

A Survey of Tuberculosis Among Diabetics

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Both in the literature and as a matter of clinical experience, there has been a general impression that diabetics have an increased susceptibility to tuberculosis. The largest study in the literature is that of Root,¹ who obtained roentgenograms on 1659 consecutive diabetic patients between 1927 and 1930.

The present study was launched as a joint project of the Philadelphia Tuberculosis and Health Association and of the Philadelphia County Medical Society, with a committee of 14 specialists representing the fields of tuberculosis, roentgenology and diabetes. This paper is a condensation of the full report recently published, which consists of 50 pages, including 56 tables.²

From December 1945 through February 1947, dia-

betics were interviewed and data were recorded on two questionnaires—one during the patient interview and the other by the private or clinic physician. The diabetics were x-rayed at two units and the films mixed with those of many hundreds of nondiabetics being routinely surveyed. Two of us (K.R.B. and D.A.C.) interpreted every film of the diabetics and each was unaware whether the film being interpreted was of a diabetic or of a nondiabetic. There was no possibility of any unconscious bias.

ANALYSIS OF THE CASES SURVEYED

Of 3167 individuals submitted by 22 diabetes clinics and 95 private physicians, 3106 satisfied the committee's

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criteria for diabetes. 82.6 per cent of the cases were from the 22 hospital clinics and 17.4 per cent were referred by the 95 private physicians. The prevalence of tuberculosis among the clinic patients and among the private patients was practically the same, 8.3 per cent and 8.9 per cent, respectively.

Among the items of information collected were the severity of the diabetes as measured by the amount of insulin taken, the duration of the diabetes, control of the diabetes, age at survey, age at onset of diabetes, sex, race, per cent standard weight, history of coma, history of gangrene and amputations, history of boils and carbuncles, history of pleurisy, history of contact with tuberculosis, presence of survey tuberculosis, presence of active tuberculosis, stage of tuberculosis, site of tuberculosis, site of cavities. These data were transferred to punch cards and the statistician produced over 100 tables, each table correlating two, three or more items. In this large number of tables it was necessary to seek for some order and meaning.

AGE, SEX AND RACE

The distribution of the 3106 diabetics by age, sex and race is shown in Figure 1. The group was preponderantly older, female and white. There were 430 individuals younger than 40—14 per cent of the total and hereafter we shall refer to these as the younger group. 86 per cent were 40 or older. 30.7 per cent were males and 69.3 per cent were females. There were 861 nonwhites, 27.7 per cent of the whole diabetic group. The nonwhite population of Philadelphia was estimated to be 14.5 per cent. It will be noted that the peak of the nonwhite members is about a decade earlier than for the whites, probably due chiefly to the shorter expectation of life of the nonwhites in the general population.

COMPARISON WITH CONTROL GROUP

The first problem which needed to be investigated was how the prevalence of tuberculosis in the diabetic group compared with the prevalence in the general population. While it was not an ideal control group, 71,767 apparently healthy Philadelphia industrial workers who had been surveyed between October 1942 and May 1945 were used (Figure 2). This large group was broken down into subgroups to correspond to the distribution by age, sex and race of the diabetic group. The prevalence of tuberculosis in the industrial group thus adjusted was 4.3 per cent. Of the 3106 diabetics 261 were found to have tuberculosis. This is a prevalence of 8.4 per cent, nearly double that of the in-

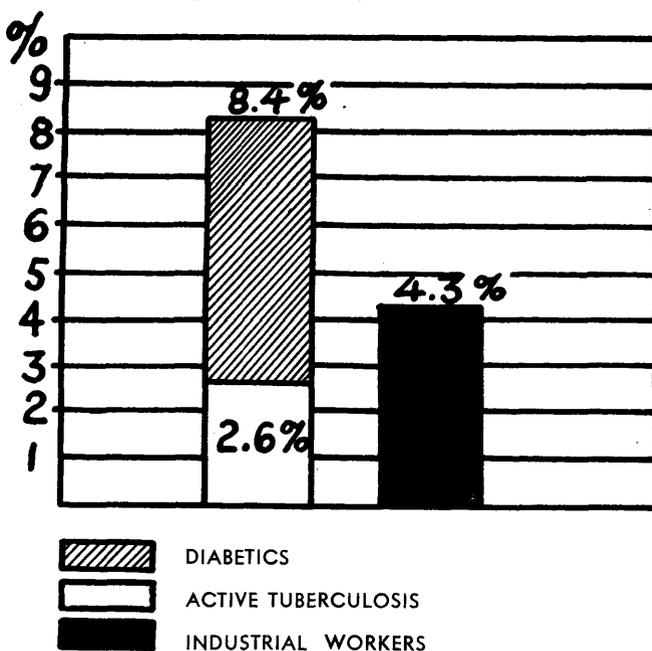


FIGURE 2 Prevalence of tuberculosis in diabetics and in industrial workers (adjusted)

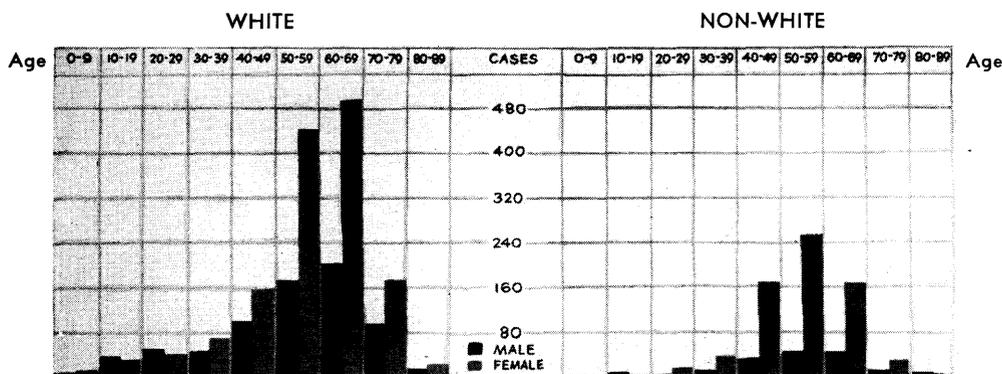


FIGURE 1 Age, race and sex distribution

dustrial group. 80 cases were classified as active tuberculosis, a prevalence of 2.6 per cent. The prevalence of total survey tuberculosis in the general population is known to increase markedly with advancing years. To a small extent this was found to be true in the diabetic group.

There was more than twice as much survey tuberculosis among the white diabetics as among the Negroes—almost 10 per cent contrasted with 4.3 per cent. Surveys of the general population have also shown a higher figure for whites. However, the tuberculosis mortality rate of the general population of Philadelphia was more than five times greater for Negroes than for whites. Presumably, tuberculosis runs a more acute course in the Negro diabetic and many do not live long enough to be counted in a survey.

Almost twice as much tuberculosis was found in male diabetics (12.3 per cent) as in female diabetics (6.7 per cent).

THE INFLUENCE OF SEVERITY OF DIABETES

While we were studying certain diabetes factors in relation to the increased tuberculosis prevalence among diabetics, we noted that tuberculosis read as "probably active" seemed more relevant than did total tuberculosis. Probably fibrocalcific and strand-like lesions often antedated the diabetes.

The prevalence of active tuberculosis was 2.6 per cent in the whole group. Of course, it occurred to us at once that the severity of the diabetes as measured by the amount of insulin taken might have something to do with the prevalence of active tuberculosis, and indeed this proved to be the case. In Figure 3 one will notice that the prevalence of active tuberculosis is approximately twice as great in the younger group as in the older group. One will notice, too, that when the

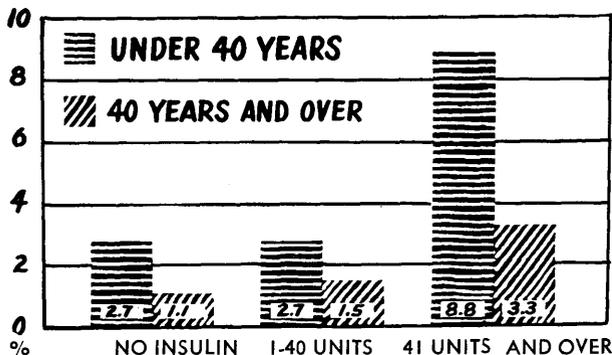


FIGURE 3 Prevalence of active tuberculosis by severity of diabetes and age

patient is taking 41 units of insulin and upward (severe group) the prevalence of active tuberculosis for both the younger and older diabetics is about three times as great as in the mild and moderate cases.

When one considers the relationship between severity of the diabetes and the prevalence of total survey tuberculosis in the younger age group, the same increase of prevalence with increase of severity obtains. In the older age group, however, there is so much old inactive tuberculosis in all three degrees of severity that no clear relationship of prevalence and severity can be demonstrated.

THE INFLUENCE OF DURATION OF DIABETES

One would think that the duration of the diabetes might be a contributing factor to the prevalence of active tuberculosis. In Figure 4 it is shown again that the prevalence of active tuberculosis is greater in the younger group than in the older group. It is also shown that when duration of under 10 years is compared with duration of 10 years and over in the younger group, there is a marked increase of prevalence from 3.2 per cent to 11.4 per cent. In the older group there is no such increase; in fact, there is slight decrease. When total survey tuberculosis is considered, the same relationships are found. The prevalence of survey tuberculosis in the younger group with duration of 10 years and over was 16.7 per cent.

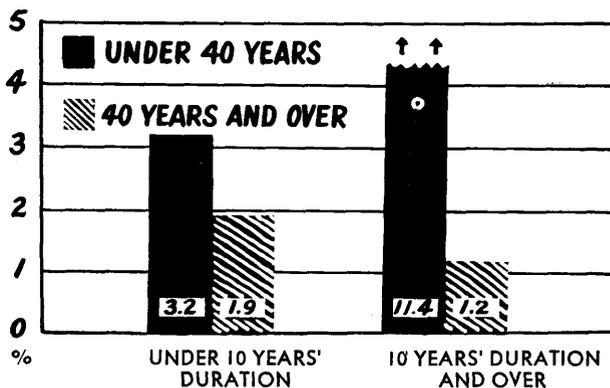


FIGURE 4 Prevalence of active tuberculosis by duration of diabetes and age

THE INFLUENCE OF A HISTORY OF DIABETES COMA

It was anticipated that the degree of control of the diabetes might prove to be an important factor in the prevalence of tuberculosis. To estimate control one should have available a whole body of information which it was impossible to collect. Furthermore, phy-

sicians are by no means in accord as to what standards constitute good control.

It was impossible to draw any valid conclusions regarding the relationship of tuberculosis to our observations of blood sugar levels. However, another approach to the problem of diabetes control is through a study of a history of coma, the end result of the disease when uncontrolled. Of the group under age 40, approximately 39 per cent had been in coma one or more times and 61 per cent had had no coma. Of the older group, age 40 and over, only 13 per cent had had coma. In Figure 5 is shown the prevalence of active tuberculosis in the younger and older groups, with and without coma. As in the previous figures, the prevalence of active tuberculosis is much higher in the younger group. But

in the younger group the prevalence of active tuberculosis with coma is only a little higher than without coma, 6.0 per cent compared with 4.7 per cent; and in the older group the prevalence is slightly lower when coma is present, the figures being 1.4 per cent with coma and 1.6 per cent without coma. When total tuberculosis is considered in the younger group the prevalence is 9.6 per cent with coma and 5.8 per cent without coma; in the older group 6.9 per cent with coma and 8.2 per cent without coma. When the younger group only is considered, it would seem that a history of coma does have a slight influence in increasing the prevalence of tuberculosis, probably because cases of diabetes which get coma as a whole are more severe, or less well controlled, than those which do not.

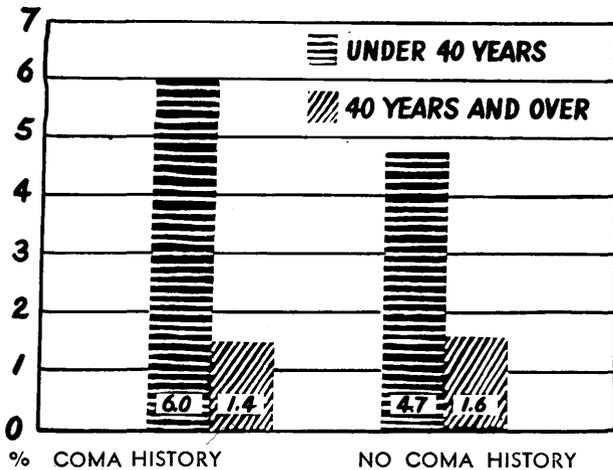


FIGURE 5 Prevalence of active tuberculosis by coma history

THE INFLUENCE OF BODY WEIGHT

It has long been recognized that obesity predisposes to diabetes; in like manner thinness predisposes to tuberculosis. It seemed, therefore, that it would be of interest to study the relationship between standard weight and the prevalence of tuberculosis in the diabetic. In Figure 6 the prevalence of total tuberculosis is compared in diabetics and in industrial workers, each divided into groups of underweight, standard weight and overweight. In both the diabetics and industrial workers tuberculosis was twice as prevalent in the light weights as in the heavy weights. It will be noted, too, that the prevalence of tuberculosis is much larger in the diabetics than in the industrial workers.

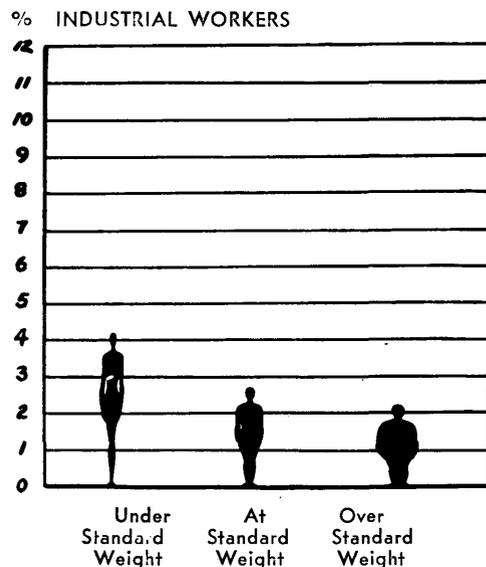
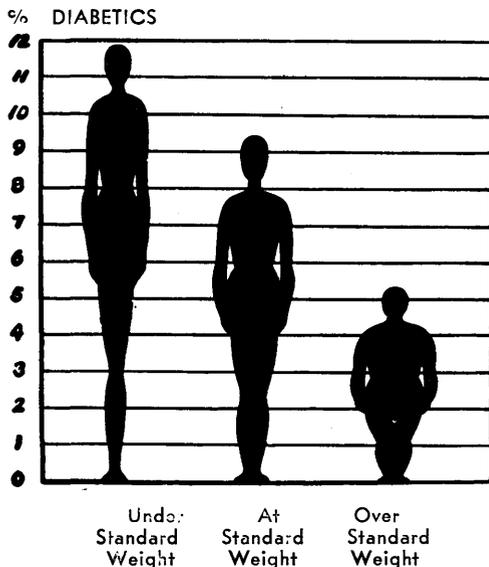


FIGURE 6 Prevalence of total tuberculosis by standard weight

When we study the prevalence of active tuberculosis by age and standard weight, as is done in Figure 7, it will be noted that weight makes a great difference in the prevalence of active tuberculosis in both age groups, the figures being 6.2, 6.7 and 3.0 per cent for the younger group, and 3.9, 1.4 and 0.7 per cent in the older group. Figure 7 also shows that the younger group has three times as much active tuberculosis as the older group—5.3 per cent compared with 1.7 per cent.

This marked influence of the weight factor was found to be present throughout the whole study, no matter what other factors were correlated with the weight factor. Because of the emphasis which has been generally put on control of overweight in the treatment of diabetes, it might be well to point out that underweight very distinctly adds to the hazard of tuberculosis. This is true at all ages but particularly in the younger group. The hazard also increases as the severity and the duration increase.

There was twice the prevalence of active tuberculosis in the 298 patients with a history of contact with tuberculosis as in those without such a history. There was also twice the prevalence of active tuberculosis in the 457 cases with a history of pleurisy as in those without such a history.

There was no marked difference in the prevalence of tuberculosis in diabetics having histories of gangrene or

amputations, which merely means that increased prevalence of arteriosclerosis in diabetics does not have any obvious relation to increased susceptibility to tuberculosis. Nor did a history of boils and carbuncles have any effect on the prevalence of tuberculosis, indicating that the increased susceptibilities of diabetics to tuberculosis and to pyogenic infections are hypersusceptibilities having nothing in common which can be demonstrated.

THE NATURE OF THE PULMONARY LESIONS

We were interested in possible differences between diabetics and nondiabetics as regards extent of disease, site of lesions, and impression of activity. We therefore obtained a matched sample of nondiabetics whose films had been read as showing tuberculosis during the same general time period. The percentage of minimal disease was about 70 per cent in both groups. However, there was no pleural effusion in the comparison group while there were three pleural effusions and one tuberculous pericarditis among the diabetics. Only one individual had an active primary tuberculosis in the comparison group whereas there were three in the diabetic group, suggesting hypersensitivity among the diabetics.

There is a clinical impression that tuberculosis in the diabetic is characterized by mid-lung and basal lesions. We studied site of tuberculosis lesions in the diabetics

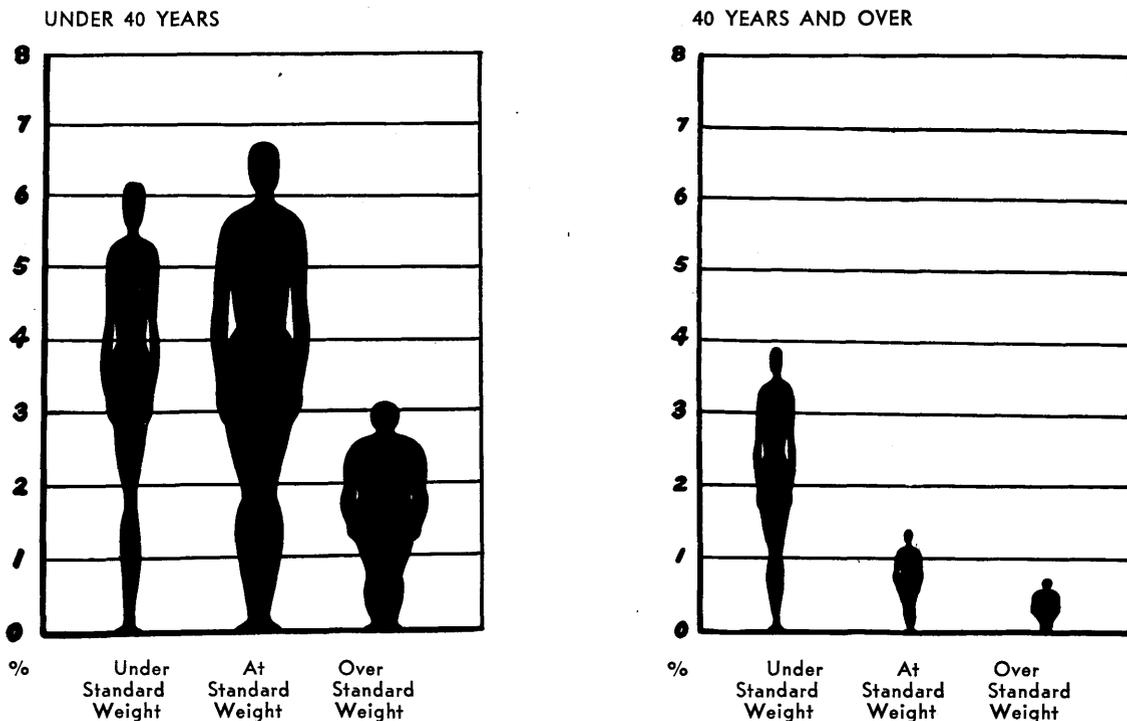


FIGURE 7 Prevalence of active tuberculosis by age and standard weight, in diabetics

TUBERCULOSIS AMONG DIABETICS

TABLE I Proportion of active cases of tuberculosis among diabetics compared with those in a comparison group

Stage	Diabetics			Comparison Group		
	Total Number	Number Active	Per Cent Active	Total Number	Number Active	Per Cent Active
Minimal	165	15	9.1	184	6	3.3
Advanced	85	58	68.2	59	21	35.6
Pleural, pericardial and active primary	11	7	63.6	7	1	14.1
	261	80	30.6	250	28	11.2

and in the comparison group. Since serial films were not available, an attempt was made to gauge the site of origin by excluding all cases with involvement of more than one lung third.

The proportion of tuberculosis found in the lower two-thirds was higher in the diabetics than in the matched sample. However, this was due to the higher proportion of active tuberculosis among the diabetics. When active tuberculosis alone was considered there was no difference between the diabetics and the sample. The clinical impression of increased basal tuberculosis among diabetics may be due to their older age.

While it is impossible to evaluate tuberculosis activity on the basis of one film, the presence of definite cavitation or extensive soft mottling can somewhat justifiably be interpreted as indicating a "probably active" condition.

The films of 31 per cent of the tuberculous diabetics were read as probably active, which is a percentage three times higher than the figure for the comparison group. The increased proportion of active cases was maintained in all stages and in both races (Table I and Figure 8).

There is a clinical impression that tuberculosis in the diabetic runs a more acute course than in the nondiabetic. While a follow-up study on our tuberculous diabetics is now under way, no systematic data are yet available.

SUMMARY

1. The prevalence of tuberculosis in cases of diabetes was found to be 8.4 per cent, compared with 4.3 per cent in an industrial group adjusted to correspond in age, sex and race.

2. The tuberculossi was active in 2.6 per cent of the diabetics.

3. Active tuberculosis was three times as prevalent in those under 40 years of age as in those 40 and over.

4. The prevalence of active tuberculosis increased markedly with the severity of the diabetes.

5. In the younger age group the prevalence of active

% ACTIVE

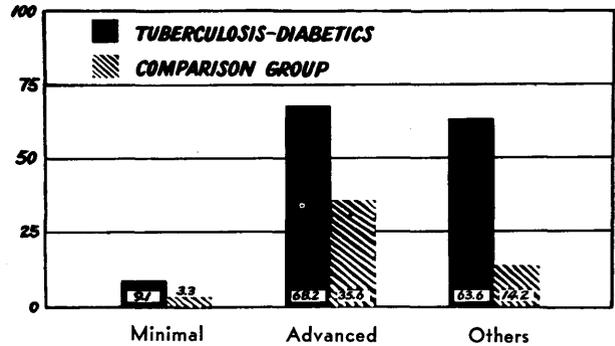


FIGURE 8 Activity by stage of disease

tuberculosis was much greater in those having had diabetes ten years or more.

6. The prevalence of tuberculosis was much greater in underweights than in overweights.

7. Tuberculosis was much more likely to be active in diabetics than in nondiabetics.

ACKNOWLEDGMENT

The cost of the investigation reported herewith was borne by the Philadelphia Tuberculosis and Health Association.

REFERENCES

¹ Root, H. F.: Association of diabetes and tuberculosis: clinical features. *New England J. Med.* 210:127-47, January 18, 1934.
² Boucot, K. R., Cooper, D. A., Dillon, E. S., Meier, P., and Richardson, R.: Tuberculosis among diabetics. *Am. Rev. Tuberc.* 65:1-50, January 1952.

DISCUSSION

DR. JOSEPH B. STOCKLEN (*Cleveland*): Any investigation into influences affecting the course of tuberculosis requires a large number of observations on an adequately controlled group. Dr. Dillon and his associates appear to have a sufficiently large group of patients in their study to yield statistically valid results. There might be some criticism of the use of a control group consisting of industrial workers. It is quite probable that this group was of higher economic status than the diabetic group, most of whom were clinic patients. How-

ever, it is doubtful that this factor would account for the rather large difference in the prevalence of tuberculosis between the two groups.

This extensive study, coupled with the work of other investigators, leaves little room for doubt that tuberculosis is more prevalent among diabetics than nondiabetics and that it is also more serious. In regard to no other complicating condition, with the possible exception of silicosis, is there better evidence of hazard to the tuberculous patient. Therefore it would seem that a routine chest roentgenogram, at possibly six month intervals, should be included in the management of every case of diabetes.

As a suggestion, it is hoped that some investigator may become interested in an experiment parallel to that reported in 1950 by Vorwald in relation to silicosis. He found that guinea pigs having silicosis succumbed to tuberculosis after inoculation with BCG. Organisms obtained at necropsy were then inoculated into normal guinea pigs. These animals survived, indicating that the fatal tuberculosis in cases with silicosis depended on the decreased resistance of the host, rather than on increased virulence of the organism.

DR. ELLIOTT P. JOSLIN (*Boston*): First of all, I want to show my pleasure and extend my congratulations to Dr. Dillon for his beautiful charts. I think they repre-

sent an example that would be fine for all of us to follow.

I have just one new figure on tuberculosis which has not been reported. Among 656 diabetics who have died in the last two years, 0.9 per cent died with tuberculosis. That is the lowest figure we have ever had. Of course, 656 deaths is not great among 12,000 diabetic deaths. The tuberculosis percentage has been between 4 and 5 per cent; in the last ten or fifteen years it has dropped to between 2 and 3 per cent, and now to 0.9 per cent. When one thinks of how half of the diabetics at the beginning of the century died with tuberculosis, the change is wonderful.

DR. EDWARD S. DILLON (*Closing*): I wish to thank Dr. Stocklen and Dr. Joslin for their comments.

Of course, this study has a disadvantage inasmuch as it was a survey of incidence and not a study of mortality. We hope to follow up this survey. We have already set the wheels in motion to survey these patients again after a period of five or six years, to see what has become of them.

As Dr. Joslin pointed out, the mortality from tuberculosis in diabetics in general is relatively small. Nevertheless, in a small select group, namely the young patients who are underweight, the dangers of tuberculosis are still quite large.

INSTRUCTIONS FOR PATIENTS

One of the commonest complaints voiced by patients concerns the failure of their physicians to provide adequate instructions to follow after they leave the offices of the physicians. These patients complain that sometimes they think they must be clairvoyant to do what their doctors expect of them. Even those who seem to expect only general directions often mildly voice a suggestion that the medical profession be more explicit when instructions are given to someone who is ill or to his relatives. If prescriptions for drugs can be written in detail so can other instructions, say these critics. . . .

Any act that convinces people that the patients' comfort and health are always uppermost in the thoughts of physicians will do much to offset the statements of those who wish to pervert the thinking of persons receiving medical care.

—From an editorial in *The Journal of the American Medical Association*, October 20, 1951.