MORTALITY IN TUBERCULIN-POSITIVE INFANTS[1]

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THE material for this note is derived from the experience of the special outpatient clinic for childhood tuberculosis which has been in operation under the direction of Dr. E. A. Park at the Harriet Lane Home of the Johns Hopkins Hospital since 1928. Admissions to the special clinic are limited to infants who, before two years of age, are shown to be either infected with tuberculosis as demonstrated by a positive tuberculin test, or who are in imminent risk of infection because of familial contact with sputum-positive tuberculosis. After the patient has been registered in the clinic, supervision and study are continued as long as possible, but as the clinic was established only in 1928, not many of these patients have been under observation more than five years.

This study deals with the record, up to November 1, 1934, of the patients registered in the clinic during the five-year period from November 1, 1928, to November 1, 1933. From the total registration of 358 have been selected all those who had a positive tuberculin test prior to two years of age, an X-ray of the chest taken at the time of the test, and had remained under observation at least one year subsequent to this test unless dying sooner. The third condition excluded five patients otherwise eligible, four of the families having refused cooperation and the other having removed from the City after seven months. Patients fulfilling all three conditions totaled 170,[3] of whom seventy-two were white and ninety-eight were colored.

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3 Twelve of these children were already known to the Harriet Lane as infected infants

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Time-Period in Months After First X-Ray	Number Under Observation at the Beginning of the Time-Period	Number Withdrawn Alive From Observation During Period[1]	Number Dying During Time-Period	Average Number Under Observation for Computing Mortality	Percentage Dying During the Time-Period	Percentage Surviving During the Time-Period	Percentage Surviving Through Preceding and Current Time-Periods	Percentage Dying During Preceding and Current Time-Periods
x	l_x	w_x	d_x	$l_x - \frac{w_x}{2}$	$100q_x$	$100p_x$	$100P_x$	$100(1-P_x)$
	WHITE							
0-6	72	0	5	72.0	6.9	93.1	93.1	6.9
6-12	67	0	2	67.0	3.0	97.0	90.3	9.7
0-12	72	0	7	72.0	9.7	90.3	90.3	9.7
12-24	65	16	0	57.0	—	100.0	90.3	9.7
24-36	49	12	0	43.0	—	100.0	90.3	9.7
36-48	37	6	0	34.0	—	100.0	90.3	9.7
48-60	31	9	1	26.5	3.8	96.2	86.9	13.1
	COLORED							
0-6	98	0	14	98.0	14.3	85.7	85.7	14.3
6-12	84	0	7	84.0	8.3	91.7	78.6	21.4
0-12	98	0	21	98.0	21.4	78.6	78.6	21.4
12-24	77	24	2	65.0	3.1	96.9	76.2	23.8
24-36	51	16	2	43.0	4.6	95.4	72.6	27.4
36-48	33	5	0	30.5	—	100.0	72.6	27.4
48-60	28	16	1	20.0	5.0	95.0	69.0	31.0

[1]Period of observation less than five years because of registration in clinic subsequent to November 1, 1929.

Table 1. Total observed life experience and mortality following first X-ray in 170 children infected with tuberculosis before two years of age.

On November 1, 1934, when these records were compiled, all of the 170 children in the group had been on the clinic register as tuberculin-positive for at least one year; hence the rate of mortality during the first year following the discovery of infection may be

prior to November 1, 1928, when they were transferred to the clinic. Three of the twelve, although less than two years of age when found to be infected, were more than two years old when the special clinic opened. On November 1, 1928, their ages were respectively 24 months, 29 months, and 44 months. For these twelve patients observation has been dated from the discovery of infection rather than from the date of registration in the special clinic.

expressed very simply by stating the number of deaths within the first year as a percentage of the whole number registered (Table 1). To express accurately the rate of mortality for a longer period—say five years—it is necessary to take into account the fact that the numbers available for calculation are necessarily diminished as time is extended, since many of the children included came into the clinic considerably less than five years prior to November 1, 1934. Therefore, the computation must be made step by step, following conventional actuarial procedures as shown in Table 1. Obviously the numbers under observation are much too small to yield stable rates of mortality in each single year. However, the rates indicated for the first year under observation and for the whole five-year period have a fairly definite significance.

Table 2 shows in summary, as derived from Table 1, the mortality for white and colored children separately, in the first six months; the second six months; the entire first year; the next four years; and for the five-year period following the discovery of infection. It should be borne in mind that all children of the series were less than two years old when found to be tuberculin-positive, the average age for each race at the time of the first[4] positive tuberculin test being thirteen months.

Table 2. Mortality during various periods after discovery of infection in 72 white and 98 colored children found to be tuberculin-positive before two years of age.

Interval in Months From Discovery of Positive Tuberculin	Number of Deaths		Mortality Per Cent During Interval	
	White	Colored	White	Colored
0-6	5	14	6.9	14.3
6-12	2	7	3.0	8.3
0-12	7	21	9.7	21.4
12-60	1	5	3.4	9.6
0-60	8	26	13.1	31.0

4 Very rarely could the time of infection be more accurately dated by preceding negative tests.

In both races the mortality within the first six months after the discovery of infection is approximately twice as great as in the second six months; and within the first year as a whole it is approximately two and one-half times greater than in the whole of the next four years. About 70 per cent of the mortality for the entire five-year period occurs during the first year of observation.

With reference to Table 2, it is to be noted that, at every time interval shown, the colored children suffered a mortality more than twice that suffered by white children. Within the first year of observation the mortality was about 10 per cent in white children and 21 per cent in colored children, and for the whole five-year period it was 13 per cent for white and 31 per cent for colored children. Stated conversely, these observations indicate that the chance of survival through five years subsequent to infection discovered before two years of age was 87 per cent for the white and 69 per cent for colored children.

When the 170 patients are classified according to X-ray findings at the first examination, sixty-seven of them showed definite lesions in the parenchyma of the lung, usually accompanied by enlarged tracheo-bronchial nodes. About one-third of these (twenty-two) were actually ill when first seen and presented fairly conclusive evidence of pulmonary tuberculosis apart from X-ray findings. In the remaining forty-five who were brought for observation and not because of illness, ordinary physical examination was negative, and the diagnosis could not have been made without the use of tuberculin and X-rays.

There were 103 children whose initial X-rays showed no definite involvement of the lung parenchyma. Of these, thirty-six showed enlargement of the mediastinal shadow with definite bulging of the tracheo-bronchial nodes; while sixty-seven showed no definitely abnormal shadows at first X-ray, and were therefore designated as roentgenologically negative on admission.

The mortality in these three classes of patients during the first

year of observation and during the whole five-year period is shown in Table 3. In group A of the table, of sixty-seven children showing unquestioned pulmonary involvement when first X-rayed, twenty-one were dead within the first year, a rate of 31 per cent, while three additional deaths (two of which were not attributable to tuberculosis) occurred during the next four years, raising the five-year rate to 40 per cent. It is to be noted that the rates for white and colored, once parenchymal lesion was found to be present, were practically identical.

If we select from group A the twenty-two patients who were ill with tuberculosis when first examined and whose lesions were sufficiently far-advanced to produce physical signs, the extremely high first-year mortality of 68 per cent was found; and this rose to 82 per cent for the entire five-year period. The mortality for such extensive disease was the same for children of both races.

Table 3. Mortality in 170 tuberculin-positive infants during (1) the first year, and (2) the five years following discovery of infection: according to lesion shown at initial X-ray.

Findings on First Examination	Race	Number of Cases	Deaths			
			Within One Year		Within Five Years	
			Number	Per Cent	Number	Per Cent
A. Parenchymal Lesion	W	23	7	30.4	8*	38.6
	C	44	14	31.8	16*	40.5
	Total	67	21	31.3	24**	40.0
B. Bulging Tracheo-bronchial Nodes	W	18	0	—	0	—
	C	18	2	11.1	4*	25.3
	Total	36	2	5.6	4*	12.7
C. Negative Chest X-rays	W	31	0	—	0	—
	C	36	5**	13.9	6**	17.3
	Total	67	5**	7.5	6**	9.2
B and C Combined	W	49	0	—	0	—
	C	54	7**	13.0	10***	21.3
	Total	103	7**	6.8	10***	11.1

*Indicates 1 death from nontuberculous cause, there being a total of five in five years.

Of the twenty-four deaths which occurred during the five-year period of observation in group A of Table 3, twenty-two were due to tuberculosis. The immediate cause of death in eleven of the twenty-two was tuberculous meningitis, while generalized tuberculosis brought about death in six others. The five remaining patients were thought to have merely extensive pulmonary lesions, but in three of these upon whom a postmortem examination was performed, an unsuspected miliary tuberculosis was found to be present. It is clear that extrapulmonary involvement was responsible for at least 75 per cent of the tuberculous deaths.

Referring to children of group B and C as shown in Table 3, there were 103 of these patients who displayed no parenchymal lesion at initial X-ray; they were either X-ray-negative when first seen, or they showed only enlarged tracheo-bronchial nodes on first examination. Their combined mortality for the first year of observation was 6.8 per cent, and for all five years 11.1 per cent. These rates are roughly one-fourth those for children coming under observation with parenchymal lesion and followed during the same time-periods.

The observations show no significant difference in total mortality between children admitted with bulging nodes (B) and those admitted as X-ray-negative (C).

However, mortality in the two races in children admitted without parenchymal lesion is significantly different. Among fifty-four

Table 4. Classification of initial chest findings in 170 tuberculin-positive infants, white and colored.

Findings on First Examination	White		Colored	
	Number of Cases	Per Cent	Number of Cases	Per Cent
Parenchymal Lesion	23	31.9	44	44.9
No Parenchymal Lesion	49	68.1	54	55.1
Total	72	100.0	98	100.0

colored children seven deaths occurred during the first year of observation, a rate of 13 per cent. This rate increased to 21 per cent by the end of five years of observation. During the same five-year period of time, no deaths occurred among forty-nine white children.

Of the ten deaths occurring among these fifty-four colored children during the five years of observation, seven were attributable to tuberculosis, five falling in the first year of observation and two somewhat later. One child died of miliary tuberculosis without meningitis. Tuberculous meningitis was the immediate cause of death in the remaining six. In two of the six the meningeal involvement was preceded by miliary tuberculosis. The remaining four of the six meningeal patients were thought, during life, to have no parenchymal lesion, but in three who underwent postmortem examination, well-defined pulmonary lesions were discovered. All the deaths due to tuberculosis in children admitted without parenchymal lesion were due to extrapulmonary involvement.

The higher mortality observed in the colored children of this series appears to be attributable to their greater tendency to develop parenchymal lesion. This is shown partially by the results of the initial X-ray examination, at which 45 per cent of the colored and 32 per cent of the white infants showed pulmonary involvement. It is still further shown by the greater frequency in colored children of subsequent development of parenchymal lesions in those who showed none when first admitted, as is seen in Table 5.

In this table are included only those children who, on first examination, showed no parenchymal lesion and for whom there was at least one subsequent X-ray. For the first year subsequent to admission parenchymal lesions developed at the rate of 2.1 per cent in the white and 24 per cent in the colored children. For the five-year period subsequent to admission, as nearly as can be estimated from the scant data available, the indicated proportions developing parenchymal lesions are 5.8 per cent in white and 28 per cent in colored infants.

Race	Number of Cases	Parenchymal Lesions			
		Within First Year		Within Five Years	
		Number	Per Cent	Number	Per Cent
White	48	1	2.1	2	5.8
Colored	54	12	24.0	13	28.0
Total	102	13	13.4	15	17.2

Table 5. Rate of development of parenchymal involvement during (1) the first year and (2) the five years subsequent to discovery of infection in 102 infants showing no parenchymal involvement at first X-ray, white and colored.

It is thus evident that in this series colored children infected with tuberculosis developed parenchymal lesion much more frequently than did the white, but once such lesion had developed, the risk of death was not materially different in the two races.

Clinical experience would appear to indicate that mortality is related to age at which infection develops, the prognosis being more unfavorable the younger the child. That this is so in our series is shown in Table 6, where the patients are grouped according to the age at which the tuberculin test was found to be positive. The proportions of white and colored, respectively, are substantially identical in the three age-groups shown in this table and in consequence no separation is made for race. Children found to be infected before six months of age had a mortality of 33.3 per cent within the first year of observation, and of nearly 78 per cent within five years subsequent to the discovery of infection. Both the first-year and five-year rates drop sharply for children whose infection was demonstrated after six months of age, the rates being much alike for infections discovered during the second six months of life or during the second year of life. Combining the two latter age-groups, the first-year mortality was 14 per cent and the five-year mortality was about 16 per cent. These rates vary significantly from those for infants *known* to have been infected before six months of age.

It is quite reasonable to suppose that the mortality in this whole

Age in Months at Discovery of Infection	Number of Cases	Deaths			
		Within First Year		Within Five Years	
		Number	Per Cent	Number	Per Cent
0-6	21	7	33.3	11	77.6
6-12	45	7	15.6	8	18.0
12-24	104	14	13.5	15	15.1
0-24	170	28	16.5	34	23.2

Table 6. Mortality during first year and during five years of observation in 170 tuberculin-positive infants, according to age when infection was discovered.

series has been higher than the average for children infected within the same age limit; because the children in this study come from the poorer strata of the population and a large proportion of them had been in intimate and more or less prolonged household contact with open cases of pulmonary tuberculosis. Such contact was definitely established in 78 per cent of the white and 64 per cent of the colored children. In the remainder of the cases careful investigation revealed no intrafamilial source of infection; but, as it was not possible to make a complete examination of every member of every family, it is possible that there have been undiscovered cases of tuberculosis in some of the families which gave negative histories.

Since it is generally believed that the severity of infection with the tubercle bacillus is directly related to the size of the infective dose or to the frequency and duration of repeated infection, the records of these children have been carefully studied to ascertain whether or not they show such a relationship; that is, whether the children exposed to demonstrable intrafamilial sources of infection tended to suffer a higher mortality than those for whom no such exposure could be found. The questions involved are more complex than at first appears and can be discussed fully only in a more detailed presentation than can be given at this time. For the present it can only be said that no obvious relationship of this kind has been shown. White children of this series in contact with a sputum-

positive case showed a mortality of 14.8 per cent for the first five years, while those not known to have had such contact within the family suffered a mortality of 6 per cent in the same period. Colored children in known familial exposure had a five-year mortality of 33.9 per cent, as against 25 per cent in those with negative contact history. However, while these differences are suggestive they are not definitely significant in such a small series; and further study of a larger series of cases is required for definitive information.

SUMMARY

1. One hundred seventy children, of whom seventy-two were white and ninety-eight colored, found to be infected with tuberculosis before reaching two years of age, have been kept under observation for periods ranging from one to five years.

2. They can be divided into sixty-seven who showed parenchymal involvement of the lungs at initial X-ray and 103 who showed no definite parenchymal lesion when first examined. Twenty-two, roughly one-third of those with pulmonary lesion when infection was discovered, were ill and presented signs of disease such that a diagnosis could usually have been made by ordinary clinical means. The remaining patients gave no indication of their infection, and a diagnosis could not have been made without the tuberculin reaction and the use of the X-ray.

3. By calculation, following actuarial procedures, the total five-year mortality for white children was found to be 13 per cent and for the colored 31 per cent.

4. Approximately 70 per cent of the deaths which occurred in five years of observation fell within the first year, mostly within the first six months following the discovery of infection. This refers to deaths from all causes, but, with very few exceptions, tuberculosis was the immediate cause of death.

5. Of those admitted with involvement of the lung parenchyma, 31 per cent were dead within the first year of observation, no difference being observed between the two races in case fatality.

6. Among those whose initial chest plates showed no parenchymal involvement, mortality during the first year subsequent to the discovery of infection was 6.8 per cent. No deaths occurred among the forty-nine white children of this group, but there were seven deaths among fifty-four colored children.

7. In the entire group of colored children observed, mortality has been more than twice that observed in white children.

8. When the pulmonary lesion has developed sufficiently to be readily demonstrable by X-ray, the fatality is about the same in white as in colored children. However, lesions of this extent are very much more frequent in the colored than in the white, and this appears to account for the fact that the gross mortality in the colored is so much higher.

9. In both white and colored children, mortality has been more than twice as high in those known to be infected during the first six months of life, as in those whose infection was discovered between the ages of six months and two years.

10. In about 78 per cent of the white and 64 per cent of the colored children of this study there was intrafamilial contact with a proved sputum-positive case. The children of each race with known exposure showed a slightly higher mortality than children not known to have been exposed. The difference in mortality is not statistically significant and a detailed study of a larger series must be made to determine the bearing which continued exposure may have upon severity of lesion.