THE ERADICATION OF TUBERCULOSIS

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The word 'eradication' suggests complete abolition. It means destruction by uprooting. The roots of tuberculosis lie deep and have extensive ramifications. They reach to every infecting bacillus and include all the pathological lesions resulting from the reaction of the tissues in the many thousands of infected individuals. It is not possible to uproot all these numerous tendrils, but the main trunk can be destroyed leaving only the terminal branches, which must be dealt with as and when they begin to sprout. The meaning of eradication for the present purpose will therefore be modified to something less comprehensive than complete elimination. In connection with tuberculosis it will be used to mean the reduction of the mortality and morbidity to such a state that they are no longer of clinical or ecological importance.

It is not a Utopian dream to entertain such thoughts. Have not plague, typhoid, smallpox, leprosy and, more recently, diphtheria become terrors of the past? Why should not the menace of tuberculosis be reduced to similar insignificance? A glance at the statistics for the County of London¹ (Table 1) will show that there is a possibility of tuberculosis disappearing as a major cause of death in the future.

TABLE 1

THE COUNTY OF LONDON

PULMONARY TUBERCULOSIS—DEATHS (PER 1,000)

	Males	Females
1900	2.26	1.22
1910	1.62	0.87
1920	1.32	0.85
1930	1.14	0.65
1939	0.92	0.42
1950	0.51	0.22

NON-PULMONARY TUBERCULOSIS—DEATHS (PER 1,000)

	Males	Females
1900	0.60	0.44
1910	0.50	0.36
1920	0.24	0.19
1930	0.13	0.11
1939	0.08	0.07
1950	0.04	0.03

The fall in mortality from tuberculosis in children gives similar cause for optimism as will be seen in the following graph (Fig. 1), which shows the fall in the crude death rates per million living in the age group 0 to 4 years and 5 to 14 years for England and Wales during the period from 1907 to 1945. (I am indebted to Dr. Norman Smith for the production of these graphs.)

In the diseases already mentioned, a number of factors have caused the reduction in incidence and mortality, but the general decline in the number of cases can usually be attributed to the influence of one factor more than the others. In plague it was the control of the carriers of the bacillus, in leprosy the avoidance of contact with infectious cases, in typhoid and smallpox the introduction of a protective vaccine, and in diphtheria inoculation by an immunizing serum. To these factors must be added the general raising of the standard of public health, which is the common denominator in all progress against disease.

In reviewing these infections it is only in leprosy that the history of the past can give us guidance in the future eradication of tuberculosis. The other diseases are acute conditions in which either death occurs or complete immunity is conferred on recovery. In tuberculosis the immunity against the disease is incomplete, so that a state of partial healing occurs, accompanied usually by the persistence of infectivity. In leprosy the disease is chronic but not so infectious as tuberculosis and rarely a danger to uninfected persons after the second decade of life. Segregation of the infectious cases from the younger generation can, therefore, be a most effective measure in stamping out the disease. Tuberculosis, on the other hand, in any individual, has that awkward characteristic of relapsing and becoming infectious without giving rise to disturbing constitutional symptoms. It is, therefore, possible for individuals to be infectious without knowing it. Furthermore, there is the somewhat paradoxical fact that in any community the uninfected individual is very vulnerable to the infection, and not infrequently develops an acute progressive lesion.

TUBERCULOSIS.
ENGLAND AND WALES 1907-1950.
CRUDE DEATH RATES PER MILLION LIVING.

Fig. 1

From observations over many years and in a number of countries, it seems certain that when tuberculosis has been indigenous in any country for a hundred or more years, the population begin to acquire an immunity to the infection that becomes progressively stronger with the lapse of time, so that the incidence of chronic fibrotic lesions becomes more frequent as the centuries pass. It is, however, these chronic fibroid lesions that are so persistently infectious and a danger to the uninfected. Although it is difficult to prove, it is probable that the converse is also true; that the less contact a community has with infectious cases of tuberculosis the lower the acquired immunity against the disease. Consequently if by any chance the risk of infection suddenly rises, there will be a crop of acute lesions.

Some evidence to support these statements may be gathered from the general character of pulmonary lesions seen in countries where the incidence of infection remains high or has become very low.

In Denmark the mortality rate is at present 17 per 100,000. The facilities for the segregation of infectious cases are very good, the milk supply is free from tubercle bacilli and therefore the possibility of the average person becoming infected is

small. It is probable that in consequence of this the usual pulmonary lesion is much less fibroid in character than that seen in England and Wales.

In China, where the disease has been indigenous for hundreds of years without any great attempt at treatment or control, the lesions are usually densely fibrosed and often calcified, without giving rise to much constitutional disturbance, but are frequently infectious.

The investigations of John Francis² indicate that the mortality rate from pulmonary tuberculosis is highest in counties in England and Wales where the incidence of tuberculosis in cattle is lowest. This may mean that the acquisition of bovine tuberculosis in humans in infancy confers some immunity to later infection by the human bacillus. It does not, as might be thought, in any way support the suggestion that drinking tuberculous milk is the way to prevent tuberculosis in adults.

In countries in which tuberculosis is not indigenous, members of the population often develop an acute form of the disease when infected, particularly when individuals from such countries acquire a primary infection in infancy or late in life.

It appears that the chances of developing active tuberculosis depend upon:

1. The native resistance in the individual, and this depends on the length of time the ancestors of the individual have been exposed to infection.

2. The capacity for developing an acquired resistance following the primary infection. This will depend on heredity, age and sex.

3. The frequency of the infection. The highest resistance will eventually be overcome if the magnitude and frequency of the infection are great enough to ensure continuous multiplication of the organism in the tissues.

4. The virulence of the organism. Although the virulence of tubercle bacilli from lesions of different grades of activity shows little variation, there is considerable variation in the reaction of different animals to bacilli of the same virulence. It is also possible to produce strains of tubercle bacilli that have varying grades of virulence, and these produce lesions of different character when injected into animals of different species.

These factors have an important bearing on the course of the disease, both in the individual and in the community. They have been operating for a number of years in England and Wales. The aggregate effect is shown in the present state of tuberculosis in the country.

1. The death rate per 100,000 population for all forms of tuberculosis has fallen from 94 to 36.4 during the last 25 years, and from 56 to 36.4 per 100,000 population during the last five years.

2. The mortality in the 0 to 4 age group is also falling. In 1907 it was 263.0 and in 1950 it was 16.5 per 100,000 living.

3. The age group in which the death rate from pulmonary tuberculosis is highest is rising, particularly in males.

4. The age when primary infection takes place is rising. This means that there are more persons highly susceptible to infection in the early age groups.

5. The possibility of becoming non-infectious after treatment is more likely than in the past. The observations of Snell³ are interesting in this respect. He found that the proportion of sputum positive cases converted in 1938-41 was 15-19 per cent. and 63 per cent. in 1950.

6. The figures of Bradbury⁴ and Stocks⁵ show that the treated tuberculous person has a greater expectancy of life today than 20 years ago. In Denmark, Anderson⁶ has shown that the length of life of the fatal case of pulmonary tuberculosis has increased by 300 per cent. during the last 30 years, although it is still only 59.4 and 62 months for males and females respectively.

7. The number of new cases discovered each year remains about the same, showing that infection is still as prevalent, but that as the ex-

pectancy of life has lengthened and resistance to the infection has increased, except in elderly males where there may be some decrease. The high mortality in young girls is probably due to the considerable number of primary infections taking place during the unstable period of adolescence.

8. Treatment is more successful, particularly by antibiotics and thoracic surgery, both of which are rendering infectious cases sputum negative.

9. The milk supply of the country is rapidly improving so that bovine infection in childhood is becoming much rarer in towns and cities, but is still frequent in rural districts.

10. Added to these conditions, B.C.G. vaccinations are being carried out more and more frequently on the non-infected exposed to the risk of infection.

The interplay between infection and resistance is so far resulting in a gradual submission of the disease to the biological defence mechanisms of the race. In Denmark the victory has been more complete than in England, but even there the hard core of infectious active cases remains, and the rate of fall of the mortality curve is becoming slower. Eradication of the disease demands that the curve shall continue to fall.

The process of the eradication of tuberculosis is one in which natural evolution plays the major part, but for a successful result it is necessary to assist nature by raising the resistance of the tissues and controlling the infecting bacillus. In a community in which no anti-tuberculous measures are taken the disease becomes almost universal and develops into a very chronic fibroid type. If in a community every possible means of suppressing the disease was undertaken and carried out with success, it is highly probable that a race with low resistance would develop so that any subsequent contact with the bacillus in any individual would cause an acute and fatal type of lesion to develop. The problem of eradication therefore resolves itself into controlling the infection and at the same time retaining native resistance against it.

The solution lies in breaking, as far as is possible, the contact between infectious and non-infected persons. This cannot be done absolutely in any community. The resistance of the uninfected must therefore be maintained and, if possible, increased by a high standard of living and by injection of substances that will stimulate the formation of antibodies. If it is agreed that the person who possesses a healed primary lesion withstands subsequent infections better than one who has never been infected, and if a benign primary infection can be given without risk by vaccination with B.C.G. or the vole vaccine, then it is illogical to allow non-infected persons to come into contact with virulent infection without pro-

tecting them by vaccination. Where it is possible to ensure that contact with virulent tubercle bacilli will not take place, then vaccination is not necessary, but except in a few remote areas and sparsely populated countries, this assurance cannot be given.

The treatment of infectious cases is still a long way from perfect. A case that at some time has discharged tubercle bacilli may do so again without warning. If such infectious people are released among a population that has been protected from virulent infection for many years, the number of acutely active cases of tuberculosis that will result may be considerable. To assist further in preventing the spread of infection it is necessary to do all that is possible to treat and educate infectious persons. It is not possible to say how many new cases arise from every infectious case of tuberculosis, but none can arise from a non-infectious one, and very few from those that are segregated either in village settlements, hostels or hospitals.

Two factors prevent the reduction of the tuberculosis mortality and morbidity figures to zero. The first is the gradual decrease in resistance in a community in which precautions against spread of infection are particularly successful. This means that the few remaining infectious individuals can cause progressive primary lesions in those persons whom they infect, as there are no primary infections of small magnitude by which individuals can obtain acquired immunity. A lowered general resistance to the disease is the result of completely protecting the majority of individuals from infection; but haphazard infection must not be relied upon as a means of conferring immunity as it always involves the possible development of progressive active disease in susceptible individuals. Fortunately, by vaccination, it is possible to produce benign primary lesions that confer a certain degree of acquired immunity. This acquired immunity may not be as great as that obtained from a healed primary lesion following natural infection, but it does not involve the risk of the production of active disease.

The loss of native and acquired resistance is a serious matter to any individual who emigrates from the sheltered conditions of a country in which the incidence of infection is very low to one where it is high. The risk of developing a progressive lesion following primary infection becomes great. The eradication of tuberculous disease, therefore, becomes an international problem, and is closely associated with the movement of populations both collectively or individually.

So long as there are infectious cases in any population the possibility of new cases of active disease arising is always present, particularly in the

susceptible age groups of 0 to 5 years and 18 to 25 years. The prevention of contact with infection and the raising of resistance by a good standard of living must be the main feature of any scheme to eradicate tuberculosis. This part of the scheme is naturally much more difficult than instituting a vaccination programme, but just as essential. Compulsory segregation of infectious cases is impracticable and unwise, so that where persuasive measures fail reliance has to be placed on education and antibiotics. There is still much new ground to be covered in the education of the public in precautionary methods of preventing infection. The use of antibiotics as a method of preventing the spread of infection is new and should be seriously considered. The complication of producing infectious persons with tubercle bacilli resistant to the antibiotic must be remembered, but if 50 per cent. of chronic advanced cases can be made non-infectious for one or two years of their lives, a great number of new cases will be prevented. The last months of the advanced case will probably be bedridden, when the sphere of influence as regards infection is strictly limited. It, therefore, becomes a matter for serious consideration that chronic, ambulant, infectious cases should be given antibiotic treatment as a preventive measure, in addition to general public health measures.

A scheme for the eradication of tuberculosis therefore requires that:—

1. Tubercle bacilli emitted from infectious persons or animals must be collected and destroyed.
2. Contact between non-infected persons and virulent tubercle bacilli must be broken.
3. Treatment must be attempted to render infectious cases non-infective.
4. The resistance of the infected and non-infected must be maintained by a high standard of living and good conditions of work.
5. Acquired resistance must be conferred upon the non-infected by producing benign primary tuberculosis with antibody-producing vaccines. This immunity must be reinforced by further vaccination whenever there is evidence that it has waned or disappeared. Only in groups of population where the incidence of infection is very low and the community relatively static can the protection of vaccination be omitted.

By these methods tuberculosis can be eradicated, but to carry them out needs money, labour and the co-operation of all concerned.

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