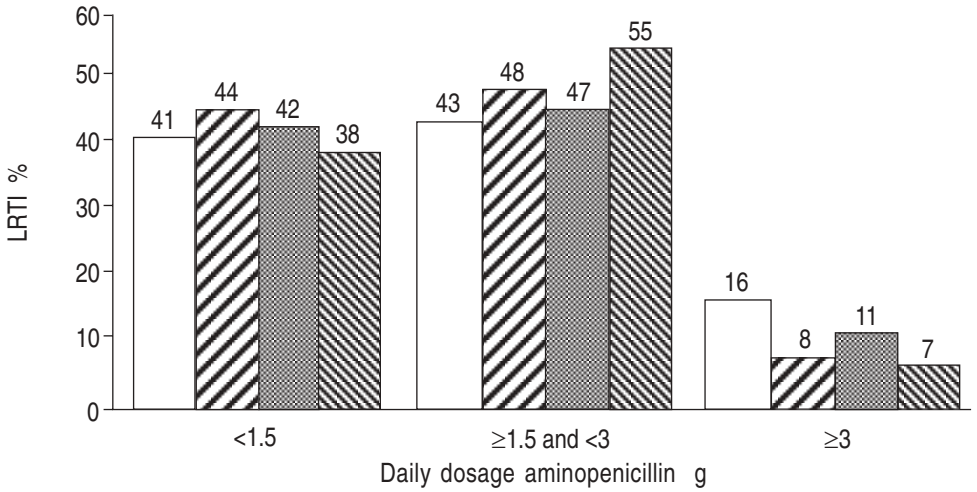

Fig. 2. – Daily dosages of aminopenicillins prescribed in community-acquired pneumonia (CAP), acute bronchitis (AB), exacerbation of chronic bronchitis (ECB) and viral lower respiratory tract infection (VRTI). ▭ : CAP; ▨ : AB; ▩ : ECB; ▧ : VRTI. LRTI: lower respiratory tract infection.

and France (27%). Rates of employment and residence in an institution among patients with respect to age provided interesting economic and cultural observations: employment was lowest in the UK and highest in Germany; residence in an institution was highest in the UK and lowest in Italy. The rate of associated chronic diseases varied both qualitatively and quantitatively. Italy was the country with the highest rate of associated chronic diseases (52%) and Spain the lowest (38%); chronic bronchitis ranked first in France (9%) and Italy (28%), asthma (14%) in the UK, and cardiac failure (13%) in Germany.

The physicians LRTI diagnoses were comparable in each country: 18% CAP, 19% ECB, 33% AB and 30% VRTI. One striking finding was the high frequency of CAP, accounting for 1 in 5 of all infections, compared for example to 1 in 25 in a previous study [4]. The similar frequency in the five countries, the high performance of chest radiographs (53% in the CAP group) and the frequency of abnormal chest radiographs (69%) to some extent validated the CAP diagnosis by GPs. Another striking finding was the higher number of VRTI in France, which matched the appearance of an epidemic of influenza that occurred during the survey; however, the increase in the number of VRTI was almost completely balanced by a reduction in the cases of AB, so that it might simply be a matter of labelling of the groups.

Most previous surveys have reported antibiotic prescription for LRTI in hospitalized patients, not in out-patients as in this study. ORTQVIST [3] reviewed the prescription pattern of empirical antibiotic treatment of CAP in the community in seven European countries on data from published studies [4, 5] and prescription surveys, including a worldwide survey performed by Inter-continental Medical Statistics Ltd (IMS), London, UK [3]. The findings were similar overall to ours: the three most commonly used compounds for out-patient treatment were aminopenicillins with and without clavulanic acid, macrolides and cephalosporins, the relative order varying between countries. Aminopenicillin was the first or second choice in four of seven countries; cephalosporins were used mainly in Germany and in Southern Europe; parenteral treatment with third-generation cephalosporins or imipenem was the commonest choice in Italy. WOODHEAD *et al.* [4] reported that the initial antibiotics prescribed by GPs for CAP in the UK were aminopenicillin (64%), erythromycin (20%), co-trimoxazole (11%) and tetracycline (4%) in 1984–1985. MACFARLANE *et al.* [5] reported that the initial antibiotics prescribed by GPs for LRTI in one UK practice were amoxycillin (80%), erythromycin (12%), cephalosporins (4%) and co-trimoxazole (2%) in 1990–1991. However, both studies included GPs with an interest in LRTI and may, therefore, not be representative of the GPs in that country. It is difficult to make any comparison of the studies in which the treatment was applied to in-patients and not to out-patients as in our survey, but overall the most prescribed antibiotics were similar to those in our study [11–14].

General trends associated with some countries are difficult to explain, such as the injection of antibiotics, mainly third-generation cephalosporins, in Italy, the 23% nonprescription of antibiotic in CAP in Germany and 16% in the UK. In Germany, this could be explained by a higher recourse to complementary investigations and later prescription depending on results; and in the UK by more frequent hospitalization, which could delay antibiotic prescription until after hospital admission. In contrast, overall antibiotics were prescribed in 87% of AB and in 71% of VRTI; even in Germany, where the level of prescription was the lowest, 70 and 59% of patients with AB and VRTI, respectively, received antibiotics. In patients with ECB, the prescription of antibiotics was normal in four of the five countries (94–99%), but less so in Germany (74%). Such prescriptions may be questionable, since there is no consensus on the need for antibiotics in patients with AB, VRTI or ECB, but it is likely that most AB and VRTI and many mild ECB do not need antibiotics [15–18].

Whatever the diagnosis, there was a link between antibiotic category and country. For example, in Germany, tetracycline was the most frequently prescribed antibiotic not only in AB, VRTI and ECB, but also in CAP; third-generation cephalosporin in Italy, macrolide in Spain and penicillins with or without betalactamase inhibitor in France and in the UK. Since the causative pathogens are probably very similar in the five countries studied, the only microbial reason for different prescribing would be differences in antibiotic resistance. Whilst microbial epidemiology may explain some of the prescriptions, it remains difficult to explain why in Italy 33% of prescriptions for AB and 25% for VRTI were third-generation cephalosporin. Nevertheless, the ideal therapy for LRTI due to some resistant bacteria (*i.e.* penicillin-resistant *Streptococcus pneumoniae*) has not been determined.

When the diagnosis of CAP was made, the rationale for antibiotic prescription was very often questionable. In the two countries, France and Spain, where the resistance of *Streptococcus pneumoniae* to antibiotics was and still is high [19, 20], the choice of antibiotic and its dosage may sometimes have been inadequate to deal with the problem. Thus, in France where resistance to macrolide was 25% in 1991, and in Spain 11% in 1992, macrolides were prescribed in 17 and 23% of patients with CAP, respectively. Whilst the decreased sensitivity of *Streptococcus pneumoniae* to penicillins was 33% in Spain in 1992 and 20% in France, penicillin was prescribed in CAP in 19% of patients in Spain and in 42% in France; moreover, in 87% of patients in France and 92% in Spain, dosage may have been insufficient, being <3 g·day^{-1}.

On the other hand, it is impossible to demonstrate whether the low resistance of *Streptococcus pneumoniae* to antibiotics in Germany and Italy is the consequence of therapeutic habits, such as prescription of high dosage of penicillins (30% >3 g·day^{-1} in Germany and 33% in Italy) and antibiotic injection in Italy. *Haemophilus influenzae*, involved in CAP and ECB, was reported to be resistant to penicillins in 22% of cases in France in 1992 and in 14% of cases in the UK in 1991 [21, 22]; the prescriptions for CAP of penicillins together with a betalactamase inhibitor in 20% of cases in France and 16% in the UK, and for ECB in 18% of cases in France and 17% in the UK might result from this betalactamase activity of *Haemophilus influenzae*.

There are many other possible reasons for such differences in prescriptions. There were large variations in GP's sources of information, which varied from one country to another, but were mainly provided by medical journals and the pharmaceutical industry. The choice of antibiotic is very likely to have been influenced by the

industry marketing directly to GPs or through advertising in medical journals, which might account for some prescriptions with limited medical rationale.

Published recommendations on the management of outpatients with CAP existed in only France and Spain at the time of the study [23, 24]; nevertheless, GPs reported that the input of recommendations was only 3% in France and 4% in Spain. In fact, the recommendations were not followed in these countries, raising the problem of the diffusion of such information to GPs. In the UK, 28% of GPs reported to know about national recommendations; but the current British recommendations deal with hospitalized patients with CAP and not with patients seen in the community [25]. More surprising, was the claim to have received information from recommendations by 25% of GPs in Germany and 24% in Italy, when such recommendations did not exist in these two countries at the time of the study [26, 27]! However, it is likely that GPs interpreted what is written in textbooks or what they learnt at medical school as being "guidelines".

Finally, some differences in health systems and in drug availability might account for differences in management. Germany was organized in a way that minimized the number of antibiotic prescriptions, and favoured low cost antibiotics and complementary examinations. The UK health system favoured hospitalization and prescription by specialists.

In conclusion, there were large variations in the management of patients with lower respiratory tract infection within the five Western European countries investigated. Considering what is known about lower respiratory tract infection, a large proportion of antibiotic prescriptions did not appear satisfactory, when considering the debated need for antibiotics in lower respiratory tract infection, the rising resistance of bacteria to antibiotics, and the cost of such management. It was beyond the scope of this study to evaluate whether differences in management had consequences on morbidity and mortality.

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