Reactivation of Apparently Inactive Cases of Pulmonary Tuberculosis

I. D. LITWACK, M.D., and JOHN GARDNER, M.D.

MEDICAL authorities concerned with pulmonary tuberculosis have theorized about a probable reactivation rate among persons with inactive disease and the presumed spread of tuberculosis to their contacts. This study is a followup investigation to establish the extent of reactivation among persons with apparently inactive disease known to the Long Beach (Calif.) Department of Public Health. Also sought was an adequate method for supervising those with inactive tuberculosis to insure continued inactivity of their disease.

The desirability of continued supervision of patients with inactive pulmonary tuberculosis was suggested at the Arden House Conference on Tuberculosis (*1*). In Los Angeles County, efforts toward this goal are being made by the Inter-Agency Council Committee for Tuberculosis Control (*2*).

The reactivation of apparently inactive cases of pulmonary tuberculosis has drawn increasing attention from both clinicians and those in public health. Low in 1959 reported on the relapse rates in a 2- to 11-year followup of patients with pulmonary tuberculosis. He found that 8.08 percent of his group, which had received multiple drug therapy containing isoniazid for 6 months or more, had reactivated disease (*3*). In an Olso study, Garegg, who followed 509 patients with apical fibrosis during the years 1936–45 through a maximum of 20 years, found the disease of 3.08 percent of the male patients and 3.02 percent of the female patients became reactivated (*4*). A study at the Veterans Administration Hospital in Memphis, Tenn., reported by Phillips, showed the disease of 23 percent was reactivated. The subjects were 726 patients with pulmonary tuberculosis treated between 1947 and 1953 who were followed for 3 years after their first discharge from the hospital (*5*).

The subjects in most studies of reactivated disease have been Veterans Administration hospital patients or patients discharged from sanatoriums. The Long Beach study is unique in using patients from the tuberculosis registry of a local health department.

The authors are with the Long Beach (Calif.) Department of Public Health. Dr. Litwack is health officer and Dr. Gardner is chief, division of preventive medical services. Dr. Leroy Hyde, chief, pulmonary services, Veterans Administration Hospital, Long Beach, read the X-ray films in this study. *A grant from the Long Beach Tuberculosis and Health Association supported the study.*

Objectives

The study had several objectives. These were (*a*) to determine the number of reactivated cases among persons with apparently inactive pulmonary tuberculosis; (*b*) to obtain data, for both the reactivated and inactive groups, on sex, age, extent of disease, and type and duration of treatment; (*c*) to compare the extent of disease in the reactivated group with diagnosis at the time of inactivation; (*d*) to establish and maintain a register of inactive cases of pulmonary tuberculosis; and (*e*) to determine an effective method of following inactive cases to prevent reactivation.

Methodology

The study began on October 2, 1961, and ended June 30, 1963. During this period, 7,590 records were reviewed. The records were those

of all persons with a diagnosis of active pulmonary tuberculosis known to the Long Beach Health Department from 1935 to 1960. Of these, 2,536 with evidence that the person's disease had become inactive were selected for study. In making this determination, the definitions of active and inactive tuberculosis given in "Diagnostic Standards and Classification of Tuberculosis," published in 1961, were followed (*6*).

Several reasons were responsible for excluding 5,054 records from selection for the study. These were death (635 persons had died); birth in 1875 or earlier (these persons, if still alive, were assumed to be too old to participate in the study); the criteria for the diagnosis of "active" given in their records did not conform to present standards for the definition of this status; or information on X-rays or results of bacteriological studies was incomplete.

Current addresses for the 2,536 persons were sought in telephone and city directories or by contacting relatives and physicians mentioned in the records. Names of those 60 years or older without a current address were checked with vital statistics records to determine if they had died. Valid addresses could not be obtained for 1,028 persons.

The remaining 1,508 persons were invited by letter to participate in the study. Letters sent to those living in the Long Beach metropolitan area, which includes portions of Los Angeles and Orange Counties, asked former patients to visit the health department for a chest X-ray and bacteriological studies. The letters suggested that, if they preferred, the patients' private physicians could perform these examinations.

Invitational letters to those currently residing outside the Long Beach area asked them to visit their physicians or local health departments for chest X-rays and bacteriological studies. Results were to be forwarded to the Long Beach Health Department. Letters were also sent to the health department of jurisdiction and to hospitals and other health agencies. Mailing record cards with notations of letters, calls, and results of attempts to contact patients were kept for each person.

Incorrect addresses caused 285 letters to be returned, and another 539 brought no response.

Table 1. Persons with reactivated and inactive tuberculosis by age, sex, and extent of disease

Age (years)	Total	Sex		Extent of disease		
		Male	Female	Minimal	Moderately advanced	Far advanced
	Reactivated group					
Total	31	17	14	7	18	6
Under 25	0	0	0	0	0	0
25–34	2	1	1	1	0	1
35–44	6	3	3	3	2	1
45–54	8	5	3	0	7	1
55–64	8	5	3	1	5	2
65–74	5	3	2	1	3	1
75 or older	2	0	2	1	1	0
	Inactive group					
Total	352	211	141	144	149	57
Under 25	[1] 3	1	2	2	0	0
25–34	25	18	7	15	10	0
35–44	[2] 76	45	31	35	32	8
45–54	101	55	46	40	38	23
55–64	84	51	33	29	40	15
65–74	45	29	16	18	20	7
75 or older	18	12	6	5	9	4

[1] Includes one person with primary tuberculosis.
[2] Includes one person with miliary tuberculosis.

Table 2. Treatment received by patients with reactivated and inactive tuberculosis

Type of treatment	Patients with reactivated disease		Patients with inactive disease	
	Number	Percent	Number	Percent
Drugs:				
Received treatment	11	35. 5	150	42. 6
No treatment	20	64. 5	202	57. 4
Surgery:				
Received treatment	7	22. 6	105	29. 8
No treatment	24	77. 4	247	70. 2

Relatives of some patients informed the department that the patients were not available for a variety of reasons.

A total of 399 responses were received to the letters. Of these, 343 persons visited the Long Beach Health Department, and 28 others, under the care of a private physician, gave the health department permission to obtain the desired information from him. Information concerning another 28 was received from sources such as hospitals and health departments. Only 16 refused to participate in the study.

Nurses interviewed each person who visited the health department in response to the letters. They completed an interval history consisting of present address, occupation, and medical and therapeutic regimens followed since the person's last contact with the health department. A 14-inch by 17-inch chest X-ray film was taken, and the person was asked to submit sputum specimens for study. (Each was a 3-day accumulation of morning expectoration, kept in the refrigerator and brought to the health department on the third day.) If unable to raise sputum, the patient was asked to have a gastric examination. The respondent also signed a form giving the department permission to obtain information from his private physician and other health agencies. Other members of his family were encouraged to have a chest X-ray taken at the health department.

Bacteriological studies were extended over a 2-month period to allow time for adequate cultures. All studies included a Niacin test to exclude unclassified mycobacteria. A health department physician reviewed the test results and completed the study history form. The latest chest X-ray was compared with earlier films available in the patient's records.

Cards for the tuberculosis register were filled out for all patients currently residing in Long Beach. These contained identifying data and information on type, extent, and status of disease.

A summary of findings was sent to the patient's private physician, and the patient was notified by mail of the test results. Persons with positive chest X-rays or bacteriological findings indicating active disease were urged to obtain medical care. Continued supervision and treatment was to be provided by private physicians or the health department, depending on the patient's choice and his financial eligibility for health department care.

Results

Evaluations were completed on 383 persons, or 15 percent, of the 2,536 selected from the records. Thirty-one persons, or 8.09 percent, were found to have reactivated disease, and the status of 352 persons remained inactive.

Moderately advanced tuberculosis was the most frequent diagnosis in both the inactive and reactivated groups: 58 percent of those with reactivated disease and 42 percent of the

Table 3. Duration of drug therapy by extent of disease for persons with reactivated and inactive tuberculosis

Disease status [1]	Total	Chemotherapy		
		None	Less than 2 years	2 years or more
Reactivated	31	20	5	6
Minimal	7	4	1	2
Moderately advanced	18	12	3	3
Far advanced	6	4	1	1
Inactive	352	202	92	58
Minimal	144	87	35	22
Moderately advanced	149	89	38	22
Far advanced	57	26	19	12
Primary	1	0	0	1
Miliary	1	0	0	1

[1] Disease status was classified according to definitions in reference 6.

inactive group. In the reactivated group about 23 percent had minimal disease, and 19 percent, far advanced; among those with inactive disease, 41 percent had a diagnosis of minimal disease and 16 percent far advanced (table 1).

Men outnumbered women in both groups, comprising 55 percent of the reactivated group and 60 percent of those with inactive tuberculosis. Most of the 383 persons in the study were in the 35–64-year age category, forming 71 percent of the reactivated group and 74 percent of the inactive group. Of the reactivated group, only 2 were under 35 and 7 were 65 or older. In the inactive group, 8 percent were under 35 and 18 percent were 65 or older.

At the start of the study, we attempted to collect data on other factors such as changes of occupation, social status, and presence or absence of alcoholism which other researchers have found significant in determining risk of reactivation. However, because this information was difficult to obtain and added an unmanageable number of variables, it was decided to omit such factors from the study.

Table 4. Results of X-ray and bacteriological studies of patients with reactivated tuberculosis

Patient and diagnosis	Sputum concentrate tests			Sputum cultures			Gastric cultures			X-ray change
	1st	2d	3d	1st	2d	3d	1st	2d	3d	
Minimal:										
1. P.A.		+			+		+Rare			None.
2. A.C.	+			+						Do.
3. E.C.	−	−		+Few	−					Do.
4. M.D.	+	+		+Rare	+Mod.					Do.
5. D.J.							+Rare	+Few	+In.	Do.
6. S.T.	+Few			+Few						Do.
7. G.W.							+Rare	−		New infiltrate.
Moderately advanced:										
8. E.B.	+	+Few		+	+In.					None.
9. S.C.	+			+						Do.
10. L.D.	+			+						Do.
11. H.H.	+Few			+Few						Do.
12. B.H.	−			+In.						New infiltrate.
13. G.H.	−			+In.						Do.
14. A.K.				+Rare	+Rare					Do.
15. M.L.	+Mod.			+Con.						Do.
16. J.M.				+Rare						None.
17. J.M.	+Few	−	−	+Few	+	+				Do.
18. J.N.	−			+Rare						Do.
19. W.M.	+Rare			+Rare						Do.
20. C.P.	−	+Rare	+Few	+In.	+Mod.	+In.				New infiltrate.
21. R.P.	+			+						None.
22. N.S.	+In.			+Few						Do.
23. N.S.							−	−		New infiltrate.
24. M.W.[1]	+			+						None.
25. L.Z.	−			+Rare						Do.
Far advanced:										
26. H.A.	+			+						Do.
27. P.A.	+	−		+	−			+		Do.
28. R.A.	+Few			+Few						Do.
29. W.H.	+			+						New infiltrate.
30. J.T.[1]	+			+						None.
31. R.W.	−	+		−	+					New infiltrate.

+Rare=1–6 colonies per tube.
+Few=7–20 colonies per tube.
+Moderate=21–60 colonies per tube.
+Innumerable=more than 100 colonies per tube, but colonies are separate.
+Confluent=Innumerable colonies per tube but not separated.
[1] Deceased. Laboratory tests performed during hospitilization prior to death.

Data on types of treatment and duration of chemotherapy for the study groups were obtained from the interval histories. The drugs commonly prescribed for tuberculosis patients are isoniazid, para-aminosalicylic acid, and streptomycin.

A smaller percentage of the persons with reactivated disease had received drug treatment (35.5 percent) and had undergone one or more surgical operations (22.6 percent) than those in the inactive group, of whom 42.6 percent had taken drugs and 29.5 percent had been treated surgically (table 2).

Analysis of data on duration of drug therapy showed that of those with reactivated disease, 6 had had antituberculosis drugs for 2 years or more, 5, for less than 2 years, and 20 received no drugs (table 3). In the larger inactive group, 58 had received chemotherapy for more than 2 years, 92 for less than 2 years, and 202 had had none.

Details of bacteriological findings and evaluations of X-rays of the 31 persons with reactivated disease are given in table 4. Two of the group were deceased. Their deaths came to our attention for the first time during the routine followup by letter, and they were therefore included in the study. Previous X-rays in the patients' records were compared with those taken during the study to ascertain changes. Films of 22, or 71 percent, showed no evidence of change; 9 revealed a new infiltrate. Chest X-rays of those in the inactive group showed no change in disease status.

Diagnoses of 10 patients with reactivated tuberculosis changed from that recorded at the time of inactivation (table 5). Films and bacteriological studies indicated improvements in the disease status of five; two had changed from moderately advanced to minimal and three from far advanced to moderately advanced. The only relationships between treatment received and X-ray change appeared in these films showing evidence of healing.

Cases of reactivated pulmonary tuberculosis undoubtedly exist among those who did not respond to letters inviting them to participate in the study and among those for whom no current address could be obtained. We will recommend that additional efforts be made to investigate this group at a later date. The records of the 635 deceased persons will be followed to determine if active pulmonary tuberculosis was a cause of death.

Summary

To investigate the degree of reactivation among persons with inactive pulmonary tuberculosis, the records of 2,536 such persons known to the Long Beach (Calif.) Department of Public Health during the period from 1935 to 1960 were selected for study. Examinations, including X-rays, sputum and gastric cultures, and interval histories, were completed for 383 persons. Thirty-one, or 8.09 percent, of these were found to have reactivated disease; 7 were diagnosed as minimal, 18 as moderately advanced, and 6 as far advanced. X-ray films taken during the study were compared with available earlier films; those of 22 patients with reactivated disease showed no evidence of change. In the reactivated group, 20 had received no chemotherapy, 5 had had antituberculosis drugs for less than 2 years, and 6, for 2 years or more.

The disease of 352 persons remained inactive. Of the 144 with a diagnosis of minimal tuberculosis, 122 had received no drugs or had taken them for less than 2 years; 22 had had drugs for 2 or more years. Of the 149 with moderately advanced tuberculosis, 127 had taken no drugs or taken them for less than 2 years, and 22 had had chemotherapy for 2 or more years. In the group of 57 with far advanced tuberculosis, 45 had had no drugs or had taken drugs for less than 2 years, and 12 had received drugs for 2 years or more.

Table 5. Changes in diagnoses of patients with reactivated tuberculosis

Diagnosis at inactivation and at reactivation	Number of patients
No change	21
Minimal to moderately advanced	1
Moderately advanced to minimal	2
Moderately advanced to far advanced	3
Far advanced to moderately advanced	3
Etiology undetermined [1] to moderately advanced	1
Total	31

[1] Diagnosis at time of inactivation made on X-ray evidence only; no laboratory confirmation.

Conclusions and Recommendations

This study of cases of inactive tuberculosis known to the Long Beach Health Department shows that reactivation does occur; the 8.09 percent of the study group which became reactive is equal to 80.9 reactivations per 1,000 cases. Obviously, inactive cases are an important source for casefinding and represent a possible reservoir of infection in the community.

Based on the results of the study, we make the following recommendations concerning cases of inactive pulmonary tuberculosis.

1. Annual medical supervision is needed for years following inactivation and possibly for the rest of the patient's life.
2. Include in medical supervision bacteriological studies as well as a comparison of the latest chest X-ray film with earlier films.
3. Place all patients who have not received adequate antituberculosis therapy on a prophylactic medical regimen for 2 years to avoid reactivation.
4. Institute an extensive orientation program so that both physicians and patients understand the necessity for continuing medical supervision.

REFERENCES

(*1*) U.S. Public Health Service: The Arden House conference on tuberculosis. PHS Publication No. 784, U.S. Government Printing Office, Washington, D.C., 1960.

(*2*) Los Angeles County Tuberculosis and Health Association: A report submitted by the ad hoc sub-committee on basic information to achieve tuberculosis control—January 17, 1963. Los Angeles, Calif., 1963. Mimeographed.

(*3*) Low, E.: Relapse rate in a 2–11 year follow-up study of patients with pulmonary tuberculosis treated with and without antimicrobials and discharged from 1946–1955. Amer Rev Tuberc 79: 612–621, May 1959.

(*4*) Garegg, S.: The frequency of relapse in apical pulmonary tuberculosis. Acta Tuberc Scand 33: 120–137 (1957).

(*5*) Phillips, S.: Three year post-discharge status of patients with pulmonary tuberculosis treated 1947 through 1953. Tuberculology 17: 8–12, December 1957.

(*6*) National Tuberculosis Association: Diagnostic standards and classification of tuberculosis. New York, 1961.

Conference Calendar

October 3–4, 1964: Society of Public Health Educators, New York, N.Y.

October 5–9, 1964: American Public Health Association; Association of Management in Public Health; Association of Public Health Physicians; American College of Preventive Medicine; all New York, N.Y.

October 8–10, 1964: American College of Physicians, Hotel Biltmore, Los Angeles, Calif. Edward C. Rosenow, Jr., M.D., Executive Director, 4200 Pine Street, Philadelphia, Pa.

October 11–15, 1964: International Congress on Diseases of the Chest, Mexico.

October 12–14, 1964: Armed Forces Institute of Pathology. The Secretary, Joint Committee on Aviation Pathology, Armed Forces Institute of Pathology, Washington, D.C., 20305.

October 19–22, 1964: National Pest Control Association, New York, N.Y.

October 26–29, 1964: Interscience Conference on Antimicrobial Agents and Chemotherapy, New York, N.Y.

October 29–31, 1964: AMA National Stroke Congress, Palmer House, Chicago. Ralph E. De Forest, M.D., Executive Secretary, National Stroke Congress, 535 North Dearborn Street, Chicago, Ill.

October 29–31, 1964: Gerontological Society, Minneapolis, Minn.

November 10–12, 1964 (date changed): Conference of State and Territorial Health Officers, Washington, D.C.

November 12–13, 1964 (tentative, date changed): Conference of State and Territorial Hospital and Medical Survey and Construction Authorities, Washington, D.C.

November 18–21, 1964: National Association for Mental Health, San Francisco, Calif.

November 22–24, 1964 (date changed): National Conference on Cardiovascular Diseases, Sheraton-Park Hotel, Washington, D.C.

November 29–December 2, 1964: American Medical Association (clinical meeting), Miami Beach, Fla.

November 1964: American School Health Association, New York, N.Y.

December 1–2, 1964: National Social Welfare Assembly (annual meeting), New York, N.Y.

March 17–20, 1965: American Orthopsychiatric Association, New York Hilton Hotel. Reservations: American Orthopsychiatric Association, 1790 Broadway, New York, N.Y., 10019.