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Tuberculosis "La Belle Dame sans Merci"

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Aims, sources and area of study

The 1990s have brought with them a resurgence of tuberculosis not only in the developing countries, but also in regions were Tuberculosis for decades has been regarded as a minor or even non-existing health problem. Today the increase of incidence of tuberculosis in Eastern Europe is among the highest in the world, even surpassing some African countries. For example in Latvia, the incidence has increased 2.5 times in the 1990s, to 74 new cases per 100 000 population in 1998. The incidence in prisons has been reported to be up to 50-100 times this figure.

The last decade also brought with it the emergence of an epidemic of MDR-TB (Multi Drug Resistant Tuberculosis) in Russia and the Baltic countries, reaching levels rendering these parts of the world hot spots for primary MDR-TB. Up to 14% of the newly detected tuberculosis cases, as seen in Estonia 1998, are due to MDR-TB. Among chronic cases and in prisoners this proportion is much higher. For patients with MDR-TB, treatment is expensive, of long duration and with much lower cure rates. The treatment cost for one patient with fully susceptible tuberculosis is about 50-60 US$, contrasting to at least a 100 times higher cost for a patient with MDR-TB. The development and spread of MDR-TB has resulted in increasing case fatality and mortality rates.

The sources of the problem are to be found among both medical and socio-economic factors. Poverty means bad nutritional status in parts of the population. Tuberculosis has struck hardest among marginalised groups, such as alcohol and drug abusers. Especially in these groups non-adherence to treatment is a problem. Tuberculosis in the prisons is a problem that has to be addressed. Overcrowding, bad nutrition and poor general conditions facilitate the spread of infection and development of disease. Inappropriate drug supply and inadequate treatment regimens contribute to the development of resistant tuberculosis. Co-ordination of tuberculosis control between health-care in prisons and other parts of the health services must be improved.
With this development on hand, what can future learn from history? What can a long time perspective add to the understanding of the current situation with the global spreading of TB and MDR-TB on hand?

A common criticism of analyses based on causes of death is that earlier diagnoses were not exact, that they changed over a period of time, and that they were based on symptoms (nosology) and not causes (etiology). Pulmonary tuberculosis, however, is a disease that is relatively easy to diagnose in its lethal stages. The genus of the bacillus epidemicus is also stable and the extent of the disease is sufficiently wide to allow statistical analysis.

You can distinguish a complex set of factors which each contribute to an explanation of the appearance and course of the disease. Certain of these factors are absolutely necessary preconditions for the outbreak of the disease, for example the presence of the germ itself, while other factors are more conditional. These can be roughly sorted into biological and social determinants. In my earlier research on TB, I´ve tried to test the following hypotheses:

- that the extent of tuberculosis in a given society is governed by immunological processes resulting in an epidemic wave, and
- that the variations in the tuberculosis mortality rate can be see as an expression of changes in the standard of living.

An adequate treatment of these main hypotheses presupposes that the following problems also will be examined:

- the possibility to measure deaths due to tuberculosis in historical populations,
- the stability and changes in TB age and sex distribution, possible changes in the virulence of the bacillus,
- the effects of changes due to competition from other diseases.

THE OVERALL AIM of this paper is to increase the understanding of the relationship between tuberculosis, man and society. This means that not only aggregate and quantitative information, but even the disease's histoire de mentalités is treated.

Tuberculosis, like most other biological phenomena, occurs in a cyclical pattern in waves.
The first hypothesis is based on changes in the occurrence of tuberculosis being seen as an immunological process. In demographic as well as medical research, it has been claime that the decrease in the mortality rate during the last centuries was caused by the termination of such a cycle. This has been seen as the effects of a natural selection process, primarily because of improvements in the immunity defences against the most serious diseases.

The second hypothesis implies that the TB mortality rate from the middle of the 18th century to the introduction of modern therapy is treated as an expression of changes in the standard of living.

Background and research design

Tuberculosis is a social disease that is extremely sensitive to changes in the standard of living. The disease is an infection that is primarily spread directly from human being to human being. The degree of crowding and the standard of housing are therefore important factors when it comes to the spreading of the disease. Usually, steady contact is required in order that the disease should be transmitted. Tuberculosis is also sensitive to nutrition. Persons with good diets are far more resistant to the disease than those suffering from malnutrition or those with a poor diet. Protein deficiency is

particularly dangerous, especially a lack of animal proteins. A reduction of nutritional intake together with a greater degree of crowding should thus lead to an increased TB frequency in societies where the disease is endemic. On the other hand, a decrease in the tuberculosis frequency presupposes better standards of nutrition and housing, at least for the period prior to modern chemotherapy, and to a certain extent even afterwards. Where diet and housing conditions operate against each other, the frequency and occurrence of tuberculosis functions as measure of the net result.

The major perspective is socio-economic, but the disease's "histoire de mentalité" has been treated. These two approaches are by no means mutually exclusive. On the contrary, in this context they operate as necessary complements to one another. Because of its extent and its nature, tuberculosis was a disease that affected both the economy and the attitudes of the society at the same time as it caused considerable human suffering.

The hypotheses that are to be examined here involve access to information covering a period of 230 years. Few sources remain unchanged over such a long period. By combining different source types, and by looking for information at a number of different geographical levels, it is possible to study the disease over such a long period. There-fore, records of deaths and burials were used from the time that these began to include the cause of death, and mortality statistics were used from their introduction in 1749. Various TB mortality sources are traced up to 1980. An analysis of primary sources, i.e. records of deaths and burials, makes it possible to judge the validity and reliability of these sources. This also gives us detailed knowledge of different social and demographic conditions which are not explicit in an analysis of the causes of death gleaned from secondary sources.

For this reason, local studies were undertaken on parish and individual levels in seven parish districts. These represent widely differing societies, from a prosperous farming community in Skåne to a far bleaker community in the very upper part of Norrland. Although the seven parish districts consist of villages with differing natural conditions, nutritional status, social structures and geographic location, they are too few in number to constitute a basis for broad
generalisations. The material is also too meagre to permit statistically reliable conclusions to be drawn concerning the tuberculosis mortality rate within and between the different districts. On the other hand, a combination of different sources on a local social level combined with regional studies provide a clearer picture of the extent of TB in different areas of Sweden during the period of study.

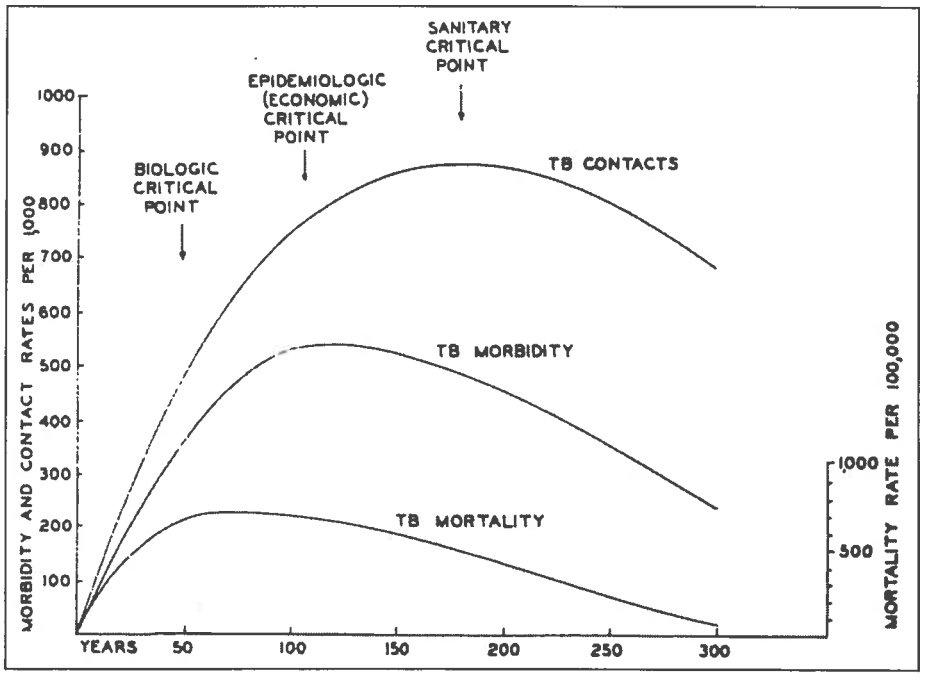
For local studies, the source material is plentiful. The major source was the above-mentioned cause of death and burial records, but background material concerning the deceased and their families has also been found in other church records-cathecetical records (parish records), records of births and baptisms, banns and marriage records, and documents concerning migration. When all this information is collated for a certain individual or a certain family, the result is a good framework of biographical data. In addition to the church records, a great number of other sources have been used-for example, census records, accounts, journals, probate records, topographic records and public statistics. For the year 1805, a cross-sectional study is made of all counties, towns and clerical districts in Sweden. Information concerning deaths caused by lung- or chest diseases are standardised in order to provide an indication of the impact of differences in age and sex structures on the TB frequency. In order to obtain longer series more exact mortality statistics are treated for the period 1750-1830 in four rural regions and the towns of Norrland. These regions cover altogether 54 parishes and 121 390 deaths. The regions studies are Norrbotten, northern Ångermanland, Medelpad and northern Hälsingland.

The differences in TB mortality on the national level between different counties and towns are studied for periods where such information is available. The extremely high tuberculosis mortality rate in Stockholm is closely studied. Comparisons are made between different types of towns according to a number of criteria such as size, location and type of employment. The town of Eskilstuna and its surrounding area and Kiruna are the subjects of particular attention. Eskilstuna was an early centre for the metal industry and the combined effects of TB, silicosis and other pneumoconiosis are studied. The Kiruna study is focused as the connection between the mining activity and changes in the way of living.

General information concerning TB morbidity is not available until 1939 for the whole country. On the other hand, morbidity statistics can be obtained for specific groups, e.g. from hospital records and documents left by patients with lung diseases.

In order to further test the importance of immunity, the secular occurrence of the disease is treated. If immunity is the decisive factor for a decline in tuberculosis, then the TB deaths should drop afterwards in an area with a previously high TB mortality rate as a result of acquired immunity. The disease should show a cyclical pattern. (See fig.1.) Two areas, Gotland and Österbotten, are treated. The former had a low TB mortality rate, and the latter had a high rate. Both showed a low degree of change in the trend and level of TB mortality.

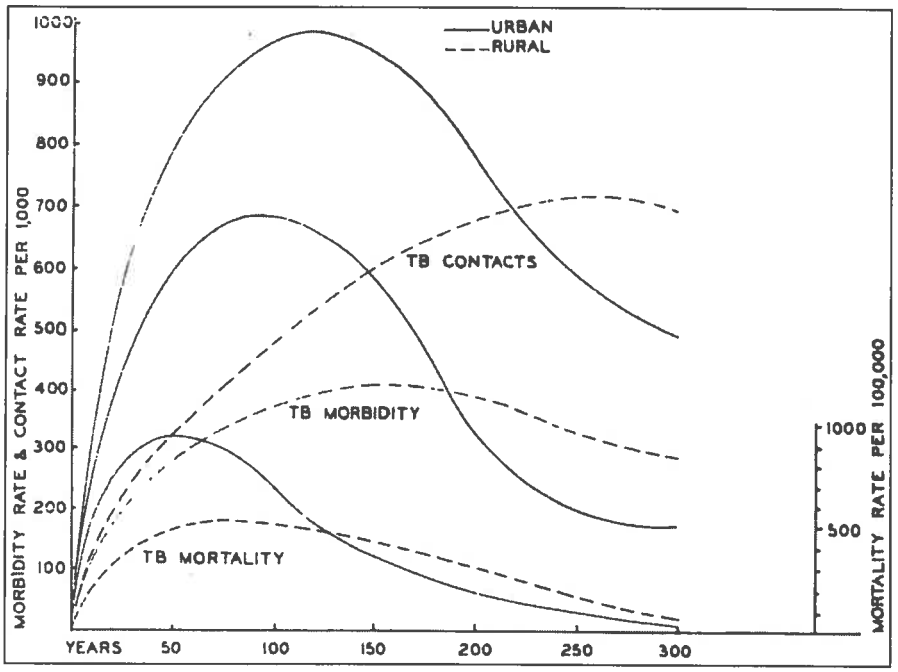
Fig.1. Model for a secular tuberculosis wave; mortality, morbidity and TB-contacts



Source: Grigg, E:R:N:, "The Arcana of Tuberculosis", The American of Tuberculosis and Pulmonary Diseases, 78 (1958) p 160.

Bovine tuberculosis has been considered to have an immunising effect, so that persons drinking milk containing bovine TB bacteria can be infected and either become sick or immune. If this is the case, then the infection should lead to an increase in infant TB mortality, while young people or middle-aged people should have a lower mortality rate compared with areas where bovine tuberculosis does not occur. During the latter part of the 19th century, Sörmland and Uppland were severely hit by bovine tuberculosis, while in Norrland the infection was almost unknown. By comparing the age distribution of TB mortality in these different areas, an attempt is made here to measure the effects of this form of immunisation. Following this, there is a discussion of possible changes in the virulence of the tuberculosis bacillus. The degree of competition from other diseases is treated. By studying the occurrence of tuberculosis in different areas during periods of low and periods of high mortality for various epidemic diseases, an attempt is made to measure the impact of other diseases on TB mortality. The second hypothesis, that variations in the numbers of deaths from tuberculosis depend on changes in the standards of living is also tested. By studying and comparing the TB frequency in groups with extremely high and extremely low standards of living, an attempt is made to measure a possible correlation between changes in the standard of living and tuberculosis. Diet, work, hygiene and education are used as vital criteria in the analysis.

Fig .2. Model for a secular tuberculosis wave; urban versus rural populations

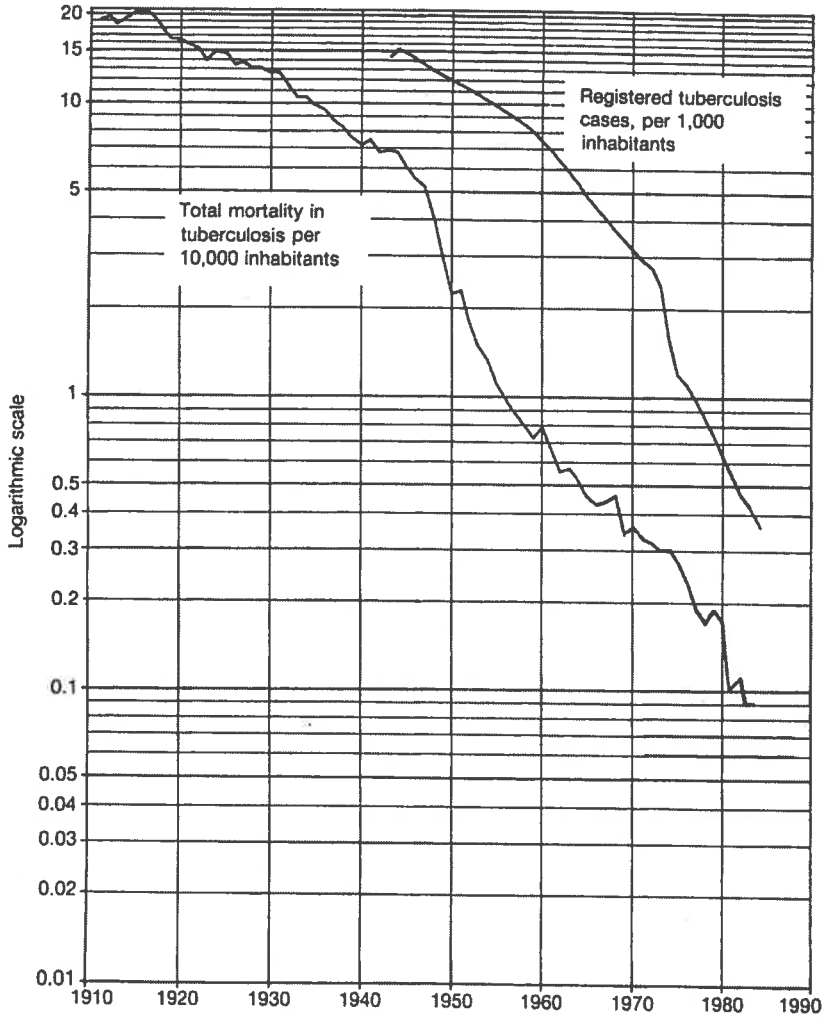


Source: Grigg, E:R:N:, "The Arcana of Tuberculosis", The American of Tuberculosis and Pulmonary Diseases, 78 (1958) p 162.

To begin with, the capital of Sweden, Stockholm is studied, with its extremely high TB mortality rate and its wide social differences. An analysis is made of consumption death among members of the Royal court, among poorhouse inmates, and among female prisoners living in barrack conditions. The importance of diet and exposition is discussed with respect to the frequency of consumption in the different groups.

In the towns, where people live in crowded conditions, there is a concentration of the negative factors that promote the spread of disease and decrease resistance. It is difficult to identify individual agents, particularly in the large and more heterogeneous towns. By studying towns with a low frequency and those with a high frequency of industrial workers, an attempt is also made to study the effect of industrialisation together with urbanisation and size of town, in relation to the surrounding area's TB frequency. Following this, a study is made of tuberculosis in three population groups: Eskilstuna's industrial worker families, Kiruna's mining families, and the inhabitants of three villages on the coast of Norrland. The aim of these partial studies is to illustrate the influence of different socio-economic factors on TB mortality in different groups in 18th, 19th and 20th century Swedish society.

Fig.3. Numbers of registered cases of tuberculosis and number deaths from the disease in Sweden in relation to the whole population.



The effects of therapy and preventive care are also treated. Here, tuberculosis is discussed as a model disease for the organisation of preventive and public medical health care. The steps that were taken to fight TB are treated as a part of the level of living standard, and are studied in the light of the widespread discussion concerning the role of medicine.

The level and trend of the mortality rate is discussed from a secular perspective together with the causes of the changes that took place over the centuries in different population groups. An attempt is made using a model to illustrate the context of the cause factors in the case of tuberculosis in a population.

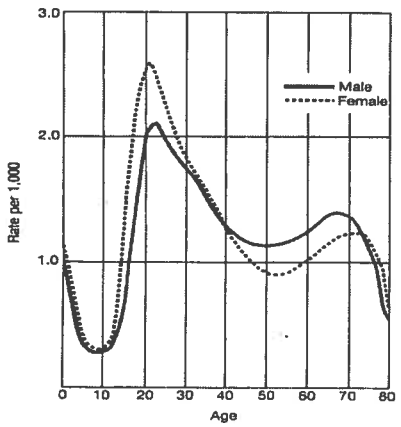
Results

The study of early cause of death registration for lung diseases with special attention to pulmonary TB has, despite changes that took place in diagnosis and in the reliability of the source material, been found to be totally applicable for the desired requirements. At the local level, a dependency on the care and knowledge of local clergy-men was much in evidence.
With regard to the overall questions, primarily studied at an aggregate level, these local deviations were of less importance. The sources show a certain under-registration of the number of persons who died of pulmonary tuberculosis. By adding the number of deaths with given causes that were in fact probably deaths from pulmonary TB, a more adequate number of such deaths has been achieved. Other forms of tuberculosis had such varied symptoms that using the nosological diagnoses of the day, made it hard to distinguish those forms from non-tuberculosis diseases.

The question of whether there was any age transition, or whether the age and sex structure was stable with regard to TB mortality is one of central importance when it comes to estimating influence of social or immunological factors on tuberculosis mortality in different age and sex groups. The study showed that there are certain constants in the age structure, but that there is great variation in the sex pattern for different types of TB. The age distribution in Sweden over the 230 year period can be roughly summarised as follows: high infant mortality followed by a sharp decline, particularly between 5 and 10 years of age, followed by an increase in the following ages. During the latter part of the 18th century, TB in upper age groups was widespread. TB was not a function of changes in the age pattern, but rather one of changes in the level of TB mortality between generations.

The residue of a higher TB mortality in earlier cohorts was greater than the youth peak in later cohorts The early youth peak reflects the natural course of the disease. A large number of cases of TB in upper age group could therefore be a result of increased relapses because of a generic deterioration in health for these age groups.

Fig 4. Specific death rates per 1000 by age and sex in Sweden



The study also showed that there was a general increase in consumption mortality for men during the 18th and 19th centuries. In the 20th century, on the other hand, women had a higher TB mortality rate. TB mortality in women is more pronounced age specific. The disease is concentrated to the early youth and to the woman's reproductive period.

Men dominate in the upper age groups, particularly in the towns.

Changes in the virulence have been cited to explain changes in the total mortality rate. When it comes to the tuberculosis bacillus, no such changes have been proven. The examples that exist; for example the production of BCG vaccine from weakened bovine tuberculosis bacilli and the bacteria resistance developed due to chemotherapy-have shown that the tuberculosis bacillus' virulence is very stable. Neither is it likely that changes in virulence took place at one and the same point in time throughout the western world. The epidemics that have occurred in populations that were previously protected show that the bacillus is still extremely virulent.

Side by side with the social and biological determinants on TB mortality that were studied, account has also been taken of other diseases and the changes undergone there. No clear correlation between changes in the TB level and changes in the causes of death panorama has been found. Neither the increase in TB mortality in the late 18th and early 19th century nor the later decline have coincided with specific changes in the disease spectrum. When it comes to the early years of the 20th century, however, it is possible that the TB frequency was affected by the changes that took place in the disease and cause of death pattern. However, these changes were not so radical as to be the sole explanation of the changes that are seen in TB mortality.

A successful immunity can either be the result of a genetic inheritance or be acquired. In the case of infectious diseases that give life-long immunity-for example, measles. Or small-pox-the immunity acquired by human beings can explain the decline of the frequency of the disease after and epidemic. In the case of tuberculosis, it is nevertheless unclear how effective the acquired immunity is and how people are affected by the immunising measures. The long-term effects of the new bactericidic chemotherapy are similarly unknown. The high level of TB in higher age groups which have been documented in this dissertation over a period of over 200 years throughout the country demonstrate a high number of rescidives, i.e. cases in which immunity has not beenparticularly long-lasting.

The number of immune individuals in a society depends on occurrences in an earlier generation and on how long-lasting the acquired immunity is. When a society initially is infected by tuberculosis, the course of the disease is acute and highly lethal. It has been estimated that it takes about a hundred years for the disease to pass from an epidemic stage to an endemic. The number of immune individuals is still fairly small, many people are infected by TB, but the course of the disease is much slower, more chronic. Natural selection and child immunity are important at this stage.
The populations studied in this thesis were at this phase. As late as in the 1940s, when effective chemotherapy was introduced, the disease still had not reached a stage where acquired immunity would result in the disease no longer constituting a problem (see fig. 1). The question is whether we would ever have reached that phase without the introduction of therapeutic measures. The situation in many developing countries today indicates that acquired immunity to the disease is not sufficiently strong or long-lasting.

It is more likely that a sharp increase in the TB frequency in a given area is either the result of the area's not earlier having been infected, or that tuberculosis was found to be endemic and the increase

in this case was due to a decline in the standard of living. This line of reasoning has formed the basis for the study of death causes in 54 Norrland parishes undertaken in this thesis. The study snowed that tuberculosis was an endemic disease at least from 1750 and that 150 years later it was still of considerable proportions. These results, which go against the conclusions of earlier research that Norrland was uninfected until the latter part of the 19th century, are of central importance.

The general occurrence of tuberculosis and the high level of TB in older people would indicate that changes in the standard of living rather than immunological processes are the main causes for the changes that took place in the TB frequency. Genetics is another important factor. The child of tubercular parents is not born with the disease, it is infected. However, the child may have inherited a relative inability to resist the infection. It has earlier been assumed that the decrease in the TB mortality rate in the late 19th century depended on an intensified "weeding out" of persons with a reduced resistance to TB. In this way, the total TB resistance in a society would gradually increase with each passing generation. This line of reasoning has a number of limitations.

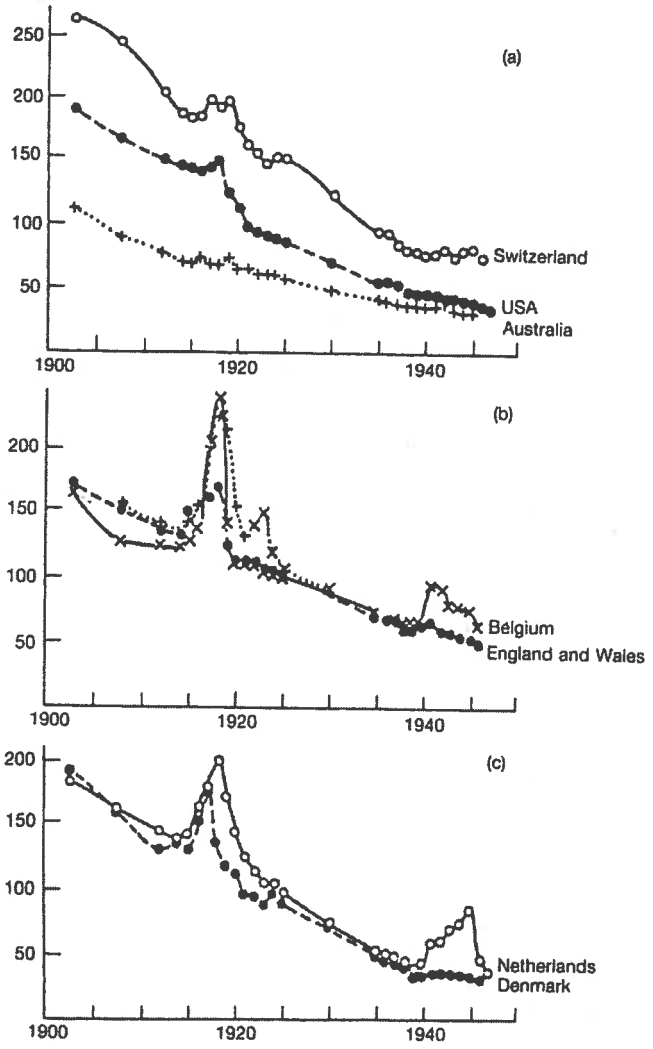
Let us take an example. The TB mortality rate increases in times of famine and deprivation. If thepopulation of a certain area withendemic tuberculosis is exposed to a decline in the standard of living, then the TB mortality rate in the affected generation will be high. By natural selection, the next generation will have more persons with a genetic resistance to TB, and the TB frequency should drop. This line of reasoning continues by pointing out that TB infected people in a '"wartime generation" do not manage to reproduce, or their children die. These conditions may apply to small groups of individuals, but this is not sufficient to explain the overall decline of tuberculosis. We know that many tubercular persons had children and that even if infant mortality was great, there were sufficient "genetically affected" survivors.

In addition, such serious periods of crisis have not preceded decreases in TB by about 30 years as would be the case if this reasoning held true. The fact of the course and slowness of tuberculosis coupled with the fact that large numbers manage to reproduce means that only genetic reasons for a drop in the TB level would seem to be highly unlikely. However, this does not mean that hereditary factors have no importance for the course of the disease.

The results of family reconstitution for the seven parishes show that the hereditary element should not be ignored. However, in retrospective studies it is not possible to distinguish heredity from the effects of the environment. By studying twins, it has been shown that there is a higher level of tuberculosis in both single-egg twins even when these have not lived in the same environment, which would indicate it is not the environment alone that contributes to poor prognosis.

Immunity does not necessarily have lobe acquired through infection from other humans.

Fig 5. Mortality from Tuberculosis in different European Countries per 100.000 population.



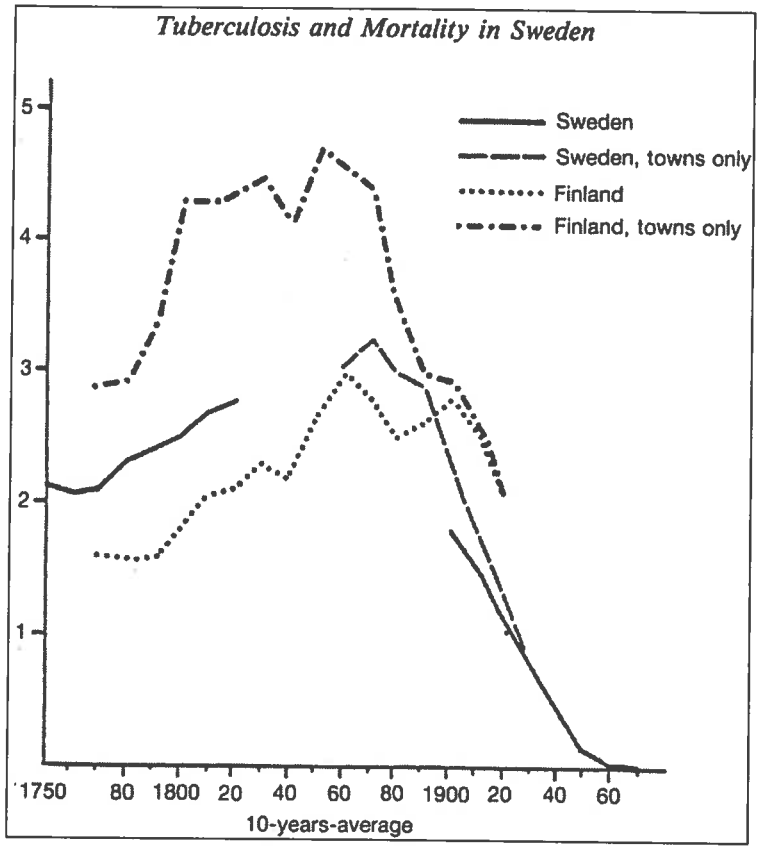
Source: Dubos and Dubos, The White Plague, Tuberculosis, Man and Society (London 1953)

In areas with widespread bovine tuberculosis the milk also contained tuberculosis bacilli. The difference between the age-specific TB mortality rate in the different parishes in areas with infected cattle and those in areas without may depend oil this type of immunisation The study shows a higher rate of infant tuberculosis mortality, but a general lower level of TB in those parishes where bovine tuberculosis was widespread. This means that the bovine tuberculosis caused increased infant TB mortality, but also provided a certain amount of protection against infection later in life to those who survived the primary infection. However, the studied populations were small and this hype thesis should be examined further. Based on the Swedish development, as discussed above, and in comparison with the TB frequency in other European countries, the course of the disease can be explained as follows.

During the 17th and 18th centuries, overcrowding, poor hygienic and housing standards in the larger cities led to a sharp increase in exposure. Many persons who had not survived a primary infection were infected by acute pulmonary tuberculosis. The results of the study of the royal court, an affluent group, indicates that it was an infectious situation rather than nutrition that governed the TB level in the

Stockholm of Gustav III. During the 19th century and the first decades of the 20th century, tuberculosis was so widespread that a large proportion of the population must have undergone a primary infection, even those moving to the towns from rural areas. The fact that the disease was consistently widespread must depend on the fact that the living standard was a sub-standard, resulting in relapses at the same time as infants were infected with acute primary infections, often tuberculosis meningitis.

Fig 6. The death rate from Consumption/Tuberculosis 1750 - 2000: Sweden and Finland



In this thesis, I show that there was a rise and fall situation in the TB death rate in Sweden and Finland and that this development was particularly apparent in the towns (see fig. 8).
These results can be seen as a confirmation of the model of TB as an epidemic wave. However, such a conclusion would be somewhat hasty. Even if the course was cyclical, the causes are not necessarily only to he found in immunological reactions on the part of the populations. The explanation is far more complex than that and will probably need a more elaborate explanation.

The standard of living operated partly through the degree of exposure, partly by affecting people's resistance. The factors that tend to increase exposure, simultaneously reduce the system of resistance. A high degree of overcrowding was often accompanied by sub-standard housing where draughts and generally unhygienic conditions conspired to reduce the general level of health of the inhabitants and thus increase the risk of infection or relapse.

One of the most important social factors behind the high TB mortality rate during the last century was the rapid rise in urbanisation. The risk of exposure to the disease was thereby increased considerably. In order to attempt to discover the extent to which a reduction in living standards increased the receptivity to the disease, a number of towns have been studied.

Conditions in Stockholm were extreme. During the 80-year period between 1750 and 1830, the pulmonary tuberculosis mortality rate was over 8 o/oo the highest known rate registered for a major city in the whole world for such a long period of time. Over 20% of the population died due to consumption. During the latter part of the 19th century, the extreme tuberculosis mortality rate generally decreased.

The strategy was to study the proportion of the mortality rate of pulmonary tuberculosis for groups with extremely good and extremely poor living conditions. The hope was that these extreme populations would give a clearer picture of the influence of the social environment than would be the case in more complex and ordinary populations where the differentials in the probability of exposure, infection and death would give a more diffuse picture. Three groups were studied: the royal court; poor women at Sabbatsberg Poor house; and finally, prisoners at Norrmalms Women's Prison. All causes of death in the court from 1749 to 1860 were studied. For the period 1766 1800, those living there were grouped into six social categories in which the royal family can be distinguished from courtiers, and these in turn from other servants. The soldiers and royal guards as well as the king's artists were categorised separately. Within each of these groups, even the members of the royal family, consumption was a common cause of death. An examination of the court food accounts shows that the diet for these highly placed individuals was nutritionally good. Despite access to good, nutritional food, the members of the court were unable to withstand the attacks of the tuberculosis bacillus. These results show that the role of nutrition in the matter of tuberculosis should not be overestimated in a society with a high general exposure risk.

The sources that are available for the poor house and the prison concerning diet give a rather positive picture as far as nutritional value is concerned. But the sources are not reliable and we have no way of knowing that the food actually reached the inmates.

Both in the poor house and the prison overcrowding was considerable. Many of the poor women were quite old and sick even on arrival at the institution. The prisoners, however, were often young and healthy women. In spite of this, the prison's medical journals show that they were quickly broken down. The majority of them had recur ring annual visits to the hospital. Many of them died before they had completed their sentences. The number of deaths from pulmonary tuberculosis and other deprivation sicknesses was very high during the first half of the 19th century, about 50%.

These groups were extreme cases. In Stockholm as a whole, there is a clear indication that pulmonary tuberculosis was the greatest killer in the poorer areas and particularly so in the areas of the poor houses. The concept of standard of living is complex, as is the Stockholm environment as such. It is difficult to isolate specific agents, although it is quite clear that the urban environment was determinant to the health of its inhabitants, not least with respect to tuberculosis. We can state clearly that the high tuberculosis mortality rate was caused by an increased exposure risk and a decrease in resistance caused by poor living standards, poor hygiene, difficult working conditions and sub-standard nutrition.

In an attempt to sort the above causes into their order of importance, different types of towns were studied. Particular emphasis was placed on the size of the town, the relation between the TB frequencies of the different towns and their surroundings, and the proportion industrially employed. A correlation can be seen between the size of the town and the tuberculosis frequency. At the same time, the TB level in the surrounding area affected that of the town in question, which means that small towns in areas with a generally higher TB frequency had a higher level of TB mortality than larger towns in areas with a lower TB frequency. The effect of the size of the town was nevertheless the stronger factor where they did not coincide.

The extent of urbanisation was also important. During periods of intense migration to a town, the tuberculosis mortality rate increased. In general, the TB mortality rate increased during the 1870s and subsequently decreased slowly. During this century, the disproportionate mortality rate in the towns has decreased. From the mid-1930s the trend has reversed. From 1936, Swedish towns have a lower TB mortality rate than the rural areas. For certain types of TB, e.g. tubercular meningitis, the course has been otherwise. These forms of tuberculosis are so rare in comparison with pulmonary tuberculosis, however, that they have not been able to affect the general trend.

The level of industrialisation has also shown itself to be an important factor. For example, Eskilstuna had the highest proportion of industrially employed and tuberculosis deaths during the last decades of the 19th century. But even this factor is not sufficient as a single explanation. Certain industrial towns, particularly smaller towns like Motala, had a low tuberculosis mortality rate. The tuberculosis mortality rate in the industrial towns was also affected by that of the surrounding areas. Where a town had a high level of industrialisation and was situated in an area with a generally high tuberculosis frequency, as in the case of Eskilstuna, the results were catastrophic. On the other hand, industrial towns such as Borås, in an area with a low tuberculosis frequency, were not hit as hard.

During the latter part of the 18th century and the beginning of the 19th, the tuberculosis mortality rate in Södermanland was low. However, Eskilstuna continued to have a high TB mortality rate, which indicates that the negative working and living environment factors were more important for the tuberculosis level than the general level of TB in the area. However, no decisive correlation has been found between the tuberculosis mortality rate and the degree of industrialisation.
The tuberculosis mortality rate certainly increased during the 1870s in most towns, but this did not correlate with the increase in levels of industrially employed. During the '80s and '90s, towns with increase in industrial employment and decrease in the tuberculosis mortality rate can be found. However, at the same time, the proportion of tuberculosis of all deaths increased, which indicates that competition from other diseases decreased.

Around the lake Mälaren in central Sweden, the TB rate decreased very rapidly. Earlier, this has been seen as a result of a natural immunisation process. This dissertation forwards another explanation. Because of its central location, this area was quick to learn about the measures that could be taken to prevent contamination. The general improvements in hygiene were also considerable. To the more distant areas, particularly Norrbotten in the north, this information and these hygienic improvements came much later. The high TB mortality rate in Norrbotten indicates that it was not in the first instance the level of industrialisation, but rather other living standard factors that affected the level of TB in society.

Where the negative factors, like poor housing, sub-standard nutrition, poor hygiene, followed in the wake of a rapid industrialisation, the towns with a high proportion of industrial workers were hit much harder, especially those located inareas with a generally high TB level.
Eskilstuna is an example of a town that fulfilled these criteria. However, industrial employment as such does not seem to raise a town's TB frequency where other negative factors are not present.

The kind of industrial employment is also an important factor. Certain occupations, like metalworkers, smiths and tailors, are more risky than others. In the study of Eskilstuna's iron- and steelworkers, the tuberculosis morbidity rate among grinders at the beginning of the 20th century was found to be almost five times that of other groups and with subsequent particularly poor survival prognosis. These facts are interesting in view of what we now know about the relationship between pneumoconiosis and tuberculosis. But the picture can be diffused by factors such as alcoholism, housing standards and nutrition.
Modern medical research has shown a very clear correlation between alcoholism and tuberculosis as well as between nutrition and tuberculosis. Such factors have naturally been present even in the past. We know that alcoholism was widespread at the beginning of the 19th century, and we also know that the abuse differed by occupational group. The misuse of alcohol affects the economy and the ability to work, which usually brings about a drop in living standards, but alcoholism can also in itself bring about a decline in the body's capability to utilise nutrition.

Generally, housing has been important in the communication of tuberculosis. Overcrowding was a serious problem in Sweden well into this century. The working population was generally poorly housed, entire families living in one room. This was also true of agricultural labourers and low income groups in general. In the towns, lodging was common. A higher TB mortality rate in working-class districts than that in more wealthy, central parts of town has been documented. The conditions of the buildings themselves was often a negative factor too. Damp, cold, conditions and non-existent ventilation were common. We also know that the tuberculosis bacillus can survive for long periods in dust and dirt. The fact that five or six people had to share the same bed, or that children and adults sought warmth in narrow bunks also assisted the spreading of the disease, often with catastrophic results.

The building of ordered accommodation for miners in Kiruna in northern Lapland, coincided with a change in the tuberculosis pattern. In a study of mining families in 1910, it was found that pulmonary tuberculosis was widespread among the adult population. During the decades that followed, a number of social improvements were undertaken in Kiruna, and the TB morbidity rate decreased. From the end of the First World War, the TB mortality rate also decreased, and remained lower in Kiruna than in the rest of Norrbotten, except during the
depression years of the 1930s. This can bee seen as an indication that the problems of the 1930s affected the mining population harder than it hit other groups in Norrbotten, and that this is reflected in the increase in the TB frequency.

At the beginning of this century, a study was made of the occurrence of tuberculosis in the population of some Norrland coastal villages. The disease was found on almost half of the farms (48%). A social-hygienic experiment was conducted in the area whereby the inhabitants' living conditions and general health were documented at the same time that all measures then known for combating tuberculosis were put into effect. One of the most important of these measures was the improvement of the general housing situation, and this was successfully carried out. The level of tuberculosis dropped

considerably, much more rapidly in the experimental area than in similar villages outside the area. It is clear from housing studies that living conditions had an important effect on the level of exposure and that the extent of tuberculosis decreased when overcrowding and hygiene standards were improved. The whole set of social factors often operated together in a complicated pattern and it is often impossible to establish exactly which of them bore the most blame. An extreme example of such a conglomeration of negative factors could be seen in the Nazi concentration camps. In Auschwitz, the tuberculosis mortality rate was astronomic.

The tuberculosis level of a social group in a particular region at a given period of time is the result of a complicated pattern of causes, which may not be statistically documented or verifiable. More often, there are more or less strong indications which taken together can give a convincing picture of a course of events.

Preventive and therapeutic care can and should be seen as indications of improved living standards. The considerable improvements that were made in the battle against tuberculosis would not have been possible if society could not afford to make the considerable investments in medical health care facilities and in research that took place during the last century. Private initiatives also played an important part in these developments.

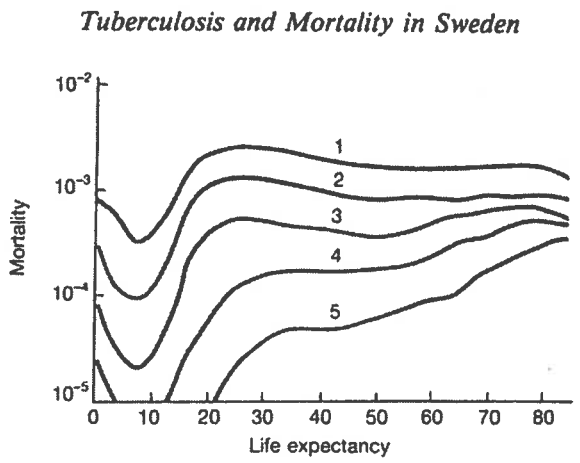
In earlier centuries, the role of medical science has been rather minimal. The importance that one is prepared to assign therapy is naturally a matter that is closely associated with the definition of the term. In addition to direct therapy, several other medical factors can be taken into consideration.

The classic sanatorium treatment was based on rest, fresh air and good nutrition, measures that certainly had a therapeutic effect. Sanatorium care was later combined with other medical therapy methods. Surgical measures, pneumothorax, and thoracoplastic surgery were in use until the 1960s, despite the fact that chemotherapeutic treatment was in broad clinical use. It is not possible to isolate the effects of the different treatments. Taken as a whole, they were beneficial to tuberculosis patients. The tuberculosis mortality rate dropped drastically. In 1943, the year before the introduction of chemotherapy, 4 396 people in Sweden died of TB, or 0.69 o/oo. In 1951, the TB mortality rate was less than half this figure, or 0.23 0/00. In 1976, it was 0.02 0/00!

This study shows a complex relation between immunological processes and different living standard factors as an explanation of the changes in the -TB level in Sweden over the past 230 years. A close correlation has not been found between changes in immunity and changes in the tuberculosis mortality rate. Despite this, immunological factors have played a vital part.

Immunological processes and living standard factors have separate time horizons. A quarter of a millennium, the time-span of this dissertation, is too short a time seen from a genetic and immunological point of view. For the entire study period, Sweden has been in phase II, based on Grigg's model (figs. 1 and 2). At this stage, there is a certain ecological balance between the host and the parasite.

Fig 7. Average age-specific mortality in quiniles of life expectancy in female populations from 43 nations 1861 - 1964.



Source: Preston, SH, Mortality Patterns in National Populations, with special reference to recorded causes of death (New York 1976)

According to the model, the great waves created by the decease going from one phase to another are continually supplemented by waves of much lower amplitude, "mini-epidemics". These mini-epidemics are a result of changes in the pattern of contacts and of living standards. Despite the fact that the disease is characterised by slow biological processes, it reacts surprisingly quickly to changes in the living standard. The wave found in this investigation is clearly identified as a mini epidemic. While immunological conditions affect TB morbidity and the overall level of mortality in a society, the changes in living standards change the short-term fluctuations and trends over a period of decades. The set of explanatory factors are illustrated in a model in fig. 32. Exposure to TB is primarily a result of living conditions, especially hygienic standards and population density, but also occupational conditions and location. Towns provide a far greater risk of exposure than rural areas, but even regional differences are great. Awareness of the risk of contamination and social measures such as sanatorium care-which prevented patients from communicating the disease to their environment-also affect the degree of exposure.

The result of a primary infection-cure, sickness or death depends on virulence and immunity as well as other factors that affect resistance. Worth mentioning is nutrition, but also the level of general health, the presence of other diseases, psychological stress, age, alcoholism, etc. A society's immunological status is not only affected by earlier infections, but can also be affected by vaccines (BCG). On the other hand, virulence is difficult to influence. In the case of TB, no significant change in the virulence of the bacillus has been demonstrated.

In brief, it has been established that the main living standard factors (particularly housing and work) have a very marked influence both on the risk of exposure, infection and death. These socio-economic factors directly affect the variation of the TB curve, while virulence and immunity conditions operate as factors underlying TB disease and the general level of TB mortality.

Present and Future

The tuberculosis curve for the West is plunging downwards. The annual TB mortality rate in countries such as Sweden is not even 1 in 100.000, i.e. 100 persons. Charts illustrating prevalence and incidence of the disease show registrations that only hover the x-axle's zero level. But the West is not the whole world, and today is not tomorrow.

World-wide, at least three million people die each year from TB. Every year there are another four or five million contagious cases. Two out of three of these people will die within a period of two years. At least 10 million people suffer from open TB. To these serious cases should be added a similar number of cases in which the disease is less contagious-at an earlier stage-and other forms of TB. These figures are conservative. Large numbers of cases never reach medical health centres and therefore remain undiscovered. The number of reported cases of TB in Africa is on the same level as in Europe, i.e. 60 per 100,000, while the true figures are
probably between 20 and 50 times as high as in Europe.

In a society where cases of open TB are found, the risk of exposure is high. An untreated case infects an average of twelve people a year.

If these conditions are not improved, an estimated 40-50 million people will contract TB within a period of ten years. Two-thirds of these will die without receiving any treatment. This enormous suffering can be prevented. Tuberculosis is a disease that can be cured using medicine. At the same time, general living conditions have an import. and influence on creating resistance to the disease. In this thesis, the complex relations between tuberculosis, man and society have been presented from using Sweden as an example. The majority of the factors that have been discussed are universal and are widespread in the developing world today and on the rise in many countries in Eastern Europé with Latvia and Estonia as examples were the incidence of TB has increased 2.5 times in the 1990s.

Even more worrying is the rapid spreading MDR-TB, the hard cured very severe form of the disease. In a WHO study 1994 on Estonia, around 10% of newly detected tuberculosis patients were infected with MDR-TB strains. In 1998, the figure was over 14%. This places Estonia among the countries with the highest MDR-TB incidence in the world. The problem is not related to immigration. Resistant tuberculosis hits the Estonian patient in different parts of the society, including the health care sector. Previous hospitalisation and ever being a health care worker are identified risk factors for developing MDR-TB.

In a global perspective, one of the main topics right now is the crucial importance in co-ordinating our common resources - national governments, international organisations, NGOs and not least the world of science - in order to combat the communicable diseases, as tuberculosis. In this work we have a lot to learn from the history of treating TB.

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