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A M E R I C A N C O L L E G E O F



C H E S T

P H Y S I C I A N S<sup>®</sup>

## Is Serious Pulmonary Disease Caused by Nonphotochromogenic ("Atypical") Acid-Fast Mycobacteria Communicable?\*

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It is indeed an honor to be invited to speak to you on this occasion. The many local, national and international honors already conferred upon Dr. Waksman for his many scientific contributions to the welfare of humanity are revealed in the almost innumerable citations in his biography.

I am happy to have a part in perpetuating the recognition of Dr. Waksman's many accomplishments, and, in so doing, I would like to talk to you on a subject which needs extensive research. We need to know the source of an infection of the lungs by certain acid-fast mycobacteria and to know if these organisms are communicated from person to person. Furthermore, there is great need for more effective drugs than are now available for treating this infection when it becomes pathogenic to man. We sincerely hope that Dr. Waksman can make another important contribution to medicine by discovering the answers to these problems.

For several years there has been a need for epidemiological studies, particularly in some of the southeastern states, in regard to a serious pulmonary disease caused by one of the several strains of "atypical" acid-fast bacilli. The need for this study is not because of a high prevalence of the disease, but because the source of these organisms and the manner in which man becomes infected with them are unknown. The known incidence of disease in Georgia is low, as only about 1 per cent of 15,180 patients admitted to our tuberculosis hospital during the past 10 years had demonstrable pulmonary lesions associated with these mycobacteria in the sputum.

In a previous report it was pointed out that of 69 patients, the sputum cultures of 64 grew out the same strain of "atypical" organisms.<sup>1</sup> The cultures of the 64 strains were smooth, moist, slightly chromogenic, slow-growing, dysgonic in appearance at the end of six weeks and not subject to appreciable color change when exposed to light.

According to Runyon,<sup>2</sup> these strains were characterized, in part at least, as nonphotochromogenic acid-fast mycobacteria, Group III. For the most part they were nonpathogenic to the guinea pig.

In our previous report it was pointed out that only 17 per cent of the patients were under the age of 40, whereas 50 per cent of all tuberculous patients admitted to the hospital during the preceding five years were under 40. Many of the patients had had repeated episodes of respiratory illness, and 59 per cent were white men. Forty-one per cent of all tuberculous patients admitted during the period were Negroes, but only 13

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per cent of the 69 patients were of this race. There were 63 married patients, but no spouse had ever had tuberculosis. No two patients had ever been discovered in the same family or among household contacts. Surgically resected materials of pulmonary lesions of seven patients were grossly and microscopically indistinguishable from tuberculosis. Only 68 per cent were positive reactors to first strength OT, and only 29 per cent of 122 family or household contacts tested by the health departments<sup>24</sup> were found to be positive to the same dose. At that time most of the reactors that were considered positive were read in terms of plus 1, 2, 3 or 4. Plus 1 was equivalent to a measured induration of more than 5, but not exceeding 10 mm. induration, etc., in accordance with NTA standards. Such terms will subsequently be used in stating the results of tests with OT or PPD among additional contacts.

Some of the foregoing observations raised the question of communicability of this disease and, since it was shown that 70 per cent of the patients remained sputum positive under chemotherapy, a clinical as well as a potential epidemiological problem was encountered.

Since that report was made, 104 additional patients have been admitted with "atypical" acid-fast mycobacteria in the sputa. Of the 104, the cultured sputa of 94 grew out only nonphotochromogens. Without going into detail it can safely be said that the age, sex, race, history, the

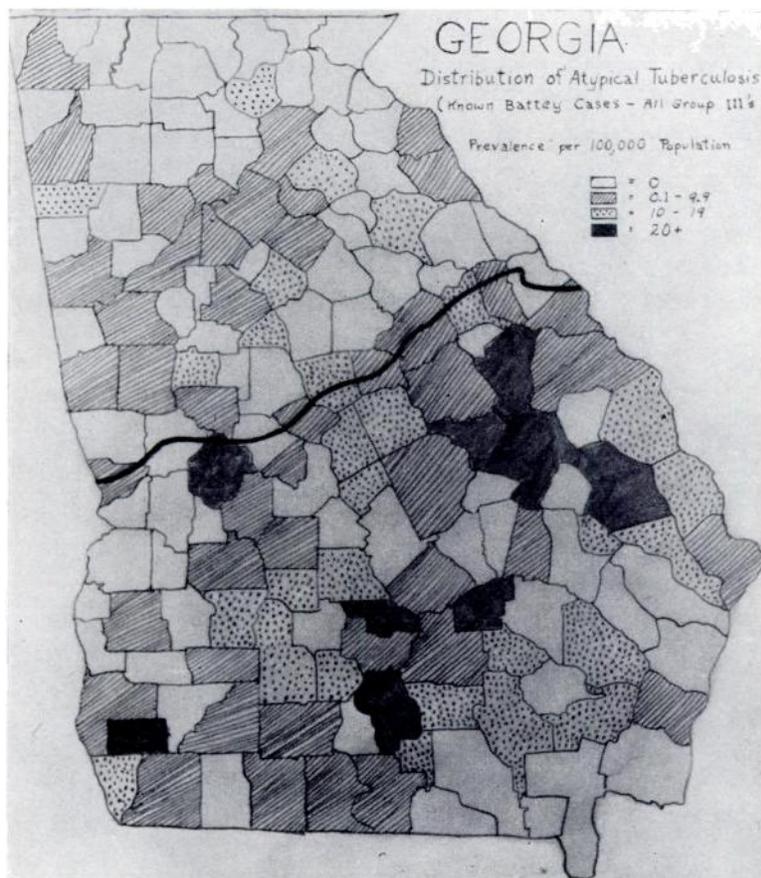


FIGURE 1

tuberculin reaction and other clinical features of the 94 patients fell into the same pattern as the 64 previously reported, making a total of 158. Additional information has been gathered, however, on 95 patients of both groups regarding all previous occupations and it was found that 81 per cent had, at one time or another, lived on farms. Of the two groups, 152 were married or widowed. One, a 76 year old widowed white woman, said that her husband had died of tuberculosis years ago. He was never hospitalized and there was no bacteriologic or roentgenographic confirmation of the diagnosis. Otherwise, there has been no history of tuberculosis in the spouse among the other married or widowed patients.

The majority of the 158 patients were over 60 years of age. There might be some question if the low incidence of a significant tuberculin reaction could be attributed to age. However, none was so acutely ill from pulmonary disease to be anergic. Moreover, the majority who were negative were between the ages of 50 and 59.

Figure 1<sup>s</sup> shows the prevalence of disease by counties in the state. It will be noted that the state is divided into two areas by a somewhat diagonal line crossing from west to east, and is known as the Fall Line. The northern area is mostly mountainous or hilly, while the southern area is, for the most part, rolling or flat. The white or unshaded counties denote that no patient has been admitted from such counties. The cross-hatched counties denote that the prevalence is 0.1-9.9 patients per 100,000 population; the dotted counties denote 10 to 19, and the black areas denote 20+ per 100,000.

Although there are no blacked-out counties in the northern portion, the largest and perhaps the most densely populated counties in the state are in two counties of the northern portion, but each of these counties shows a prevalence of only 1.9 per 100,000 in contrast to 10 to 30 in some of the southern, mostly rural counties. It is found from a map furnished us by the Georgia Division of Mines, Mining and Geology, that the greatest incidence of this disease has been found in counties where the surface soil is fine, grain-size silica, and is classified as "Hawthorne" soil (sedimentary rocks). Practically all of this type of soil is found below the Fall Line.

Pretreatment susceptibility studies of these organisms to streptomycin were done on 81 patient strains of the 94 patients previously mentioned.

TABLE 1—REACTION TO PPD-S AND PPD-B AMONG 51 PATIENTS

	Patients
Non-reactors to both antigens	2
To PPD-S alone	
(a) 6 mm. or over	3
(b) Under 6 mm.	2
To PPD-B alone	
(a) 6 mm. or over	16
(b) Under 6 mm.	1
Six mm. or over to B, under 6 to S	3
Six mm. or more to S and B	24
Total	51

Of this number 58 were sensitive, 23 partially resistant and none completely resistant. A growth of 10 mcg./ml. comparable with the control was considered to be complete *in vitro* resistant. Studies of susceptibility to INH were done on strains of 80 patients prior to treatment. All 80 had growth on 1 mcg./ml. comparable with the control, indicating complete *in vitro* resistance.

Response to streptomycin plus PAS, INH plus PAS, or, to all three drugs given simultaneously has been equally as poor among the latter as the former group of patients, thus, again, posing a possible potential epidemiological problem.

One hundred seventy-three patients are mentioned in the abstract furnished for this program. However, the sputum of 15 patients, five of the first group and 10 of the second group, either produced different strains of "atypical" organisms, or both group III "atypical" and *M. tuberculosis* were concurrently or alternately isolated. (One patient converted from "typical" to "atypical" and one from "atypical" to "typical"). After submitting the abstract it was decided to withhold at this time discussion of these patients and their contacts because of the need for individualization of the patients and further studies of the contacts.

This has been a very limited study in epidemiology of this disease. For the lack of much needed research to establish the source and mode of transmission of infection, the study, of necessity, had to be limited to the clinical aspects of the patients; the tuberculin reaction to OT or PPD among household contacts; the reaction of patients and contacts to an antigen prepared from a nonphotochromogenic strain obtained from a patient in the hospital; a re-evaluation of the geographic distribution of this disease in Georgia, since our previous report, and a continuing search for a contact case.

In order to illustrate some of the features of this disease and the findings among contacts, the following case history is presented (Fig. 2). This is the chest x-ray film of a white man, 39 years of age, when first admitted in December, 1955. It is felt that roentgenographically these lesions are indistinguishable from pulmonary tuberculosis (however, in many patients the location of the lesion, or lesions, and the extensive amount of fibrosis and emphysema are not necessarily considered characteristic of tuberculosis). No mycobacteria or fungi have at any time been isolated from the sputa of this patient except nonphotochromogens. He had had symptoms suggestive of tuberculosis for about one and one-half years prior to admission. His family and marital history were negative for tuberculosis and there was no known contact with the disease. Other than chest findings and being underweight, the physical examination was not remarkable. At the time of his admission, his wife said that she and their six minor children had continuously lived in the home with the patient, and that he had been coughing for over a year. She stated

TABLE 2—NUMBER AND PER CENT OF 51 PATIENTS WITH 6 MM. OR MORE INDURATION

	Patients	Per cent
To PPD-S	28	55
To PPD-B	43	84

that she and all the children were tested with tuberculin and had x-ray films by the health department, shortly after the husband was found to have pulmonary disease, and they were all negative to both tuberculin and chest x-ray film inspection. Guinea pig inoculation was done with raw sputum from the patient and when the animal was sacrificed, it was considered to be grossly non-infected. However, a macerated portion of the spleen planted on culture grew out the same atypical organisms as originally isolated. Pretreatment drug susceptibility evaluation showed complete sensitivity to streptomycin and a 4+ growth on 1 mcg./ml. of INH. He has had streptomycin, PAS, INH, viomycin and cycloserine in various combinations, but no PZA because of slight abnormal liver function at the time the drug was considered. He has never been considered a surgical candidate. His sputum cultures remain positive. Figure 3 shows progressive disease and the prognosis would seem to be hopeless.

Information furnished us by the local health departments and the Division of Tuberculosis Control<sup>1,4</sup> showed that 336 household contacts of the 94 patients had been skin tested with first or intermediate strength OT or PPD. The results of those who were given 250 TU were excluded from this study because of the question of cross reaction if positive. Only 87 (26 per cent) were positive by the criteria of plus 1, 2, 3 or 4. This compares favorably with the 29 per cent of 122 contacts previously mentioned.

During our early observations of the clinical aspects of these patients and the low rate of tuberculin sensitivity to OT or PPD among them and their contacts, it became desirous to have an antigen prepared from the nonphotochromogenic strains to be used for tuberculin testing of patients and their household contacts. The purpose was for correlating the results with those usually found among "typical" cases of tubercu-

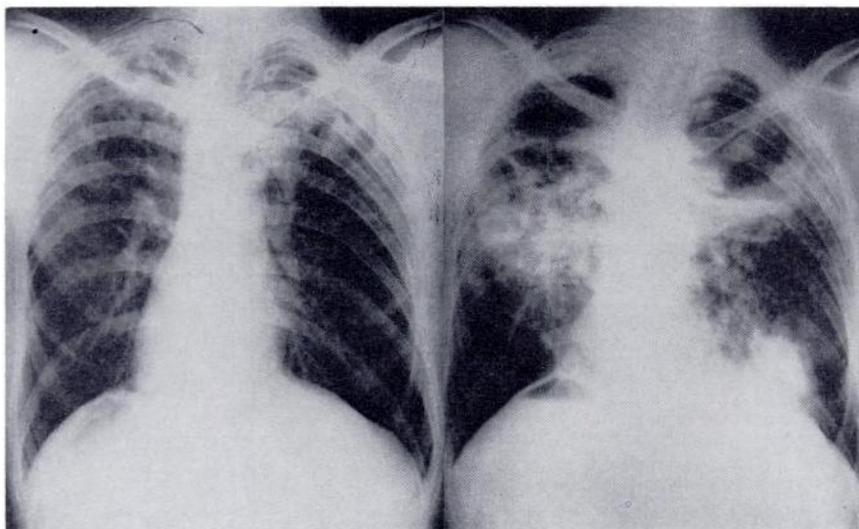


FIGURE 2

FIGURE 3

FIGURE 2: Chest roentgenogram on admission to hospital, showing bilateral infiltration with cavitory disease in each apex. FIGURE 3: Chest roentgenogram made approximately 50 months after admission, showing progressive infiltration and cavitory disease.

losis and their household contacts when tuberculin tested with OT or PPD. It was anticipated that should infection with these "atypical" organisms occur by reason of contact then the frequency of positive reactors among household contacts, when tested with an homologous antigen, should be similar to that usually found among household contacts of known "typical" cases of tuberculosis when tested with an homologous antigen, that of *M. tuberculosis*.

Drs. Florence Seibert and Lewis Affronti of Phipp's Institute were furnished cultures obtained from the sputum of patients in Battey Hospital, and they were kind enough to prepare antigens from two of these strains, known as Battey I and Battey II. Only the antigen prepared from Battey I, and referred to as PPD-B, was used in this study.

Beginning in September, 1958, a sufficient amount of this antigen, along with the standard PPD, prepared by Dr. Seibert and referred to as PPD-S, was obtained, as needed, to begin skin testing all patients admitted to the hospital. The dose of each antigen was 0.0001 mg., or 5 TU. The results of these tests are being studied by some of the staff, but are incomplete. (As a progress note it can be said, however, that among hundreds of tuberculous patients tested, the incidence of a 6 mm. or more induration to PPD-B among Negro patients had been considerably higher, thus far, than among white patients).

So far, 51 patients with "atypical" tuberculosis, including several discharged before this antigen was obtained, have been simultaneously tested with these two antigens. The criterion used to indicate a positive reaction was 6 or more millimeters of measured induration (Table 1). For convenience the letters, S and B, are used to indicate PPD-S and PPD-B, respectively. Table 2 shows the number and per cent who had a 6 mm. or more induration to S and B. Table 3 shows a comparison of induration among these patients.

Two hundred ninety-six of approximately 500 known household contacts of these patients have been tested with the same dose (5 TU) of the two antigens. Circumstances beyond our control made it impossible to test all contacts at this time. Two sets of tuberculin syringes and needles were used, one for PPD-S and one for PPD-B. At no time was there any mixing of the sets. They were sterilized in separate sterilizers and packaged separately. The antigens were given simultaneously in opposite arms. The criterion used for a positive reaction was the same as that used among patients. Table 4 shows the results of these tests among contacts of all ages, sex and race. Of these, four had the same number of millimeters, 16 had a greater reaction to S than B, and 15 had a greater reaction to B than to S. It was found that the total number that had 6 or more millimeters induration to PPD-B was 103, or 35 per cent,

TABLE 3—COMPARISON OF INDURATION AMONG 51 PATIENTS

	Patients	Per cent
Greater to PPD-S than to PPD-B	15	29
Greater to PPD-B than to PPD-S	33	65
Equal induration	1	2
Non-reactors	2	4
Total	51	100

Table 5. This percentage is considerably less than the known percentage of positive reactors to OT or PPD among some 1500 contacts of culturally proved cases of "typical" tuberculosis.<sup>3,4,6</sup>

When the 296 contacts were broken down according to age and sex, the number in each group was insufficient to be of any significance. However, it was found that the per cent of men reactors to PPD-B was considerably higher than women for all age groups except from 45-54. There were 117 men and 179 women tested. Of the 117 men, 100 were white and 17 were Negroes. Fifty of the whites and eight of the Negroes were positive. Of the 179 women tested, 161 were white and 18 were Negroes. Thirty-four of the whites and nine of the Negroes were positive.

A group of 140 *non-contacts* of different ages of white and Negro persons have been tested with PPD-S and PPD-B. Of 63 white men tested with PPD-S, 19 had a positive reaction of 6 mm. or more, and of 25 white women tested three were positive. Of the white men tested with PPD-B, 15 were positive while none of the white women had any reaction at all. Of 33 Negro men tested with PPD-S, 16 were positive, and seven of 19 Negro women tested were positive. Eighteen of the 33 Negro men tested with PPD-B were positive, and eight of the 19 Negro women were positive.

Information available at this time shows that the incidence of positive reactors to PPD-B among "typical" tuberculous patients, contacts of "atypical" patients and *non-contacts* to either form of disease is higher in the Negro than in the white race.

Edwards and Palmer<sup>7</sup> reported 68 per cent of 800 men Navy recruits from the southeastern part of the United States had 6 mm. or more induration to 5 TU of PPD-B. This was in contrast to their findings of only 39 per cent in the mideast, 29 per cent in the northeast and only about 20 per cent<sup>8</sup> in the northwest.

In an unpublished report, Dr. Charles LeMaistre,<sup>9</sup> who recently skin tested 600 men kaolin workers of varying ages in Washington County, Georgia, with the same dose of PPD-B, found that 459 (76.5 per cent) had 5 or more millimeter induration. The exact number who had only 5 mm. induration has not been obtained at this writing.

TABLE 4—REACTION AMONG HOUSEHOLD CONTACTS TO PPD-S AND PPD-B OF ALL AGES, SEX, AND RACE

	Number	Per cent
Non-reactors to both antigens	157	53
Reactors to PPD-S alone		
(a) 6 mm. or over	7	2
(b) Under 6 mm.	6	2
Reactors to PPD-B alone		
(a) 6 mm. or over	59	20
(b) Under 6 mm.	15	5
Reactors to both "S" and "B"		
(a) 6 mm. or over	35	12
(b) Under 6 mm.	6	2
(c) 6 mm. or over to "S" and under 6 to "B"	2	1
(d) 6 mm. or over to "B" and under 6 to "S"	9	3
Total	296	100

TABLE 5—NUMBER AND PER CENT OF CONTACTS WITH 6 MM. OR MORE INDURATION

	Contacts	Per cent
To PPD-B	103	35
To PPD-S	44	15

### Discussion

During our early observations these organisms were thought to be saprophytes. After failure to recover *M. tuberculosis* from serial sputum cultures and failure to produce progressive tuberculosis in guinea pigs inoculated with the same specimen of sputa, three of these patients were discharged as being non-tuberculous. Further studies in our laboratory, however, convinced us that these organisms definitely were not saprophytes, as the term is commonly used, in that their growth rate was slower; there was little or no pigment production, and the repeated occurrence of these strains in the sputum and surgically resected specimens of pulmonary tissue indicated the existence of more than a casual relationship.

It became obvious that the incidence of a significant tuberculin reaction among these patients and their contacts was not as high as had been found among culturally proved cases of "typical" tuberculosis and their contacts.

It seemed paradoxical not to find a contact case among approximately 500 known contacts, including the spouse, of 151 married or widowed patients.

For some unexplained reason, the ratio of the patients per 100,000 population ranged from 4 to 15 times higher in some of the rural and small town areas than in the urban or more densely populated centers.

It will be recalled that among two different groups of 122 and 336 (458) contacts of "atypical" cases, the percentage of reactors to OT or PPD, showing not less than 6 mm. induration, was 29 and 26 per cent respectively. It has been shown that of the 296 contacts tested with PPD-S, only 44, or about 15 per cent, had 6 or more millimeters induration. This 15 per cent is only about half of that seen in the group of 458 tested with OT or PPD. This discrepancy may be due to several factors, such as the difference in numbers tested, the difference in antigens, the possibility that some of the contacts had more exposure to cases of "typical" tuberculosis than others, etc.

Since it was found that the per cent of reactors, among contacts, to PPD-S was about equal between men and women and the per cent of reactors to PPD-B among men was twice that of women, there should be a large group of women tested, particularly white women. There is also great need for testing a large group of *non-contacts* of all ages, sex and race with PPD-B, and used as a control.

In addition to focusing our attention on the source of infection and the question of communicability, it must be borne in mind that impaired function of one or both lungs from previous respiratory episodes may play a significant role as a predisposing factor in subsequent development of disease.

Despite the apparent high prevalence of infection in the southeast, the incidence of disease is extremely low. However, once the disease develops, it poses a much greater treatment problem than does "typical" tuberculosis.

There is great need for further epidemiological studies, and other approaches should be made to discover the source of infection, and the mode of transmission. More effective drug therapy is needed to treat this rare but serious disease.

### SUMMARY

It has been shown that 158 patients, about one per cent of 15,180 patients, admitted during the past 10 years had demonstrable pulmonary lesions associated with non-photochromogenic mycobacteria in the sputum.

At one time or another, 81 per cent of them had lived on a farm. The ratio of patients per 100,000 population ranged from 4 to 15 times higher in rural and small town areas than in the large, urban centers. The incidence of the disease was higher in the southern than in the northern part of the state.

There was no history or evidence that the spouses of 151 married or widowed patients had ever had tuberculosis.

Pretreatment susceptibility of these organisms to streptomycin showed that 58 patient strains of 81 examined were susceptible, 23 partially resistant and none resistant. The strains of 80 patients were examined for susceptibility to isoniazid and all of whom were resistant.

Response to streptomycin plus PAS, INH plus PAS, or, to all three drugs given simultaneously, was poor. The sputum of about 70 per cent remained positive after many months and even years of treatment.

Only 68 per cent were positive to OT or PPD. Of 51 tested with PPD-S and PPD-B, 54 per cent were positive to S, and 85 per cent were positive to B.

Among 458 household contacts, 27 per cent were positive to OT or PPD. Among 296 household contacts tested with PPD-S and PPD-B, only 15 per cent were positive to S and only 35 per cent were positive to B.

The percentage of positive reactors to B was twice as high in men as in women. The percentage of reactors of all contacts was only 6 per cent greater than that found among a group of 140 *non-contacts*.

The incidence of positive reactors to PPD-B has been found to be greater in the Negro, in all groups tested, than in the white race. However, the incidence of disease in the Negro was found to be only 11.7 per cent of that found in the two races combined. Yet, of the 15,180 patients admitted, 41 per cent were Negroes.

If a 6 mm. or greater induration to PPD-B is accepted as being specific, the incidence of infection is high. However, the incidence of known disease is rare.

From the evidence at hand, we conclude that the source of infection may well be environmental, and that the organisms may be avirulent to man except under certain circumstances or predisposing conditions.

#### RESUMEN

Se ha mostrado que entre 15,180 enfermos admitidos durante los pasados 10 años, se encontraron 158 con lesiones pulmonares demostrables, asociadas con la presencia de micobacterias no fotocromógenas en el esputo, o sea en el 1 por ciento aproximadamente.

En alguna ocasión en 81 por ciento de ellos habían vivido en una granja, la proporción de enfermos por 100,000 fué de 4 a 15 veces mas alta en los de origen rural o de los pequeños poblados que lo encontrado en los grandes centros urbanos. La incidencia de la enfermedad fué mas alta en el Sur que en el Norte del estado.

No hubo prueba de que el cónyuge de 151 casados o viudos, haya sufrido tuberculosis jamás.

La susceptibilidad de estos gérmenes a la estreptomycin antes del tratamiento, mostró que 58 cepas de enfermos entre las 81 examinadas, eran susceptibles, 23 parcialmente resistentes y ninguno resistente.

Las cepas de 80 enfermos se examinaron respecto de la susceptibilidad a la isoniacida y todas ellas eran resistentes.

La respuesta a la estreptomycin mas PAS, INH mas PAS o a las tres drogas dadas simultáneamente, fué deficiente. El esputo de alrededor de 70 por ciento, permaneció positivo después de muchos meses y aún años de tratamiento.

Sólo 68 por ciento eran positivos a la OT o PPD. De 51 probados con PPD-S y PPD-B 54 por ciento fueron positivos a S y 85 por ciento positivos a B.

Entre los 458 contactos familiares, 27 por ciento fueron positivos a OT o a PPD. Entre los 296 contactos intrafamiliares probados con PPD-S y PPD-B, sólo 15 por ciento fueron positivos a S y sólo 35 por ciento las fueron a B.

El porcentaje de reactores positivos a B, fué doble en los hombres en comparación con las mujeres. El porcentaje de reactores de todos los contactos fué solo ó por ciento mayor que el encontrado en el grupo de 140 no contactos.

La incidencia de los reactores positivos a PPD-B se encontró mayor en negros en todos los grupos estudiados, que en los blancos.

Sin embargo la incidencia de la enfermedad en el negro se encontró que sólo era de 11.7 por ciento de la encontrada en las dos razas combinadas.

Sin embargo, de los 14,180 admitidos el 41 por ciento fueron negros. Si se acepta que una induración de 6 mm. o mas, como respuesta al PPD-B es específica, la incidencia de la infección es alta. Sin embargo la incidencia de enfermedad conocida es rara.

De lo encontrado concluimos que la fuente de la infección bien puede ser ambiental y que los organismos pueden ser avirulentos al hombre excepto bajo ciertas circunstancias o condiciones predisponentes.

#### RESUMÉ

Sur 15,180 malades hospitalisés durant les dix dernières années, 158, soit environ 1%, eurent des lésions pulmonaires décelables, associées à des mycobactéries non photochromogènes dans l'expectoration.

A un moment ou à un autre, 81% de ces malades ont vécu dans une ferme. Le taux de malades pour 100,000 habitants fut de 4 à 15 fois plus élevé chez la population rurale et les zones de petites villes que dans les grands centres urbains. La fréquence de la maladie fut plus importante dans les régions sud que dans les régions nord de l'état.

Il n'y a pas d'histoire ou de preuve montrant que les épouses des 151 malades ou leurs veuves avaient jamais été atteintes de tuberculose.

La sensibilité de ces germes à la streptomycine avant tout traitement montra que 58 souches sur 81 examinées étaient sensibles, 23 partiellement résistantes, et aucune complètement résistante. Les souches de 80 malades furent examinées au point de vue de la sensibilité à l'isoniazide et toutes se montrèrent résistantes.

Le résultat thérapeutique de la streptomycine associée au P.A.S., de l'isoniazide associé au P.A.S. ou de toutes ces drogues données simultanément se montra médiocre. L'expectoration d'environ 70 malades resta positive après plusieurs mois et même plusieurs années de traitement.

68% seulement furent positifs à la tuberculine brute ou à la tuberculine purifiée. Sur 51 testés avec la P.P.D.-S et la P.P.D.-B, 6.54% furent positifs à la tuberculine S et 85% avec la tuberculine B.

Sur 458 tests pratiqués chez des gens en contact dans leur foyer 27% furent positifs à la tuberculine brute ou à la purifiée. Sur 296 tests pratiqués avec la tuberculine purifiée S et la tuberculine purifiée B, 15% seulement furent positifs à la tuberculine S et 35% seulement à la tuberculine B.

Le pourcentage des réactions positives à la tuberculine B fut deux fois plus élevé chez les hommes que chez les femmes. Le pourcentage des réactions provenant de tous les tests fut seulement plus élevé de 6% par rapport à celui trouvé dans un groupe de 140 personnes n'ayant eu aucun contact avec les tuberculeux.

La fréquence des réactions positives à la tuberculine purifiée B a été trouvée plus élevée chez les Noirs, dans tous les groupes testés, que dans la race blanche. Cependant la fréquence de la maladie chez le Noir ne fut que de 11.7% par rapport à celle constatée dans les deux groupes de races. Notons que, sur 15,180 malades hospitalisés, 41% étaient des Noirs.

Si on admet qu'une induration de 6 mm. au minimum peut être considérée comme spécifique, la fréquence de la maladie à proprement parler est rare.

En possession de faits évidents, l'auteur conclut que la source de l'infection peut parfaitement provenir du milieu environnant, et que d'autre part les bacilles peuvent être avirulents pour l'homme, sauf dans certaines circonstances ou conditions favorables.

#### ZUSAMMENFASSUNG

Es wurde nachgewiesen, daß 158 Patienten d.h. ungefähr 1% von 15,180 während der vergangenen 10 Jahre aufgenommenen Patienten an nachweisbaren Lungenveränderungen in Verbindung mit nicht photochromogenen Mycobakterien im Sputum litten.

Zu irgendeiner Zeit hatten 81% von ihnen auf einem Bauernhof gelebt. Die Verhältniszahl von Patienten auf 100,000 Einwohnern lag zwischen 4 und 15 mal höher im ländlichen Bezirken und Kleinstädten als in großen Städten. Die Krankheitshäufigkeit lag höher im Süden als im Norden des Landes.

E fand sich keine Krankengeschichte oder Anhaltspunkte dafür, daß der Ehepartner von 151 verheirateten oder verwitweten Patienten jemals eine Tuberkulose gehabt hätte.

Die Empfindlichkeit dieser Keime gegen Streptomycin vor Beginn der Behandlung zeigte, daß 58 Patienten-Stämme von 81 geprüften empfindlich waren, 23 teilweise resistent und keiner vollresistent. Die Stämme von 80 Patienten wurden hinsichtlich der INH-Empfindlichkeit geprüft, und sie waren sämtlich resistent.

Die Reaktion auf Streptomycin + PAS, INH + PAS oder auch alle drei gleichzeitig gegebene Medikamente war dürrtig. Das Sputum von ungefähr 70% blieb noch positiv viele Monate nach der Behandlung und sogar nach vieljähriger Behandlung.

Nur 68% reagierten auf Alttuberkulin oder PPD positiv. Von den 51 mit PPD-S und PPD-B getesteten Fällen waren 54% positiv auf S und 85 positiv auf B.

Unter 458 Umgebungsfällen im Haushalt reagierten 22% positiv auf Alttuberkulin oder PPD. Von 296 Umgebungsfällen im Haushalt, die mit PPD-S und PPD-B getestet wurden, waren nur 15% positiv auf S und nur 35% positiv auf B.

Der Prozentsatz positiver Reaktoren auf B war bei Männern doppelt so hoch wie bei Frauen. Der Prozentsatz von Reaktoren unter allen Umgebungsfällen lag nur um 6% höher als in einer Gruppe von 140 nicht Umgebungsfällen.

Das Auftreten positiver Reaktionen auf PPD war in allen getesteten Gruppen häufiger bei Negern als bei angehörigen der weißen Rasse. Jedoch betrug die Krankheitshäufigkeit bei Negern nur 11.7% der-jenigen, die bei beiden Rassen kombiniert gefunden wurde. Gleichwohl befanden sich unter den 15,180 aufgenommenen Kranken 41% Neger.

Sofern man von einer Induration von 6 mm Durchmesser oder mehr annimmt, daß sie spezifisch sei, so ist die Häufigkeit der Infektion beträchtlich. Jedoch ist die Häufigkeit bekannter Er-Krankungen gering.

Aus den auf der Hand liegenden Befunden schliessen wir, daß die Keime für den Menschen avirulent sein können, außer unter bestimmten Bedingungen oder prädisponierenden Umständen.

Complete reference list will appear in the reprints.

**Is Serious Pulmonary Disease Caused by Nonphotochromogenic ("Atypical")  
Acid-Fast Mycobacteria Communicable**

HORACE E. CROW, RAYMOND F. CORPE and C. EDWIN SMITH

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