Chapter VI
Resistance to antimicrobials in France: statistical data from ONERBA's networks

1 Methodology Review

The data presented in this report and the themes discussed in this chapter are classified into the four major information categories defined in ONERBA's methodological guidelines [1], briefly reviewed below.

Subpopulations analysis of major bacterial species, according to their susceptibility level (type 1 information)

The objective is to identify and describe subpopulations of isolates according to their susceptibility level. This requires access to quantitative data (inhibition diameters or MICs). This type of data is useful for establishing the critical values that delimit clinical categories, and for detecting the emergence of strains with atypical susceptibility level that would remain undetected by qualitative S, I, or R classification; for example, strains with reduced susceptibility level remaining within the susceptible category, or highly-resistant strains.

Global statistics of antibiotic resistance for the major bacterial species of medical interest (type 2 information)

The objective is to assess the percentage of strains with acquired resistance; that is, to identify susceptible, intermediate and resistant strains within a species. The strains are isolated from diagnostic samples, whether or not there is a documented infection (colonization, carrier-state).

Global resistance statistics for the major bacterial species are extracted from databases of the laboratories of the networks.

This type of data is useful for defining the spectrum of activity of antimicrobial agents or their clinical indications.

Resistance of bacterial isolates from well-documented infections in specific epidemiological Settings (type 3 information)

The objective is to determine, in specific epidemio-clinical settings, the probability of activity for the major antibiotics. This requires clinical data, except for close site samples (for example, cerebrospinal fluid) or blood cultures, whose interpretation is generally unambiguous aside from rare specific cases (for example, blood cultures yielding coagulase-negative staphylococci).

This type of data is essential for defining indications for antibiotics as they appear in product description summaries. It is invaluable for clinicians who are prescribers, as well as for Scientific Societies and Health Authorities who establish good practice recommendations for antibiotic use.

Surveillance of multidrug-resistant bacteria: prevalence, incidence, Characteristics (type 4 information)

The objective is to assess the magnitude of the problem presented by multidrug-resistant bacteria (MDR): methicillin-resistant *S. aureus* (MRSA), extended-spectrum beta-lactamase producing enterobacteria (ESBL), carbapenem-resistant enterobacteria, glycopeptide-resistant enterococci (GRE), etc.

Because of their frequency or therapeutic consequences, MDR bacteria warrant specific surveillance in individuals, hospitals and the community, and even in animals and the environment.

Several National Reference Centres or veterinarian networks are responsible for the monitoring of some community-acquired species (*Streptococcus pneumoniae, Mycobacterium tuberculosis, salmonella* Typhimurium). C-CLIN networks are in charge of the surveillance of MRSA and ESBL enterobacteria, and sometimes other MDR bacteria. Some indicators (incidence per 100 admissions and per 1000 patient-days, place of acquisition) have been standardised within the framework of the Alert, Investigation and Surveillance of Nosocomial Infection network (RAISIN). The results generated by RAISIN are presented elsewhere [2]. Other indicators (percentage of MDR bacteria in the species, co-resistance to other antibiotics, etc.) are collected by some networks independently from RAISIN.

2 Presentation of statistical data

2.1 Subpopulation analysis of major bacterial species, according to their susceptibility level (type 1 information)

Data in humans:

Figures 1.1, 1.2, 1.10, 1.11, and 1.13 to 1.15 allow to compare the activity of amoxicillin + clavulanate (AMC) to amoxicillin alone (AMX) against *Escherichia coli*. The behaviour of this species with respect to AMX (Figure 1.1) is bimodal, with one clearly susceptible subpopulation (mode, 24-26 mm) and a clearly resistant one (mode, 6 mm) widely separated by the two critical values. *E. coli* behaviour toward AMC shows an

unimodal distribution (mode, 21 mm) spread over a wide zone on either side of « D » (21 mm), the upper critical diameter (Figure 1.2 and 1.13). Stratification on AMX susceptibility (susceptible strains (S) *versus* non-susceptible strains, i.e. intermediate susceptibility and resistant, R) shows two distinct subpopulations (Figures 1.10, 1.14 and 1.11, 1.15). The behaviour of AMX-S strains toward AMC is comparable to that of AMX alone, with unimodal distribution (mode, 24-26 mm). However, for AMX-R strains, AMC diameters distribution is highly heterogeneous. AMC restored susceptibility (diameter ≥ 21 mm) in a very small proportion of AMX-R strains, suggesting high level of resistance to amoxicillin. The observed distributions are similar to those observed in 2003 and 2004 [3,4].

Figure 1.3 shows that *E. coli* susceptibility to cefotaxime is highly homogenous, most strains being very susceptible (inhibition diameter ≥ 35 mm). As already observed in 2003 and 2004, a small proportion of strains is highly resistant, possibly due to the emergence of strains producing ESBL of CTX-M type [5,6].

Figure 1.4 shows *E. coli* behaviour toward imipenem. The distribution is unimodal (mode, 31 mm), although there is a small peak at 35 mm relative to the upper detection limit of some automated cameras. Similar results are observed for *P. mirabilis* (Figure 1.16), and *P. vulgaris* (Figure 1.18), both distribution with a modal inhibition diameter of 29 mm. On the contrary, for *M. morganii*, the distribution of inhibition diameters is slightly different with a lower modal inhibition diameter of 25 mm and a small proportion of strains in the intermediate or the resistant zones with inhibition diameters spread from 16 to 21 mm.

Figure 1.5 shows that *E. coli* susceptibility to nalidixic acid (NAL) is trimodal as in the previous years: a susceptible subpopulation with 26 mm modal inhibition diameter, a highly resistant subpopulation (mode, 6 mm) that is more important than previously reported in 2004, and an intermediate subpopulation whose limits extend between both previous subpopulations. Figure 1.7 shows the behaviour of *E. coli* isolates toward ciprofloxacin (CIP). Three populations are delineated. Isolates resistant to CIP are more prevalent and reached now the proportion of 10% (+4% compared to 2004). All isolates susceptible to NAL are also fully susceptible to CIP (Figure 1.8), but the distribution is bimodal (modes, 23-34 mm et > 34 mm) suggesting the presence of an acquired mechanism of resistance in the least susceptible population. For NAL non-susceptible isolates (Figure 1.9), there are 4 subpopulations (modes: 6 mm, 9-10 mm, 25-33 mm, and >34 mm). Over half of NAL-R isolates are CIP-resistant. There is no change in distributions, when compared to the previous years [3,4].

Figure 1.12 shows *E. coli* susceptibility to cotrimoxazole to be trimodal: a susceptible population with 28 mm modal inhibition diameter, a highly resistant population (mode, 6 mm) and an intermediate population located between « d » and « D ».

Figure 1.6 displays *E. coli* behaviour towards gentamicin. The distribution of diameters is trimodal, with a susceptible population (mode, 24 mm), a resistant to intermediate population located between 8 and 17 mm, and a highly resistant population (mode, 6 mm). The latter (2.5% of all isolates) is less prevalent than in 2004 (4.5%).

For *Pseudomonas aeruginosa*, the piperacillin-susceptible population with 30 mm mode (Figure 1.20) is more clearly defined in relation to « D » than the ticarcillin-susceptible population, which extends on either side of « D » (Figure 1.19) as observed in previous years. *P. aeruginosa* susceptibility to piperacillin (Figure 1.20) is quite similar to that for the piperacillin-tazobactam combination (Figure 1.21). The slightly different distribution existing between both drugs is illustrated in Figures 1.22 and 1.23 which show susceptibility to piperacillin-tazobactam combination in piperacillin-susceptible and non-susceptible strains. Among piperacillin-resistant isolates, susceptibility to the combination is restored for only a small proportion of isolates.

Figure 1.25 displays inhibition zone diameters for imipenem towards *P. aeruginosa*. The distribution of diameters is trimodal, with a susceptible population (mode, 27 mm), a resistant to intermediate population located between 8 and 21 mm, and a highly resistant population (mode, 6 mm).

Figure 1.27 shows *E. faecalis* behaviour towards ampicillin and amoxicillin. For both drugs, the distribution of the susceptible population is unimodal with modes of 26 mm and 28 mm, respectively. For *E. faecium*, the distribution of diameters is strikingly different (Figure 1.29). Indeed, there is a highly resistant sub-population (mode, 6 mm) for both drugs, although slightly more prevalent for ampicillin. The remaining non-highly-resistant population spans from the resistant to the susceptible zones without sub-population being clearly distinguishable.

Distribution of diameters for teicoplanin is unimodal and very homogeneous for both species (Figure 1.28 and 1.30). A very small proportion of strains is resistant to teicoplanin, and the level of resistance is not very high when referred to diameters sizes.

Data from food animals

Figure 1.33 shows the susceptibility of *E. coli* cattle isolates to ceftiofur (third generation cephalosporin used in veterinary medicine). Data gathered in 2005 are line with those from 2004 and underline the persistence of isolates harbouring decreased susceptibility (or resistance) to this molecule in animal production. ESBL-producing *E. coli* of animal origin were first identified in France in cattle, swine and poultry in 2006 [7] and their significant prevalence identified through dedicated studies [8] constitute the best hypothesis for an explanation of these observations in the network. In Figure 1.35, the distribution of diameters for enrofloxacin is bimodal (modes, 6 and 30 mm), and almost 20 % of *E. coli* isolates from cattle have decreased susceptibility (or resistance) to this drug. These data emphasize the constant need for a prudent use of beta-lactams and fluoroquinolones in veterinary medicine, even if co-selection with other antimicrobials should not be excluded. When regards to *S. uberis* isolates of bovine origin, Figures 1.36 to 1.38 show that distribution of diameters are tri-modal for erythromycin, spiramicin and lincomycin, and that around 10% of isolates are resistant to these drugs.

2.2 Summary statistics of antibiotic resistance for the major bacterial species of medical interest (type 2 information)

Staphylococcus aureus

In the MedQual network of private laboratories (Table 2.23), around 16% of *S. aureus* isolated in the community are resistant to methicillin (MRSA). This does not mean that these are community-acquired MRSA as previous history of patients is not recorded herein. Most (99%) of *S. aureus* strains are gentamicin-susceptible, and 88% are tobramycin-susceptible. Of interest, only 81% of the strains are susceptible to fluoroquinolones, suggesting that at least 4 to 5% of methicillin-susceptible strains are fluoroquinolone-resistant. Finally, 10% of all *S. aureus* isolated in private laboratories are resistant to fusidic acid.

More data on MRSA are given in appendix 4 regarding multidrug-resistant organisms.

Enterobacteria

Tables 2.1 to 2.26 show susceptibility rates of enterobacterial species:

- to amoxicillin (AMX) : 53% and 59% of *E. coli* strains are susceptible to this antibiotic when considering the REUSSIR network of hospital laboratories (Table 2.1) and the MedQual network of private laboratories (Table 2.22);
- to the amoxicillin-clavulanic acid combination:
- 66% of *E. coli* strains are susceptible to this antibiotic when considering the REUSSIR network (Table 2.1) and 79% for the MedQual network (Table 2.22), resulting in only 10% more susceptible strains than for AMX in both networks;
- 77% among *P. mirabilis* (Table 2.9), 84% among *K. pneumoniae* (Table 2.7) and 79% among *K. oxytoca* (Table 2.6);
- to cefotaxime for group 1 and 2 enterobacteria (susceptibility rates between 96% and 98%) compared to group 3 enterobacteria that naturally produce AmpC enzyme (susceptible rates 52% to 90%). Of note, the least susceptible species is *E. aerogenes* that display a rate of only 52% of susceptible strains (Table 2.4);
- to fluoroquinolones (mainly ciprofloxacin) for group 1 and 2 enterobacteria (79% to 94%) compared to group 3 enterobacteria (30% to 81%). Some species remain very susceptible (90% of susceptibility for *E. coli*, 97% for *P. vulgaris*), while others are susceptible in less than 90% of cases (81% of susceptible for *P. mirabilis* and *M. morganii*), and finally some species are rarely susceptible (55% of susceptible for *E. aerogenes*, 30% for *P. stuartii*);
- to amikacin where it can be noticed that *E. aerogenes* and *S. marcescens* remain less frequently susceptible (74% and 71%, respectively) than other species (susceptible rates >95%).

Susceptibility in strains isolated from animals

Amongst *E. coli* strains isolated from poultry and swine (Tables 2.24 and 2.25), between 45% and 49% were susceptible to amoxicillin in 2005. For non-susceptible strains, susceptibility is often restored by clavulanic acid, and over 99% of strains are susceptible to ceftiofur (third generation cephalosporin). Between 88% and 95% of *E. coli* strains isolated from poultry and swine, respectively are susceptible to fluoroquinolones and more than 93% of strains are susceptible to gentamicin in these two animal productions. Percentages of cotrimoxazole-susceptible *E. coli* are significantly different between poultry (60%) and swine (35%) ($p < 0.01$). Only 15% of *E. coli* strains are susceptible to tetracycline.

When considering cattle, comparison of data gathered in 2003, 2004 and 2005 (Table 2.26) shows a constant and low level of susceptibility of *E. coli* to amoxicillin (around 20%), which is being poorly restored by clavulanic acid (38,8 % of susceptible isolates in 2005). Susceptibility to third generation cephalosporins does not demonstrate any clear trend in the present network. Susceptibility to fuoroquinolones remains stable as well, albeit at a level of 70 to 80% of susceptible strains, below the level observed in pork and poultry. Low levels of susceptibility to streptomycin (19,2 %) and tetracyclin (25,2 %) are also to be underlined.

Trends in susceptibility

Trends in susceptibility rates are given in Tables 2.13 to 2.21.

E. coli

No trend in *E. coli* susceptibility was observed for most antibiotics during the last 6 years (Table 2.13). However, there is a slight decrease in fluoroquinolone susceptibility of *E. coli* isolates, from 95% in 2000 to 90% in 2005. In addition, no strain resistant to cefotaxim was recorded in 2005 when 2% of isolates are resistant to this antibiotic in 2005.

E. aerogenes

E. aerogenes susceptibility rates to cefotaxime, amikacin and fluoroquinolones (Table 2.15) increased significantly, from 35% in 2000 to 52% in 2005 for cefotaxim, from 55% to 74% for amikacine, and from 36% to 56% for fluoroquinolones, respectively. Such an increase in susceptibility is probably related to a decrease in the number of ESBL-producing strains (Tables 4.10 to 4.13).

E. cloacae

In contrast to *E. aerogenes*, *E. cloacae* susceptibility to third generation cephalosporins and to fluoroquinolones remained very stable since 2000 (Table 2.16). However, there is a slight decrease in fluoroquinolone (87% in 2000 to 80% in 2005) and cotrimoxazole susceptibility (93% in 2000 to 89% in 2005).

K. pneumoniae

K. pneumoniae susceptibility to most antibiotics did not vary between 2000 and 2005 (Table 2.18).

P. mirabilis

As for *E. cloacae*, there is a slight decrease in fluoroquinolones (87% en 2000 à 82% en 2005) and cotrimoxazole susceptibility (81% en 2000 à 77% en 2005) in the last years.

2.3 Bacterial resistance of isolates in documented infection or in specific epidemiological settings (type 3 information)

Tables 3.1 to 3.42 give examples of resistance statistics established within several networks for documented infections or in specific epidemiological settings (type of infection, nosocomial/community-acquired, etc.).

Bacteraemia: trends in antibiotic susceptibility

Analysis of trends relative distribution of species recovered from bacteraemia shows that while a majority of species isolated in community-acquired bacteraemia are gram-negative since 2001, it is now the case in 2005 for hospital-acquired bacteraemia (Table 3.9).

Table 3.5 shows that, between 1996 and 2005, there was a constant increase in *S. aureus* susceptibility to gentamicin, that now reached nearly 100%. This trend is linked to the increase in MRSA susceptibility to gentamicin: from 53% in 1996 to 90% in 2005, while susceptibility to gentamicin in MSSA strains remained stable, at nearly 100% during the same period of time.

The increase in susceptibility of *S. pneumoniae* invasive strains to beta-lactams and erythromycin, observed in the previous years in confirmed in 2005 (Figures 3.21 and 3.22).

Between 1996 and 2005, susceptibility of *E. coli* strains isolated from blood cultures remained stable for most antibiotics, except two drugs for which there was a decrease in susceptibility: a drop from 60% to 48% for amoxicillin and a decrease from 98% to 89% for ciprofloxacin (Table 3.6 and Figure 3.2). Of interest, 1.7% to 3.4% of *E. coli* strains isolated from bacteraemia in 2005 produced extended-spectrum beta-lactamases, while in 2001 this proportion was only 0.2% to 0.3% (Tables 3.6 and 3.15).

Stratification on amoxicillin susceptibility shows that amoxicillin-resistant strains are less frequently susceptibility to gentamicin, cefotaxime and fluoroquinolones than amoxicillin-susceptible strains (Table 3.17).

Table 3.16 shows that susceptibility rates of *E. coli* strains isolated between 2001 and 2005 from community-acquired bacteraemia remained stable; on the contrary, there was a decreased in rates of antibiotic susceptibility for strains isolated in hospital-acquired bacteraemia during the same period. Among the latter, about 70% of amoxicillin-resistant strains are susceptible to ciprofloxacin (Table 3.17) and less than 30% of nalidixic acid-resistant strains are susceptible to ciprofloxacin (Table 3.18).

For *S. aureus* strains isolated from bacteraemia, it is well known that nosocomial origin is closely linked to a higher risk of resistance to beta-lactams (Table 3.10). Overall, nosocomial MSSA strains are as susceptible to aminoglycosides, rifampicin and fusidic acid than community-acquired strains, but less often susceptible to fluoroquinolones (Table 3.11).

The frequency of resistance in coagulase-negative staphylococci isolated from bacteraemia is a cause for concern, since about 60% of these strains are methicillin-resistant (Table 3.13). In addition, susceptibility rates to other antimicrobials are seldom higher than 50%, excepted for vancomycin, rifampicin and pristinamycin.

For enterobacteria isolated from community-acquired bacteraemia, susceptibility to the major antimicrobials used in the treatment of serious infections (third generation cephalosporins, aminosides, fluoroquinolones) remains almost stable (92 to 98%). However, susceptibility to these antimicrobials in enterobacteria isolated from hospital-acquired bacteraemia only reaches 80% to 89%. Therefore, the risk of failure may not be overlooked when these antimicrobials are used in monotherapy (Table 3.16). The difference is linked to two factors. First, differences in susceptibility rates within a species, whether strains are community- or hospital-acquired, susceptible or resistant to amoxicillin or nalidixic acid as it is the case for *E. coli*, (Tables 3.16, 3.17, 3.18). Second, it is also linked to the much higher proportion of « hospital » species with usually higher resistance rates (*Enterobacter spp, Serratia spp*…) in hospital-acquired than in community-acquired bacteraemia (Table 3.9).

Community-acquired infections

Streptococcus pneumoniae

Analysis of *S. pneumoniae* resistance according to age and type of sample is presented in Tables 3.23 to 3.34. In 2005, strains isolated from paediatric (<16 years) meningitis or bacteraemia are not more often resistant to beta-lactams or macrolides than strains isolated from meningitis or bacteraemia in adults. On the opposite, fluoroquinolone-resistant strains are more frequent in adults than in children.

In children, strains isolated from otitis media are more often resistant to antibiotics than strains isolated from meningitis or bacteraemia. The proportion of susceptible strains is significantly different between these locations for penicillin G (42,0% *vs* 67,6%; p <0,001), amoxicillin (70,0% *vs* 83,6% ; p < 0,001) and erythromycin (39,7 % *vs* 65,6 %; p <0,01), but not for cefotaxime (89,0 % *vs* 94,6% ; p = 0,09). This could be explain by the fact that in France, tympanocentesis is performed only in case of failure of medical treatment, therefore selecting the more resistant strains for culture.

Between 2001 and 2005, the proportion of invasive strains susceptible to beta-lactams or macrolides increased significantly among children (Figure 3.21). In adults, the same significant downward trend is observed for beta-lactams, while it is not the case for macrolides (Figure 3.22). Such decreases could be explained by at least two Public Health measures: the national campaign for better use of antibiotic [9], and recommendations for widely use of the 7-valent vaccine (mars 2002). When considering fluoroquinolone resistance, proportion remained stable between 2001 and 2005.

Mycobacterium tuberculosis

The WHO recommends that *Mycobacterium tuberculosis* resistance statistics be stratified on prior antituberculosis treatment.

Table 3.38 shows that percentages of strains susceptible to isoniazid, rifampicin and ethambutol, three of the four first line drugs reach 94% (95.7% in 2004) in the absence of prior

treatment history (« primary » or « initial » resistance). These percentages fall around 85% (81% in 2004) in case of prior treatment (« secondary » or « acquired » resistance). As in the previous years, the most frequent resistance is isoniazid resistance (5.5% of primary resistance and 14.3% of secondary resistance). Primary resistance to rifampicin remains around 1%, and most of the resistant strains are multi-resistant (i.e. resistant to both rifampicin and isoniazid). Acquired resistance to rifampicin is 7 times higher than among new patients (8%). Patients with unknown or doubtful previous history of treatment have resistance rates similar or close to those of new patients. As in previous years, the region with higher resistant rates is the « Ile-de-France » region (Table 3.39). Primary and secondary resistance rates are relatively stable since 2000, and close to values observed in other Western European countries [10].

Documented infections in animals

Neonatal diarrhoea in calf constitutes the major pathological setting for antimicrobial use in cattle. The main target species is *E. coli*, and the particularly low and constant percentage (around 10 %) of susceptible *E. coli* isolates to amoxicillin over the years is to note (table 3.35). Resistance rates to third generation cephalosporins and fluoroquinolones should be a matter of worry as well.

Bacterial respiratory infections in cattle are mainly due to the two species Pasteurella multocida et Mannheimia haemolytica. Even if both of them retain very high susceptibility rates to most antimicrobials (tables 3.36 and 3.37), data from 2005 show a decreased susceptibility to tetracyclin (*Pasteurella multocida, Mannheimia haemolytica*), as to amoxicillin, sulfonamides and quinolones (*Mannheimia haemolytica*).

2.4 Surveillance of multidrug-resistant bacteria (type 4 information)

Methicillin-resistant *Staphylococcus aureus* (MRSA)

The global MRSA proportion among *S. aureus* is very homogenous in French hospitals: between 28 and 39% for most networks in 2005, regardless of the type of clinical sample (Tables 4.1 to 4.4). The proportion of MRSA varies depending on the type of hospitalisation: between 24% and 34% in acute care, and between 60 and 69% in chronic or long-term care facilities. MRSA proportion remained stable circa 40% in the Paris and North region of the nosocomial network (CCLIN) between 1998 and 2005 (Table 4.1). However, this proportion decreased in acute-care facilities of the « Assistance Publique-Hôpitaux de Paris » network during the same period of time. Indeed, MRSA proportion fell from 39% in 1993 to 24% in 2005 (Table 4.2 and Figure 4.2). This decrease was even more significant in Intensive Care Units of the AP-HP network, where MRSA proportion fell from 55% in 1993 to 23% in 2005 (Figure 4.4). In the other networks, MRSA trends is encouraging, with a decreased MRSA percentage among *S. aureus* for most networks, although observed decreases are less pronounced than in Paris area. Such a downward trend is observed while at the international level, and particularly in Europe, there is an almost generalized rise of this indicator [11].

Most MRSA strains (between 87 and 93%) are gentamicin-susceptible, and the percentage of tobramycin-susceptible strains has shown constant increase since 2000, reaching 23% to 34% in 2005 according to the network (Tables 4.5 to 4.7). Between 45 and 50% of MRSA strains are erythromycin-susceptible, with a constant increase in susceptibility rates. Finally, resistance to fluoroquinolones remains high, above 90%.

Extended-spectrum beta-lactamase-producing enterobacteria (ESBL)

In the past few years, the distribution of enterobacterial species producing extended-spectrum beta-lactamases has considerably changed. Indeed, there was a drastic increase in *Escherichia coli* and a concomitant decrease in *Enterobacter aerogenes* and *Klebsiella pneumoniae*, depending on the network (Tables 4.9 to 4.13, and Figures 4.7 and 3.8). In 2005, in the AP-HP network, 55% of ESBL strains belong to *E. coli* species, while it was only 9% in 1995. This trend is also observed in other regions of France, with a slight time lag. It occurs as a result of the spread of CTX-M producing strains resulting in an increase in the global ESBL-positive enterobacteria incidence. In the yearly survey of the ColBVH network, the overall prevalence of ESBL-positive enterobacteria was 1.6% (1% in blood cultures and 4.2% in pulmonary samples). Among all *E. coli* isolated, the prevalence of ESBL-positive *E. coli* was 1% (Table 4.17). Among the 82 strains of ESBL-positive *E. coli*, 62 produce were positive for blaCTX-M by PCR (Table 4.18).

Risk of dissemination in the community and the situation observed in neighbouring countries such as Spain and the United Kingdom [11] must prompt us to the greatest vigilance concerning these MDR strains that requires specific monitoring and control procedures. Overall, ESBL-positive strains remain highly resistant to all antimicrobials except carbapenems (Tables 4.14 to 4.16, Figure 4.9).

Other multidrug-resistant bacteria

Multidrug-resistance among *Acinetobacter baumannii* isolates, as defined by resistance to all beta-lactams except imipenem, is similar in 2004 and 2005 (Table 4.19) around 35%. Among the resistant strains, 12.8% were also resistant to imipenem. Multidrug-resistant isolates are mainly isolated in ICUs (Table 4.20) and are observed in all departments under surveillance by the regional South-West network, included overseas departments, but the Limousin region (Table 4.21).

The number of patients harbouring multidrug-resistant *Mycobacterium tuberculosis*, (defined as simultaneous resistance to isoniazid and rifampicin) remains below 70 for the last two years of the surveillance. Since the increase in prevalence and incidence observed in 2002, yearly MDR rates among all *M. tuberculosis* isolates remain stable around 1.3 to 1.4% (Table 4.22). Such rates are closed to those observed in other European countries such as Switzerland, Norway or Belgium, but lower than rates observed in Spain (4.7%), Portugal (2.1%) or Germany (2.7%) [10].

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