TUBERCULARIZATION AND LEPROSY

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The thesis of enhancement of resistance against leprosy infection resulting from a previous tuberculosis infection has been accepted by some authors, who advocate BCG vaccination for the prevention of leprosy. Nevertheless, many observations are not in agreement with that view of the role of tuberculosis infection. This is a subject which should be cleared up once and for all.

Lepromin positivity has been found to accompany negative results of tuberculin tests, and the well-known phenomenon of anallergy[1] has been taken to account for this dissociation. Reactivity against tuberculin could be lost consequent to the repetition or great intensity of the stimulus leading to exhaustion of antibody elaboration—i. e., of sensitivity to tuberculin—while immunity persists ([3]). A study whose results would be free from a possible anallergic interference should be available, to demonstrate whether or not cosensitization or cross-immunization really exists.

PLAN OF STUDY

For that demonstration I believe it to be necessary to compare the epidemiologic aspects of both diseases within the population of a given city. Rio de Janeiro is a good place for a study of this kind, for both diseases are prevalent there in a high degree. The prevalence of leprosy is on the order of about 2 per thousand. The annual tuberculosis mortality was 335 per 100,000 in 1944, when one tuberculosis patient died every 15 minutes. This mortality rate has been diminishing lately, to 88 in 1955, but the epidemiologists assert that tuberculosis morbidity, the rate of which is difficult to determine, has increased coincidentally.

Tuberculosis infection is very common in Rio de Janeiro, so that its population of more than 2,500,000 shows high percentages of positive tuberculin reactions; until 10 years ago the rate used to be at about 95 per cent after the age of 35. It must be pointed out that most of the leprosy patients included in this statistical study arose during that time. Even today, the percentages of tuberculariza tion revealed by tuberculin testing have not diminished very greatly, as can be seen in Table 1 ([5]). The positives in the people aged 20 or more were 96 per cent in 1950, and 82 per cent in 1955.

[1] According to those authors who defend the cosensitization or cross-immunity between tuberculosis and leprosy, the term *anallergy* means a condition in which a previous allergic state has lost its capability to react, by exhausting its antibody elaboration.

TABLE 1.—*Rio de Janeiro City: positive tuberculin reactors. 1950 and 1955 by age groups.*[a]

Age group	1950			1955		
	No. of persons tested	Positives		No. of persons tested	Positives	
		Number	Per cent		Number	Per cent
0- 4	960	508	52.9	1,342	238	17.7
5- 9	1,173	833	71.0	932	381	40.9
10-14	959	752	78.4	948	547	57.7
15-19	754	627	83.1	5,342	3,852	72.1
Other ages	1,303	1,249	95.8	6,543	5,389	82.4
Total	5,149	3,969	77.1	15,112	10,407	68.9

[a] Taken from a report by Drs. Rodrigues de Albuquerque and Villas Boas.

FEATURES OF TUBERCULOSIS EPIDEMIOLOGY

The proportions of tuberculosis infections revealed by tuberculin testing increase gradually throughout the age groups from childhood to the oldest ages. Children are really less commonly infected by tuberculosis, although morbidity and mortality are very high among them. (See Fig. 1.)

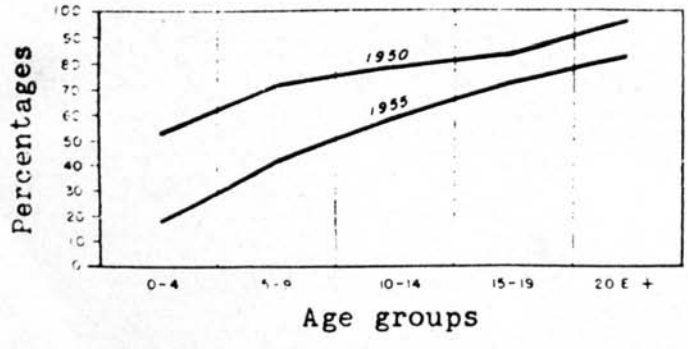


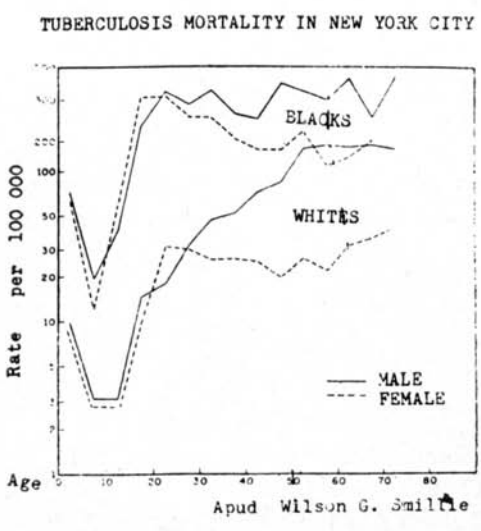
FIG. 1. Percentages of positive tuberculin reactors, Rio de Janeiro City, 1950 and 1955, by age groups.

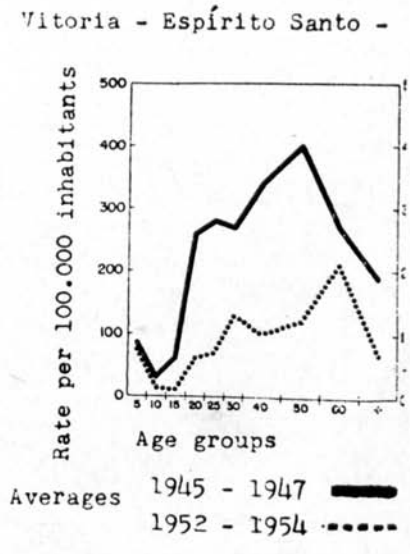
On the other hand, there is in childhood a well-known period, generally between the ages of 3 and 12 years in the United States and between 7 and 14 in Brazil, in which the children exhibit a notable resistance against tuberculosis as measured by the mortality rates, although as seen infections continue to go up. The examples shown in Figs. 2, 3 and 4 demonstrate this period of low mortality in childhood in New York ([8]), Vitória (State of Espírito Santo, Brazil) ([6]), and Rio de Janeiro ([5]). They show that in a certain period of childhood there develops a resistance against tuberculosis in those places, as everywhere in the world.

This is a general rule in tuberculosis epidemiology, and the data are available for comparison with those of leprosy epidemiology to ascertain whether or not there is correlation between the two diseases.

EPIDEMIOLOGIC ASPECTS OF LEPROSY

Leprosy in Brazil is most frequent among adults, in spite of the fact that, as has been seen, adults are most frequently infected by tuberculosis as indicated by the results of tuberculin tests. The statistics of the leprosy records of Rio de Janeiro show that of the persons with leprosy 75 per cent are adults, and 25 per cent children, as shown in





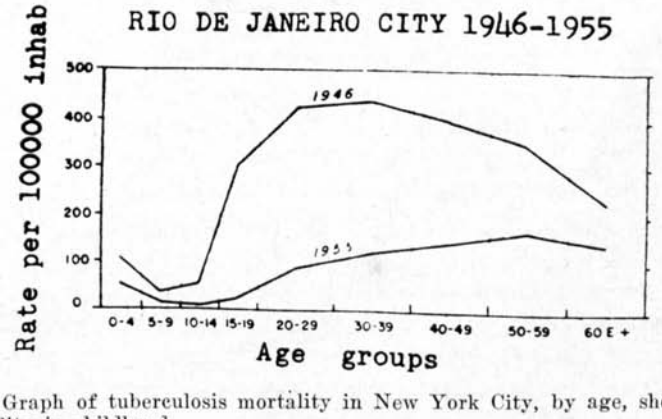


FIG. 2. Graph of tuberculosis mortality in New York City, by age, showing the period of low mortality in childhood.

FIG. 3. Graph of tuberculosis mortality in Vitória, Espírito Santo, Brazil, showing the same period of low mortality in childhood.

FIG. 4. Graph of tuberculosis mortality in Rio de Janeiro, showing the same period of low mortality in childhood.

Table 2. These percentages are to be compared with those of the age distribution of the general population of Rio de Janeiro, of whom fully 60 per cent are adults and nearly 40 per cent are children. Thus, the childhood age groups are less represented among the leprosy patients than among the general population.

TABLE 2.—*Age distribution of leprosy patients and of the general population in Rio de Janeiro, in percentages.*

Subject group	0-4	5-9	10-14	15-19	20-29	30-39	40-49	50-59	60>
Leprosy patients	0.9	4.1	8.8	11.4	23.6	19.8	15.5	10.0	5.9
	25.2				74.8				
General population	10.9	8.7	8.8	10.2	21.1	15.6	11.5	7.2	6.0
	38.5				61.5				

[a]The data for leprosy patients are based on a total of 4,960 cases registered up to 1957.

It should be explained that the limit between children and adults has been taken at age 20, because those in whom leprosy appeared in the 15-19 age group were really infected in childhood, and so they are included in that group.

The predominance of leprosy among adults is as found in areas recently invaded by the disease, of which is said that leprosy "turned to the right." Leprosy turns to the left, with predominance among children, in areas heavily affected for a long time. As the disease goes on toward extinction, however, there will be a turning to right again because of lesser frequency of new cases among children.

As a matter of fact, the distribution in Rio de Janeiro is due not only to the fact that the adults are more exposed than children, as is the general rule in areas recently invaded by leprosy, but also to the further fact that the younger children are really more resistant, for they show relatively higher percentages of the tuberculoid type (1). This is in accord with observations in Brazil generally, as I reported with Fonte at the Havana congress in 1948 (2). What we found at that time is shown in Table 3.

It is to be seen in this total figures that the tuberculoid type never predominated in any age group, but what is interesting is that its percentages go down as the age increases in childhood.

The same investigation has been repeated for Rio de Janeiro City, the population of which is heavily infected by tuberculosis, as has been seen from the data of the tuberculin surveys and the morbidity and mortality rates.

For this purpose only those leprosy patients who not only dwell in

TABLE 3.—*Age groups and leprosy types in Brazil* (1948).

Age group	No. of cases	Type of leprosy					
		Lepromatous		Indeterminate		Tuberculoid	
		No.	%	No.	%	No.	%
0- 4	268	76	28.4	55	20.5	137	51.1
5- 9	1,442	605	42.0	174	12.1	663	46.0
10-14	2,904	1,649	46.8	223	7.7	1,032	35.5
15-19	3,853	2,467	64.0	273	7.1	1,113	28.9
20-29	9,000	5,677	63.1	735	8.2	2,588	28.8
30-39	7,152	4,546	63.6	537	7.5	2,069	28.9
40-49	3,834	2,231	58.2	349	9.1	1,254	32.7
50-59	1,621	868	53.6	175	10.8	578	35.7
60+	641	318	49.6	68	10.6	255	39.8
Total	30,715	18,437	60.0	2,589	8.4	9,689	31.5

the city but also were born there were taken into consideration, which reduced the sample from 4,960 cases to only 1,689. This procedure, although actually exaggerated, nevertheless permits the separation of a sample upon which the influence of tuberculosis infection had been very concentrated, the purpose being to see what influence the tuberculosis factor might have had on the occurrence of leprosy.

TABLE 4 .—*Distribution of leprosy types among* 1,689 *patients who were born and reside in Rio de Janeiro City.*

Age group	No. of cases	Type of leprosy					
		Lepromatous		Indeterminate		Tuberculoid	
		No.	%	No.	%	No.	%
0- 4	31	5	16.1	14	45.2	12	38.7
5- 9	127	54	42.6	37	29.1	36	28.3
10-14	261	143	54.8	46	17.6	72	27.6
15-19	273	173	63.4	38	13.9	62	22.7
20-29	414	258	62.3	70	16.9	86	20.8
30-39	256	148	57.8	42	16.4	66	25.8
40-49	181	87	48.1	42	23.2	52	28.7
50-59	107	49	45.8	30	28.0	28	26.2
60+	39	18	46.2	10	25.6	11	28.2
Total	1,689	935	55.3	329	19.4	425	25.1

It is again to be seen that the rates of the tuberculoid type decrease with increasing age in childhood, from the youngest to the oldest groups, while on the contrary the lepromatous rates increase. In this case, in all but the first age group, which is the least affected by tuberculosis, the lepromatous rates are invariably the highest. Among the

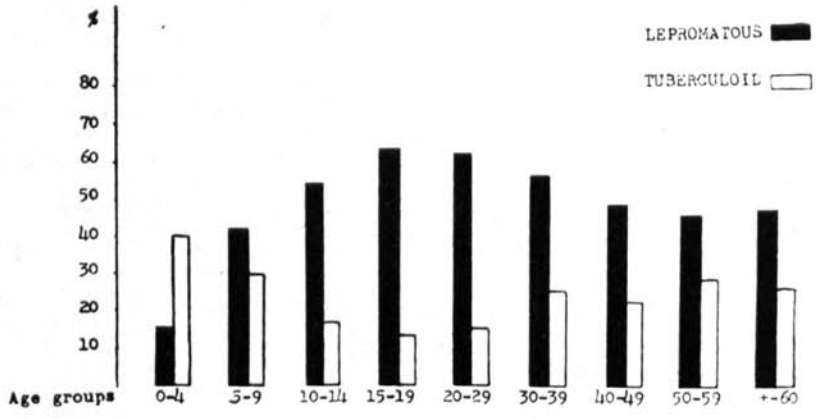


FIG. 5. Illustrating the decrease of percentages of tuberculoid cases in childhood after the youngest group in Rio de Janeiro and the relative predominance of lepromatous cases in all age groups after the first one.

total of 1,689 patients, selected as stated, the percentages of the leprosy types were: lepromatous, 55.3; tuberculoid, 19.4; indeterminate, 25.1.

The same things are to be seen in similar tables pertaining to other places in Brazil. For example, the data of 33,926 cases in the State of São Paulo are given in Table 5. Here the total type percentages are: lepromatous, 57; tuberculoid, 14; and indeterminate 27.

TABLE 5.—*Distribution of leprosy types by the age grouping of* 33,926 *patients in São Paulo State.*

Age group	No. of cases	Type of leprosy					
		Lepromatous		Tuberculoid		Indeterminate	
		No.	%	No.	%	No.	%
0- 4	220	41	18.6	48	21.8	131	59.6
5- 9	1,289	372	28.9	182	14.1	735	57.0
10-14	2,661	1,364	51.2	300	11.3	997	37.5
15-19	3,914	2,390	61.1	431	11.0	1,093	27.9
20-29	8,972	5,571	62.1	1,202	13.4	2,199	24.5
30-39	7,416	4,682	63.1	979	13.2	1,755	23.7
40-49	4,839	2,908	60.1	744	15.4	1,187	24.5
50-59	2,870	1,604	55.9	565	19.7	701	24.4
60+	1,745	924	53.0	412	23.6	409	23.4
Total	33,926	19,856	57.0	4,863	14.0	9,207	27.0

APPARENT CONTRADICTION

It has been shown that among children the tuberculoid form of leprosy occurs most frequently in those of the youngest age group, diminishing rapidly in the next age groups. On the other hand, it has long since been demonstrated that positive reactivity to the lepromin

test is least frequent in children of the lowest age groups and increases regularly with age. Here is an apparent contradiction.

Children actually have a potential capability of reaction to lepromin which is manifested as a result of a stimulus stronger than a single injection of lepromin, and cannot help being effective when infection with leprosy occurs. Sometimes a simple repetition of the lepromin test induces a positive result (7). That happened in, for example, a recent study in Brazil (Rabelo Neto and Silva); negative reactors became positive at the same rate in the two groups of the study, one vaccinated with BCG and the other not vaccinated.

COMPARISON OF LEPROSY AND TUBERCULOSIS

Now, let us make a comparison between leprosy and tuberculosis, using the sample of Rio de Janeiro City. The following has been seen.

(1) Predominance of the tuberculoid type only in the first age group, when the tuberculosis infection is lowest.

(2) In the other age groups, the lepromatous type predominates, in spite of their higher degrees of tuberculosis infection as evidenced by the results of tuberculin testing.

(3) The groups most attacked by tuberculosis (20-29 and 30-39) are also those most attacked by leprosy.

(4) While children develop resistance against the disease tuberculosis in the period between the ages of 7 and 14 years, the same thing does not happen with respect to leprosy.

(5) On the contrary, the opposite is observed: The tuberculoid-type percentages dwindle from 45 per cent to 18 per cent exactly when resistance against tuberculosis develops.

(6) Such being the case, it follows that there is no influence of tuberculosis over leprosy. Both diseases develop in the same population quite independently, without mutual interference.

This kind of epidemiologic investigation, by comparison, leads to the conviction that tuberculosis infection cannot detain leprosy. The supposed protection by tuberculosis has far from extinguished leprosy in Rio de Janeiro, where the statistics demonstrate high rates of both diseases.

Dissociation between tuberculosis and resistance against leprosy may be found in some further examples, free from argument of a possible tuberculin anallergy. Mention may be made of certain further observations.

(1) Recently, in cooperation with two specialists in tuberculosis (Drs. Saboia and Serebrenick), I applied the lepromin test to 150 tuberculosis patients carefully selected from the standpoint of certainty of diagnosis and good general conditions to avoid a possible

anergic state. The Mitsuda reaction could be read in 118 cases, of which 68 per cent were positive, 27 per cent doubtful, and 5 per cent negative. These rates are the same as are usually seen in healthy communities.

(2) Another interesting finding against cosensitization has been recorded by other authors (Magarão and Silvano Lima): Of a group of lepromatous patients also suffering from tuberculosis, 61 per cent were able to react to an intradermal injection of BCG, at a dose of 400,000 bacilli, producing 8 mm. nodules within four weeks, while of course these patients are unable to react to lepromin. In tuberculosis patients who do not react against intradermal BCG, it was found, the prognosis is bad (4).

Now, the cross-immunity theory is becoming more and more complicated, and its maintenance requires more and more hypotheses like those of priority of tuberculosis and emphasis on interference by tuberculin anallergy. Those who adopt it have had to limit its possibilities. They recognize it would work in one direction only, namely, against leprosy. Tuberculosis protects against leprosy, although the latter does not protect against the former. That is a "broken-cross-immunity. . . ."

SUMMARY

This paper considers the possibility, maintained by some workers, of a correlation between leprosy and tuberculosis, with a supposed protective effect against the former by infection with the latter. The similarity of the epidemiologic aspects of both diseases in the same population gives grounds for this type of investigation.

The investigations were made in the city of Rio de Janeiro, a city with a population of more than 2,500,000 inhabitants in which both tuberculosis and leprosy are prevalent.

Tuberculosis infection increases according to age from childhood to old age. After the age of 35 years almost all of the inhabitants, more than 90 per cent, have been infected as evidenced by the results of the tuberculin test.

Leprosy, however, is most frequent in adults, who are also the most affected by tuberculosis. Of the leprosy patients in Rio de Janeiro, 75 per cent are adults and only 25 per cent are children, whereas in the general population the children are nearly 40 per cent of the whole and the adults are about 60 per cent.

The first age group (0-4 years), the least infected with tuberculosis, is the only group in which the tuberculoid type of leprosy (45%) exceeds the lepromatous type (16%).

During the age period between 3 and 12 years, in which the children evidence resistance to tuberculosis in terms of mortality, the percentages of the tuberculoid type decrease considerably (from 45% to

18%) instead of increasing, as it should be if there is any connection in the resistance against both diseases.

This investigation leads to the conclusion that tuberculosis infection affords no protection against leprosy.

RESUMEN

Considérase aquí la posibilidad, mantenida por algunos técnicos, de que exista una correlación entre la lepra y la tuberculosis, con un supuesto efecto protector contra la primera por infección con la última. La semejanza de los aspectos epidemiológicos de ambas dolencias en la misma población constituye la base para una onvestigación de este género.

Los estudios se llevaron a cabo en Río de Janeiro, ciudad con una población de más de 2,500,000 habitantes, en los cuales son frecuentes tanto la tuberculosis como la lepra.

La infección tuberculosa aumenta de acuerdo con la edad desde la infancia hasta la ancianidad. A partir de la edad de 35 años, casi todos los habitantes, más de 90 por ciento, se han infectado según demuestran los resultados de la comprobación con tuberculina.

En cambio, la lepra es más frecuente en los adultos, que son también los más afectados por la tuberculosis. De los leprosos en Río de Janeiro, 75 por ciento son adultos y solamente 25 por ciento niños, mientras que en la población general los niños representan casi 40 por ciento y los adultos aproximadamente 60 por ciento.

El primer grupo por edad (0-4 años), el menos infectado con tuberculosis, es el único en le que la forma tuberculoidea de la lepra (45 por ciento) exceda la forma lepromatosa (16 por ciento).

Durante el período entre 3 y 12 años de edad, en le que los niños muestran resistencia a la tuberculosis en términos de mortalidad, los porcentajes de la forma tuberculoidea desciencen considerablemente (de 45 a 18 por ciento), en vez de aumentar, como deberían hacer si existe alguna relación en la resistencia a ambas enfermedades.

Esta investigación lleva a la conclusión de que la infección tuberculosa no suministra protección contra la lepra.

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