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WORKING GROUP REPORT

Standardization of antituberculosis drug resistance surveillance in Europe

Recommendations of a World Health Organization (WHO) and International Union Against Tuberculosis and Lung Disease (IUATLD) Working Group

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Standardization of antituberculosis drug resistance surveillance in Europe. Recommendations of a World Health Organization (WHO) and International Union Against Tuberculosis and Lung Disease (IUATLD) Working Group. V. Schwœbel, C.S.B. Lambregts-van Weezenbeek, M-L. Moro, F. Drobniewski, S.E. Hoffner, M.C. Raviglione, H.L. Rieder. ©ERS Journals Ltd 2000.

ABSTRACT: Surveillance of antituberculosis drug resistance is an essential tool for evaluating the quality of tuberculosis control programmes. Consensus-based recommendations on uniform reporting of antituberculosis drug resistance surveillance data in Europe have been developed by a Working Group of the World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (IUATLD).

Laboratories should use standardized methods for testing drug susceptibility with a quality assurance programme including national and international proficiency testing. The proportion of drug resistance, particularly resistance to isoniazid, rifampicin or both (multidrug resistance) among all definite, *i.e.* culture-positive, tuberculosis cases at the start of treatment is the major indicator of interest. It should be calculated separately among patients treated previously and among those who have never been treated with ≥1 month of combined antituberculosis drugs.

The Working Group recommends that, in countries in which resources allow, laboratories report drug susceptibility test results on all isolates of the *Mycobacterium tuberculosis* complex. Test results of the specimen at the start of treatment and clinical data from the notification should be linked using a suitable identifier. Results should be presented by calendar year and analysed by age, sex, place of birth, site of disease and sputum smear results.

In countries in which a routine system cannot be organized, representative surveys or sentinel systems are possible alternatives. In some countries, the annual prevalence of multidrug-resistant tuberculosis may be estimated through a national laboratory reporting system.

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Drug resistance complicates tuberculosis treatment. In particular, treatment of patients with multidrug resistance, defined as resistance to at least isoniazid and rifampicin, is long and costly and requires the use of drugs which frequently cause severe adverse reactions [1]. The treatment outcome for multidrug-resistance (MDR) tuberculosis is poor, with low cure and increased fatality ratios [2–4], particularly among human immunodeficiency virus (HIV)-infected patients [5–7]. Moreover, MDR tuberculosis cases may remain infectious in the community for a prolonged period of time.

Drug resistance results from the selection of drug-resistant mutant bacilli following monotherapy [8], whether intentional or resulting from inadequate treatment [9]. One of the objectives of multiple drug therapy is to prevent this problem, and recommended regimens usually include four drugs in the initial 2-month intensive phase [10]. The quality of tuberculosis treatment is a key element of tuberculosis control, because effective treatment quickly renders the patient noncontagious and therefore stops the transmission of tubercle bacilli in the community [11]. Since drug resistance develops because of inadequate use of drugs, antituberculosis drug resistance surveillance is, together with the monitoring of treatment outcome [12], an essential tool for evaluating the quality of tuberculosis control programmes [13].

In 1994, a global initiative on antituberculosis drug resistance surveillance was launched by the World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (IUATLD). It was based on the observations that available data often lacked

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representativeness, standardization of laboratory methods and valid clinical information were often missing, and results were therefore frequently neither comparable nor meaningful [14]. General principles and standard methods for antituberculosis drug resistance surveillance have been proposed by the WHO and the IUATLD [15]. A few countries in Europe have participated in the global initiative, with some reporting high levels of drug resistance [16]. Some countries have also recently reported MDR tuberculosis outbreaks in HIV-infected patients [17–20]. However, outside of the WHO/IUATLD initiative, data on antituberculosis drug resistance surveillance in Europe are still scarce and suffer from the limitations described above. In addition, major factors associated with drug-resistant tuberculosis in Europe, such as migration and the age of tuberculosis patients, are rarely taken into account.

A Working Group was set up in 1998 to address these issues and to elaborate specific recommendations for the standardization of antituberculosis drug resistance surveillance in Europe, taking into account the usual procedures of diagnosis and treatment of tuberculosis in the region. This report provides a review of currently existing European systems and offers recommendations in line with the international WHO/IUATLD recommendations for antituberculosis drug resistance surveillance. They are a direct extension of the recommendations elaborated by prior European WHO/IUATLD Working Groups on uniform reporting of tuberculosis cases [21] and standardization of treatment outcome monitoring [12].

Review of existing European antituberculosis drug resistance surveillance systems

In 1998, as part of the EuroTB programme [22], a postal survey was conducted among the co-ordinators for tuberculosis surveillance in the 51 countries of the WHO European Region. The main results for the 47 responding countries are presented in table 1.

Drug susceptibility testing was performed as a routine examination in most of the responding countries in 1998. The number of laboratories (public or private) offering drug susceptibility testing varied widely by country.

Most countries had an established national reference laboratory for mycobacteria, with various responsibilities including expertise, training, research and quality assurance programmes. The majority of these laboratories participated in an international proficiency testing programme, but only a few organized proficiency testing for other laboratories in their own country.

Within the 5-yr period 1992–1997, 39 countries conducted antituberculosis drug resistance surveillance, of which 24 had one or more ongoing national systems: 22 systems were based on the reporting of all drug susceptibility test results or of drug-resistant cases, and four were based on the reporting of MDR tuberculosis cases only. However, drug susceptibility test results were linked with data from tuberculosis notification in 65% of these national systems. National surveys were conducted in four countries. Systems not covering the entire country were also organized in 15 countries: some were representative of one or several districts or regions, whereas others were not (sometimes described as sentinel systems).

These data indicate that there is a need to improve the standardization of antituberculosis drug resistance surveillance in Europe with quality assurance in the laboratory, representativeness of data and linkage of laboratory data with clinical information. It appears feasible to implement such a standardization, in view of the general practice of drug susceptibility testing and the current process of improvement of surveillance in many countries.

Objectives of antituberculosis drug resistance surveillance

The overall aim of antituberculosis drug resistance surveillance is to help reduce morbidity and mortality due to tuberculosis, including that due to drug-resistant disease.

The main public health objectives at a national level are as follows: 1) Evaluation and improvement of the quality of tuberculosis treatment. Antituberculosis drug resistance surveillance provides information on present and past misuse of antituberculosis drugs in the country. Analysis of trends in drug resistance allows monitoring of the performances of the tuberculosis control programme (including public and private sector activities) over time. Since standard treatment regimens [10] constitute the best means of prevention of drug resistance, results of antituberculosis drug resistance surveillance are mainly useful in the design of interventions for implementing such regimens or improving their use, *e.g.* by improving drug prescription or delivery, patient follow-up and adherence to therapy [9]. 2) Identification of population groups at high risk of drug resistance in order to target interventions for preventing the development and transmission of drug-resistant tuberculosis.

A secondary national objective of antituberculosis drug resistance surveillance is to obtain indications regarding recent tuberculosis transmission. At a local level, the observation of more than one case with similar drug resistance patterns may be indicative of an outbreak, particularly in patients who have not previously received tuberculosis treatment and in whom it is suspected that tuberculosis infection may be recent (*e.g.* children or immunodeficient patients). Investigation using conventional contact tracing [23], complemented with deoxyribonucleic acid (DNA) fingerprinting of the strains in cases in which it is feasible [24], should be conducted to confirm transmission. Information regarding recent transmission can be used to improve contact tracing strategies, and to devise or adapt infection control policies in hospitals and other institutional environments.

At an international (European) level, an antituberculosis drug resistance surveillance system has additional objectives: 1) to compare drug resistance levels and trends in different countries in order to identify those which have been more successful in controlling drug resistance and learn from their experience; and 2) to identify population groups at high risk of drug resistance common to several countries in order to co-ordinate control efforts.

Definitions

"Resistance" is defined as a decrease in susceptibility of sufficient degree to be reasonably certain that the strain concerned is different from a sample of wild-type strains

Table 1. – Survey on antituberculosis drug susceptibility testing (DST) practices and surveillance systems in 1998 in 47 countries of the WHO European Region

Country	DST done on >90% cases	Laboratories doing DST n		National Reference Laboratory			Surveillance systems	
		Total	pm	Established	Organizes national PT	Participates in International PT	No. 1	No. 2
Albania	No	1	0.3	Yes	No	No	Regional system	–
Armenia	No	0	0.0	No	No	No	–	–
Austria	Yes	12	1.5	Yes	No	No	National system	–
Belarus	Yes	31	3.1	Yes	No	No	Regional system	–
Belgium	Yes	20	2.0	Yes	Yes	Yes	National system	National system (MDR)
Bosnia and Herzegovina	No	4	1.2	Yes	No	No	Regional system	–
Bulgaria	No	10	1.1	No	No	No	–	–
Croatia	Yes	12	2.7	Yes	Yes	Yes	National system	–
Czech Republic	Yes	15	1.5	Yes	Yes	Yes	National system	–
Denmark	Yes	1	0.2	Yes	No	Yes	National system	National system (MDR)
Estonia	Yes	3	2.0	Yes	No	Yes	National system	–
Finland	Yes	1	0.2	Yes	No	Yes	National system	–
France	Yes	158	2.7	Yes	No	Yes	Sentinel system	National system (MDR)
Georgia	No	1	0.2	Yes	No	No	–	–
Germany	Yes	100	1.2	Yes	No	Yes	Regional system	–
Greece	Yes	4	0.4	Yes	No	No	Other survey	–
Hungary	No	13	1.3	Yes	Yes	Yes	Regional system	–
Iceland	Yes	0	0.0	No*	No	No	National system	–
Ireland	Yes	9	2.5	No	No	No	Regional system	–
Israel	Yes	2	0.4	Yes	No	Yes	National system	–
Italy	No	60	1.0	Yes	No	Yes	Sentinel system	Regional system
Kazakhstan	Yes	16	0.9	Yes	No	No	Regional system	–
Kyrgyzstan	Yes	1	0.2	Yes	No	No	National system	–
Latvia	Yes	1	0.4	Yes	No	Yes	National system	–
Lithuania	Yes	8	2.2	Yes	Yes	Yes	National system	–
Luxembourg	Yes	1	2.5	Yes	No	No	National system	–
FYROM	No	1	0.5	No	No	No	Other system	–
Malta	Yes	0	0.0	No*	No	No	National system	–
Moldova, Republic of	Yes	8	1.8	Yes	No	No	Other system	–
Monaco	Yes	0	0.0	No*	No	No	–	–
The Netherlands	Yes	12	0.8	Yes	No	Yes	National system	–
Norway	Yes	3	0.7	Yes	No	Yes	National system	–
Poland	Yes	38	1.0	Yes	Yes	Yes	National system	–
Portugal	No	8	0.8	Yes	No	Yes	National system	National system (MDR)
Romania	No	55	2.4	Yes	No	Yes	National system	National survey
Russian Federation	Yes	300	2.0	No	No	No	Regional system	–
San Marino	Yes	0	0.0	No*	No	No	–	–
Slovakia	Yes	8	1.5	Yes	Yes	No	National system	–
Slovenia	Yes	2	1.0	Yes	Yes	Yes	National system	–
Spain	No	30	0.8	Yes	No	No	Regional system	–
Sweden	Yes	5	0.6	Yes	Yes	Yes	National system	–
Switzerland	Yes	16	2.2	Yes	Yes	Yes	National system	–
Tajikistan	No	5	0.8	Yes	No	No	–	–
Ukraine	Yes	28	0.5	No	No	No	Regional system	–
UK	Yes	7	0.1	Yes	Yes	Yes	National system	National survey
Uzbekistan	No	14	0.6	No	No	No	–	–
Yugoslavia	Yes	12	1.1	No	No	No	–	–

*: the National Reference Laboratory of another country is utlized. pm: per million; PT: proficiency testing; (MDR): concerns only multidrug-resistant cases; FYROM: Former Yugoslav Republic of Macedonia.

that have never come into contact with the drug [25]. Resistance is measured in the laboratory by drug susceptibility tests on isolates of the *Mycobacterium tuberculosis* complex. Results should be given as "resistant" or "susceptible" for each specific drug tested ("intermediate" results should be avoided). The first-line drugs tested for susceptibility are isoniazid, rifampicin, ethambutol and streptomycin (results of tests for susceptibility to pyrazinamide are not reported or compared internationally because of specific methodological problems [25]).

"Monoresistance" is defined as resistance to one first-line drug only.

"Polyresistance" is defined as resistance to two or more first-line drugs [26].

"Multidrug resistance" (MDR) is a specific type of polyresistance defined as resistance to both isoniazid and rifampicin, with or without resistance to other drugs.

"Primary resistance" is defined as resistance in a patient who has active tuberculosis following infection by drug-resistant bacilli.

"Acquired resistance" is defined as resistance which has emerged in a patient during treatment as a consequence of selection of drug-resistant mutant bacilli.

Because the true frequency of primary and acquired resistance cannot be reliably measured, surveillance indicators are recommended following the definitions below.

"Start of treatment", which is the reference date for the notification of a tuberculosis case [21], should also be the reference date for antituberculosis drug resistance surveillance (for patients not starting treatment after diagnosis, *e.g.* patients diagnosed after death, the reference should be the date of diagnosis). For patients who have received previous treatment, a new start of treatment should be considered only if the case satisfies national criteria for renotification. Since patients with chronic tuberculosis or intermittently defaulting and returning patients should not be repeatedly notified [21], it is recommended that patients are notified only once within the same calendar year.

"Proportion of drug resistance at start of treatment" is the proportion of tuberculosis cases whose bacilli are resistant to a drug or a combination of drugs, calculated at the start of treatment among all definite (culture-positive) cases notified over a calendar year. The proportions of resistance to isoniazid, rifampicin, and both (MDR), at start of treatment, are major indicators of interest. These proportions should be calculated separately: 1) among patients treated previously: previous treatment is defined as treatment for active tuberculosis with ≥1 month of a combination of antituberculosis drugs and excludes preventive chemotherapy; and 2) among those who have never been treated, *i.e.* who have never received previous treatment as defined above.

"Annual prevalence of MDR tuberculosis" is the number of tuberculosis patients with at least one MDR isolate at any point in time during the calendar year, divided by the total population.

"Quality assurance" in the laboratory [27] includes three major components: 1) internal quality control, which covers all aspects of the laboratory procedures for monitoring the accuracy and reproducibility of results; 2) quality improvement; and 3) proficiency testing, which allows laboratories to assess their capabilities by comparing their results to those obtained in other laboratories.

Laboratory methods

Drug susceptibility tests should be performed using one of the several published methods for measuring susceptibility to antituberculosis drugs [28–33], *i.e.* the proportion method on Löwenstein-Jensen or Middlebrook 7H10 medium, the radiometric proportion method, the resistance ratio method or the absolute concentration method. For surveillance purposes, the speed of the method is not the main criterion for choice, although rapid susceptibility tests may be indicated for clinical and public health reasons. If the proportion method is used, resistance is defined as ≥1% colony growth at critical concentrations of the relevant drug.

Whatever method is adopted, quality assurance is essential. Rigorous internal quality control should be conducted [15]. In addition, in cases in which several laboratories are performing drug susceptibility tests, proficiency testing should be organized, whereby panels of coded strains are periodically exchanged with the national reference laboratory for blind retesting. At least 90% agreement for each drug should be achieved between the national reference laboratory and the local laboratory.

At an international level, the reliability and comparability of national results should be ensured by a similar proficiency testing programme. The WHO and the IUATLD have established a network of supranational laboratories [34], which analyse in blinded fashion a panel of *M. tuberculosis* isolates for susceptibility to isoniazid, rifampicin, ethambutol and streptomycin. All national reference laboratories in Europe should participate in such an international proficiency testing programme. A European subnetwork of supranational laboratories has been established by the WHO and the IUATLD for this purpose.

At both a national and an international level, appropriate feedback should be provided by the co-ordinating laboratory to the laboratories participating in the proficiency testing programme in order to correct any discrepancies.

Surveillance of drug resistance at start of treatment

Design

The system should allow the measurement of the proportion of drug resistance at start of treatment among all definite (culture-positive) tuberculosis cases notified in the country on an ongoing basis, as illustrated in figure 1.

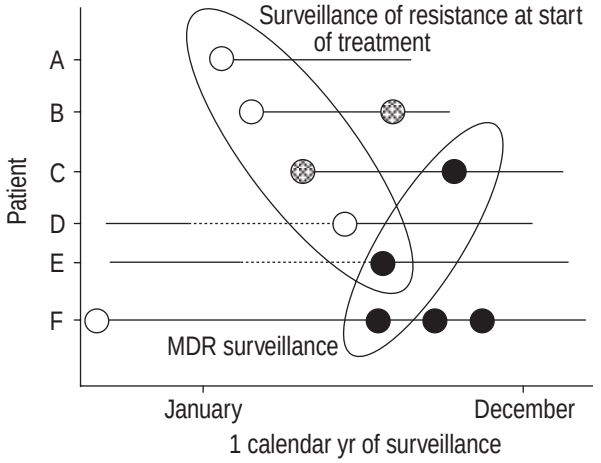

Fig. 1. – Isolates from tuberculosis patients in relation to tuberculosis treatment and antituberculosis drug resistance surveillance systems. Each circle represents one isolate, and each horizontal line one patient (only some examples are presented). Patients A–E are included in the surveillance of resistance at start of treatment since their treatment started during the calendar year of surveillance (A–C had not been treated previously, and D and E had been treated in a previous calendar year). Patients C, E and F are included in the multidrug-resistant (MDR) surveillance since they yielded an MDR isolate during the calendar year of surveillance, regardless of when their treatment started. ○: susceptible isolate; ◍: monoresistant isolate; ●: MDR isolate; —— : treatment.

In Europe, it has been recommended that laboratory reporting of all isolates of the *M. tuberculosis* complex is made mandatory, and that these reports are linked with clinical reports within 3 months [21]. It is now recommended that, in addition, laboratories report drug susceptibility test results for all these isolates.

Laboratories should preferably report full drug susceptibility test results. These results should be reported either simultaneously with the culture results on a single reporting form or on separate forms using the same identifier. Linkage of laboratory reports with the clinical data of the notification should then be performed as early as possible, depending on the organization of the reporting system.

Only results concerning isolates from specimens obtained at start of treatment (or, for patients not starting treatment, concerning the isolate which confirmed the diagnosis) should be included in antituberculosis drug resistance surveillance. Linkage of data may be performed based on the patient′s name or other identifier at the local, regional or national level, depending on the country′s resources and legal requirements.

In countries in which such a system cannot be organized, alternative options may be considered. 1) a representative survey may be conducted over a limited period of time and repeated periodically to evaluate trends. The representativeness of the survey, whether national or regional, should be ensured by appropriate sampling [15]. 2) sentinel surveillance may be organized through nonrandom selection of laboratories or diagnostic centres. However, results obtained from this scheme are not representative, thus geographical comparisons cannot be made. Moreover, time trends are difficult to interpret, especially since the recruitment of patients may change with time. In these latter two options, clinical data are obtained either through linkage with the tuberculosis notification or through a separate questionnaire.

Essential information

Laboratory reports on drug susceptibility should include at least: 1) the full name of the patient or another suitable identifier; 2) the date on which the specimen was taken; and 3) separate susceptibility results for each drug tested. The surveillance of susceptibility to isoniazid and rifampicin is a priority in Europe since these are the most potent drugs used and are almost universally included in the initial phase of standard regimens. Susceptibility to streptomycin and ethambutol, if routinely tested, may also be included in the surveillance [15].

In addition to the patient′s full name or other identifier, clinical data which should be collected or retrieved through linkage with the notification are those which it is recommended to collect for each notified tuberculosis case in Europe [21]: 1) date of start of treatment (or date of diagnosis); 2) patient′s place of residence; 3) patient′s sex and age at start of treatment (or at diagnosis); 4) country of birth of the patient; 5) history of previous tuberculosis; 6) site of disease; and 7) culture and sputum smear results.

The specimen for which drug susceptibility test results should be included is the one with the date corresponding (or closest) to that of the patient′s start of treatment.

History of previous tuberculosis should enable patients who have received previous treatment with chemotherapy to be distinguished from those who have not. Patients diagnosed before the chemotherapy era may be numerous in some European countries. In practice, cases diagnosed in Europe before 1950 may be considered as never having been treated.

Data analysis

The proportion of drug resistance at start of treatment should be reported by calendar year among the total number of definite cases, and separately among patients who have never been treated and patients treated previously, as proposed in table 2.

The proportion of drug resistance among patients treated previously reflects, to a large extent, inadequate treatment (acquired resistance). However, it represents a mixture of both primary and acquired resistance, since patients may have been initially infected by drug-resistant bacilli. The proportion of drug resistance among patients who have never been treated reflects the extent to which drug-resistant bacilli have been transmitted in the community and is the best indicator for primary resistance. Results in patients whose treatment history is doubtful should be analysed and presented separately.

There is major epidemiological interest in knowing the resistance patterns of the strains presently circulating in the community. These could be determined from strains obtained from very young children, for whom it is certain that tuberculosis infection has been acquired very recently. It is not usually feasible, however, to obtain a large enough number of strains from young children with tuberculosis to allow meaningful interpretation. To provide, nevertheless, some idea of the change in resistance patterns with time, age-specific proportions of resistance in a given calendar year can be calculated among patients who have never previously been treated and who were born in the country. Since younger patients have been, on average, infected much more recently than older patients, trends in this proportion by age provide indirect insight into the development of drug resistance over time. The slope that might be seen is, however, not an exact reflection of the trend over calendar time, since patients may have acquired their infection at various points in their lifetime.

The likelihood of foreign-born patients harbouring drug resistant-bacilli is different from that of patients born in the country of diagnosis, since they may have been infected abroad, or have acquired drug resistance while under treatment outside the country. Thus, drug susceptibility test results in foreign-born patients may not reflect the quality of the national tuberculosis control programme. Patients originating from countries with a high incidence of tuberculosis contribute greatly to the epidemiological situation in several European countries [22], some of which report high proportions of drug resistance in immigrants [35–39]. In these countries, results should be analysed and presented separately according to the patient′s geographic origin. Intercountry comparisons within Europe should be conducted separately among patients born in the country and foreign-born patients.

Results in sputum smear-positive pulmonary cases can be presented separately from results in other cases. This will facilitate international comparisons since, at an international level, antituberculosis drug resistance surveillance

Table 2. – Form for reporting antituberculosis drug susceptibility testing (DST) results

DST results		Number of culture-positive patients tested for drug susceptibility			
		Never treated (or <1 month)	Previously treated (≥1 month)	Unclassified treatment status	Total
Total tested					
I	Any isoniazid (H) resistance				
	Any rifampicin (R) resistance				
	Any ethambutol (E) resistance				
	Any streptomycin (S) resistance				
II	H only				
	R only				
	E only				
	S only				
	Total monoresistance				
III	H + R				
	H + R + E				
	H + R + S				
	H + R + E + S				
	Total multi-drug resistance (MDR)				
IV	H + E				
	H + S				
	H + E + S				
	R + E				
	R + S				
	R + E + S				
	E + S				
	Total polyresistance other than MDR				

is conducted as a priority among smear-positive pulmonary cases [15].

In order to evaluate the representativeness of results, the characteristics (age, sex, *etc.*) of the cases for which drug susceptibility test results are available should be compared with those of other culture-positive cases without drug susceptibility test results diagnosed in the same country within the same time period.

Multidrug resistance surveillance

Multidrug resistance may develop during the course of treatment and thus not be present at the time of notification. In addition, MDR tuberculosis cases may remain infectious for a long period without being repeatedly notified. The surveillance of drug resistance at start of treatment therefore captures only a subset of MDR tuberculosis cases (fig. 1). In order to assess the total number of MDR tuberculosis cases present in the community, a specific system may be established, provided bacteriological examination with drug susceptibility tests is performed at least once a year in such patients.

In countries in which drug susceptibility test results are reported at a national level, multidrug resistance surveillance should include all patients with at least one reported MDR isolate during the calendar year, whether or not the specimen was taken at the start of treatment.

In countries in which drug susceptibility test results are not reported at a national level, the reporting of MDR isolates by laboratories may nevertheless be possible because their number is usually limited. Furthermore, even in countries in which culture and drug susceptibility tests are not performed routinely among all patients, bacteriological diagnosis of multidrug resistance is often made on the basis of cases not responding to standard treatment. Such a system has proven feasible in some countries (*e.g.* Belgium, France and Portugal).

Clinical data may be obtained through linkage with the tuberculosis notification, or through a separate questionnaire. Clinical information should be obtained at least once a year. Apart from the essential information listed in the

previous section, the following additional clinical, therapeutic or epidemiological information could be obtained if required.

1) Detailed information regarding previous treatment and the drug susceptibility of the first reported isolate of the patient may allow distinction between primary and acquired multidrug resistance. 2) Outbreaks of MDR tuberculosis have been described in HIV-infected patients [17–20], and association between HIV infection and primary MDR tuberculosis has been observed [40]. Countries may thus consider reporting a patient's HIV infection status or other immunosuppressing conditions. 3) Monitoring treatment and treatment outcome may be useful in countries in which specialized management of MDR tuberculosis patients can be organized and regularly evaluated [36].

Multidrug resistance surveillance allows an estimate of the annual prevalence of MDR tuberculosis to be made. This information is complementary to that provided by the surveillance of the proportion of resistance at start of treatment. Indeed, it allows assessment of the emergence of multidrug resistance (cases newly diagnosed as MDR during the calendar year) and the burden of patients with chronic tuberculosis remaining MDR in the community (cases known as MDR in previous years). If the information is available, primary and acquired multidrug resistance should be analysed separately.

Conclusion

Antituberculosis drug resistance surveillance should become an integral component of tuberculosis control and be implemented in all countries in which resources are available. Quality assurance in the laboratory and adequate surveillance methodology are crucial to the interpretation of results, international comparison and monitoring of the performance of tuberculosis control in Europe.

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