Commentary: Tuberculosis down the generations—a comment on ‘Continued studies of Tuberculosis as a generation illness’ by Kr F Andvord

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Introduction
It is 70 years since Andvord first looked at the way tuberculosis affects the human race within successive generations.1 His object was to find the incidence of disease and so the risk of disease to an individual over that person’s life time. A method of describing the incidence for different age groups for successive years provides the means to observe the way tuberculosis affects and afflicts a generation from birth, through adult life and into old age. Frost describes this analysis of the change in mortality by age as the most significant of all analyses. ‘For every change in the rate of mortality as we pass from one age to another represents a shift in the balance established between the destructive forces of the invading bacillus and the sum total of host resistance. If we could accurately interpret this record, analyzing in detail each movement upward or downward and assigning to each factor its due share in the change, then we would be well on the way of knowing the epidemiology of tuberculosis’.2
The analysis
The need for accurate data for tuberculosis mortality is the main prerequisite for such analysis and the Scandinavian nations were the first to excel in this. Andvord, a Norwegian, initially looked at 5 year age groups stating with those aged 0–5 from 1871 to 1875. This group would have been aged 20–25 in the 5 year interval 1891–95. These two time intervals represented two snapshot shots of the same generation cohort. He then looked at rates of mortality for these two age groups (0–5 and 20–25) at sequential 5 year intervals. Rates in the generation born in 1871–75 were 35.1 when aged 0–5 but 42.3 when aged 20–25. He then carried out the same analysis for 12 succeeding 5 year generations for those aged 0–5 and looked at the 20- to 25-year-olds from the same generations 20 years on. A table of succeeding 5 year generations until 1926–30, therefore, gives 12 successive generation 'cohorts'.

The striking finding about this table is that though infant mortality rates declined successively across the 60 year period from 35.1 to 20.3 cases per 1000 a year, rates among the young adults remained stubbornly high at 42–47. This reduction in rates among infants showed that transmission from adult to child was lessening over the years studied, perhaps as a result of improved living conditions and nutrition.

The generation curves
By applying the same analysis for all generations at each time interval from 1895 to 1929, the most recent available years for his paper published in 1932, Andvord was able to plot generation curves from birth to those aged up to 35 years. A clear sinusoidal pattern emerges with highest rates during infancy, declining to a nadir aged 4–14, then climbing to a second peak in the 20–24 age groups and declining thereafter.

Those born from 1895 to 1905 had higher rates in infancy than at age 20–25. For those born subsequently the highest rates moved from infant to early adult life. Each curve for succeeding generations is identical in shape but slightly lower than the preceding one demonstrating that mortality declined for each succeeding generation but that rates in each generation remained highest in infancy and in those aged 20–24.

Further evidence from generation curves
Others who have used this type of analysis to investigate trends in tuberculosis were Frost and Springett.2,3 The latter looked at mortality trends in men and women separately in England and France. His data show a much smaller mortality in the infant group and a comparatively larger mortality in young adults so that the generation curves appear to be like a large inverted 'U' with the highest incidence in young adults aged 20–35. The trends were less clear in females than males.

Since the mid 1950s and the introduction of effective chemotherapy for the treatment of tuberculosis morbidity or notification data has to be used as a clearer measure of the incidence of tuberculosis than mortality. One of the important conclusions to draw for both Andvord and Springett is that once a generation passes early adult life the risk of tuberculosis diminishes. The reason that at any point in time rates are higher in older than younger age groups is that the older age groups are part of a higher (earlier) generation curve.

Modern studies
We have undertaken a similar analysis of data from England and Wales, and Hong Kong.4 Figure 1 shows the rates of disease for different 5 year age groups at 5 year intervals from 1958 to 1993. Rates for the older age groups are generally higher than for the younger age group. To obtain a generation plot from these data, lines for succeeding birth generations need to be drawn. The examples shown are for those born in 1909–13 and those born in 1929–33 (arrows). It can be seen that particularly for those born in 1929–33 there is a nadir around the age of 45–59 and thereafter a steady but definite increase so that the curve no longer resembles and inverted ‘U’ with the highest incidence in the young adult range but a capital ‘N’ with rates increasing with increasing age.

The implication of this is that once a certain age is reached around the mid-60s the likelihood of tuberculosis, that is the risk, actually increases. The curve above a given age is rising rather than falling. This means that for the elderly their chance of developing tuberculosis increases as they age, a finding at variance with the earlier work of Andvord and Springett.

Conclusion
Our recent analysis of tuberculosis as a generation illness may have uncovered a new and potentially important trend in the balance between host and pathogen suggesting that the elderly are at increasing risk of disease as they grow older. This might be expected as if an individual is infected the chances of disease developing tuberculosis once a certain age is reached, increases as the aging process diminishes the host’s immunity.

Earlier studies may not have revealed this trend as previously there were too few people living beyond a certain age from which to draw clear data. Whether this is a true reflection on the continuing struggle of the human race and the tubercle bacillus, as Andvord and Frost would maintain, or a spurious finding
based on faulty data will depend on other workers carrying out similar analyses over subsequent generations.

References

1 Andvord KF. Norsk Mag. Løvevidensk 1930;91:642.

Commentary: Kristian Andvord—an under recognized star in the epidemiological firmament

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The article ‘Continued Studies of Tuberculosis considered as a generation illness’ by Andvord published in this Journal in translation by Otto Jervell, makes available to a wide modern audience one of the milestones of research methods in medicine. This article is the text of a presentation in 1932 describing the concept of ‘birth cohort’, which is now a fundamental concept in medical research.