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How Much Control of Tuberculosis?*

W. H. FROST, M.D., F.A.P.H.A.

*Professor of Epidemiology, School of Hygiene and Public Health,
Johns Hopkins University, Baltimore, Md.*

THE impetus for the modern campaign against tuberculosis came from Koch's discovery of the tubercle bacillus and his demonstration of its necessary rôle in the causation of the disease. From his evidence the inference was plain that the disease could be prevented if infection with the tubercle bacillus could be avoided. There was then, and there has been since, no reason to doubt the soundness of the thesis that complete protection against exposure to the tubercle bacillus would completely prevent tuberculosis; but there has been and is still grave doubt as to whether it is practicable to set up and maintain protective measures which will be sufficient to give this result.

The years that have elapsed since the campaign began have extended our knowledge of tuberculosis in every direction. They have brought improvements of great importance in methods of diagnosis and treatment, and have seen the building up of a tremendous

machinery for the care of the tuberculous. But they have not brought forth any really new principle of prevention; they have produced no well proved and dependable method for lasting and effective specific immunization by artificial means and no simple specific cure for the disease. Thus, while organization and weapons have been improved, the essential strategy of the attack against tuberculosis remains the same as it was 50 years ago. The main objective is still avoidance of exposure, and the strategy is still that of a frontal assault on discoverable sources of infection. From the standpoint of prevention, curative treatment and measures designed to increase resistance to infection may be regarded as supplementary.

If we could measure the success of this strategy by the decline in mortality from tuberculosis, the results must be considered gratifying beyond expectation, for in this country, and quite generally in others where the progress of civilization has been comparable, mortality has steadily declined. For instance, in that part of the United States for which we have

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continuous mortality statistics since 1900—an area made up largely of the northeastern states—the crude mortality rate from tuberculosis in 1933 was less than one-third of the rate in 1900. And, what is still more gratifying, the rate of decline has been more rapid in the latter than in the early years of this period.

There are, however, many and sound reasons for doubting that the general and rapid decline of tuberculosis during the last 50 years has been due *principally* to the measures which have been taken for the specific purpose of preventing infection. To mention only a few of these reasons; it is readily apparent that even in areas best provided with sanatorium facilities the isolation of open cases of tuberculosis is far from complete. Also, as has often been pointed out, the decline in mortality is not limited to those areas in which vigorous control measures have been carried out and when studied broadly shows no clear correlation with the extent of these measures. There is also conclusive evidence that although tuberculosis as a manifest disease has declined greatly, tuberculous infection remains high. It has not been uncommon in recent years to find, in cities, that more than one-half of the children attending public schools show evidence of infection (that is, a positive tuberculin reaction) before they have passed the age of 15, and that of adults past 30 few indeed remain uninfected.¹

Moreover, the general doctrine that communicable disease may be prevented satisfactorily by avoidance of infection has fallen somewhat into disrepute as applied to those diseases which, like tuberculosis, are transmitted directly from person to person by way of the

1. It is generally conceded that the control of human infection from bovine sources has already been highly effective in this country and that further control is practicable. All that follows refers to infection from *human* sources.

respiratory tract. The physical difficulties in the way of preventing this kind of person-to-person transmission are obvious enough; and, as bacteriological and immunological observations on the diseases of this class have been extended, it has been more and more convincingly demonstrated that even when the diseases themselves are of limited occurrence, as is true for instance of diphtheria, scarlet fever, and cerebrospinal meningitis, infection with the specific microorganisms which cause them is almost universal. It may, in fact, be accepted as a general principle that it is impracticable, in populous communities, so to isolate an individual from his neighbors as to insulate him continuously against exposure to infections transmitted directly in this way from other people. Such relative isolation as the most favored classes of society enjoy may serve to postpone the average age at which first infections occur; it does not nearly suffice to afford complete and continuous protection over such a period as 20, 30, or 40 years.

Therefore, for protection against diseases of this class, we have ceased to rely greatly upon simple avoidance of exposure and have turned to other measures, such as specific immunization and treatment and, in certain diseases such as measles and whooping cough, the device of postponing exposure from infancy until later childhood, when infection is less dangerous.

It has, moreover, become recognized that protection against exposure to highly prevalent, endemic infections, unless it can be kept up through life, may in the end prove more harmful than beneficial. For the same con-

2. This and preceding paragraphs should not be interpreted as implying that the isolation of known cases of the diseases of this group is useless. There is reason to believe that infections contracted from carriers at large in the general population may be less dangerous than those contracted in the immediate environment of clinical cases.

cealed infections which spread disease producing bacteria and viruses so widely through the population serve at the same time to build up a protective immunity. And since a good many infectious diseases are apt to be more severe in adults than in children between 5 and 15 years of age, the postponement of first infections from childhood to adult age may be actually disadvantageous.²

Finally, it is highly probable that the cyclic changes in prevalence which are observed in some diseases are brought about chiefly by evolutionary changes in the characteristics of the specific microorganisms, the causes of which are to be found in uncontrolled natural forces. Thus, within the last 100 years we have seen both diphtheria and scarlet fever, which previously were of widespread occurrence but relatively low prevalence, rather suddenly take on a much more malignant character and attain a much higher prevalence more or less throughout the world. Then, after some decades of high prevalence and malignancy, they have in the last 40 years gradually declined both in prevalence and severity. With respect to these and a number of other epidemic diseases, such as influenza, cerebrospinal meningitis and poliomyelitis, the explanation of such cyclic changes in severity and prevalence remains obscure, but we are obliged to recognize at least the possibility that they may be due to the operation of natural forces beyond human control.

When these epidemiological conceptions, which are firmly enough established with respect to various of the acute epidemic diseases, are applied in interpreting the epidemiology of tuberculosis, they tend obviously to cast doubt upon the efficacy of the measures which have been taken to control tuberculosis by limiting ex-

posure to the tubercle bacillus and upon the possibility of establishing permanent and complete control on this principle. However, the extremely pessimistic view of tuberculosis control which has been taken by many eminent students of the subject overlooks some important considerations which bear upon the question.

One of these considerations is the probability that infection established by a small number of microorganisms may be less severe in its course than infection resulting from a larger or frequently repeated dosage.³ As regards human infection with the tubercle bacillus, the epidemiological evidence to this effect is fairly impressive and is supported by a good deal of evidence from experiments on lower animals. It may well be, therefore, that the measures which have been taken to limit the spread of the tubercle bacillus in our environment, even though they are insufficient to prevent eventual infection of nearly everybody, may still be of great effect in mitigating the severity of resulting infections, because of reduced frequency and dosage of infection. If this is so, it is a consideration of real importance.

It is also to be remembered that the frequency of exposure to the tubercle bacillus may have been reduced much more than would appear to be indicated by the results of tuberculin tests. For instance, if we find that at 15 years of age 60 per cent of the population show a positive tuberculin reaction, which we may take as evidence of prior infection with the tubercle bacillus, it is obvious that, under the worst conditions which can have existed in the past, the proportion infected before reaching this age could not have been greater than 100 per cent. It may therefore appear that there can have been no more than a

3. See reference 2.

40 per cent reduction in the prevalence of infection, whereas we know that there has been a much greater reduction in mortality. However, assuming a random distribution of exposure, the rate which would result in infecting approximately 99 per cent within 15 years is some 4 times the rate which would infect only 60 per cent within that period.⁴ Therefore, the simple fact that under present conditions nearly everybody who reaches middle age shows evidence of having been infected with the tubercle bacillus does not at all imply that there has been no great reduction in the rate of exposure to infection.

A still more important consideration which has been too frequently overlooked when tuberculosis is compared with other communicable diseases transmitted directly from person to person by way of the respiratory tract, is that the tubercle bacillus is differentiated from other disease producing organisms of this group by the conditions governing its growth within the body and its escape from the infected host. When the tubercle bacillus invades the body it does not multiply upon the surface or in the superficial layers of the mucous membrane. It penetrates to the deeper tissues and, as it multiplies, is surrounded by a protective cell-wall which the body throws around it. In order to escape into the outside world and infect others it must break through this defensive wall. In pulmonary tuberculosis—the type of most consequence in the spread of infection—this result is relatively infrequent. In the great majority of infections the bacillus is walled off within the body,

and the lesion eventually heals without breaking through to the external air passages. Thus, the conditions which limit the propagation of the tubercle bacillus are: (1) that in order to escape from its host it must cause a lesion which breaks through to the surface—in general an extensive lesion which severely damages the host—and (2) that it succeeds in producing such lesions in only a limited proportion of infected persons.

Various other pathogens of man are subject to one or the other of these conditions, but not to both. For instance, the virus of measles appears to be spread only from persons actually suffering from or in process of developing the eruptive disease; but the virus is so highly infective and pathogenic that it succeeds in producing this effect in nearly all persons who survive to adult age. On the other hand, the diphtheria bacillus, the pneumococcus, the virus of poliomyelitis, and various other pathogens transmitted by way of the respiratory tract, cause clinical disease in only a small proportion of those who are infected; but actual disease is not essential to propagation of these microorganisms, since sub-clinical or "carrier" infections, being equally "open," suffice to spread them from host to host, and to perpetuate the species.

The combination of these *two* limiting conditions is the peculiarity of the tubercle bacillus which makes it more amenable to control by case-isolation than are diseases such as diphtheria, scarlet fever, and measles. For notwithstanding that the tubercle bacillus infects nearly everybody sooner or later, most of the infections are "sterile," in the sense that although the bacilli multiply within the body they do not escape to reach other hosts. Only the relatively small proportion of infections which progress to the stage of open lesion are successful

4. The conditions assumed in making these calculations are of course entirely hypothetical, and much simpler than obtain in nature. The figures given are to be interpreted only as illustrating the principle that exposure rates may differ much more widely than would be indicated by casual comparison of the results of tuberculin tests.

in spreading the infection to others,⁵ and it is only these sputum-positive cases that need to be isolated in order to prevent the spread of infection.

If the effective control of tuberculosis required *complete* isolation of *all* open cases, throughout the whole of their open stage, the present status could not be considered encouraging, for a large proportion of such cases are discovered only after they have reached a fairly advanced stage; and the isolation even of cases known to the health authorities is probably less than 50 per cent complete.

However, for the eventual eradication of tuberculosis it is not necessary that transmission be *immediately* and *completely* prevented. It is necessary only that the rate of transmission be held permanently below the level at which a given number of infection spreading (*i.e.*, open) cases succeed in establishing an equivalent number to carry on the succession. If, in successive periods of time, the number of infectious hosts is continuously reduced, the end-result of this diminishing ratio, if continued long enough, must be extermination of the tubercle bacillus.

Bearing in mind this principle, it is a fair inference that in this country as a whole we have already reached the stage at which the biological balance is against the survival of the tubercle bacillus, for year by year the mortality from tuberculosis is decreasing. It is true that we do not have equally direct statistical evidence of a proportionate decrease in the prevalence of infective cases, taking into account not only the number of cases but duration of the open stage; but there appears to be no good reason to doubt that the prevalence of open cases is

diminishing at something like the same rate as mortality from phthisis. This means that under present conditions of human resistance and environment the tubercle bacillus is losing ground, and that the eventual eradication of tuberculosis requires only that the present balance against it be maintained.

As to maintenance of this balance—favorable to us, unfavorable to the tubercle bacillus—there are, of course, elements of uncertainty, among them uncertainty as to the stability of our civilization. But if it be assumed that environmental control affecting the spread of tubercle bacilli from existing foci can be maintained at its present level (and we may justly expect to improve it), we know of only two forces which, singly or together, would check or reverse the downward trend of tuberculosis. These are: (1) a decrease in human resistance to the disease, or (2) some fundamental change in the adaptation of the tubercle bacillus to its host, tending to favor survival of the parasite.

With respect to the latter possibility, we can do no better than base future expectations on past experience. Upon this basis, if we were discussing diphtheria, scarlet fever, or influenza, their past history would lead us to expect future changes, more or less sudden, in the disease-producing properties of their causative organisms. But present knowledge of tuberculosis is consistent with the view that the specific properties of the tubercle bacillus have not changed appreciably in modern times; and in the absence of compelling evidence for such variation in the past, we are under no necessity of anticipating it in the future. Therefore, while we have no means of excluding this possibility, I do not know of any reason why we should expect it.

A question of more immediate concern is whether, with progressively diminished exposure to tuberculous in-

5. It is quite possible that tubercle bacilli may escape from apparently "closed" lesions more frequently than is implied here; but epidemiological evidence indicates that demonstrably open pulmonary lesions are of predominant importance in the spread of infection.

fection, we must expect such decrease in human resistance to this infection as would check or reverse the present downward trend.

It is probable that one of the most important factors in the decline of tuberculosis has been progressively increasing human resistance, due to the influence of selective mortality and to environmental improvements such as better nutrition and relief from physical stress, tending to raise what may be called nonspecific resistance. It is, however, a reasonable expectation that the increase in average resistance due to these causes will be maintained, for, while complete elimination of the mortality from tuberculosis would check this process of raising genetic resistance, there is no apparent reason why it should result in reversion to a state of higher average susceptibility than exists today. Also, any gains due to better nutrition and to other elements of personal hygiene should be permanent if civilization continues at its present level or a higher one.

The kind of resistance which is of a less permanent order and which seems more likely to be lost, is individual specific immunization by so-called latent infection. At present a majority of the population in many areas acquire their first infection with the tubercle bacillus between late infancy and adolescence, precisely at the age when the immediate reaction to infection is most favorable. However, further reduction in the prevalence of tubercle bacilli in the environment must necessarily postpone first infections to a later average age; and, as it is believed by some authorities that primary infection is more dangerous in adults than in children, it is feared that such postponement of infection will in the end prove disadvantageous.

The question which is thus raised cannot at present be answered with assurance. We do not yet know enough

about the nature and durability of any immunity which may be conferred by infection acquired in childhood. It is, however, significant that in those areas where childhood infection is most common, we find the highest mortality in adult life; and that in areas such as Cattaraugus County, N. Y., where a majority of adolescents are demonstrably tuberculin negative, the mortality in adult life is low. Also, occupational statistics show that in adult life the mortality from tuberculosis is lowest in the professional group who, as a class, have been least exposed to infection in childhood. Therefore, while this whole question obviously needs much more study, there is at present no compelling evidence that the downward course of tuberculosis must be checked by eventual loss of mass immunity.

We need not assume, then, that tuberculosis is permanently and ineradicably engrafted upon our civilization. On the contrary, the evidence indicates that in this country the balance is already against the survival of the tubercle bacillus; and we may reasonably expect that the disease will eventually be eradicated. There can be no certainty of this result, but it is an expectation sufficiently well grounded to justify shaping our tuberculosis control program toward this definite end.

As regards means to this end, an effective program of tuberculosis control must first of all be definite and specific, aiming at the prevention of tuberculosis by the most direct methods possible. At the same time it cannot be too greatly narrowed; it must not only provide for the discovery and medical care of tuberculosis and isolation of open cases, but must equally include a generous plan of social assistance. It is impossible, within a brief space, to discuss the details of such a program, extending as it must in many directions. The most that can be done is to summarize the principal

kinds of activity and to set them in an order of relative importance. This I think should be about as follows:

1. The isolation in sanatoria of *all known* open cases of pulmonary tuberculosis, continuing isolation so long as the cases remain open.

2. Adequate medical care, preferably in institutions, for the *known* cases of tuberculosis which are active but not in an open stage, since these cases constitute the group most likely in the immediate future to become infectious.

3. More vigorous effort to find cases of tuberculosis earlier and to bring them more promptly under medical care and under isolation if they are discharging bacilli

4. Special protection, including medical observation and advice, and financial aid as needed, for those groups who, though not at the time suffering from tuberculosis, are most imminently endangered.

The isolation of *known open* cases is placed first because it is the most direct method that we have for reducing the prevalence of tubercle bacilli in our environment; the measure which, applied to the smallest number of people, gives the maximum of protection to the community. It is also one of the measures at present often neglected or compromised by makeshift attempts at home isolation. But the broader reason for giving first place to the isolation of open cases is that if this is carried out thoroughly it leads up to all the other measures indicated. For it is in the household associates of the open case that the search for additional cases should begin, with the certainty of finding some that are in need of medical care; and, if prevention of tuberculosis is the aim, nowhere is generous financial aid more urgently needed or better justified than in the families of the tuberculous poor who bear the double risk of intimate exposure to the tubercle bacillus and poverty.

Thus the known open case is the logical center from which to develop protective measures of all kinds. And

merely to carry out *thoroughly* this one item in the program, the institutional isolation of all known open cases, is no simple matter. It involves much more than diagnosing the cases and providing beds for them at public cost. It equally involves inducing the patients not only to enter the institutions, but to remain there as long as may be necessary, and making it possible for them to do so. The medical and social organization which best meets all these needs in all discovered cases of open tuberculosis will, I think, be the organization best prepared to spread its activities more widely from this center.

How far the tuberculosis control program should extend in the direction of general social betterment is a question which, perhaps, need not be answered. Probably nothing has been more influential in bringing about the decline of tuberculosis than progressive improvement in the social order as a whole; and nothing, perhaps, is more essential to the further effective control of the disease than to hold up, and so far as possible to improve, the standards of living of the lower economic strata. Obviously, the tuberculosis control program cannot expand to include the whole scheme of social betterment; but it can, and I think it should be concerned with raising the standards of living of those groups who are in most imminent danger of tuberculosis, beginning with the families of the tuberculous, and extending thence as far as practicable.

As regards the families of persons suffering with open tuberculosis, I think a clear distinction should be made between the kind of public aid given them and that which is given generally to the poor who are disabled. For if we are to require the isolation of open tuberculosis as a matter of public protection, it becomes a public responsibility to bear not only the cost of medical care, but the whole cost to the

patient's family, or as large a share as may be required. Moreover, it should be recognized that what is needed is not bare maintenance on a minimum or average "relief" standard, that it is not sufficient merely to prevent their dropping lower in the economic scale; it may often be necessary to raise them to a higher level. The two conditions which most favor tuberculosis are intimate exposure and poverty. Where these two meet is where double protection is needed, and it implies more than free medical care and hospital beds.

As the prevalence of tuberculosis is progressively diminished, the control program must necessarily be readjusted, at least in a quantitative way, and I think it should also be changed somewhat in direction. The soundest principle to follow seems to me to be that as the cases become fewer and fewer, preventive measures should be centered more and more upon the open cases; that the protection thrown around these infective cases and their

immediate contacts be not relaxed, but steadily and progressively increased. This is a sound principle of epidemiology, for it is to be expected that as the prevalence of the tubercle bacillus in the general environment is diminished, infection and disease will become more distinctly focalized. In fact, there is already evidence of increasingly wide differentiation between the most sheltered and the most exposed groups of our population; and even now we should take more cognizance of this in directing our efforts.

The principle of centering effort increasingly upon the open cases themselves is also sound psychology. As the menace of tuberculosis becomes less imminent, the public will naturally take less interest in general and diffuse measures of protection. But in proportion as the disease becomes rarer, less a matter of everyday experience, we may be assured that public opinion will not only support but will even demand more rigid isolation.

Living Conditions

IT is often overlooked, parenthetically, that in writing of disease physicians did not limit themselves to its clinical aspects. They were necessarily concerned with ultimate as well as immediate causes, with the predisposing social environment as well as with the actual infections. There is much valuable information on general living conditions among the poorer classes in this country, whether they were Negro slaves or Irish laborers, in the papers and reports of socially-minded medical men. The same is true for other nations. If your library happens to contain the English poor law board report of 1842, for instance, it possesses one

of the most systematic accounts in existence of the living conditions in British cities in early Victorian days. This was essentially a medical survey.

In like manner the whole early literature on hygiene, both personal and public, possesses social meaning. Much of it found its way in the old days into the general libraries. When Sir John Sinclair prepared his bibliography of this subject about 1800, he was able to list nearly 1,900 items in European languages, which suggests that it was even then no small literature.—Richard H. Shryock. *Library Collections in Social Medicine*, Am. Library Assoc., 1936.