A STUDY OF MORTALITY AMONG INDIVIDUALS WITH ACTIVE PULMONARY TUBERCULOSIS[1,2]

by JEAN DOWNES

TODAY it is generally recognized that tuberculosis is an infectious disease which frequently results in prolonged disability and often causes premature death. The modern campaign against tuberculosis which includes efforts toward provision of sanatorium facilities for care and treatment of the disease, prevention of the spread of infection in the tuberculous family, and early diagnosis of cases is a forceful acknowledgment of the importance of control of the disease. One of the most striking ways of indicating the seriousness of tuberculosis is to show the risk of mortality for persons with manifest disease. Observation over a period of years of all individuals within a rural area, Cattaraugus County, who were known to have active disease makes it now possible to present the mortality experience for a group of unselected cases.

Drolet has studied the fatality of tuberculosis cases by ascertaining the ratio of deaths to new cases of the disease reported in various communities.[3] However, studies of the mortality of tuberculosis cases have been largely confined to groups of individuals discharged from sanatoria. Hilleboe[4] has pointed out that in only a few of these

[1] From the Milbank Memorial Fund.

[2] Acknowledgments are made to the Cattaraugus County Department of Health for permission to use the records of the Bureau of Tuberculosis, especially to Dr. John H. Korns, director of the Bureau, whose interest and cooperation have contributed to the value of this study; and to the late Dr. W. H. Frost, of The Johns Hopkins University School of Hygiene and Public Health, who gave helpful suggestions and criticisms concerning the analysis and presentation of the data. Acknowledgments are made also to Drs. J. Burns Amberson, R. L. Gauld, Godias J. Drolet, and Selwyn D. Collins for a critical reading of the manuscript.

[3] Drolet, Godias J.: Present Trend of Case Fatality Rates in Tuberculosis. *The American Review of Tuberculosis,* February, 1938, xxxvii, No. 2.

[4] Hilleboe, H. E.: The Comparative Mortality of Patients Discharged from Tuberculosis Sanatoria. *The American Review of Tuberculosis,* December, 1936, xxxiv, No. 6.

studies of post-sanatorium cases has there been adequate follow-up of patients and employment of a precise method of analysis, both of which are essential for an accurate presentation of mortality. The post-sanatorium mortality experience of cases from studies using suitable control populations for comparison has indicated that persons discharged from sanatoria do suffer a mortality considerably in excess of that in the general population. Britten has shown also that policy holders who gave a history of one attack of pulmonary tuberculosis two years or more prior to application for life insurance suffered a death rate from seven to ten times the expected mortality among persons of the same age and sex.[5]

DATA AND METHOD OF STUDY

The data presented in this particular study include essentially all of the active cases of the adult pulmonary form of tuberculosis reported or discovered in the County during the twelve-year period, 1923-1935. A special effort has been made by the Bureau of Tuberculosis of the County Department of Health to follow carefully the progress of every known active case. Those who enter sanatoria outside of the County are reported upon at various time intervals, at least once a year, and those who after arrest of the disease leave the County temporarily or permanently are asked to report upon their condition from time to time. Such a careful follow-up of cases offers data which are unique because of their completeness. Furthermore, for the most part the cases have been classified as to stage and condition of activity at varying time intervals by one person, Dr. John H. Korns, director of the Bureau of Tuberculosis since 1928. This insures a high degree of uniformity as to diagnosis and classification of the cases.

Since it is desired to arrive at an annual rate of mortality among tuberculosis cases, it is necessary to use as a population base the total

5 Britten, Rollo H.: Risk of Mortality among Persons with Chronic Disease. The Milbank Memorial Fund *Quarterly*, October, 1937, xv, No. 4, pp. 303-318.

observation of cases after first diagnosis or knowledge of the disease. Each year of life of the tuberculosis case is considered as a unit and the life experience of each case is calculated from the date of diagnosis or from the date the case was first known to the County Department of Health to the end of the period of observation, namely, December, 1936.[6] The longest possible period of observation was thirteen years, and the shortest was from one to two years.

For the more precise study of mortality of tuberculous persons, it is necessary to classify them according to the stage of the disease when first diagnosed or reported. The data include 135 cases classed as minimal, 207 classed as moderately advanced, and 160 classed as far advanced.[7] Thirty-eight per cent of the 135 minimal cases had a period of sanatorium care (three months or longer); 43 per cent of the 207 moderately advanced cases had a period of sanatorium care (three months or longer); and 58 per cent of the 160 far advanced cases had some sanatorium or hospital care.

MORTALITY AND RATE OF CESSATION OF CLINICAL ACTIVITY (ARREST) OF TUBERCULOSIS CASES[8]

Mortality of Tuberculosis Cases. Table 1 shows the average an-

[6] This is essentially the life-table method used and described by the late Dr. W. H. Frost in a paper, "Risk of Persons in Familial Contact with Pulmonary Tuberculosis," which he presented, at the annual meeting of the American Public Health Association, in 1932. Dr. Frost at that time pointed out the value of the method and the fact that it had been applied very little to data readily available from the experience of public health organizations and clinics. At that time he urged that it be used more widely. *See* Frost, W. H.: Risk of Persons in Familial Contact with Pulmonary Tuberculosis. *The American Journal of Public Health,* May, 1933, xxiii, No. 5.

[7] From the group of minimal cases, one case was excluded because the case moved from the County shortly after diagnosis and could not be traced. This case was observed less than five months. From the group of moderately advanced cases, 4, or 1.8 per cent, were excluded because they were not known of until after death. Six cases, or 2.8 per cent, of the total 217 cases were excluded because they were observed less than five months. From the group of far advanced cases, 15, or 8.6 per cent, of the total 175 cases were excluded because they were not known of until after death. Also, only a few cases (9) of active adult pulmonary tuberculosis have been diagnosed or reported among children under 15 years of age in Cattaraugus County during the period 1923-1935; consequently, all cases under 15 years of age have been excluded. In all, 35 cases, or approximately 7 per cent of the total 537 cases, have been excluded for one or another of the above reasons.

[8] No important sex differences were noted in preliminary analyses of the data; consequently, all data are shown for both sexes combined.

Age Groups	Mortality per 100 Persons per Year			Number of Deaths			Population (Years of Observation)[2]		
	Minimal	Moderately Advanced	Far Advanced	Minimal	Moderately Advanced	Far Advanced	Minimal	Moderately Advanced	Far Advanced
15-69	4.1	9.2	46.8	28	85	130	676.0	924.0	278.0
Rates Adjusted for Age[1]	4.2	9.2	47.1						
15-24	3.1	10.9	56.2	4	22	36	127.5	202.5	64.0
25-34	4.1	9.3	28.9	9	25	25	219.5	270.0	86.5
35-44	4.0	7.9	58.4	7	14	26	174.5	178.0	44.5
45-69	5.2	8.8	51.8	8	24	43	154.5	273.5	83.0

[1] Rates adjusted to the age distribution of the combined years of life for all three types of cases (minimal, moderately advanced, and advanced).
[2] Based on total years that each case was observed, both during period of clinical activity of disease and after cessation of activity.

Table 1. Annual mortality from all causes among active cases of adult pulmonary tuberculosis classed as minimal, moderately advanced, or far advanced when first diagnosed or reported.

nual mortality from all causes for cases in each of the three groups: minimal, moderately advanced, and far advanced.[9] In this table the years of observation of the cases, that is, the population, are years of observation at specific ages. They include all of the years each case was observed, both those during the period of clinical activity and those after clinical activity had ceased. Cases diagnosed in the minimal stage suffered the lowest mortality with a rate of 4.1 per 100 persons per year. Moderately advanced cases had an average annual mortality slightly more than twice as high as for minimal cases, namely, 9.2 per 100 persons. Far advanced cases suffered a mortality far in excess of either moderately advanced or minimal cases. The average annual death rate, 46.8 per 100, was more than four times the rate noted for moderately advanced cases, and more than ten times the rate among minimal cases. The differences between the death rates noted for each of the three groups are statistically significant, that is, they are greater than would be expected

[9] The mortality data for all cases include all deaths, both those which occurred in Cattaraugus County and those which occurred outside the County.

to occur as chance variations.[10] It is thus apparent that the mortality increases as the anatomical extent of the tuberculous process, designated by stage, increases. This is entirely in accord with conclusions drawn from clinical observation.

The death rates at specific ages for each of the three groups, as shown in Table 1, are based upon such small numbers that it is unwise to attach significance to variations at different ages for any of the three classes of cases; nevertheless, it is of interest to note that there is some indication that aging as a factor in increasing the chances of mortality has a greater opportunity to operate among minimal cases than among moderately advanced or far advanced cases.

The force of mortality among each of the three classes of cases of active adult pulmonary tuberculosis can best be portrayed by contrasting the actual number of deaths in each class with the number of deaths which under normal conditions might be expected to occur within a group of the same size with such an age distribution.[11] Table 2 shows that among the individuals with minimal tuberculosis 5.3 deaths would be expected, whereas 28 deaths actually occurred, or slightly more than five times the expected number. Deaths occurred among persons with moderately advanced tuberculosis approximately ten times as frequently as would be expected

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Average Annual Rate per 100		
Minimal	Moderately Advanced	Differences
4.1 ± 0.46	9.2 ± 0.67	5.1 ± 0.55
Moderately Advanced	Far Advanced	
9.2 ± 0.67	46.8 ± 1.15	37.6 ± 0.90

[11] This comparison can be made by applying the life table mortality for Cattaraugus County at specific ages to the population of each group of cases to ascertain the number of deaths which might be expected if the tuberculous individuals died at the rate prevailing in the County generally. The life table for Cattaraugus County for the period 1926-1928 was used.

Age Groups	Minimal		Moderately Advanced		Advanced		Cattaraugus County (1926-1928)[1] Rate per 1,000 Persons Per Year
	Observed Deaths	Expected Deaths	Observed Deaths	Expected Deaths	Observed Deaths	Expected Deaths	
15-69	28	5.3	85	8.6	130	2.7	
15-24	4	0.4	22	0.6	36	0.2	3.0
25-34	9	0.9	25	1.1	25	0.3	3.9
35-44	7	1.2	14	1.2	26	0.3	7.0
45-54	5	1.1	8	1.5	20	0.4	11.5
55-69	3	1.7	16	4.2	23	1.5	29.5

[1] Data from: Life Expectancy in Cattaraugus County. Milbank Memorial Fund *Quarterly Bulletin*, January, 1930, viii, No. 1, pp. 13–16.

Table 2. Observed number of deaths from all causes in each of three population groups composed of active cases of adult pulmonary tuberculosis contrasted with the expected number of deaths in the same populations if the community rate is applied to these populations.

under normal conditions; 85 deaths were observed in this group and the expected number was 8.6 deaths. The observed number of deaths, 130, among persons with far advanced tuberculosis was slightly more than fifty times the expected number of 2.7.

Though the data of this study are not strictly comparable with data of post-sanatorium patients, it is of interest that the mortality of these cases drawn from Cattaraugus County, representing an average experience, was similar to the results of studies of a more selected group (post-sanatorium patients), cited by Hilleboe.[4] For example, data drawn from the Midhurst Sanatorium and the Brompton Sanatorium in England, the Trudeau Sanatorium, and the Metropolitan Life Insurance Company's sanatorium in New York State indicated that in general a person with minimal tuberculosis has his risk of dying increased approximately four times; moderately advanced, sixteen times; and far advanced, forty times over that of persons in the general population.

Cessation of Clinical Activity or Arrest of Disease. In a study of the outcome of active cases of pulmonary tuberculosis, it seems suitable to show the average annual rate at which cases obtained a

Age Groups	Arrests per 100 Persons per Year		Number Becoming Arrested		Population (Years of Observation)[2]	
	Minimal	Moderately Advanced	Minimal	Moderately Advanced	Minimal	Moderately Advanced
15-69	27.1	15.8	94	98	346.5	622.0
Rates Adjusted for Age[1]	27.9	15.8				
15-24	25.4	15.6	23	25	90.5	160.0
25-34	26.9	13.8	33	26	122.5	188.5
35-44	23.9	20.0	19	20	79.5	100.0
45-69	35.2	15.6	19	27	54.0	173.5

[1] Rates adjusted to the age distribution of the combined population of the two groups (minimal and moderately advanced).
[2] Based only on years of observation during period of clinical activity.

Table 3. Annual rate of arrest of activity of disease among surviving individuals with adult pulmonary tuberculosis classified according to stage of disease when first reported or diagnosed.

cessation of clinical activity of disease.[12] Table 3 shows the rate at which clinical activity of disease ceased for minimal and moderately advanced cases. In Table 3 the population, or years of observation, for each case is limited to the total years when the disease was considered clinically active. Years of observation at specific ages are shown. The data in Table 3 indicate that improvement in the status of the disease is obtained with much greater frequency among individuals classed as minimal when first diagnosed than among those with moderately advanced disease. The average annual rate of cessation of clinical activity was 27.1 per 100 persons in the minimal group contrasted with 15.8 among cases classed as moderately advanced. Adjustment of these rates in order to take account of the influence of differences in the age distribution of the two groups affects them only slightly. Since the difference between the

[12] Cessation of clinical activity of disease (arrest) means complete cessation of a known previously active tuberculous process as nearly as can be determined by X-ray and clinical examination. All constitutional symptoms absent; sputum, if any, must be concentrated and found microscopically negative for tubercle bacilli; lesions stationary or retrogressive; no evidence of pulmonary activity. These conditions shall have existed for a period of six months, during the last two of which the patient has been taking one hour's walking exercise twice daily or its equivalent.

crude rates, 11.3 ± 1.24, is slightly more than nine times its probable error, it may be considered as significant and not due to chance variations. This experience among active cases in Cattaraugus County with respect to cessation of clinical activity of the disease is in agreement with the conclusion drawn from clinical observation that the mortality risk is much lower in cases which, when first diagnosed, show minimal lesions than in cases which show moderately advanced lesions; consequently, the chances of improvement are greater for the minimal cases.

Reactivation of Cases in Which Clinical Activity Has Ceased. A question which deserves consideration by those engaged in combating tuberculosis is what is the frequency of occurrence of reactivation or breakdown among cases in which clinical activity of the disease apparently has ceased. The data of cases drawn from Cattaraugus, even though small in number, offer some interesting indications concerning this question. Table 4 shows the reactivation rate among improved cases in the minimal and in the moderately advanced classes. The population in Table 4 (years of observation) is restricted to the total years observed for each case after clinical activity of the disease had ceased and the case had been classed as arrested. Also, years of observation at specific ages are shown. The

Table 4. Annual rate at which surviving cases classed as arrested (clinical activity having ceased) again became active.

Age Groups	Rate per 100 Persons per Year		Number Becoming Active Again		Population (Years of Observation)[1]	
	Minimal	Moderately Advanced	Minimal	Moderately Advanced	Minimal	Moderately Advanced
15-69	4.9	5.9	16	18	327.5	303.0
15-29	8.4	9.7	7	8	83.5	82.5
30-49	4.1	4.3	7	6	170.5	140.5
50-69	2.7	5.0	2	4	73.5	80.0

[1] Based only on years of observation during period of arrest of disease. Includes only cases known and observed to have had active clinical tuberculosis before arrest or cessation of activity.

reactivation rates, 4.9 and 5.9 per 100 persons per year, for minimal and moderately advanced, respectively, are strikingly similar. It is also interesting to note that the rates at specific ages are generally similar. Furthermore, among both minimal and moderately advanced cases, the reactivation rate at ages 15-29 is twice as high as that for any of the other age groups. These data are based upon such a small sample of cases that it is unwise to go far in the interpretation of their meaning; however, they suggest that the anatomical extent of the tuberculous process is not necessarily the dominant factor in producing reactivation or a second breakdown from the disease. Rather, the inference may be drawn that physiological factors, as well as social and economic factors, play important roles.

MORTALITY AND CESSATION OF CLINICAL ACTIVITY OR ARREST OF DISEASE WITHIN SPECIFIED INTERVALS AFTER DIAGNOSIS

The period of time within which the risk of mortality among active cases of tuberculosis is concentrated is of considerable interest to those engaged in tuberculosis work. Conversely, the period of time within which the frequency of cessation of activity of disease among cases is greatest is also of importance. The data of this study can be used to show for a five-year period the experience of minimal and moderately advanced cases with respect to the two factors, mortality and arrest of disease.

The data presented in the first part of this study are in life-table terminology and have shown the average experience of tuberculous individuals with clinically active disease with respect to mortality and arrest of disease. To indicate the relation between time and the operation of the factors, mortality and cessation of clinical activity of disease, a special calculation has been made which shows the mortality and rate of arrest for successive annual periods of observation following the diagnosis. These rates are shown for minimal and moderately advanced cases in Tables 5 and 6. In obtaining these rates, all cases observed during one complete year

Years After Diagnosis	Minimal			Moderately Advanced		
	Observed Population (Active and Arrested Cases)	Number of Deaths in Each Year	Rate per 100	Observed Population (Active and Arrested Cases)	Number of Deaths in Each Year	Rate per 100
1st	135	5	3.7	207	21	10.1
2nd	115	5	4.3	170	15	8.8
3rd	91	4	4.4	138	17	12.3
4th	77	4	5.2	103	10	9.7
5th	50	3	6.0	83	10	12.0

Table 5. Observed rate of mortality among active minimal and moderately advanced cases of adult pulmonary tuberculosis in successive years after diagnosis.

are used to determine the outcome of the cases within twelve months of diagnosis. Similarly, in determining the chances of an active case becoming arrested in the second year following diagnosis, all cases active at the end of one year and observed for another twelve-month period are included. In the same manner, mortality in the first year is shown for all cases observed during that year and in the second year for all cases alive at the end of the first year. The outcome in successive years up to five years is obtained by this method for all cases observed for each specified annual period.

The values or rates shown in Tables 5 and 6, which represent the

Table 6. Observed rate of arrest (cessation of clinical activity) among active minimal and moderately advanced cases of adult pulmonary tuberculosis in successive years after diagnosis.

Years after Diagnosis	Minimal			Moderately Advanced		
	Observed Population (Active Cases)	Number of Arrests of Clinical Activity in Each Year	Rate per 100	Observed Population (Active Cases)	Number of Arrests of Clinical Activity in Each Year	Rate per 100
1st	135	21	15.6	207	6	2.9
2nd	98	37	37.8	165	40	24.2
3rd	46	16	34.8	100	20	20.0
4th	30	5	16.7	61	13	21.3
5th	26	6	23.1	36	7	19.4

observed experience in a changing population, may be utilized to calculate the probabilities of mortality or arrest among a group of cases followed continuously for a five-year period. Such a calculation is presented in Table 7 for a theoretical series of 100 minimal cases and 100 moderately advanced cases. The method may be explained by briefly stating the steps followed for determining the rate of arrest and mortality for the first two years. As shown in Table 5, the observed mortality within the first year after diagnosis was 3.7 per cent for minimal cases, and, therefore, in the theoretical group of 100 cases, 3.7 cases would die in the first year. Among the surviving cases, 96.3, the mortality would be 4.3 per cent in the second year and 4.3 per cent of 96.3 is 4.1, or the number of cases that die in the second year. Cumulating the deaths in the first year

Table 7. Calculated cumulative mortality and rate of arrest among active minimal and moderately advanced cases of adult pulmonary tuberculosis.

Years After Diagnosis	Number Alive (Active or Arrested)	Observed Per Cent Died[1]	Number Died	Cumulated Mortality Out of 100 Cases	Number of Active Cases[3]	Observed Per Cent Arrested[2]	Number Arrested	Cumulated Number of Arrests Out of 100 Cases
	MINIMAL CASES							
	Col. 1	Col. 2	Col. 3	Col. 4	Col. 5	Col. 6	Col. 7	Col. 8
1st	100.0	3.7	3.7	3.7	100.0	15.6	15.6	15.6
2nd	96.3	4.3	4.1	7.8	80.7	37.8	30.5	46.1
3rd	92.2	4.4	4.1	11.9	46.1	34.8	16.0	62.1
4th	88.1	5.2	4.6	16.5	26.0	16.7	4.3	66.4
5th	83.5	6.0	5.0	21.5	17.1	23.1	4.0	70.4
	MODERATELY ADVANCED CASES							
1st	100.0	10.1	10.1	10.1	100.0	2.9	2.9	2.9
2nd	89.9	8.8	7.9	18.0	87.0	24.2	21.1	24.0
3rd	82.0	12.3	10.1	28.1	58.0	20.0	11.6	35.6
4th	71.9	9.7	7.0	35.1	36.3	21.3	7.7	43.3
5th	64.9	12.0	7.8	42.9	21.6	19.4	4.2	47.5

[1] Values taken from Table 5.
[2] Values taken from Table 6.
[3] The number of active cases in each year is 100 less the cumulated number of arrested and dead in the preceding years.

and the second year (Col. 4, Table 7), the deaths within a two-year period equal 7.8 and the mortality rate is 7.8 per cent since the number of cases is 100. This same procedure is carried out for each specific year for both minimal and moderately advanced cases, and a comparable procedure is followed in determining the number of arrests of clinical activity in the original groups of 100 active minimal and moderately advanced cases.

The cumulated per cents of cases dying, found in Col. 4 (Table 7), indicate that 22 per cent of the active cases diagnosed as minimal was dead at the end of five years, and 43 per cent of the cases diagnosed as moderately advanced. The cumulated number of arrests at each time interval, shown in Col. 8 (Table 7), indicates that for active cases of adult pulmonary tuberculosis diagnosed in the minimal stage, it is reasonable to expect that at the end of five years 70 per cent will probably be classed as nonactive; for those diagnosed as moderately advanced, 48 per cent will have shown a cessation of clinical activity of disease.

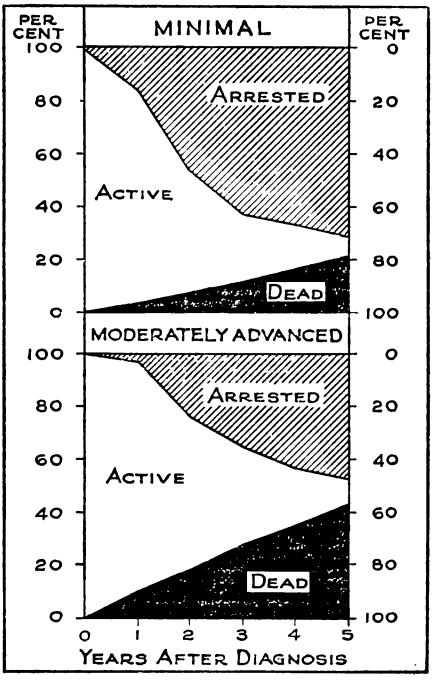

Fig. 1. Cumulated mortality and rate of arrest among active minimal and moderately advanced cases of adult pulmonary tuberculosis in successive years after diagnosis. (Rates of mortality are plotted according to the scale on the left-hand side of the chart; rates of arrest are plotted according to the scale on the right-hand side of the chart.)

The cumulated mortality and the cumulated rate of cessation of clinical activity for each of the five years after diagnosis are shown in Figure 1 for minimal and moderately advanced cases, respectively. The figure illustrates strikingly the similarities and differences between minimal and moderately advanced cases in respect

to the proportion dying or becoming arrested within the five-year period. For example, both for minimal and moderately advanced cases the proportion becoming arrested is greatest within the first three years after diagnosis; in the following two years the proportion increases more slowly for both groups of cases.

Mortality exerted its greatest force among moderately advanced cases during the first three years after diagnosis; 28 per cent died during that interval, and within the next two years an additional 15 per cent died. There is very little tendency for the cumulative curve of mortality among moderately advanced cases to reach an asymptote within the five-year period. The curve of mortality among minimal cases shows no diminution. The total mortality within five years was 21.5 per cent, and the year-to-year variation was extremely slight.

CONCLUSION

This study of mortality among cases in Cattaraugus County indicates that active pulmonary tuberculosis has an exceedingly high fatality. Even though diagnosed in the minimal stage, the disease offers a distinct hazard to life. Slightly more than five times the expected number of deaths occurred among individuals with active minimal tuberculosis; deaths occurred among those with moderately advanced tuberculosis approximately ten times as frequently as would be expected under normal conditions; and among persons with advanced tuberculosis the observed number of deaths was fifty times the expected number.

In view of the fact that from 4 to 5 per 100 cases per year suffer a breakdown after a reasonably satisfactory arrest of the disease has been obtained, it seems suitable to call attention to the need for study of causes of breakdown. Undoubtedly reactivation of disease contributes to the after-mortality of cases.

The observed experience of active cases of adult pulmonary tuberculosis in Cattaraugus, when utilized to calculate the probabilities

of mortality or arrest of clinical activity, indicated that after a period of five years 22 per cent of the active cases diagnosed in the minimal stage was dead and 70 per cent was classed as nonactive. Among moderately advanced cases 43 per cent had died and 48 per cent had shown a cessation of clinical activity of disease.

In conclusion it is pertinent to point out that these data show clearly the seriousness of the adult pulmonary form of tuberculosis. Furthermore, the findings of this study may serve to emphasize anew that it is important that the program of control be directed toward prevention of the spread of infection so that active cases of the disease will develop much less frequently.