

## Tuberculosis and AIDS: European and worldwide perspectives

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Recent studies demonstrate that the impact of HIV infection on the tuberculosis situation may potentially be very serious in all countries where both the prevalence of tuberculosis infection and disease and the risk of HIV infection are high<sup>1,2</sup>. Immunosuppression has always been known to worsen the course of any infection. The HIV infection, a global threat, reduces protection provided by cell-mediated immunity and may therefore change the whole course of tuberculosis epidemiology. According to WHO estimates in 1990, in the world population of 5300 million there were 1700 million people infected with tubercle bacilli and about 9–10 million infected with HIV<sup>3</sup>. Most recent WHO estimates are that in early 1992 at least 10–12 million adults and children worldwide have become infected with HIV since the start of the pandemic, and that by the year 2000 some 30–40 million people will have been infected<sup>4</sup>.

While in the pre-AIDS era usually 5–8% of those infected with tubercle bacilli developed clinical tuberculosis during their life span, there is now a growing evidence that in persons co-infected with HIV the rate of progression to clinical tuberculosis may be several times higher. This evidence is particularly strong in sub-Saharan Africa, but also in some selected population groups in highly developed countries like the USA<sup>2,5,6,7</sup>. Thus with the AIDS pandemic the fact of being infected with tubercle bacilli has become very important and the HIV infection has become the strongest risk factor so far identified for the reactivation of pre-existing tuberculosis infection<sup>2,5</sup>.

### The magnitude of the tuberculosis problem

It is a well-known fact that for many decades tuberculosis in Europe has been declining. The decline in tuberculosis mortality was demonstrated even before all the powerful drugs against tuberculosis became available. In the world as a whole, however, tuberculosis still remains the largest single cause of death, killing 3 million people every year. Other epidemiological indicators, such as incidence of the disease, have always been considered less reliable since they are strongly related to activities of health programmes, like case-finding and treatment. In the 1960s and the 1970s, for example, between 1.0 and 1.8 million new cases of tubercu-

losis were reported annually to WHO, while in the 1980s the number of new cases of tuberculosis reported annually to WHO increased to 2.5 million<sup>3,8</sup>.

Progress in tuberculosis epidemiology allows us to measure the true magnitude of the tuberculosis problem in any given population by using a reliable indicator such as the spread of infection. The annual risk of infection represents the probability for an individual of becoming infected with tubercle bacilli in a one-year period. It can be determined directly from tuberculin surveys of a population known to be uninfected at the start, or indirectly from the prevalence of infection measured, for example, among children in a given age group. It has been demonstrated that there is a linear relationship between the annual risk of infection and the incidence of smear-positive pulmonary tuberculosis, and that 1% of the annual risk of infection corresponds to 50/100 000 new smear-positive cases of tuberculosis developing each year<sup>9,10</sup>. Available data on the risk of infection have recently been collected and compiled<sup>11</sup>. The linear relationship that exists between the annual risk of infection and the incidence of smear-positive tuberculosis indicates also that by knowing one of these variables one can estimate the value of the other.

It is also known that for each smear-positive case of pulmonary tuberculosis there are 1 to 1.2 cases of other forms of tuberculosis, i.e. smear-negative but culture-positive or clinically diagnosed, for example cases in children, who seldom produce sputum, and of extra-pulmonary tuberculosis<sup>3,10</sup>. Table 1 presents the number of smear-positive cases of tuberculosis developing each year in different parts of the world, based on the annual risk of infection<sup>3,12</sup>. To the 4 million new smear-positive cases developing each year worldwide, one has to add another 4 million new cases of other forms of tuberculosis, so that the total number of new tuberculosis cases developing each year is 8 million<sup>3</sup>.

Since the majority of these cases remain undetected and untreated, the prevalence of the disease is at least 2 times the incidence, i.e. 17 millions.

The overall European contribution to the tuberculosis problem is very small. The incidence of all forms of tuberculosis, for Europe as a whole, is about 20 per 100 000 population, and the annual risk of infection about 0.1%<sup>13</sup>. In many European countries the annual decline rate in the risk of

Tab. 1. Number of smear-positive pulmonary tuberculosis cases developing each year-global estimates for 1991.

Region area	Level of annual risk (%) (average) (a)	Annual decline rate (%) (b)	Population in millions (c)	Estimated incidence of smear-positive cases per 100 000 population per year (average)	Estimated number of smear-positive cases per year (average)
1. Highly developed countries	<0.20 (0.1)	> 10	800	5	40 000
2. Other industrialized countries	0.21–0.70 (0.4)	5–10	800	20	160 000
3. Middle income countries (Latin America, North Africa)	0.71–1.50 (1.0)	5–10	600	50	300 000
4. Most Asian countries	1.00–2.50 (2.0)	< 5	1600	100	1 600 000
5. Sub-Saharan Africa and Subcontinent of India	>2	0– 3	1600	125	2 000 000
World total			5400		4 100 000

(a) see references 3 and 12

(b) see reference 3

(c) see references 15 and 16

infection and in the incidence has been in the range of about 10% for the last two or three decades, and a few years ago it was already being claimed that in another three or four decades some of these countries will reach a stage of tuberculosis elimination<sup>10, 13, 14</sup>. It is interesting to note, that the criteria for elimination of tuberculosis, as proposed, are very pragmatic, i.e. that the prevalence of tuberculosis infection will be less than 1% of the total population and that the annual incidence of smear-positive tuberculosis will be 1 per million of the total population or less. For the eradication phase it has been proposed that criteria should be the same as for the elimination phase, but 10 times lower<sup>10, 14</sup>. It means that one can claim the eradication of tuberculosis if the prevalence of tuberculosis infection is lower than 0.1% of the total population and/or the annual incidence of smear-positive tuberculosis is 1 per 10 million population. The purpose of this paper is to assess the possible influence of HIV on tuberculosis in the coming decades, both world-wide and in Europe.

With the AIDS pandemic it has become clear that the indicators for measuring the magnitude of the tuberculosis problem are the prevalence of tuberculosis infection and the annual risk of infection<sup>10, 12</sup>. For any assessment and/or projections on tuberculosis/AIDS interaction the age structure of those infected with tuberculosis is of the utmost importance. The mode of transmission of the HIV infection favours younger age groups and therefore it is important to know the prevalence of tuberculosis infection in persons below 50 years of age, since in practice mainly those below 50 are at the highest risk of becoming dually infected.

## Methods

The prevalence (P) of tuberculosis infection for selected European countries was estimated by using the following formula:

$$P = 1 - (1 - R)^a$$

where R = the average annual risk of infection  
a = the age at which the prevalence is calculated

All the calculations were made for each 10-year cohort of the population of a given country separately. Demographic projections up to the year 2025 were based on WHO data<sup>15</sup> and on data from the UN Demographic Yearbook for 1988<sup>16</sup>. The average annual risk of infection for each of the cohorts was based on data, or estimates, of the incidence of smear-positive tuberculosis at the respective time in the past, assuming that the incidence of 50 per 100 000 is equal to a 1% annual risk of infection. Thus a cohort born in 1920s has been exposed to the risk of infection of that decade and all the next decades. Since in the pre-chemotherapy era the risk of tuberculosis infection was very high, and in order to simplify calculations, for a given cohort the risk that existed during the decade the cohort was born has been used as the average annual risk of infection, with the following modifications. For cohorts younger than 30 years of age an average decline of 7% annually in the risk of infection was assumed, and for those older than 30 years a 3% annual decline was assumed. For the Netherlands the exact data in this regard are available and have been published<sup>14</sup>.

The scientific evidence on the prevalence of dual (Tb+HIV) infection is very limited. According to available estimates from WHO, of the 10 million persons in the world infected with HIV, there are at present about 3 million who are also infected with Tb<sup>3</sup>. To assess the effect of HIV infection on the tuberculosis problem it has been further assumed that among those dually infected, about 10% will develop clinical tuberculosis annually<sup>3</sup>.

It has to be mentioned that most recent WHO estimates on the HIV infection world-wide indicate that by the year 2000 some 30–40 million people will have been infected<sup>4</sup>. Consequently the number of persons dually infected may also be higher. No projections are available for the years beyond 2000 for the numbers who will be HIV infected or dually infected, although there is no doubt about the further rapid spread of HIV infection, particularly in developing countries, which is likely also to have an impact on the tuberculosis problem.

## Results

The prevalence of tuberculosis infection was calculated for the Netherlands, England and Wales, Switzerland, Germany, France, and Poland. The data are summarized in Table 2.

The data confirm that the majority of people in Europe infected with tubercle bacilli are now in the older age-groups, since they were exposed to a high risk of infection in the past. The difference between countries in both total population infected and those below 49 years of age infected is very high, the highest prevalence being more than double the lowest. The age of 49 years as a cut-off point was arbitrarily chosen because, most probably, those below 49 are at the highest risk of HIV infection and if dually infected, at the highest risk of developing clinical tuberculosis.

Among the countries for which the prevalence of tuberculosis infection was calculated, the Netherlands and Poland present the two extremes. Figures 1 and 2 illustrate the age structure of those infected with tuberculosis in these two countries. For the purpose of comparison the situation in Africa in this regard is presented in Figure 3<sup>3</sup>.

It has to be noted that while in Europe about 20 to 40% of the TB infected population is under 49 years of age (average 30%), in Africa about 80% of those infected with tubercle bacilli are less than 49. In terms of the consequences of HIV infection for the tuberculosis problem this fact is of the utmost importance.

The projections of the possible influence of HIV infection on the tuberculosis problem world-wide and for Europe up to the year 2025 are presented in Table 3.

With regard to HIV infection the estimates presented by WHO<sup>4</sup> go as far as the year 2000. In Table 3 both the prevalence of HIV infection and the prevalence of dual Tb/HIV infection for the year 2025 have been arbitrarily chosen on the assumption that in Asia, which has more than half of the world's population, there was a dramatic rise in seroprevalence in the last few years and that by the mid to late 1990s, and probably in the first decades of the next century, more Asians than Africans will be infected each year<sup>4</sup>.

For Europe it has also been assumed that the increase in the prevalence of HIV infection may be the same as in other parts of the world, owing to migration, as well as to a possible dramatic rise in seroprevalence in Eastern Europe. The prevalence of dual infection, however, will rise very moderately, because of the decline in the prevalence of tuberculosis infection due both to the decline in the annual risk of infection and to the natural demographic shift in the coming decades, as presented in Figures 4 and 5 for the Netherlands and Poland respectively.

The data presented in Table 3 indicate that by the year 2000 the 10% breakdown rate among dually infected people will produce 600 000 new tuberculosis cases annually in addition to 8 million cases which will appear without the influence of AIDS/HIV. By the year 2025 the number of additional cases of tuberculosis developing each year due to HIV infection will reach 1.5 million, which will be a 12% increase in relation to the 8 million developing annually without AIDS/HIV.

The figure of 8 million new cases of tuberculosis developing each year without the influence of AIDS/HIV has been taken as stable for the next few

Tab. 2. Prevalence of tuberculosis infection in selected countries by age (estimates for 1990).

Countries	Population total (a) (million)	Population infected with tuberculosis		Proportion of infected (%)
		(million)	% of total	aged more then 50 years
The Netherlands	14.67	2.09	14.3	81.0
England & Wales	50.5	8.90	17.6	80.0
Switzerland	6.5	1.60	24.0	74.0
Germany	77.7	21.8	28.0	72.0
France	55.8	16.3	29.0	72.0
Poland	38.0	12.1	32.0	58.0

(a) see reference 11 and 12

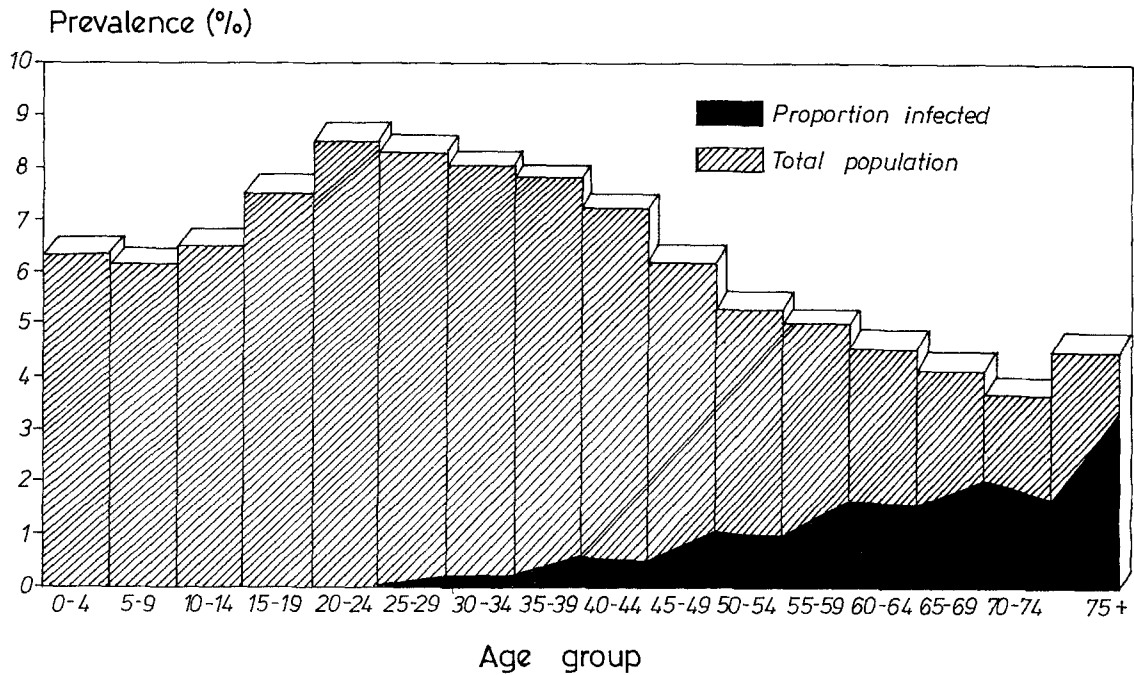


Fig. 1. Prevalence of tuberculosis infection by age – the Netherlands, 1990.

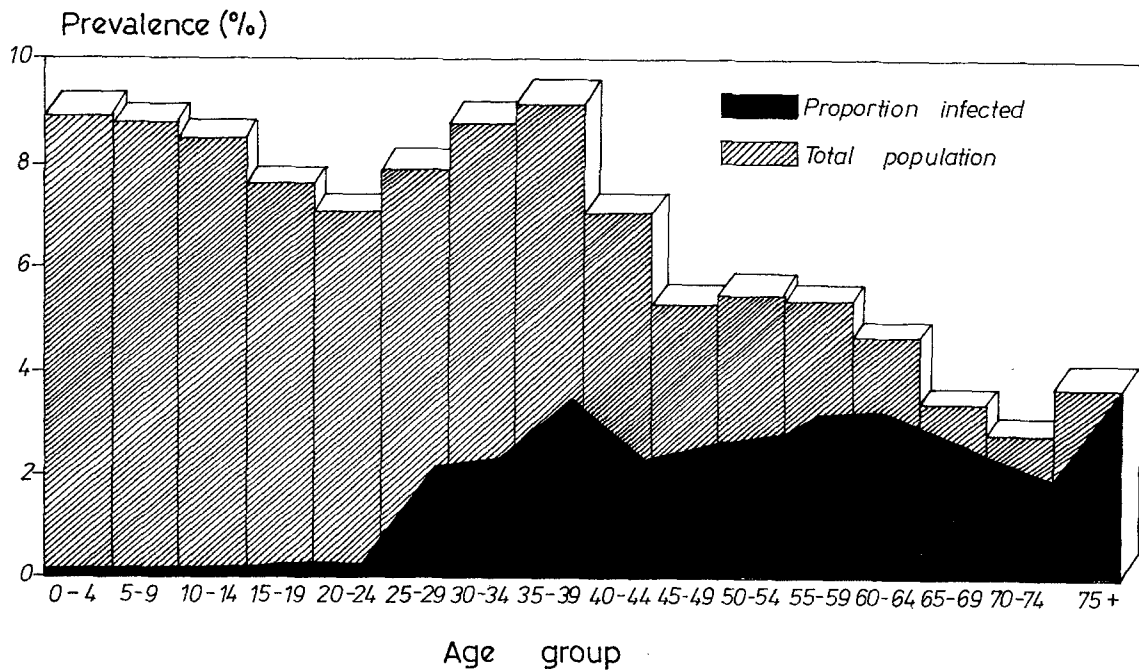
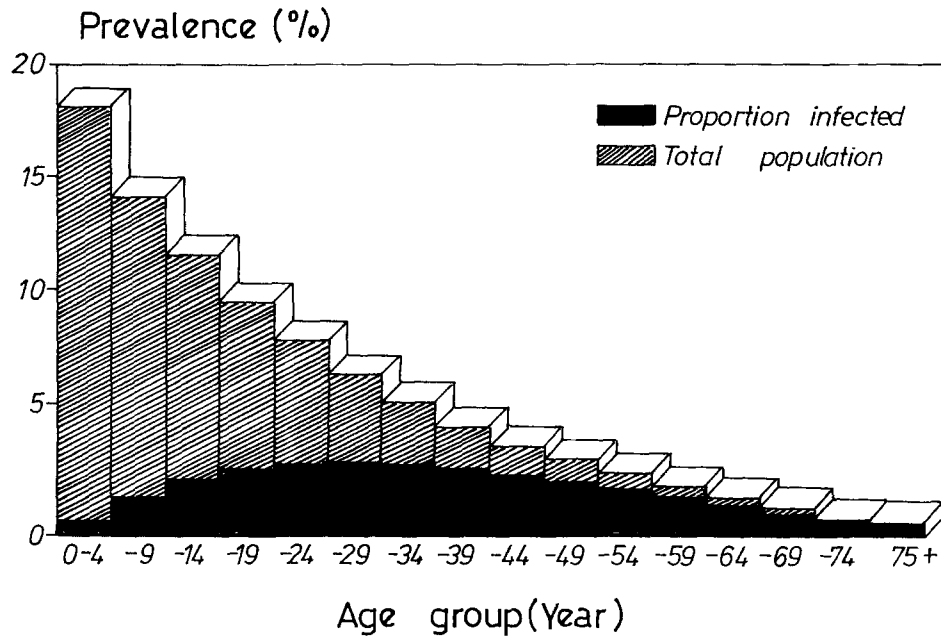


Fig. 2. Prevalence of tuberculosis infection by age – Poland, 1990.

decades on the assumption that the decline in the annual risk of infection, and consequently in the prevalence of tuberculosis infection and the incidence of the disease, will be offset by population growth so that the absolute number of persons infected with tuberculosis and the number of new cases developing annually will remain the same i.e. 1.700 million infected and 8 million new cases of tuberculosis annually. The respective rates per 100 000 i.e. incidence and prevalence will of course be much lower. For Europe, however, the figures

are not as stable as they are globally, since the size of the population is hardly changing and tuberculosis is decreasing. It is assumed that the decline in the annual risk of infection and in the incidence of tuberculosis in Europe will continue, so that the number of new cases developing annually, which in 1991 was about 135 000 (i.e. 24 per 100 000), will be about 100 000 (i.e. 16 per 100 000) in the year 2000, and by the year 2025 will be only 36 000 (i.e. 6 per 100 000). These figures do not take into account any AIDS/HIV influence, and also do not take into



Source: WHO/TUB 1990 (3)

Fig. 3. Prevalence of tuberculosis infection by age in Tropical and Southern Africa, 1990.

Tab. 3. Projection of possible influence of HIV on tuberculosis up to the year 2025 (in thousands).

1	Population (a)	Prevalence of			No. of new cases of tuberculosis all forms, per year (incidence) (b)	Possible additional cases of tuberculosis due to HIV infection (e)
		Tuberculosis infection (b)	HIV infection (c)	Dual (TB+HIV) infection (d)		
	2	3	4	5	6	7
<b>World</b>						
1991	5 400 000	1 700 000	10 000	3 000	8 000	300
2000	6 260 000	1 700 000	40 000	6 000	8 000	600
2025	8 500 000	1 700 000	100 000	15 000	8 000	1 500
<b>Europe<sup>(f)</sup></b>						
1991	560 000	128 000	500–1000	50	135	5
2000	590 000	83 000	1500–2500	100	100	10
2025	610 000	24 000	5000–7500	150	36	15

(a) see reference 15 and 16  
 (b) see text  
 (c) see reference 3 and 4 and the text  
 (d) see reference 3 and the text  
 (e) under assumption of 10% annual break down among dually infected  
 (f) without population of the previous Soviet Union, now Commonwealth of Independent States

account the situation in countries of the former Soviet Union. The expected prevalence of dual TB/HIV infection may produce some 10 000 additional tuberculosis cases annually by the year 2000, and by the year 2025 some 15 000 cases, which will represent, respectively, 10% and 40% of the number of cases expected without AIDS/HIV.

**Discussion and conclusions**

Globally the effects of the AIDS pandemic on the tuberculosis problem will be serious. In 35 years from now it is expected that in addition to some 8 million new cases of tuberculosis developing each year from the pool of those infected with tubercle bacilli, there will be an additional 1.5 million cases developing annually due to HIV infection. Although it is a known fact that almost 50% of

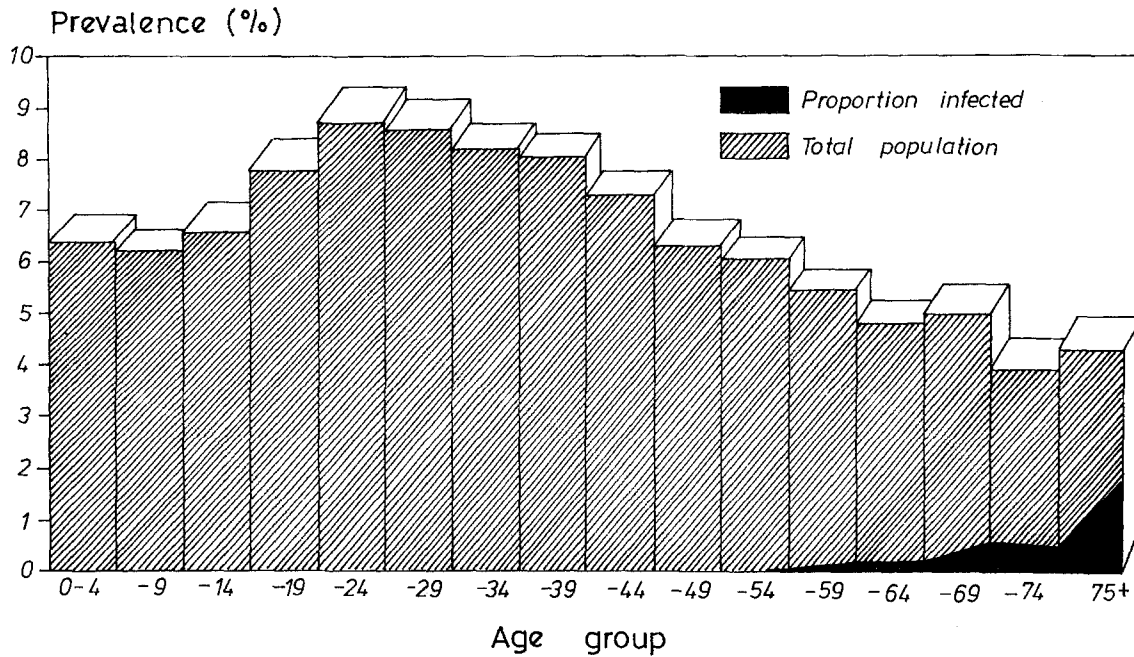


Fig. 4. Prevalence of tuberculosis infection by age – in Netherlands, 2020.

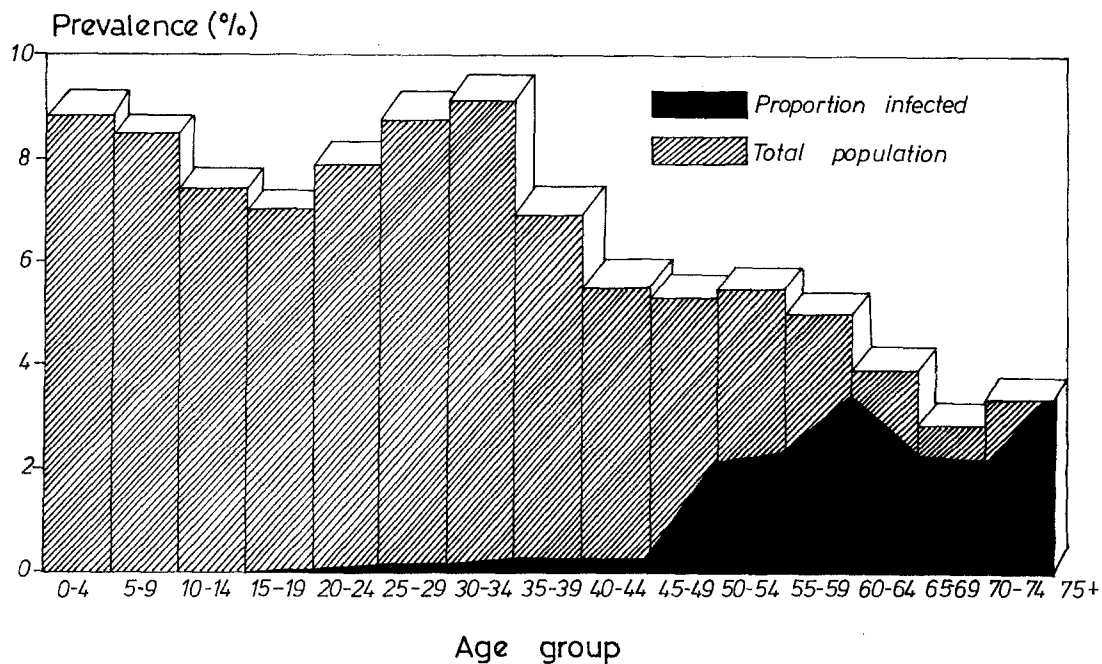


Fig. 5. Prevalence of tuberculosis infection by age – Poland, 2020.

HIV-related cases of tuberculosis are extrapulmonary tuberculosis, the question that remains unanswered is whether the recently observed decline in the annual risk of infection<sup>11</sup> will continue or will slow down because of these additional cases and the possible transmission of infection that they may produce.

For Europe, within the same time period it is expected that in addition to about 36000 cases of tuberculosis developing each year from the existing pool of persons infected, there will be some 15000

more due to HIV infection. Although the 15000 HIV-related tuberculosis cases in Europe will represent only 1% of the global number of HIV-related cases expected by the year 2025, for Europe this will represent 40% more than expected without the influence of AIDS/HIV. For Europe, therefore, the serious question is whether the rate of decline in the annual risk of infection with tubercle bacilli will remain unchanged or whether the HIV pandemic together with the increase in the number of new cases of tuberculosis will also increase the trans-

mission of infection to younger population groups, and consequently postpone the elimination of tuberculosis from Europe for a few more decades. Recent studies demonstrate that this aggravation most probably will not substantially influence the phase of elimination of tuberculosis in the countries with the currently lowest prevalence of tuberculosis infection, like the Netherlands and other Nordic countries<sup>2, 6, 7, 14</sup>. One cannot exclude the possibility however, that the phase of the elimination of tuberculosis may be postponed by one or more decades in other European countries with a higher prevalence of tuberculosis infection. The situation in Poland in 1990s is, for example, similar to the situation in the Netherlands of the 1960s, i.e. roughly 30 years behind. In the USA in the last few years there has been a reversal of the trend, i.e. an increase in the number of new tuberculosis cases registered annually, and it is claimed that this increase is due to HIV in an identified segment of the population<sup>7</sup>.

Since the purpose of this paper was to assess the possible influence of the HIV infection on the tuberculosis problem both worldwide and in Europe, the problems of diagnosing tuberculosis related to HIV and other problems related to clinical facilities needed in the future are not considered here.

The conclusions, however, are clear: in view of the magnitude of the aggravation of the tuberculosis problem caused by AIDS/HIV it is absolutely necessary to improve the current level of case-finding, diagnosis and treatment of all tuberculosis cases, irrespective of their HIV-status, since for most of the cases their HIV status is not known. What seems to be obligatory is to monitor constantly all the changes in the epidemiological situation of both tuberculosis and AIDS/HIV. Furthermore, it may be necessary to develop specific recommendations on how to cope with the increased case load of tuberculosis that is to be expected in some parts of Europe, as well as in countries/areas with high prevalence of HIV infection.

### Summary

To examine the possible influence of AIDS and HIV infection on the epidemiology of tuberculosis in Europe and worldwide in the coming decades an analysis of the available data on the two diseases and on the transmission of the two infections in relation to the demographic structure of the population was conducted, including projections for up to the year 2025. Globally, the effects of the AIDS pandemic on the tuberculosis situation will probably be very serious, adding some 1.5 million new cases of tuberculosis annually by the year 2025 as a result of HIV infection. However, this effect for Europe in the year 2025 may be in the range of

15000 additional cases only. The main factor determining the scale of aggravation of Tb is the age structure of the population infected, or at risk of being infected, with tubercle bacilli and HIV. Although the influence of HIV infection on tuberculosis in Europe may not be very high due to the fact that HIV infection involves mainly younger age groups it may, however, substantially postpone the elimination of tuberculosis from Europe. Therefore it seems necessary to monitor constantly all the changes in the epidemiological situation of both tuberculosis and AIDS/HIV.

### Résumé

#### La tuberculose et le SIDA: Les perspectives européennes et mondiales

La situation créée par l'interaction entre l'infection VIH et l'infection tuberculeuse est inquiétante tant par son ampleur que par la menace pour l'avenir de la situation mondiale de la tuberculose. L'effet de cette interaction a été étudié dans plusieurs pays européens et pour plusieurs décennies à venir, en relation avec les changements démographiques de la population infectée par M. tuberculosis. On peut prévoir qu'en 2025, à l'échelle mondiale, l'effet de la pandémie de SIDA se traduira par une augmentation du nombre des cas de tuberculose d'environ 1.5 millions. Dans les pays européens, en 2025, le SIDA n'aura pas une grande influence sur l'élimination de la tuberculose en raison de la prévalence faible de l'infection tuberculeuse chez les sujets âgés de 0 à 50 ans, chez lesquels la fréquence de l'infection par le VIH est la plus élevée. L'augmentation du nombre des cas de tuberculose en 2025 sera d'environ 15 000 cas. Néanmoins, cette augmentation peut prolonger l'élimination de la tuberculose dans la plupart des pays européens, et il est nécessaire d'étudier constamment tous les changements de la situation épidémiologique du SIDA et de la tuberculose.

### Zusammenfassung

#### Tuberkulose und Aids: Europäische und weltweite Perspektiven

Um in den kommenden Jahrzehnten den Einfluss der AIDS- und HIV-Infektionen auf die Tuberkuloseepidemie in Europa und weltweit zu untersuchen, wurde eine Analyse der vorhandenen Daten über die beiden Krankheiten und über die Übertragung dieser Infektionen in Beziehung zur demographischen Struktur der Bevölkerung durchgeführt, einschliesslich Prognosen bis ins Jahr 2025. Während weltweit der Effekt der AIDS-Pandemie auf die Tuberkulose von bis zu 1,5 Millionen neuer Tuberkulosefälle bis ins Jahr 2025 als sehr ernst bezeichnet werden kann, werden in Europa bis

dahin nur etwa 15000 zusätzlicher Fälle auftreten. Hauptfaktor, verantwortlich für diesen Unterschied, ist die Altersstruktur der infizierten Bevölkerung oder der Bevölkerung mit dem höchsten Ansteckungsrisiko für Tuberkulose oder HIV. Obschon der Einfluss der HIV-Infektion auf die Tuberkulose in Europa nicht so stark sein wird, weil HIV hauptsächlich die jungen Altersgruppen betrifft, wird sie dennoch die Elimination der Tuberkulose in Europa beträchtlich verzögern. Aus diesem Grunde ist es wichtig, dass die epidemiologische Situation der beiden Krankheiten Tuberkulose und AIDS/HIV weiterhin sorgfältig überwacht wird.

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