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Epidemiological Trends of Tuberculosis in Low and High Prevalence Countries.

by

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Abstract

The study of the epidemiology of tuberculosis and the need for a rational approach to the problem of tuberculosis control require a sound knowledge of the risk of transmission of tuberculosis infection from host to host. This knowledge is required today both in countries with a high prevalence and in those with a low prevalence of the disease.

The risk of transmission of tuberculosis infection in a given community during a particular period of time is most reliably expressed numerically in terms of a series of average annual infection risks in successive calender years.

The infection risk indicates the proportion of the population which will be primarily infected, or reinfected, with tubercle bacilli in the course of one year. The risk is usually expressed as a percentage or as a rate. The annual trend (decrease) in the risk of infection is even more important than the actual level of this risk.

Tuberculin surveys in schoolchildren, which are repeated, say every five years, in the same area provide us with the necessary information to make estimates for the annual infection risk. In areas where infections with the socalled atypical mycobacteriae are frequent, simultaneous testing with two "Sensitins", one prepared from human tubercle bacilli and one from atypical mycobacteriae will be of value for estimating the proportion of those infected with virulent bacilli and those infected with other mycobacteriae.

Introduction

In the present stage of development where tuberculosis mortality has lost its statistical significance because of effective chemotherapy, it is generally recognized that the most reliable measure of the extent of the tuberculosis problem in a population is the "annual tuberculosis infection rate" or incidence of infection. In countries where infection with the bovine type of tubercle bacilli no longer exists, as is the case in the majority of low prevalence countries, the annual infection rate expresses that proportion of the population under study which will be primarily infected, or reinfected (in those who have been previously infected) with tubercle bacilli from a human source in the course of one year.

The annual tuberculosis infection rate is also the best measure for following the trend of the tuberculosis problem in a given population and for evaluating the total effects of organized efforts to control tuberculosis.

The annual tuberculosis infection rate is derived from the results of tuberculin testing. A technique for converting information on prevalence of infection into a smooth series of annual rates of tuberculosis infection has been developed recently by TSRU and published in a comprehensive report in 1969 (TSRU, 1969). To obtain reliable estimates of the annual tuberculosis infection rates and their changes in a particular period, several tuberculin surveys are required at intervals, each in a representative sample of non-BCG vaccinated subjects of the same age, tested by the same technique.

Dependable information on annual tuberculosis infection rates, and on the trends in the rates in recent years, enables a low prevalence country to assess the relevance of current tuberculosis control measures in a rapidly changing situation, and to plan for the eventual eradication of the disease. A considerable advantage of this epidemiological index is that it is not linked with any part of a tuberculosis programme, such as diagnosis and reporting of cases.

The approach used in TSRU for estimating the average annual risks of tuberculous infection in the Netherlands is complicated, partly because nothing was previously known about the way in which the risk of infection was changing and this had to be assessed carefully, and partly because it was desirable, in the process, to make comprehensive use of the extensive prevalence data available in the Netherlands. However, for routine tuberculosis control a simple method of estimating the annual tuberculosis infection rate is described in the short section VIII of the same report.

I am going to describe once more how the annual tuberculosis infection rates can be estimated easily, because a number of people who have recently visited the International Tuberculosis Surveillance Centre, to which I will refer later, knew about the TSRU report on the transmission of infection but found the publication too technical.

There are:

Two steps in assessing the annual tuberculosis infection rates.

a. Estimation of the percentage decrease in the annual risk of infection using Appendix Table C of TSRU report no. 1.
Table 1 shows a part of this table. The percentage decrease in the annual tuberculosis infection rates can be estimated if two or more prevalence figures are available for subjects of the same age. If the prevalence of infection in children aged (say) 10 years was, for instance, 5.5% in 1966, and 2.5% in 1972, entry 80 in the table is divided by 6 years (from 1966 to 1972), to give the approximate annual percentage decrease, which is about 13%. The approximate annual percentage decrease is needed for use in Appendix Table B.

b. Using the estimate of the percentage decrease, Appendix Table B of the same report provides direct assessments of the risk of tuberculous infection in two calendar years, namely the year in which the prevalence of tuberculous infection was determined, and a few years earlier. In the above mentioned case one consults Appendix Table B for children aged 10 years, last column (13% annual decrease in risk of infection each year). The table indicates the following annual tuberculosis infection rates:

1966 : 0.25% (and in 1956 : 0.92%)

1972 : 0.11% (and in 1962 : 0.41%).

Trend in the risk of tuberculous infection with age

It is widely believed that the risk of tuberculous infection may be greater among adolescents and young adults than among children or older people. A small (though non-signifi cant) trend in infection risk with age (about $2\frac{1}{2}\%$ for each year of age during the period 1945 to 1966) was observed in TSRU report no. 1.

Further studies carried out by Sutherland and Fayers and by Waaler provide evidence of a consistent tendency for the risk of tuberculous infection to increase with age in a number of countries, both developed and developing. More detailed analyses are being made by Sutherland and Fayers on the data from a number of countries. The finding that the risk of infection is associated

with age in several countries sug-
gests that a similar association may
also exists in other countries. It is
difficult to assess how the risk va-
ries with age, but as already indica-
ted, the calendar trend in the risk,
eliminating a possible effect of age,
is readily estimated from the results
of two or more tuberculin surveys
on representative samples of the po-
pulation of the same age, (say) eve-
ry 5 to 7 years.

*The risk of tuberculous infection
and its decrease in low prevalence
countries*

Some of you know the curve shown
on Figure 1 referring to the level
and the trend of the risk of tuber-
culous infection in the Netherlands
over a long period. The risk of tu-
berculous infection in that country
is, at present, very low indeed - of
the order of 0.3 per thousand in 1973
- and it has been decreasing steadily
by about 14% annually since 1941.

We now also know more about
the risk of tuberculous infection in
other developed countries (see figu-
re 2). Junker has recently published
estimates of the risk of tuberculous
infection in Vienna (Austria) for
the first 50 years of this century.

From his curve, we have plotted
the part between the years 1922 and
1948 based on the results of tuber-
culin testing carried out in 1927
(nearly 14,000 children aged 6½
years) and in 1948 (nearly 8,000
children aged 6-7 years). The esti-

mated risk of tuberculous infection
was nearly 6% in 1922 and about
2.2% in 1948. Because of the lack
of reliable information on the pre-
valence of tuberculous infection in
children of that age between 1927
and 1948, the hypothetical straight
line of the risk presented in the fi-
gure might have differed from the
real trend of the risk. On the other
hand, estimates of the risk of tuber-
culous infection for 1922 (6%) and
1948 (2.2%) are reliable. It can be
concluded therefore, that there has
been a considerable decrease in the
risk of infection during the period
under study.

Sutherland et al., estimated the
risk of infection for Prague (Cse-
choslovakia), also for the period
1922 to 1948. Estimates are derived
from the results of tuberculin tes-
ting of 22,000 children aged 6-10
years in 1926 and about 78,000 chil-
dren aged 5-15 years tested in the
ITC in 1948. (TSRU report no 2).
The risk of tuberculous infection in
Prague was about 8% in 1922 and
about 2½% in 1948.

The results from the Netherlands,
Vienna and Prague show (a) that
the risk of tuberculous infection was
high in those three parts of Europe
before World War II, and (b) that
the risk decreased, on average, by
about 4% to 5% each year. There
are very few other historical data
available that are fully representati-
ve for any of the European countri-

es. It is therefore useful to look more to the present and to the near future.

Neumann carried out a tuberculin survey of about 500 children in Stuttgart (West Germany) with the WHO standard tuberculin test in 1965. The second tuberculin survey of nearly 2,000 school-children aged 7 to 15 years was made in June 1971, in co-operation with ITSC. Schools included in the 1965 survey were also included in the 1971 survey; in addition, a number of other schools in Stuttgart participated in the latter survey. The analysis of the material showed that the present risk of tuberculous infection in Stuttgart is very low indeed - about 0.3 per thousand. The decrease in the risk of infection with calendar year was nearly 15%. The levels of the rates and the decrease in the annual risk of infection are of the same magnitude as was found in the Netherlands.

Waaler, Galtung and Mordal estimated the risk of infection in Norway. Their estimates were derived from the results of tuberculin testing in school-children carried out on a national basis during the last two decades. The material is very reliable. Their estimates are very close to those in the Netherlands, both with regard to the level of the risk of infection and its downward trend. A full report will appear soon.

The TSRU analyses of the material from Saskatchewan (Canada) also show that the situation in Canada is similar to that in the Netherlands and other low prevalence countries. The material from Saskatchewan is very extensive and is reliable; about 140,000 tuberculin tests in subjects of all ages were made annually during the period 1954 to 1970.

Lotte is going to present the results of estimates of the risk of infection in France. A representative tuberculin survey is being made in Britain and we hope that our British colleagues will soon publish a full report of estimates of the risk of infection and its trend. Preliminary results, derived from the data on tuberculin testing completed during the first year of the study, show that the present risk of infecion in Britain is also very low.

Our team has recently made a tuberculin survey in Sardinia (Italy). The prevalence of indurations of 10 mm or more to 2 TU PPD Rt 23 in schoolchildren aged 6 to 14 years was 3.0%. This corresponds to a risk of infection of less than 3 per thousand.

We think that these results show two facts :

1. In the majority of technically developed countries there is, at present, a low or a very low risk of tuberculous infection. It is very probable that in the majori-

ty of developed countries the
present risk of tuberculous infec-
tion is below 5 per thousand; in
most of these countries the rate
may be of the order of 1 to 3 per
thousand; and in a few of those
countries the annual risk of tu-
berculous infection is even less
than 1 per thousand.

2. The risk of tuberculous infection
   continues to decrease, in develo-
   ped countries, by about 10% or
   more each year. Thus even these
   small risks may halve themsel-
   ves every 5 to 7 years.

A different situation is seen in
countries with high tuberculosis-pre-
valence-figures. The risk of infecti-
on is not only high, but what is
much more important, the decrease
of the risk is very small or not seen
at all.

Stott and collaborators have ana-
lyzed thoroughly the risk of infecti-
on in Uganda. As a first base line
for the estimate of the risk of infec-
tion the results of a tuberculin sur-
vey made in 1958 through the WHO
were used. The results of the survey
made in 1970 - 1971 were used as
second information. The same 10
areas as in this study (1958) were
visited for tuberculin-testing.

The tuberculosis infection rate for
1958 was 2.6% and for 1970 it was
2.3%. The slight decrease in the in-
fection rate was smaller than 1%

per year and this is not statistically
significant.

ITSC analyzed the data concerning
the prevalence of infection in one of
the North-Africa countries for this
same period 1950 - 1971. The first
investigations in children in this co-
untry were made in connection with
the BCG-campaign of ITC in 1948.
The ITSC-team tested in 1971 school-
children in four areas, in which the
coverage of the BCG-vaccination in
1948 had been low.

The results are given for two
areas in which the infection risk in
1950 was almost the same: 3,9% and
3,1%. The decrease in the risk of in-
fection however was substantially
different, in one of the areas (ur-
ban) it declined to 1% and in the
other (rural) it declined only to
2.3%.

We have a number of tuberculosis
infection risks from various high
prevalence countries, but unfortuna-
tely we do not yet have a trend. The
risks however, are high, e.g. in Za-
ire more than 2% and in the wes-
tern part of Java more than 3%.
The risk proved to be lower in e.g.
Suriname, 1% and in Venezuela 0,8%.

The risk itself and its downward
trend decrease much slower in these
high prevalence countries.

We are of the opinion that in these
high prevalence countries steps sho-
uld be taken in the fight against

tuberculosis, which enable and ensure a rapid decline of the risk of infection for tuberculosis.

Why is the annual tuberculosis infection rate not used on a larger scale?

There are, in our opinion, several reasons and explanations for this:

a. The method has been introduced only recently. TSRU report no. 1 appeared in 1969 and it is understandable that after the introduction of a new epidemiological index some time will elapse before it is generally used.

b. As already mentioned, the TSRU approach in report no. 1 may seem too complicated to a number of policy makers. However, it has been shown that the method is simple.

c. In a number of countries the method cannot be used at present because of compulsory BCG vaccination of newborns. Unless a representative sample of newborn children is selected and BCG vaccination is deferred in this group of children for several years, in order to assess the development of tuberculin sensitivity during this period, the annual infection rate cannot be estimated reliably.

However, it is possible, in these developed countries, to arrange regular tuberculin testing of this group of children for a number of years and to give chemoprophylaxis to those who have acquired tuberculous infection. In fact, it is essential for those countries to discover the right point at which to stop mass BCG vaccination, namely when the harm from BCG vaccination (in terms of serious complications, such as suppurative lymphadenitis, lupus vulgaris, fatal BCG-itis, loss of tuberculin allergy, etc.) is greater than the benefit from BCG vaccination. The risks of tuberculous infection shown previously indicate that in some countries such a point has been reached already or will very soon be reached.

d. In countries where there is a high prevalence of "non-specific" tuberculin sensitivity, the efficiency of the tuberculin test as a measure of tuberculous infection is somewhat reduced.

The currently available techniques, however, make it possible to determine with sufficient accuracy the proportion of persons infected with tubercle bacilli.

TABLE 1 : *Decreases in infection risk corresponding to various percentages infected by the same age at two different surveys (tsru).*

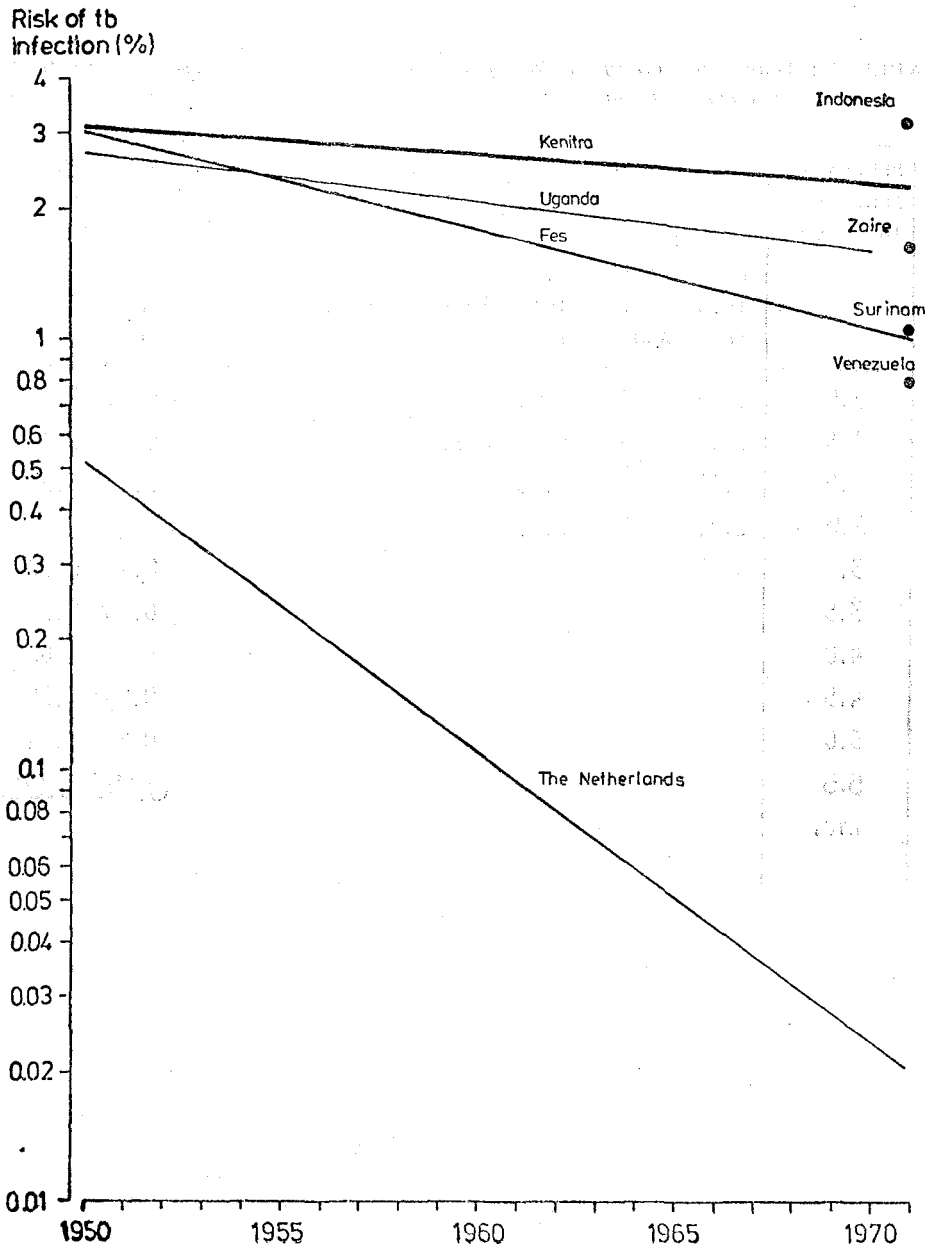| PERCENTAGE ALREADY INFECTED AT THE TIME OF		THE LATER SURVEY									
		0.2	0.4	0.6	0.8	1.0	1.5	2.0	2.5	3.0 ...	
	0.4	69									
	0.6	110	41								
	0.8	139	70	29							
	1.0	161	92	51	22						
THE EARLIER	1.5	202	133	92	63	41					
	2.0	231	162	121	92	70	29				
SURVEY	2.5	254	184	144	115	92	52	23			
	3.0	272	203	162	133	111	70	41	18		
	3.5	288	218	178	149	127	86	57	34	16	
	4.0	302	232	191	163	140	99	70	48	29 ...	
	4.5	314	244	203	175	152	111	82	60	41 ...	
	5.0	324	255	214	185	163	122	93	71	52 ...	
	5.5	334	265	224	195	173	132	103	80	62 ...	
	ETC.										

Divide the entry in the table by the interval in years between the surveys to obtain the approximate annual percentage decrease for use in app. table b.

TABLE 2 : *Annual percentage risks of tuberculous infection corresponding to the percentage already infected by the age of 10 years (tsru).*
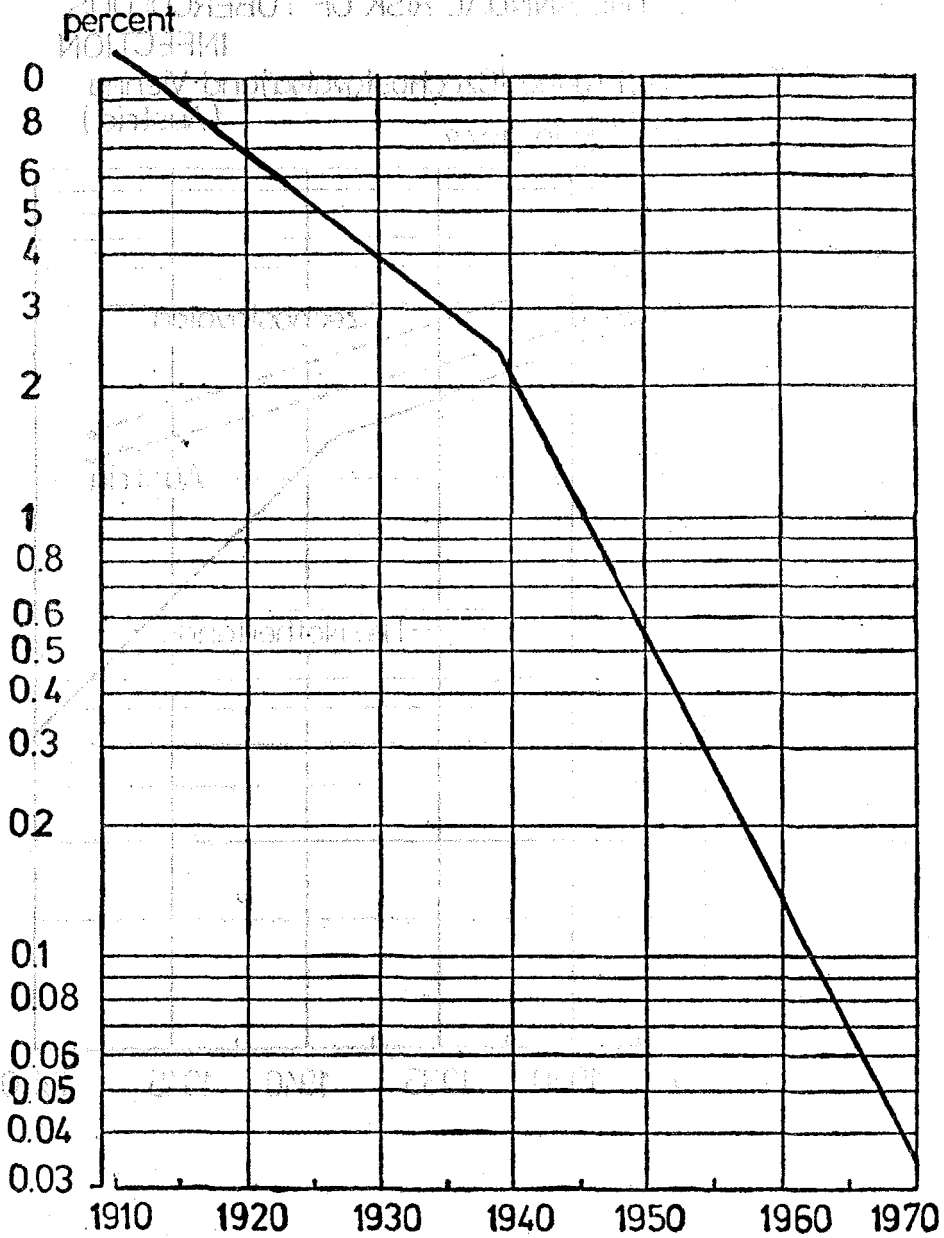
PERCENTAGE ALREADY INFECTED	APPROXIMATE PERCENTAGE DECREASE IN RISK OF INFECTION EACH YEAR						
	1		**3**		**5**	**13**	
	RISK THIS YEAR	RISK 10 YRS AGO	RISK THIS YEAR	RISK 10 YRS AGO	ETC.	RISK THIS YEAR	RISK 10 YRS AGO
1.0	0.09	0.10	0.08	0.11	ETC.	0.04	0.16
1.5	0.14	0.15	0.12	0.16		0.07	0.25
2.0	0.18	0.20	0.16	0.22		0.09	0.33
2.5	ETC.		ETC.			0.11	0.41
3.0						0.14	0.50
3.5						0.16	0.58
4.0						0.18	0.67
4.5						0.20	0.75
5.0						0.23	0.84
5.5						0.25	0.92
ETC.							

ESTIMATED ANNUAL RISK OF TUBERCULOUS INFECTION

1950_1971

**Risk of tb
Infection (%)**

ANNUAL RISK OF TUBERCULOUS INFECTION (‰)
THE NETHERLANDS, 1910 — 1970

percent

0
8
6
5
4
3
2
1
0.8
0.6
0.5
0.4
0.3
0.2
0.1
0.08
0.06
0.05
0.04
0.03

1910   1920   1930   1940   1950   1960   1970

ESTIMATES OF THE ANNUAL RISK OF TUBERCULOUS INFECTION

The Netherlands, Prague (Czechoslovakia) and Vienna (Austria)

percent · 1920—1948
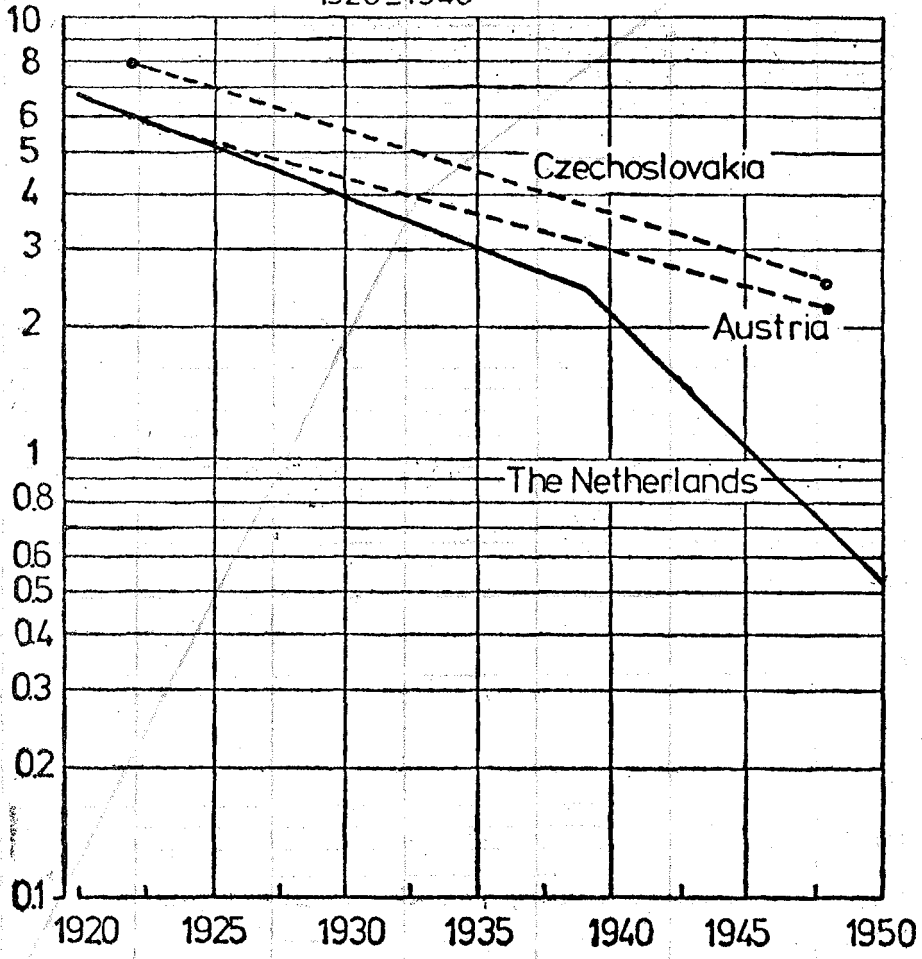
LOW PREVALENCE COUNTRIES, 1955 _ 1972

percent

- France
- Geneva (Switzerland)
- Sardinia (Italy)
- Britain
- Saskatchewan (Canada)
- Norway
- Stuttgart (West Germany)
- The Netherlands

1955   1959   1963   1967   1971