COUNTRY SURVEILLANCE SYSTEMS

Information on national TB case reporting systems in 1998 was obtained through a questionnaire survey. Detailed information referring to 1997 was published in the previous EuroTB annual report **[5].**

3.1 Inclusion of specific population groups in notifications

At European level it is recommended that all cases diagnosed in the country should be included in TB notifications. However, due to the organisation of the health systems and of surveillance, specific population groups are excluded from tuberculosis notification in some countries.

In 1998, cases diagnosed among foreigners (legal residents, asylum seekers, illegal residents), prisoners, military personnel, homeless, persons with HIV infection or AIDS and institutionalised persons were included in tuberculosis notifications in 29 countries, of which 19 countries in the West (Table 3).

Eight countries included only nationals, excluding all categories of foreigners patients (Azerbaijan, Belarus, Kyrgyzstan, Macedonia, Poland, Turkey, Turkmenistan, Uzbekistan), of which three (Kyrgyzstan, Turkey, Uzbekistan) exclude also the other population groups of interest (prisoners, military personnel, homeless, persons with HIV infection or AIDS and institutionalised persons)

Foreigners who were legal residents were included while illegal immigrants and/or asylum seekers were excluded in Andorra in the West, in four countries in the Centre (Albania, Romania, Slovakia and Yugoslavia) and in five countries in the East (Armenia, Kazakhstan, Latvia, Moldova, and Tajikistan). Compared with 1997, in 1998, one or more groups of foreigners previously excluded were included in notifications in six countries.

Prisoners were excluded from notification in 11 countries compared with 15 countries in 1997. The homeless were excluded from notifications in nine countries, military personnel in eight countries, persons with HIV infection or AIDS in six countries and institutionalised persons in six countries.

It should be noted that official inclusion of a specific group in notifications does not necessarily mean that notifications will be complete for that group. Exclusion of specific population groups from notification may particularly affect notification data in the East, where, in some countries, cases among prisoners may represent a relevant proportion of incident cases **[9]** and cases among individuals co-infected with HIV may do so in the near future **[10].**

3.2 Recommendations for notification of recurrent cases

In 1998, according to the European recommendations, all countries notified both new and recurrent TB cases except Turkmenistan where only new cases were included in notifications. However, recommendations on notifications of recurrent cases, differed across countries. In four of the 41 countries providing information no specific recommendations existed. In the majority of the other 37 countries**,** most types of recurrent cases including relapse and return after default (Table 1, cases A to F) were recommended to be included in notifications, whereas treatment failures were recommended to be included in 10 countries only (Table 1, case G) Recurrent cases to be notified included other than definite cases (Table 1 case A) in the majority of countries. Untreated recurrent cases (e.g. previous TB episode before 1950) were classified as new cases or as recurrent cases in comparable numbers of countries (Table 1, cases B, E). Limited information is available on how these recommendations are applied. In addition, information on previous history of tuberculosis is difficult to obtain and may result in misclassification of cases.

Standardised criteria for the notification and classification of recurrent cases, would improve the com-

TABLE 1 Recommendations for notification of recurrent cases, 1998, 37 countries

Case	Type of recurrent case: previous treatment	previous outcome	confirmation of current episode	No of countries in which it is recommended to notify as: new case	recurrent case	not specif	total	not to notify	No recomm.*	No answer	Total
A	yes	not specified	other than definite	2	25	1	28 †	4	1	4	9
B	no (before 1950)	–	definite	15	16		31	1	1	4	37
C	yes	completed	definite	3	29	1	33 †	0	0	4	4
D	yes	default	definite	2	22		24	2	5	6	37
E	no (<30 days)	interr > 2 mo	definite	14	12		26	2	4	5	11
F	yes	interr <2 mo	definite	8	14		22	5	4	6	15
G	yes	failure	definite	3	7		10	19	3	5	27

Note: Bosnia Herzegovina and UK not included because different recommendations in different parts of the country
* No recommendations
† including Czech Republic in which the recommendation does not specify the classification new/recurrent

parability of surveillance data at the international level, which is particularly relevant for surveillance of drug resistance and of treatment outcome.

3.3 Case definition and classification

In 1998, classification of cases as "definite" was limited to culture positive cases in 22 countries (compared to 12 countries in 1997) and included cases with both positive culture and/or positive sputum smear in 27 countries (Table 11). All countries notified TB cases with any disease localisation, except Spain, where notification of extra-respiratory cases was limited to meningeal localisations.

3.4 Estimates of over and under-notification

Estimates of under-notification for tuberculosis cases notified in 1997 were provided from 32 countries and varied widely from 0 in 8 countries to 20% or more in 4 countries. Over-notification (i.e. notification of cases, which do not correspond to case definition, or multiple reports of the same individual within a calendar year) was estimated to be 0 in 15 countries and 5% or more in 7 countries **[5]**.

3.5 Bacteriological diagnosis and laboratory reporting

In 1998, culture for *Mycobacteria* was considered to be widely available in 38 countries, available in some areas in 11 countries and not available in Armenia (Table 11). Access to culture does not necessarily mean that the culture is systematically performed for all suspected cases. In 27 of the 38 countries with widely accessible culture facilities, all level II laboratories routinely report initial isolates to the notification system.

TUBERCULOSIS CASES NOTIFIED IN 1998

4.1 Information provided

All the 51 countries in the WHO European Region provided some information on TB cases notified in 1998 (Table 4)**.** Twenty countries provided individual data and 31 provided aggregate data. Only the total number of cases was available for Belarus. In six countries, aggregate data (by sex, age, site of disease and bacteriology results) were provided on new cases only and are not presented in this report.

Compared with 1997 the number of countries providing data increased for all types of information (Table 4). Data by sex according to the requested age groups were provided by 40 countries (38 in 1997). Data by previous TB disease status (new/recurrent) were provided from 43 countries (38 in 1997), by geographic origin from 32 countries (29 in 1997), by site of disease from 42 countries (37 in 1997) and by sputum smear from 42 countries (32 in 1997). Aggregate data by culture result were collected for the first time in 1998 and were provided overall by 38 countries.

Data on the organisation of drug resistance surveillance (DRS) and on drug susceptibility testing (DST) results at the start of treatment were requested for the first time on cases notified in 1998 (in the East data were requested only from Baltic countries). DST results were provided from 29 countries (18 countries in the West, 8 in the Centre and the three Baltic countries) (Table 15). In 26 countries data refer to TB cases notified in 1998, of which 15 provided individual data (Table 4), and in three countries data are not related to TB cases notified (see 5.1).

4.2 Global 1998 figures and trends

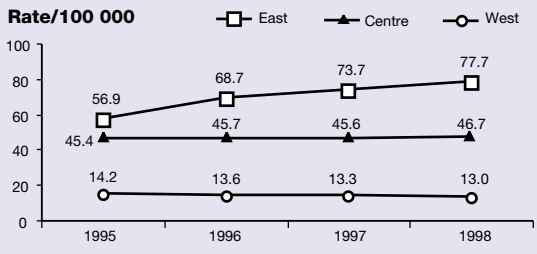
In 1998, 363 521 cases of tuberculosis were notified in the 51 countries of the WHO European Region, of which 226 575 (62%) where notified in the East. The overall notification rate in the region was 42 per 100 000 population and it ranged from 13 per 100 000 in the West, to 47 per 100 000 in the Centre to 78 per 100 000 in the East (Table 5).

TB notification rates were lower than 20 cases per 100 000 population in 22 countries in the West and in the Czech Republic; between 20 and 49 cases per 100 000 in 13 countries, including 10 countries in the Centre; and 50 cases or over per 100 000 population in 16 countries, including 13 countries in the East (Map 1).

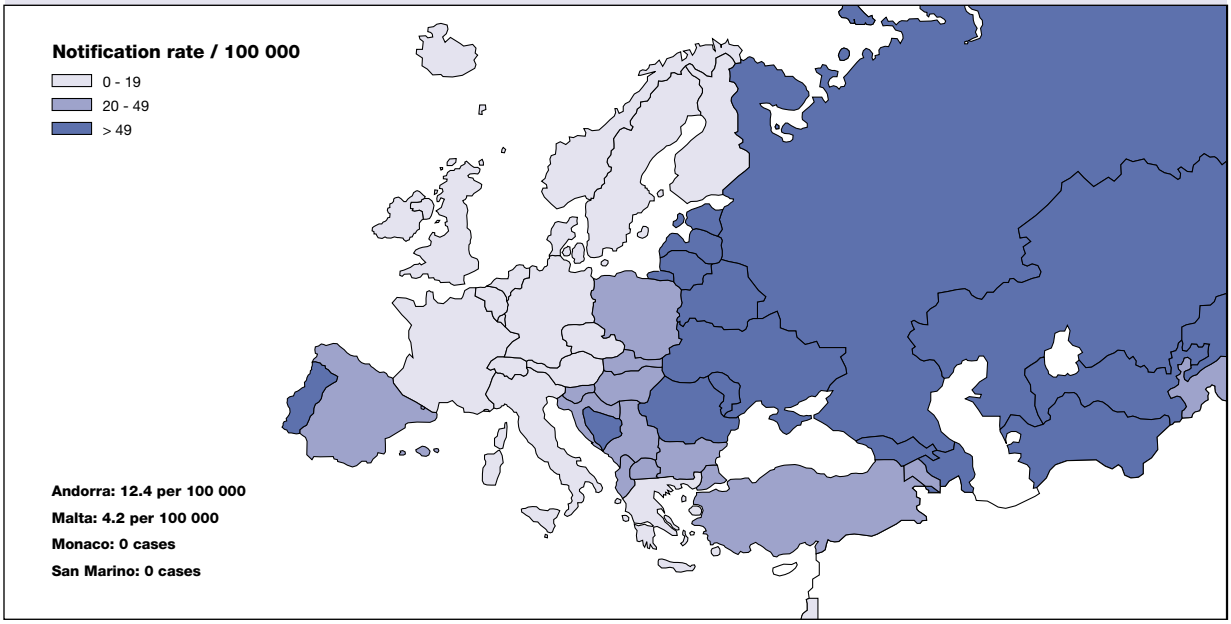
Among countries in the West notification rates ranged from zero (Monaco and San Marino) to 53 per 100 000 in Portugal. In the Centre, 60% of cases were notified from Romania and Turkey, each representing 30% of cases, and country rates ranged from 18 per 100 000 in the Czech Republic to 115 per 100 000 in Romania. In the East more than half of the cases were notified in the Russian Federation and rates ranged from 41 per 100 000 in Armenia to 128 per 100 000 in Kyrgyzstan.

Notification trends between 1995 and 1998 differed markedly by geographic area and by country (country profiles). When comparing rates in 1998 with 1995, notification rates had decreased from 14.2 to 13.0 in the West (-9%), increased slightly from 45.4 to 46.7 in the Centre (+3%) and increased markedly in the East from 56.9 to 77.7 per 100 000 (+37%). (Figure 1)

FIGURE 1 **Tuberculosis notification rates by geographic area, 1995-1998, WHO European Region**

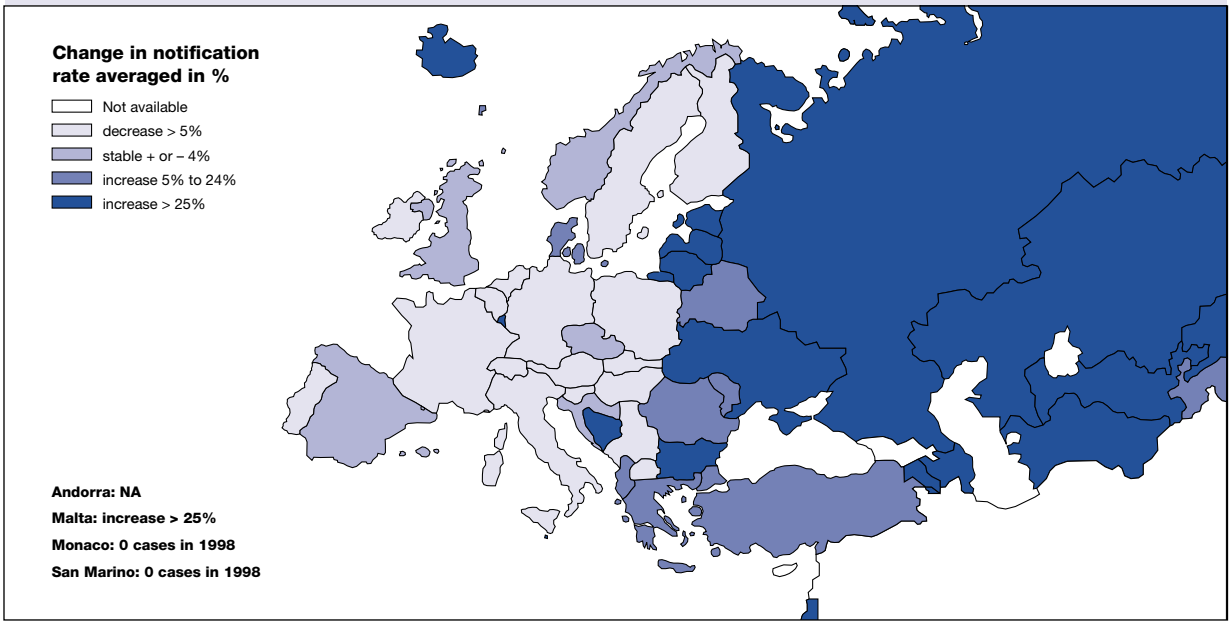


MAP 1 Tuberculosis notification rates 1998, 51 countries, WHO European Region



Trends in notification rates for the period 1995-1998 were analysed more in detail in each area. In the West, trends are not interpretable in Spain (where case definition changed in 1997 from new respiratory cases only to all respiratory and meningeal cases) and Greece and Israel, where numbers of cases notified increased by more than 50% between 1997 and 1998, due to immigration patterns and reorganisation in the TB programme (Israel) or to major changes in TB surveillance (Greece). In the other

MAP 2 Changes in tuberculosis notification rates, 1998 compared to 1995, WHO European Region



countries, annual notification rates in 1998 had decreased by 12% compared to 1995, with regular annual decreases of 4% throughout the period. Among the 14 countries with more than 50 cases notified per year, rates decreased by more than 5% between 1995 and 1998 in 11 countries, were stable in the United Kingdom (-0.4%) and Norway (+1.5%), and increased in Denmark (+16%). (Map 2).

In western Europe, notification rates in the period 1995-1998 show that incidence is decreasing again in most western European countries after the stabilisation or increases observed in many countries in the late 1980s and early 1990s [**11**]. Trends in many countries in the West are affected by increasing numbers of cases notified in patients of foreign origin (see below). Trends in notification rates among nationals were consistently decreasing in recent years in countries with increasing numbers of cases reported among foreigners, suggesting that tuberculosis in the population of foreign origin may have had a limited effect on transmission among nationals.

In the Centre notification rates were stable overall (+2% between 1995 and 1998) but contrasting trends were observed across countries (Map 2). Compared to 1995, in 1998 notification rates decreased by 8% or more in Hungary, Macedonia, Poland, Slovakia, Slovenia and Yugoslavia, decreased by 2% in the Czech Republic, were stable in Croatia and increased by more than 5% in Turkey (6%), Romania (13%), Bulgaria (34%), where limited information is available to interpret this trend and Bosnia-Herzegovina (36%) where part of the observed increase may be due to cases in the population of refugees returning after the war. Decreasing trends in several countries in the Centre may partly reflect improvements in the socio-economic situation and indicate that the quality of tuberculosis control has been maintained over recent years.

In the East data are not available for 1995 in Georgia, the only country in which rates decreased markedly in recent years (-36% between 1996 and 1998), partly due to retrospective reporting in 1996 of cases diagnosed during the early 1990s. In all the other countries, the notification rates increased by 37% overall in 1998 compared to 1995, with increases ranging widely between countries, from 6% in the Republic of Moldova to 95% in Kazakhstan.

These recent trends confirm the increases in tuberculosis mortality and morbidity observed since 1990 in Eastern Europe **[12].** The changes in the notification system in some of these countries such as increasing inclusion of some population groups at high TB incidence such as prisoners **[9]** in notifications are unlikely to explain all observed increases.

Increases in tuberculosis notifications are likely to reflect a combination of socio-economic difficulties leading to impoverishment of some population groups and to disruption of health services including tuberculosis control programmes. Delays in diagnosis and treatment may result in increased transmission of tuberculosis infection, and inadequate treatment may increase the probability of recurrence and the emergence of drug resistance, as suggested by the high proportions of multi-drug resistance reported from Baltic countries (see below and **[4])**.

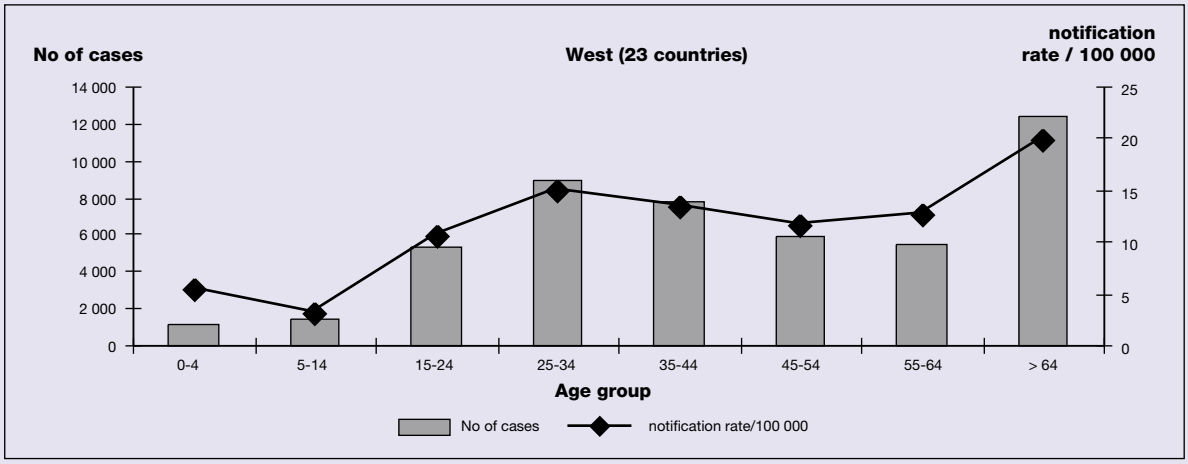
In several Eastern European countries, HIV infection is spreading at alarming rates **[13]**. Although AIDS incidence is still considerably lower than in western Europe the ongoing large scale HIV epidemics represent a serious threat for TB control and their impact on the incidence of tuberculosis could be substantial in the near future **[10]**.

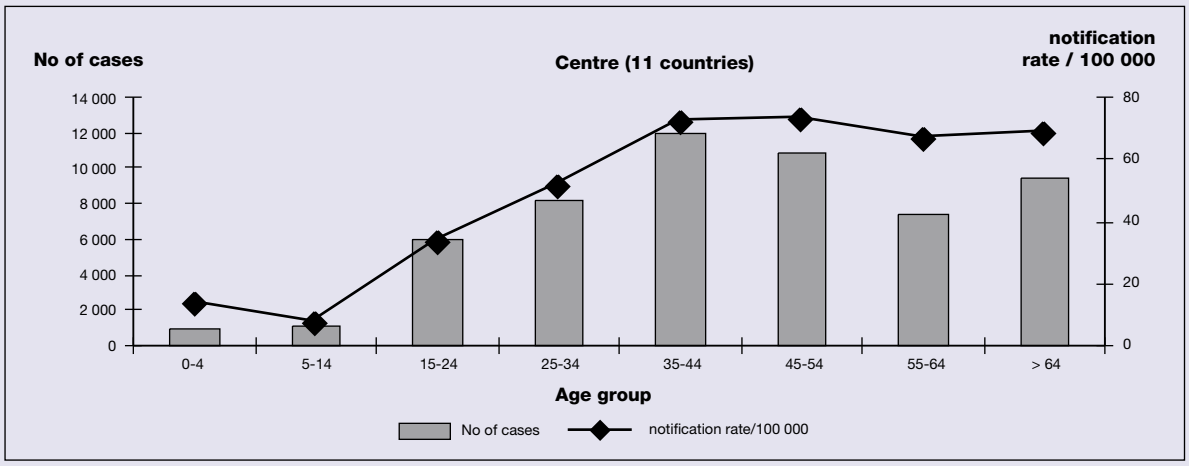
4.3 New and recurrent cases

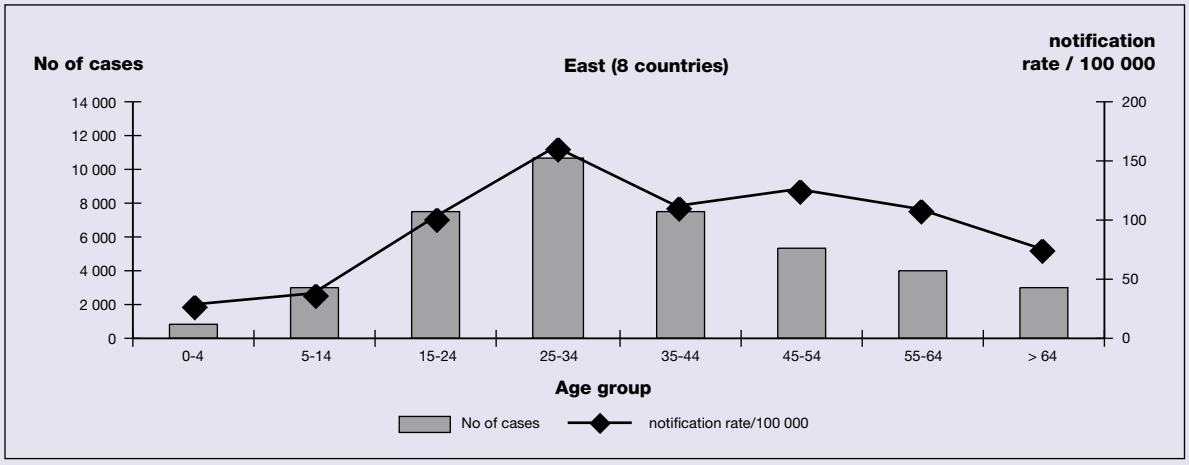
Information on previous tuberculosis diagnosis was available in 43 countries (Table 6). Overall, 88% of cases notified in 1998 were new cases, 10% were recurrent cases and 2% had no information on previous TB diagnosis. In four countries, 25% or more of cases were reported with unknown previous diagnosis (Croatia, Ireland, Spain and United Kingdom). Excluding these countries, the proportion of recurrent cases notified was 10% in the West, 13% in the Centre and 9% in the East. The proportion of recurrent cases ranged widely across countries and was lower than 5% in 8 countries, between 6 and 13% in 21 countries and 16 to 38% in 10 countries, without any clear geographic pattern. The slightly higher proportion of recurrent cases in the Centre (13%) is due to the higher proportion of recurrent cases notified in Turkey (19%), where 30% of the cases notified in the Centre were notified.

FIGURE 2

Number of TB cases and notification rates by age group, 1998, WHO European Region







Differing proportions of recurrent cases cannot easily be interpreted in terms of performance of the TB programmes. Indeed, differences between countries may be due to the differing recommendations for including recurrent cases in TB notifications (see section 3.2) and on the adherence to these recommendations, on which little information is available. For example, the high proportion of recurrent cases notified in Norway (29%) is mainly due to elderly patients with a previous episode of tuberculosis untreated (in the years before availability of anti-TB drugs) and not to failure of anti-TB treatments. The high proportion of recurrent cases notified in Georgia (26%), decreasing compared to 1997 (36%), may be due to inclusion in notifications of prevalent cases under treatment. On the opposite, proportions of recurrent cases below 5% (e.g. in five countries in the East), may be due to under-notification of recurrent cases.

4.4 Sex and age

The distribution of cases by age and sex as well as the age specific notification rates by sex varied considerably across areas (Figure 3) and countries (see country profiles).

Among the 40 countries which provided information on sex, 64% of the tuberculosis cases notified were male. The number of male cases per one female case (sex ratio) was 1.8 overall, ranging from 1.6 in the West (excluding Spain, sex not reported for 27% of cases) to 1.7 in the East and to 2.1 in the Centre. The sex ratio varied between countries, ranging from less than one in Iceland and Sweden to 4.8 in Armenia. Thirteen countries, of which 9 are situated in the Centre or East, reported at least twice as many cases in males than in females (Table 7). The sex ratio increased with age, peaked for the 45-64 years age group and then decreased for the older age groups. For the whole WHO European Region, it was 1.2 among patients under 15 years of age, 1.8 between 15 and 44 years, 2.7 between 45 and 64 years and 1.8 over 64 years.

A total of 40 countries provided information on the age and sex distribution of all notified cases (new and recurrent) according to requested age groups (Table 8, Figure 2). Paediatric cases (0-14 years of age) accounted for 6% of the reported cases of which one third were among children under 5. Proportions of cases by age group varied significantly across geographic areas. The age group 15-44 years represented 43% of the cases notified in the West, 47% of cases in the Centre and 61% of cases in the East. The elderly (64 years and over) represented 21% of cases in the West, 17% in the Centre and 7% of cases in the East.

Age specific notification rates were highest in the age group 65 years or over in the West, were similar from age 35 in the Centre and were highest in the age group 25-34 in the East (Figure 2). The highest notification rate observed in the older age group in countries of the West of Europe is mainly due to reactivation of old *M. tuberculosis* infection.

Among children, notification rates were similar in males and females in all countries. In the West and in the Centre, rates were higher in children under 5 compared to older children, probably reflecting higher risk of developing tuberculosis after infection in younger children compared to older children **[14]**. However, in the East, this was not the case, suggesting a possible under-reporting of cases in children under 5 in some countries.

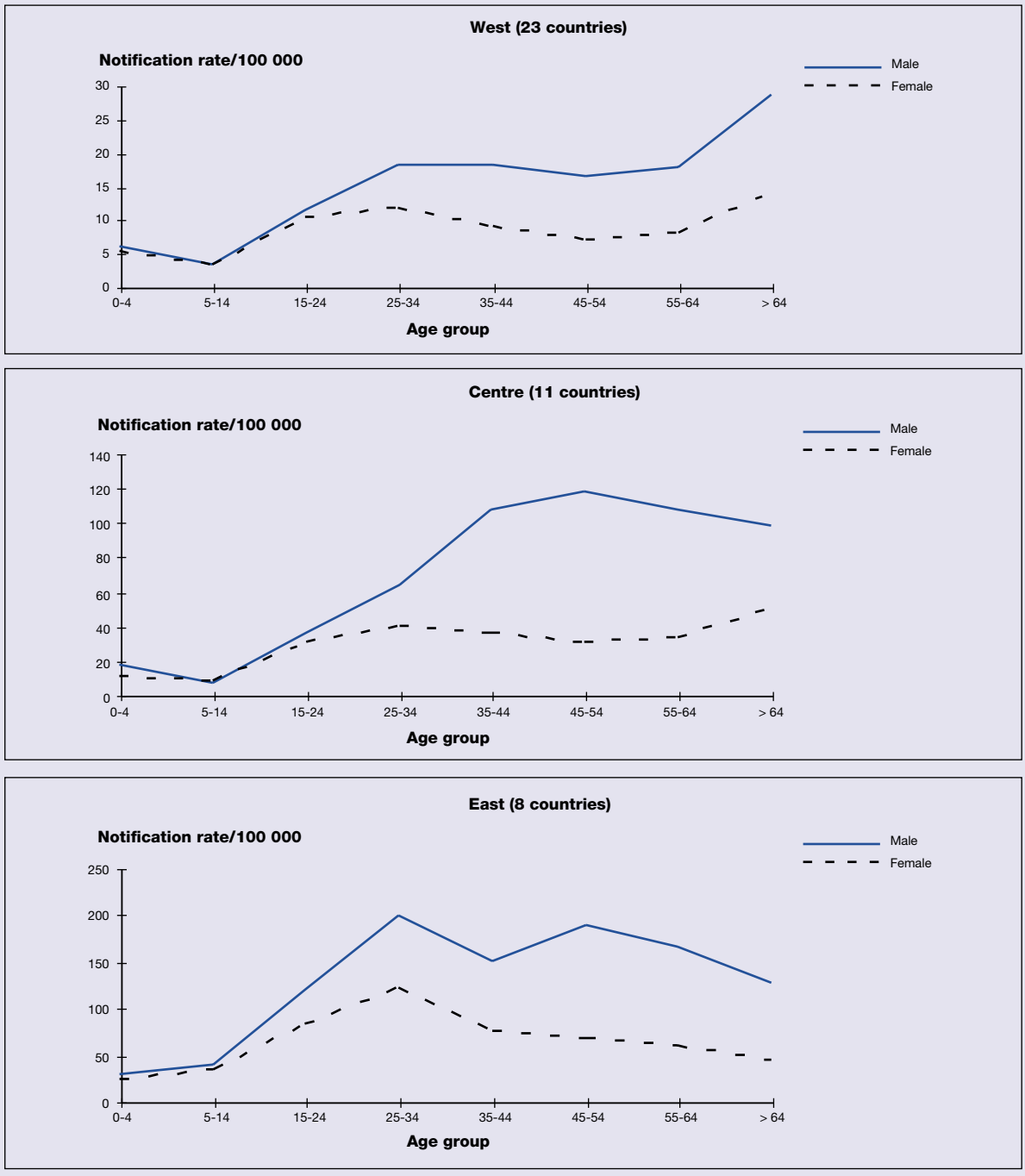
In the West, age specific notification rates among males were relatively stable across the age groups 25-34 to 55-64 and were highest among the elderly. In females, rates were highest in the age group 65 years or over. In the Centre, rates increased rapidly after age 14 in males but less rapidly in females, resulting in large sex differences, particularly between 35 and 64 years of age. In the East, rates peaked in the 25-34 age group in both sexes, with a second peak in group 45-54 among males, and decreased in older age groups.

Higher notification rates in males compared to females observed in all countries may reflect a higher prevalence of infection in males **[15]**. The larger difference in notification rates by sex observed in countries of the Centre and of the East could be also partly explained by an underreporting of females in some countries probably due to differences in access to health services **[16]**.

Additionally some of the country variations in the age distribution of cases and in age-specific notification rates were related to differences in the distribution of cases by geographic origin. In the 32 coun-

FIGURE 3

Number of TB cases and notification rates by age group, 1998, WHO European Region



tries with information available on patients' geographic origin, the proportion of cases aged 15 to 44 years was much larger in foreigners than in nationals (53% versus 16%), while the proportion aged over 44 years was lower (45% versus 81%), and proportions of male cases were higher among patients of foreign origin. These differences influence age-specific notification rates in countries with larger proportions of cases in foreigners, mostly situated in the West (see section 4.5).

4.5 Geographic origin

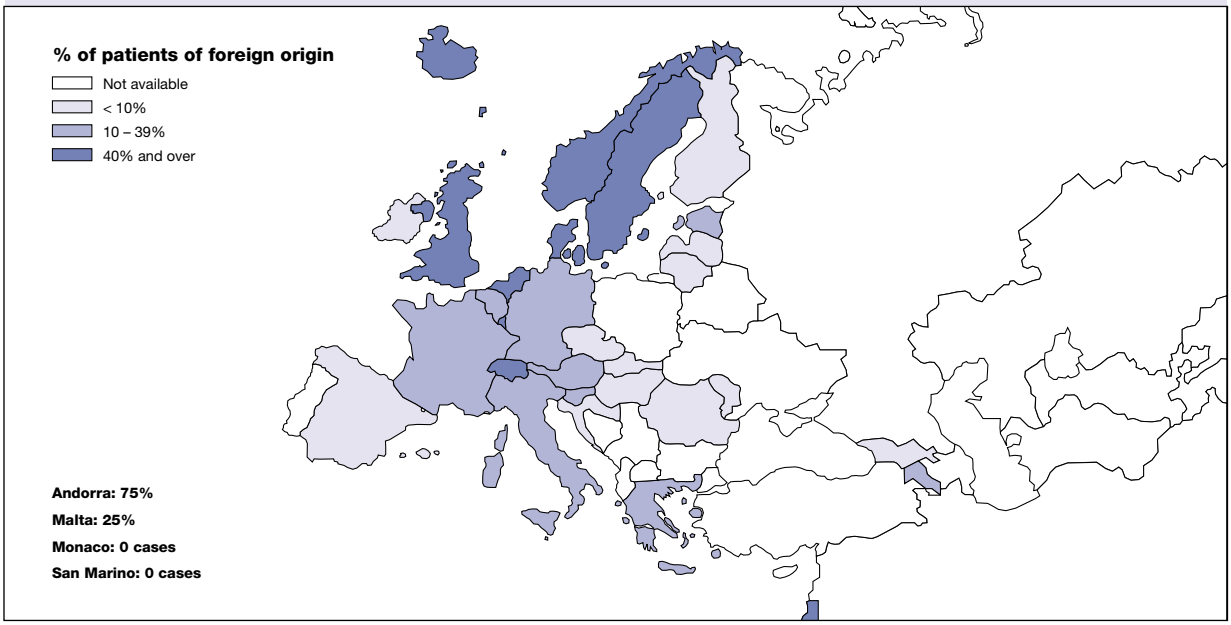
Among the 41 countries including patients of foreign origin in TB notifications (Table 3), 32 provided information on geographic origin, based on birthplace in 22 countries (recommended) or on citizenship in 10 countries.

Information was more frequently available in countries situated in the western part of Europe. All countries, except Portugal, provided information in the West, seven countries in the Centre and six countries in the East (Table 9, Map 3). The proportion of cases in foreign patients was 27% in the West and much lower in the Centre (1%) and in the East (4%). The proportion of missing information on geographic origin was less than 3 % in all countries except in France (14%), Switzerland (17%), Croatia (42%) and Spain (59%). When excluding Spain and Croatia, the proportion of TB cases in patient of foreign origin did not change in the Centre but increase to 33% in the West. In ten countries in the West, patients of foreign origin represented more than 40% of notified cases (Andorra, Denmark, Iceland, Israel, Luxembourg, Netherlands, Norway, Sweden, Switzerland and United Kingdom) (Map 3).

Comparisons of the proportion of patients of foreign origin across countries should be made with caution, taking into account differences in notification of specific groups of foreigners (e.g. asylum seekers, illegal immigrants), possible under-notification of patients of foreign origin, variations in immigration patterns, in policies regarding acquisition of nationality and in tuberculosis screening programmes for immigrants.

Trends in the proportion of TB cases in patients of foreign origin were calculated for 13 countries with available information, with at least 50 cases notified

MAP 3 **Proportion of tuberculosis cases notified in patients of foreign origin, 1998, WHO European Region**



and more than 10% of TB cases notified in foreign patients in 1998. Between 1995 and 1998, the proportion of TB cases in patients of foreign origin:

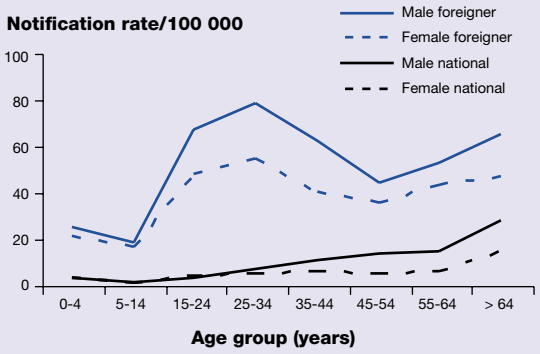
- increased regularly until 1997 and remained stable or decreased between 1997 and 1998 in Denmark, Norway and Sweden
- increased during the whole period in Belgium, Finland, Germany, Italy and Netherlands
- was relatively stable in France, Slovenia and Switzerland.

In all countries with increasing number of cases among patients of foreign origin, except Israel, the number of cases in nationals decreased during the period 1995 to 1998. However, the proportion of patients of foreign origin is difficult to interpret in Israel since the State of Israel was created recently (1948) and immigration has played and still plays a major role in the population structure of the country.

Notification rates were calculated separately for nationals and for patients of foreign origin in 13 countries with a proportion of cases in patients of foreign origin over 5%, that could provide population figures for foreigners in 1998 (Austria, Belgium, Denmark, Finland, France, Germany, Iceland, Ireland, Luxembourg, Netherlands, Norway, Slovenia and Sweden). Rates were consistently higher in foreigners than in nationals (from 1.3 times higher in Ireland to 33 times higher in Netherlands). This variation may be explained by differences in migration patterns. For example the relatively low differences in Ireland and Slovenia may results from migration coming from neighbouring countries with comparable TB incidence. By contrast, in Denmark and the Netherlands there is immigration from higher incidence countries, which could explain a notification rate under 4 per 100 000 in nationals and of 99 and 118 per 100 000 respectively in patients of foreign origin. Notification rates in the foreign population should be interpreted with particular caution considering the difficulties in obtaining accurate figures on the population of foreign origin.

Age specific rates by geographic origin were calculated in the 11 countries of the West where the proportion of patients of foreign origin is highest. Large differences in age-specific rates by geographic origin were observed (Figure 4). In the population of foreign origin, the notification rates clearly peaked in the 25-34 year age group, at a higher level in males than in females, then decreased before increasing again in the oldest age group (>64 years). Among nationals, the adult rates increased regularly with age without a peak in young adults, and were constantly at a much lower level than those in the foreign population. Differences between males and females were more marked among the foreign population than among nationals under age 55.

FIGURE 4 TB notification rates by age group, sex and geographic origin, 1998, West *



* Austria, Belgium, Denmark, Finland, France, Germany, Iceland, Luxembourg, Netherlands, Norway, Sweden

Nineteen countries in 1998 provided information on the specific country of origin of patients (Table 10). Overall, 24% of the 7055 foreign born or foreign citizen patients were from Europe (WHO European Region), 34% from Asia, and 33% from Africa.

As in the previous year, foreign patients in 1998 had very diverse origins, but almost half (47%) were born in, or were citizens of, one of the following five countries: Somalia (12%), India (11%), Pakistan (10%), Morocco (6%), Yugoslavia (4%), and Bosnia-Herzegovina (4%). The large majority of patients from India and Pakistan (84%) were reported in the United Kingdom. Patients form Somalia were reported mostly in Denmark, the Netherlands and the United Kingdom (77%) and 95% of patients from Morocco were reported in Italy, the Netherlands and the United Kingdom. Patients from Bosnia-Herzegovina and Yugoslavia were mainly (76%) notified in Austria, Croatia, Slovenia and Switzerland.

4.6 Site of disease

Information on site of disease was provided by 42 countries, based on the recommended pulmonary classification in 31 countries and on the respiratory classification in 11 countries (see technical note). The proportion of cases with unknown information on site of disease was less than 3% in all countries, except in Greece (6%). The overall proportion of pulmonary / respiratory cases was 75% in the West (excluding Spain where only meningeal cases are notified among extra-respiratory cases (range 63 - 84 %) compared to the Centre (88% ; range 56 - 96%) and to the East, where pulmonary/respiratory cases represented at least 90% of cases notified in all countries except Georgia (73%) (Table 12).

Information on both major and minor site of the disease was provided by 12 countries for a total of 37 610 patients (Austria, Belgium, Estonia, Iceland, Luxembourg, Malta, Norway, Romania, Slovakia, Slovenia, Switzerland and the United Kingdom, except Scotland) (Table 2). Pulmonary tuberculosis could be reported as a major site only, whereas extra-pulmonary localisations could be reported either as major sites (if not associated with pulmonary tuberculosis) or as minor sites (if associated with another localisation). A pulmonary localisation was reported in 80% of the patients. Pleural TB were reported as major or minor sites in 11% of the patients and lymphatic extra thoracic localisation in 5%. All other sites were reported in less than 2% of the patients. Meningeal tuberculosis was reported for 254 patients (0.7%).

The site of disease varied by age group (Table 2). The proportion of pulmonary TB increased with age and was significantly higher among patients aged over 15 years than among younger patients. Lymphatic intrathoracic tuberculosis as well as meningitis were more frequently reported in children under 15 years (4 to 4.8%) compared to adults (less than 1%). Pleural tuberculosis was more frequent among children (less than 15 years of age) and adults (15 – 44 years) than among patients aged over 45 years.

The site of disease varied also by sex. As in 1997, among patients over 15 years of age, women were 1.8 times more likely than men to have extra pulmonary TB without pulmonary localisation (28% versus 15%).

TABLE 2 Major and minor sites of TB disease by age group, 12 countries* reporting individual data

Major or minor site of disease †	Age group (years)							
	0-14		15-44		45 and over		Total ‡	
	N	(%)	N	(%)	N	(%)	N	(%)
Pulmonary	1 224	(59.6)	16 177	(80.0)	12 775	(83.4)	30 200	(80.3)
Pleural	245	(11.9)	2 563	(12.7)	1 181	(7.7)	3 998	(10.6)
Lymphatic intrathoracic	390	(19.0)	233	(1.2)	108	(0.7)	732	(1.9)
Lymphatic extrathoracic	169	(8.2)	1 018	(5.0)	634	(4.1)	1 822	(4.8)
Spine	15	(0.7)	133	(0.7)	119	(0.8)	267	(0.7)
Bone/joint other than spine	39	(1.9)	142	(0.7)	202	(1.3)	384	(1.0)
Meningeal	70	(3.4)	104	(0.5)	80	(0.5)	254	(0.7)
CNS § other than meningeal	3	(0.1)	20	(0.1)	10	(0.1)	33	(0.1)
Genito-urinary	5	(0.2)	124	(0.6)	353	(2.3)	482	(1.3)
Peritoneal/digestive	12	(0.6)	223	(1.1)	135	(0.9)	372	(1.0)
Disseminated ||	45	(2.2)	203	(1.0)	209	(1.4)	457	(1.2)
Other	40	(1.9)	290	(1.4)	286	(1.9)	616	(1.6)
Unknown	7	(0.3)	23	(0.1)	18	(0.1)	48	(0.1)

Note: added % exceed 100% because some patients were reported with more than one site of disease
* Austria, Belgium, Estonia, Iceland, Luxembourg, Malta, Norway, Romania, Slovakia, Slovenia, Switzerland, United Kingdom (except Scotland)
† Except for pulmonary localisation, which is always classified as major site
‡ Including 38 cases with unknown age
§ CNS = Central Nervous System
|| includes: – miliary tuberculosis
– tuberculosis in which *M. tuberculosis* complex has been isolated from the blood
– tuberculosis of more than two organ systems

Differences were also observed by geographic origin. Data were analysed for 16 countries providing individual data with more than 5% of TB cases in patients of foreign origin, of which 14 are situated in the West. Croatia was excluded from the analysis due to the high proportion of missing information on geographic origin (42%). In patients of foreign origin, extra pulmonary tuberculosis (without pulmonary localisation) were significantly more frequent than in nationals (37% vs 18%) while pulmonary cases were less frequent (63% vs 82%).

4.7 Bacteriology results

4.7.1 Culture

Aggregate data by culture result were collected for the first time for 1998. Data were provided overall from 38 countries, in seven of which access to culture is limited to some areas of the country (Table 11). Data from Croatia and Germany were provided through a complementary national survey including respectively 65% and 60% of cases notified in 1998. Overall, 50% of the cases notified in 1998 were culture confirmed.

In the 31 countries with access to culture in the whole country, proportions of culture confirmed cases were 57% in the West (range: 24-100%), 50% in the Centre (range 31-77%) and 54% in the Baltic countries (range: 49-66%). In countries providing individual data, proportions of culture positive cases were higher among pulmonary cases compared to extrapulmonary cases in the West (63% vs. 50%), in the Centre (61% vs. 9%, due to very low proportions of culture positive extrapulmonary cases in the Czech Republic and Romania) and in Estonia (68% vs. 37%).

The overall proportion of culture positive cases was similar in the 21 countries using culture only (49%) and in the 10 countries using both culture and/or sputum smear (51%) to classify cases as definite. However, it should be noted that several countries (Table 11) changed the definition of definite cases (culture positive only) in 1998, and the impact of this change on diagnostic practices and on notifications may not yet be fully visible.

Negative culture and unknown culture result / culture not performed were provided as separate categories from 29 countries (Table 11). In these countries, 46% of cases were culture positive, 22% were negative and 32% had unknown results or had no culture performed. The proportion of cases with unknown culture result or culture not performed was 25% or higher in 12 countries, including three countries with limited access to culture.

In countries providing individual data it was possible to separate cases with culture done but results unknown (> 10% of cases in Italy, Malta, Romania and the United Kingdom), culture not done (ranging from 0 in 10 countries to 10% in Romania, 25% in Malta and 30% in Austria) and no information on culture (6% overall, ranging from 0 in 7 countries to 22% in Finland and Italy and 48% in the Netherlands, due to incomplete follow up at time of data collection).

The differences in the proportion of culture positive cases between countries may be explained by differences in diagnostic practices or in notification systems. High proportions of cases with unknown culture result or culture not performed may be due to one or more of the following reasons:

- culture may not be available in the whole country, as in Romania.
- culture is not requested routinely for all suspected cases or not reported, especially in countries in which sputum smear is also accepted for bacteriological confirmation of the cases.
- laboratories do not participate in the case notification system (e.g. France) or are requested to report only positive culture results (e.g. Denmark and Finland). In the latter case, culture results are then recorded in the notification data set either as positive or as unknown, resulting in a high proportion of cases with unknown information on culture.
- data are still incomplete at the time of European data collection, for example in the Netherlands, where culture results are actively collected at a later time with treatment outcome results.

Time trends in the proportion of culture confirmed cases could be analysed in countries providing individual data but are inconclusive due to the varying numbers of cases with missing information.

4.7.2 Sputum smear

Results of sputum smear for pulmonary / respiratory cases were provided from 42 countries (Table 13). Overall, the proportion of cases with positive sputum smear was higher in the Centre (average 52%, range 28-66%) compared to the West (41%; range 26-60%) and the East (29%; range 20-48%).

In countries providing individual data, data could be analysed according to both culture and sputum smear results (Table 14). Among pulmonary cases with positive culture, the proportion of cases with positive sputum smear ranged from 33% to 75% with a higher proportion in countries in the Centre and East (67%) compared to the West (53%).

Several factors may affect the proportion of sputum smear positive cases including the classification used for definite cases and the use of diagnostic procedures (cases with a positive smear on bronchoalveolar lavage (BAL) may not have a subsequent sputum smear examination and are not classified as positive smear cases.

4.7.3 Bacteriologically confirmed cases

The proportions of cases with positive culture and / or positive sputum smear (bacteriologically confirmed cases) were calculated in countries providing individual data (Table 14). Overall, around two thirds of all notified cases with information on site of TB were bacteriologically confirmed (West: 64%; Centre 66%; Estonia: 68%). Proportions of bacteriologically confirmed cases among pulmonary cases were 75% overall (West: 73%; Centre 76%; Estonia: 71%).

DRUG SUSCEPTIBILITY TESTING (DST)

5.1 Data presentation

Drug susceptibility testing (DST) results as well as data on the organisation of drug resistance surveillance were requested from all countries in the West, the Centre and from Baltic countries in the East. Data were provided from 29 countries: 18 countries in the West, 8 in the Centre and the three Baltic countries.

DST results are presented divided in three groups of countries (Tables 15-18):

- 21 countries providing DST results for > 35% of all notified cases
- 5 countries providing DST results for ≤ 35% of notified cases
- 3 countries providing DST results not related to TB notifications

This grouping of countries aims to avoid over-interpretation of data and comparison of data with different characteristics and meaning. In the 26 countries providing results on notified cases, and particularly in those providing individual DST results, it is possible to compare cases with DST results to other notified cases in order to assess the representativeness of drug resistance data. The five countries providing DST results for <35% of notified cases reported low proportions of culture positive cases or provided DST results for a limited proportion of culture positive cases which may both result in low representativeness of DST results.

In the three countries reporting data not related to TB notification, information on other TB cases diagnosed in participating laboratories or clinical Centres is limited. Additional information needed to assess the representativeness of results was not collected systematically or not available, and data from these countries should not be considered as representative of the country situation.

Proportions of resistant cases presented in Tables 16-18 include cases with resistance to one drug alone or in any combination with resistance to the three other drugs on which information was collected. Proportions of drug resistant cases are calculated using as a denominator cases with available DST results. Proportions of cases resistant to ethambutol or streptomicin are not shown for some countries because resistance to these drugs was not systematically tested in all cases.

5.2 Laboratory practices

Among the 29 countries providing DST results, culture was available in the whole country in 25 countries and only in some areas in Albania, Greece, Romania and Yugoslavia. In all the countries, DST was performed using the internationally recommended methods **[2]** by a single laboratory in 10 countries, 2-10 laboratories in 10 countries and more than 10 laboratories in nine countries (Table 15). Among the 18 countries with more than one laboratory performing DST, a national proficiency testing scheme existed in 14 countries (not in Greece, Ireland, Netherlands and Yugoslavia).

A national Reference Laboratory (NRL) for *Mycobacteria* existed in all countries except Ireland, Malta and Yugoslavia. The NRL (or another laboratory) had participated, in 1998 or in a previous year, in an international proficiency testing programme in all countries except Greece, Luxembourg and the FYR of Macedonia. The proportion of agreement with the supranational reference laboratory for isoniazid and rifampicin (information provided from 20 countries) was 100% in 14 countries, 90-98% in 5 countries and 65% in one country (not shown).

5.3 Drug resistance results in 1998

5.3.1 Countries providing DST results for notified cases

In the 26 countries providing data on notified cases (Table 15), DST results refer to culture positive cases notified in the country (shown in Table 11) except:

- Germany, where data were collected through a complementary survey carried out on TB cases notified in 290/430 public health services, covering all regions and including 60% of cases notified in the country;

- Romania and Yugoslavia, where culture is available only in some regions and DST results were provided on TB cases notified respectively from 13/47 regions (30% of notified cases) and from the region of Belgrade (29% of notified cases).

- the Czech Republic, Israel, and Yugoslavia, where results were provided on pulmonary cases only.

In other countries, minor differences between Tables 11 and 15 in the numbers of culture positive cases may be due to later data collection of DST results compared to other bacteriological data.

The proportion of culture positive cases among notified cases varied widely across countries (range: 25-100%) and was lower than 50% in Albania, Hungary, Lithuania, Macedonia and Malta. DST results were available for over 97% of culture positive cases in 17 countries, 91% in Slovenia and the United Kingdom, 87% in Switzerland, 78% in Germany, 72% in Finland, 62% in the Czech Republic, 49% in Hungary and 46% in Romania. Because of the low proportion of culture positive cases, missing DST results, or both, the proportion of notified TB cases with available DST results was 35% or lower in five countries (Albania, Hungary, Macedonia, Malta and Romania, shown separately in Tables 15-18).

Countries providing DST results for > 35% of notified cases

Overall, in the 21 countries providing DST results for >35% of TB cases notified, 28.511 TB cases were notified, 17,692 (62%) were culture positive and 15,593 (55%) had DST results available. In these countries, compared to the other TB cases notified in 1998, cases with DST results were more frequently males (except in the Netherlands, Norway, Slovakia and Switzerland), aged 25-44 years and, in most western countries, of foreign origin.

Three of the countries (Czech Republic, Finland and Israel) did not provide DST data by previous treatment status. As previous treatment is a major determinant of drug resistance data from these three countries cannot be interpreted reliably. Among countries providing individual data, the proportions of cases previously treated were slightly lower among cases with DST results (7%) compared to the other notified cases (9%) except in Estonia (18% versus 13%) and Slovakia (21% versus 15%).

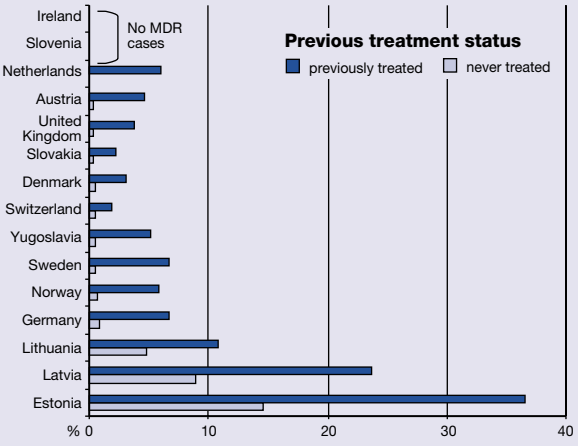
Overall results

In the 18 countries with at least 50 TB cases notified in 1998, the overall proportions of resistant cases were much higher in the Baltic countries and in Israel compared to the other 17 countries in the West and in the Centre (Table 17). Proportions of cases resistant to at least isoniazid were 13-30% in Baltic countries and Israel compared to 1-8% in the other countries (median 4.4%). For rifampicin, proportions of resistant cases were 7-20% in the Baltic countries and Israel compared to 0-2.5% (median 0.9%) in the other countries. Proportions of multidrug resistant (MDR) cases were 6-18% in the Baltic countries and Israel and 0-2.2% (median: 0.7%) in the other countries. For ethambutol proportions of resistant cases were 2-19% in the Baltic countries and Israel compared with 0-2% (median 0.4%; Germany excluded). For streptomicin proportions were respectively 12-35% compared with 1-12% (median 2%; Austria, Germany, Norway, Switzerland and United Kingdom excluded).

Previous treatment

Among cases with DST results, the proportions of previously treated cases were 18-22% in the Baltic countries and ranged from 7% in Denmark to 21% in Slovakia (median: 9%) in the countries in the West and in the Centre. Proportions of drug resistant cases were lower among patients never treated compared to patients previously treated (Table 17). For example, in the Baltic countries proportions of cases resistant to isoniazid were 12-25% among cases never treated and 17-50% among cases previously treated. In the other countries proportions were respectively 0.7-7.0% among cases never treated (median 3.9%) and 0-18% (median: 10%) among cases previously treated. Proportions of MDR cases among cases never treated were 5 - 15% in the three Baltic countries. and below 1% in the countries in the West and in the Centre (Figure 5).

FIGURE 5 **Proportion of multi drug resistant cases in countries providing DST results for > 35% of TB cases***



* and notifying at least 50 cases in 1998

The proportion of drug resistance among patients previously treated, together with the overall proportion of patients previously treated among notified patients, reflects to a large extent the quality of anti-tuberculosis treatment. However, in data presented here, numbers of resistant cases previously treated were small and proportions of resistant cases were higher in foreign-born patients, in which previous treatment may have been taken place in the countries of origin.

Geographic origin

Another important determinant of drug resistance levels is the geographic origin of TB cases, because patients born in countries with high TB incidence have a higher probability of having both primary and acquired drug resistances. DST results by geographic origin were not provided from Latvia and Yugoslavia (Table 18). Among the countries in the Centre and in the West, foreigners represented from 0 (Czech Republic and Slovakia) to 87% (Israel) of tested cases with information on geographic origin (median: 54%).

In countries in the West and Centre with >50 TB cases notified in 1998, the proportions of resistant cases were consistently higher among patients of foreign origin, except in the Netherlands and Slovenia where proportions were comparable. For example the proportions of MDR cases were 0-2.5% (median 0.3%) among nationals and 0-9% (median 1.4%) among patients of foreign origin which represented 76% of MDR cases diagnosed in these countries. Patients of African or Asian origin had higher proportions of drug resistance compared to patients originating from foreign countries in Europe (not shown).

Differences in drug resistance by geographic origin should not be over-interpreted. Drug resistance may result from infection or treatment both in the country of origin or in the country of diagnosis. In addition, the numbers of patients were too small to allow meaningful comparisons between individual countries, patterns of migration into European countries differ and no information is available on time of immigration.

Drug resistance among patients never treated and born in the country / was analysed in individual data available from 11 countries, as an indicator of transmission of drug resistant bacilli within the country. In Estonia, proportions of drug resistant cases were also slightly higher among patients under 35 years of age compared to older patients (36% versus 20% for isoniazid, 23% versus 12% for rifampicin). In the other countries, the proportions of resistant cases were higher for isoniazid in patient under 35 years (average: 3.2%) compared to older patients (average 2.3%) and were similar in the two age groups for rifampicin and for multidrug resistance. The higher level of drug resistance observed among younger patients in Estonia seems to indicate a high level of transmission of drug resistant tubercle bacilli during recent years.

Countries providing DST results for <35% of notified TB cases

Among the five countries with DST results available on less than 35% of notified cases, overall proportions of resistant cases were high in Hungary and Romania (MDR cases 5% and 4% respectively) and, as in other countries, lower among cases never treated (MDR cases 4% and 2% respectively) compared to cases previously treated. However, due the low proportion of culture positive cases with DST results (Hungary, Romania), the partial geographic coverage (Romania), and the lack of results

by previous treatment status (Albania, FYR of Macedonia) data from these countries should not be considered representative of the country situation.

5.3.2 Countries providing DST results not related to TB notifications

In France, Greece and Italy, DST results were provided from a source not linked to TB notifications (Table 15). Very little information is available on the patient population from which cases with DST results derive, and data may include an unknown proportion of cases not notified in 1998. Data from these countries represent selected samples of TB cases possibly not representative of the drug resistance situation in the countries.

In France data were collected through a network of 19 university hospital laboratories in 11/22 regions. DST results were available for 99% of culture positive cases diagnosed in those laboratories. However, information on other TB patients (not confirmed by culture) diagnosed in the clinical centres referring to the participating laboratories is not available; regional representativeness of data provided could not be estimated by comparison with notifications, due to incomplete data on culture results in France. Overall, resistance level in data from France are similar to those reported from other countries in western Europe but their representativeness should be assessed carefully.

In Greece, DST data are provided by all the three laboratories, which perform DST. However DST is performed systematically only for recurrent cases, which are rarely notified (2% of cases in 1998). This probably results in overestimated proportions of resistant cases. Total numbers of culture positive cases diagnosed in these Centres and data by previous treatment status were not available. Therefore the levels of resistance, higher compared to other countries in the West and in the Centre, are difficult to be interpreted.

In Italy, data derive from a subset of 46 laboratories and clinical centres from 13/20 regions. Proportions of resistant cases are very high (e.g. 37% of MDR cases among previously treated cases), suggesting that participating Centres are likely to care for complex cases with higher probability of resistance (Table 17). Neither the total number of TB cases nor the total number of culture positive cases diagnosed in participating centres were available. Therefore, data from Italy should not be considered as representative of the country situation.

5.4 Discussion on drug resistance data

DST results were presented in detail and compared for countries where proportions of culture confirmed cases are high and DST results are available for the majority of culture positive cases. Among these countries the level of drug resistance were found to be relatively low in the West and the Centre, particularly among patients never treated. Levels of drug resistance among patients previously treated are higher and more variable, partly due to differences in the recommendations for notification of recurrent TB cases. Data show consistently lower proportions of resistant cases among patients born in (or citizens of) the country of report compared to those originating from foreign countries. DST results presented indicate that tuberculosis control in general and tuberculosis treatment remain of good quality in many countries in the West and in the Centre. Standardised complementary information should be collected from countries in which DST results are not related to TB notification or have limited geographic coverage, in order to assess the representativeness of DST data provided.

Resistance levels were much higher in Baltic countries, among both never treated and previously treated cases indicating that in recent years resistant strains have emerged and have been transmitted in the population as a consequence of sub-optimal performance of treatment programmes. Data from other former Soviet Union countries will be collected from 1999 and should provide a more complete picture of the situation in Eastern Europe.

Although data on DST should not be taken as representative for Europe as a whole, and data standardisation and presentation need to be further improved, they demonstrate that surveillance of drug resistance as part of the tuberculosis notification system is feasible and can provide a relevant contribution to the evaluation of TB programmes.

REFERENCES

1. Rieder H., Watson J., Raviglione M., *et al*. Surveillance of tuberculosis in Europe. Recommendations of a Working Group of the World Health Organization (WHO) and the European Region of the International Union Against Tuberculosis and Lung Disease (IUATLD) for uniform reporting on tuberculosis cases. *Eur Resp J* 1996; 9:1097-1104.

2. Schwoebel V., Lambregts-van Weezenbeeck C.S.B., Moro M.L., *et al*. Standardisation 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. *Eur Resp J* 2000; 16: 364-371.

3. World Health Organization Global tuberculosis control. WHO Report 2000. Geneva, Switzerland, WHO/CDS/TB/2000.275.

4. World Health Organization. Anti tuberculosis drug resistance in the world. Report No. 2 Prevalence and trends. WHO/CDS/TB/2000.278.

5. EuroTB (CESES/KNCV) and the national coordinators for tuberculosis surveillance in the WHO European Region. Surveillance of tuberculosis in Europe. Report on tuberculosis cases notified in 1997, September 1999.

6. United Nations Population Division. Annual Populations 1950-2000 (The 1994 Revision), United Nations, New York, 1994.

7. United Nations Population Division. Annual Populations 1950-2000 (The 1998 Revision), United Nations, New York, 1998.

8. Council of Europe. Recent demographic developments in Europe, France, Strasbourg ,1997.

9. Stern V. (editor); Sentenced to die? The problem of TB in prisons in Eastern Europe and Central Asia. 1999. Int Centre for Disease Studies, London.

10. Perelman M.I. Tuberculosis in Russia. Int J Tuberc Lung Dis 2000 4(12):1097-1103.

11. Raviglione M.C., Sudre P., Rieder H.L., Spinaci S., Kochi A. Secular trends of tuberculosis in Western Europe. *Bull World Health Organ* 1993; 71:297-306.

12. Raviglione M.C., Rieder H.L., Styblo K., Khomenko A.G., Esteves K., Kochi A. Tuberculosis trends in Eastern Europe and the former USSR. *Tubercle Lung Dis* 1994; 75:400-416.

13. European Centre for the Epidemiological Monitoring of AIDS. HIV/AIDS Surveillance in Europe. N°63. Mid-year report 2000. 2001.

14. Comstock G.W., Livesay V.T., Woolpert S.F. The prognosis of a positive tuberculin reaction in childhood and adolescence. *Am J Epidemiol* 1974; 99:131-138.

15. Rieder H. Epidemiologic basis of Tuberculosis control. First Edition, International Union against Tuberculosis and Lung Diseases, Paris 1999.

16. Holmes C.B., Hausler H., Nunn P. A review of sex differences in the epidemiology of tuberculosis. Int J Tuberc Lung Dis 1998; 2:96-104.