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Abdominal Surgery and Development of Pulmonary Tuberculosis

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Summary. **We studied the effect of abdominal surgery on the development of pulmonary tuberculosis using 74 patients treated for active pulmonary tuberculosis for the first time. Group I consisted of patients (53) without a history of abdominal surgery, and Group II consisted of patients (21) with a history of abdominal surgery. Group II was divided into those patients (Group IIa, 13 patients) in whom tuberculosis developed within 10 years after surgery and those patients (Group IIb, 8 patients) in whom tuberculosis developed more than 10 years after surgery. A comparison of chest X-rays showed that the extent of lesions was clearly larger ($p < 0.05$) in Group IIa than in Group I and that Group IIa required more time ($p < 0.05$) after treatment was begun until bacterial drainage became negative. Group IIb was clearly older ($p < 0.05$) than Group I, but the group showed no difference from Group I in the extent of lesions in chest X-rays, and the group required less time ($p < 0.05$) than Group IIa until bacterial drainage became negative.**

The patients tended to have an underweight build with average degrees of obesity being −7.5% in Group I, −10.9% in Group IIa, and −6.7% in Group IIb. Total cholesterol was significantly ($p < 0.05$) lower in Group IIa than in Group I.

One reason why pulmonary tuberculosis was more severe in Group IIa than in Groups I and IIb was probably that the patients had fallen to a low nutritional, underweight condition in the 10 years after their operations, though other factors also need to be considered.

INTRODUCTION

In our treatment of pulmonary tuberculosis patients, we noticed that many had a history of abdminal surgery. We were also impressed by the fact that many patients with a history of abdominal surgery were slightly more underweight than patients without a history of abdominal surgery, that lesions in patients with a history of abdominal surgery were larger in X-rays taken at their initial treatment, and that more time was required, even after treatment, until bacterial drainage became negative. It is already known that reduced weight is a factor in the development of pulmonary tuberculosis,[1-4] but it is uncertain whether surgery for various abdominal disorders may be a determining factor in the development of pulmonary tuberculosis many years later. Therefore, we divided patients being treated for the first time for pulmonary tuberculosis into two groups depending on the presence or absence of a history of abdominal surgery, and we compared their degree of obesity and the extent of the lesions in chest X-rays at their initial treatment. Furthermore, we studied the time required after treatment was begun until bacterial drainage became negative. The results showed some definite differences between the groups.

PATIENTS AND METHODS

Patients

From among the patients treated for active pulmonary tuberculosis in our department in the last five years, we selected 74 who had been treated for the first time to be subjects of this study. All of them were shown to have tubercle bacilli in their sputum (positive niacin test results), and all underwent tuberculostat tolerance tests. In order to study the relation between a history of abdominal surgery, or lack of it, and the development of pulmonary tuberculosis, we excluded all patients complicated by diabetes, renal disease, malignant tumors, collagen disorders, gastric or duodenal ulcers, and other disorders ; also excluded were patients on immunosuppressants or steroids. Nor did we include patients for whom there was a definite source of infection in the home or workplace. Most of the patients we chose were considered to have already been infected. Their ages ranged from

15 to 83; there were 56 men and 18 women.

History of Abdominal Surgery

Patients who had undergone surgery for stomach or duodenal ulcer, stomach cancer, rectal cancer, uterine cancer, cholelithiasis, ureterolithiasis, ectopic pregnancy, or abdominal injury (surgery two times for ileus) and who had definite surgical scars on the abdominal wall were considered as having a history of abdominal surgery. Patients who had undergone an appendectomy were excluded.

Grouping

Patients without a history of abdominal surgery were put in Group I (53 patients, average age 49.8), and those with such a history were put in Group II (21 patients, average age 58.5). Since Group II showed definite trends for patients who had developed tuberculosis within 10 years after surgery and those who had developed it more than 10 years after surgery, the group was divided into Group IIa (13 patients, average age 55.8) with patients who had developed tuberculosis within 10 years after surgery (4.0 ± 2.7 years after surgery) and Group IIb (8 patients, average age 62.9) who had developed tuberculosis more than 10 years after surgery (24.5 ± 10.2 years after surgerry). Neither group had patients who had a history of surgery in places other than the the abdomen (e.g., the chest).

Items Compared Between Groups

All of the following items were compared among the groups: age, degree of obesity (obtained by Minowa's method[5]: rate (%) of body weight increase or decrease = (actual measured body weight − standard body weight)/standard body weight × 100 (unit: kg) where −10% or less was judged underweight and +10% or greater was judged overweight (obese or muscular)), serum total protein, serum albumin, albumin and globulin ratio (A/G), gamma globulin, total cholesterol, GOT, GPT, blood sedimentation rate (1 hour value), hemoglobin, peripheral blood lymphocyte count, and at their initial visit, extent of lesions in chest X-rays (according to the Japanese Society for Tuberculosis classification, revised in 1960). Bacterial drainage smears were compared based on the Gaffky table; cultures before beginning treatment were compared based on the following scale for extent of bacterial growth 8 weeks after beginning the culture: (−) no growth of bacterial colonies seen, (+) 1-200 bacterial colonies, (++) 200-500 bacterial colonies, (+++) 500-2000 bacterial colonies, (++++) more than 2000 colonies. Time until smears became negative, time until cultures became negative, and time until both smears and cultures became negative were measured. The tolerance coefficient of each drug used in treatment was measured after treatment was begun. The tolerable concentrations of drugs judged to be completely tolerable were 0.1 μg/ml for INH, 50 μg/ml for RFP, 20 μg/ml for SM, and 5 μg/ml for EB.

Test for Significance of Difference

Significance of difference was tested using the t-test, and significance was obtained at $p < 0.05$.

RESULTS

1. Comparison of age, degree of obesity, and serum total protein (Fig. 1):

The mean age in Group I was lowest at 49.8 ± 17.4 years (mean ± S.D), significantly lower ($p < 0.05$) than that in Group II (58.5 ± 14.7 years) and that in Group IIb (62.9 ± 14.1 years). A significant difference was not seen between Groups I and IIa (55.8 ± 14.9 years) and between Groups IIa and IIb.

Degree of obesity was $-7.5 \pm 12.2\%$ in Group I, $-9.3 \pm 11.2\%$ in Group II, $-10.9 \pm 11.4\%$ in Group IIa, and $-6.7 \pm 10.9\%$ in Group IIb. There were six patients (11.3%) with a degree of obesity greater than +10% in Group I, but no obese patients were found in Groups II, IIa or IIb. There were 24 patients (45.3%) in Group I with a degree of obesity of less than −10%, 10(47.6%) in Group II, 7(53.8%) in group IIa, and 3(37.5%) in Group IIb. Each group showed underweight trends, but there were no significant differences in comparisons among the groups.

Serum total protein was 7.0 ± 0.7 g/dl in Group I, 6.8 ± 0.6 g/dl in group II, 6.7 ± 0.6 g/dl in Group IIa, and 7.0 ± 0.6 g/dl in Group IIb, and all mean values were within the normal range with no significant differences being observed among groups.

2. Comparison of serum albumin, A/G, and gamma globulin (Fig. 2):

Serum albumin was 3.8 ± 0.6 g/dl in Group I, 3.7 ± 0.6 g/dl in Group II, 3.5 ± 0.6 g/dl in Group IIa, and 3.9 ± 0.5 g/dl in Group IIb, with group IIa showing the lowest value but no significant differences being observed among the groups.

The A/G ratio was 1.3 ± 0.4 in Group I, 1.2 ± 0.3 in Group II, 1.1 ± 0.3 in Group IIa, and 1.3 ± 0.2 in Group IIb, and no significant difference was observed among the groups.

Gamma globulin was 1.4 ± 0.4 g/dl in Group I, 1.4 ± 0.3 g/dl in Group II, 1.5 ± 0.4 g/dl in Group IIa, and 1.

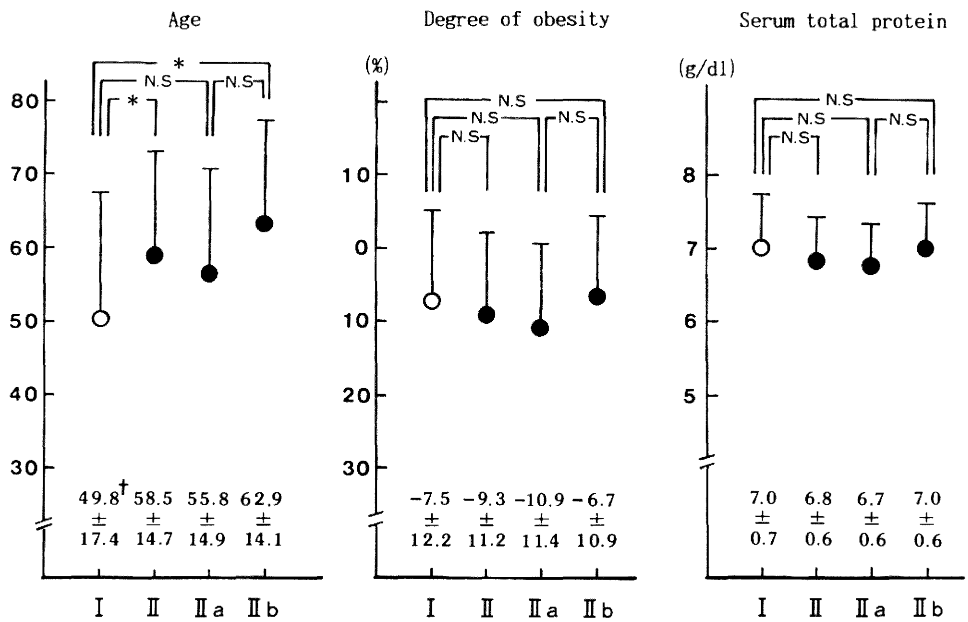

Fig. 1. Comparison of age, degree of obesity, and serum total protein. I : group without a history of abdominal surgery (53 patients) ; II : group with a history of abdominal surgery (21 patients) ; IIa : group developing tuberculosis within 10 years of abdominal surgery (13 patients) ; IIb : group developing tuberculosis more than 10 years after abdominal surgery (8 patients). + mean±S.D. ; * $p<0.05$

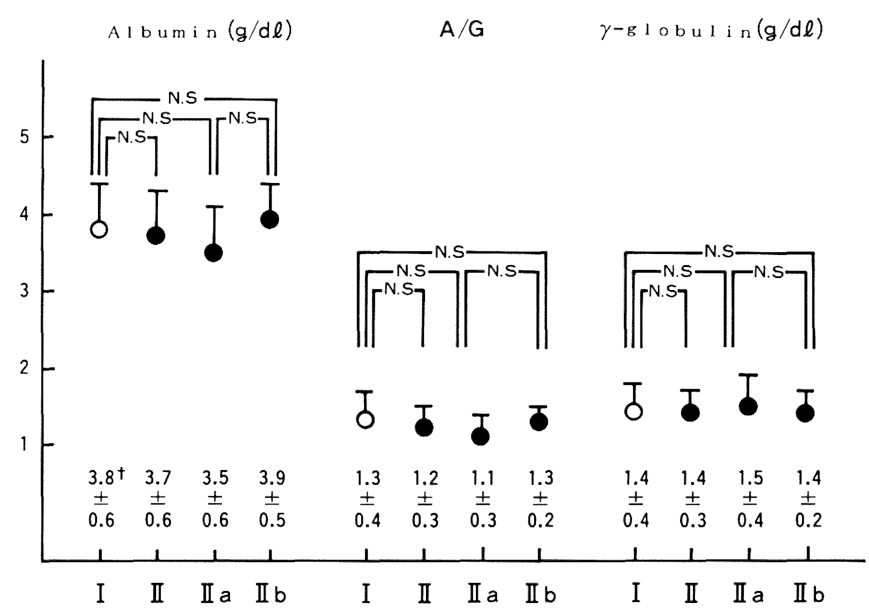

Fig. 2. Comparison of serum albumin, A/G, and gamma globulin.
I : group without a history of abdominal surgery (53 patients) ; II : group with a history of abdominal surgery (21 patients) ; IIa : group developing tuberculosis within 10 years of abdominal surgery (13 patients) ; IIb : group developing tuberculosis more than 10 years after abdominal surgery (8 patients). + mean±S.D.

4±0.2 g/dl in Group IIb, with no significant differences being observed among the groups.

3. Comparison of serum total cholesterol, GOT, and GPT (Fig.3)

Total cholesterol was 154±34 mg/dl in Group I, 140±39 mg/dl in Group II, 128±32 mg/dl in Group IIa, and 160±43 mg/dl in Group IIb. Group IIa was significantly lower than Group I ($p<0.05$), but no other comparisons showed a significant difference.

GOT was 27±19 U/ml in Group I, 28±22 U/ml in Group II, 22±12 U/ml in Group IIa, and 37±31 U/ml

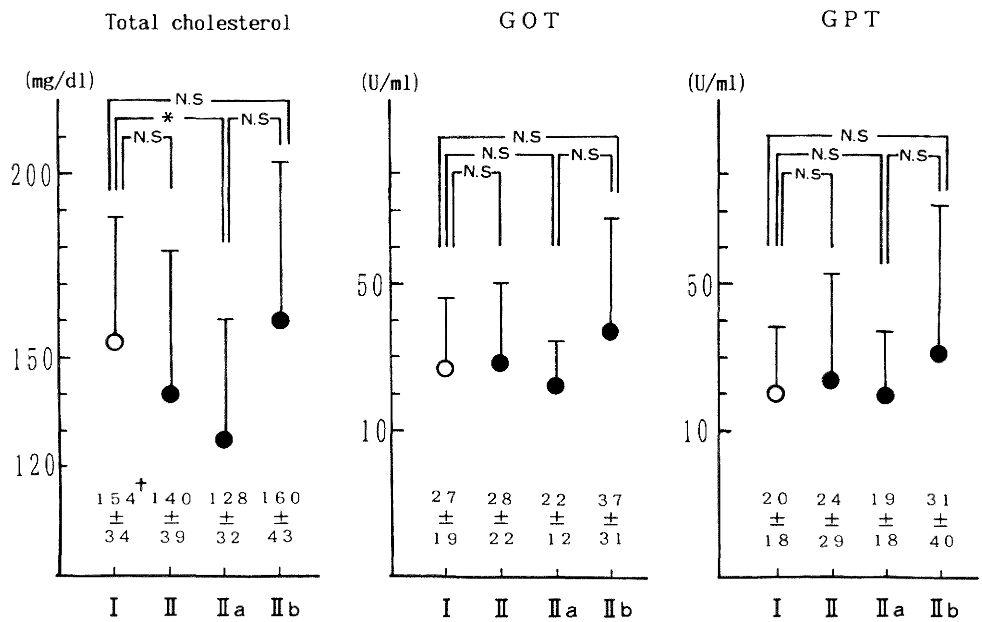

Fig. 3. Comparison of serum total cholesterol, GOT, and GPT. + mean±S.D. ; *$p<0.05$

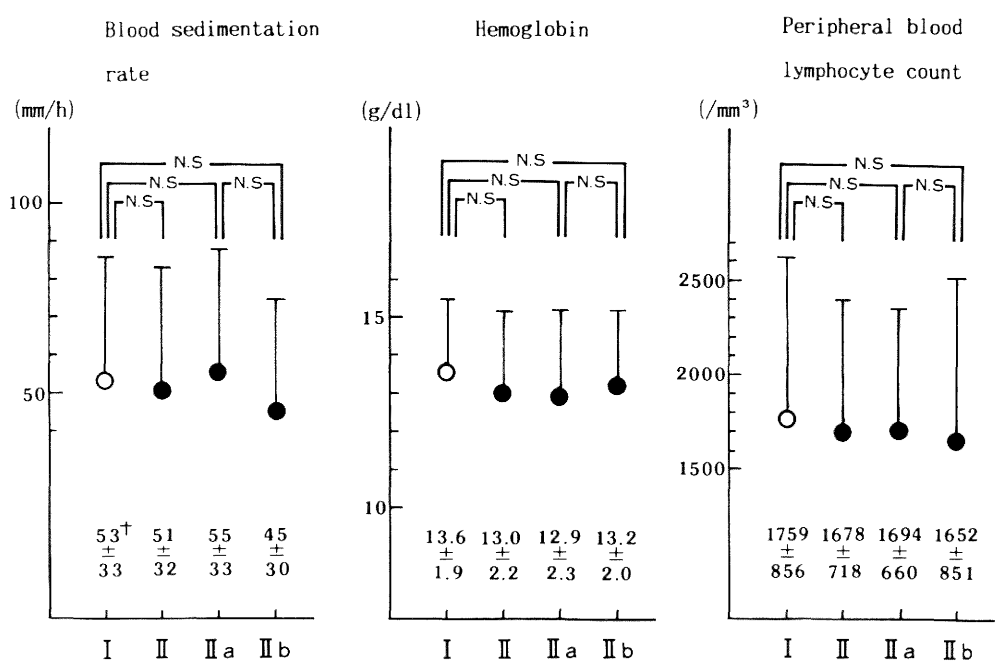

Fig. 4. Comparison of blood sedimentation rate, hemoglobin, and peripheral blood lymphocyte count.
+ mean±S.D.

in Group IIb, with no significant differences being observed among the groups.

GPT was 20±18 U/ml in Group I, 24±29 U/ml in Group II, 19±18 U/ml in Group IIa, and 31±40 U/ml in Group IIb, with no significant differences being observed among the groups.

4. Comparison of blood sedimentation rate, hemoglobin, and peripheral blood lymphocyte count (Fig. 4)

The blood sedimentation rate was 53±33 mm in Group I, 51±32 mm in Group II, 55±33 mm in Group IIa, and 45±30 mm in Group IIb, all of which were accelerated, but no significant differences among the groups were observed.

Hemoglobin was 13.6±1.9 g/dl in Group I, 13.0±2.2 g/dl in Group II, 12.9±2.3 g/dl in Group IIa, and 13.2±2.0 g/dl in Group IIb, and no significant differences were seen among the groups.

The peripheral blood lymphocyte count was 1759±856 cells/mm³ in Group I, 1678±718 cells/mm³ in Group II, 1694±660 cells/mm³ in Group IIa, and 1652±851 cells/mm³ in Group IIb, and no singnificant differences were observed among the groups.

5. Comparison of the extent of lesions in X-rays and bacterial drainage (Fig.5)

The extent of lesions in X-rays was 1.5±0.6 in Group I, 1.8±0.8 in Group II, 2.0±0.8 in Group IIa, and 1.4±0.5 in Group IIb, with Group IIa showing a significantly ($p<0.05$) larger extent of lesions than Group I. There were no differences in other group comparison.

A comparison of bacterial drainage using the Gaffky table showed no significant differences among groups, with Group I being 3.4±2.7, Group II being 3.4±2.8, Group IIa being 3.5±3.1, and Group IIb being 3.1±2.4.

In the comparison of bacterial drainage based on bacterial growth in cultures, Group I was 3.9±0.6 (where, 1.0 corresponded to (+), 2.0 to (++), 3.0 to (+++), and 4.0 to (++++)), Group II was 3.9±0.3, Group IIa was 3.8±0.6, and Group IIb was 4.0±0. No significant differeces were observed among groups.

6. Comparison of times until bacterial drainage became negative (Fig. 6)

The time until smears became negative was 1.9±1.4 months in Group I, 2.8±2.3 months in Group II, 3.5±2.5 months in group IIa, and 1.5±0.8 months in Group IIb, with Group IIa showing a significantly longer time than Groups I and IIb ($p<0.01$, $p<0.05$, respectively).

The time until cultures became negative was 1.9±1.3 months in Group I, 2.2±2.1 months in group II, 3.0±2.4 months in Group IIa, and 1.0±0 in Group IIb, with Group IIa showing a significantly longer time than Groups I and IIb (both $p<0.05$).

The time until both smears and cultures became negative was 2.1±1.6 months in Group I, 2.8±2.3

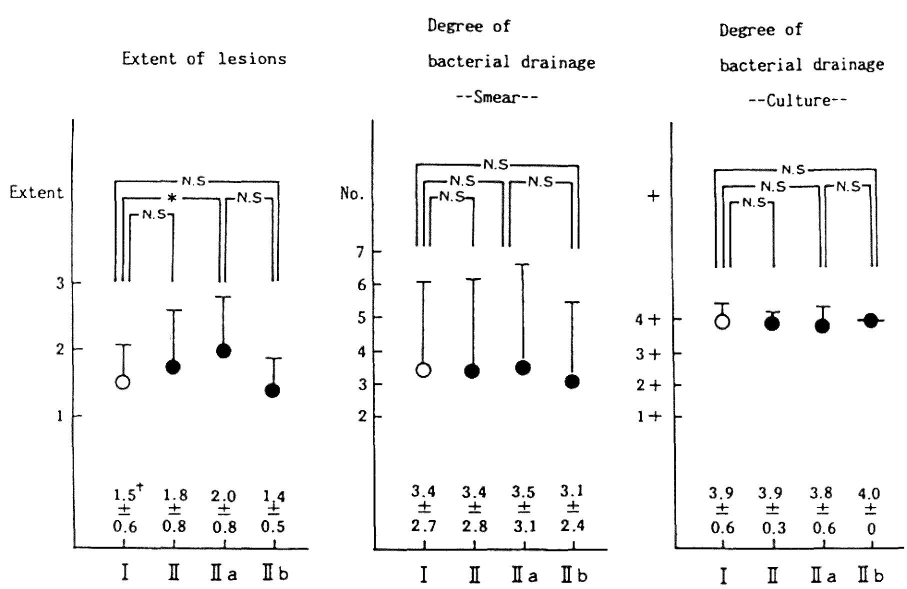

Fig. 5. Comparison of extent of lesions in X-rays and degree of bacterial drainage. + mean±S.D.; *$p<0.05$

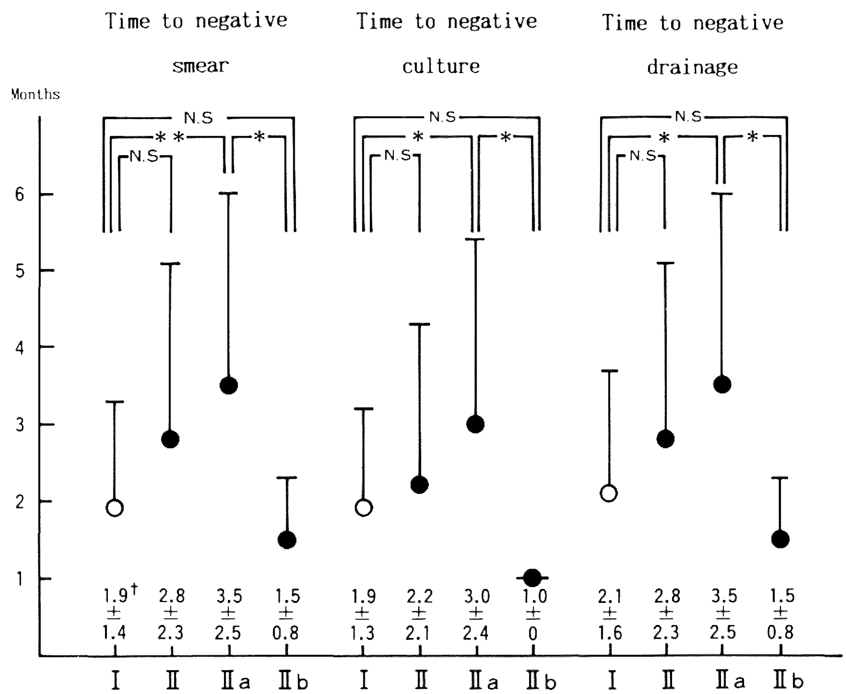

Fig. 6. Comparison of times until bacterial drainage became negative.
I : group without a history of abdominal surgery (53 patients) ; II : group with a history of abdominal surgery (21 patients) ; IIa : group developing tuberculosis within 10 years of abdominal surgery (13 patients) ; IIb : group developing tuberculosis more than 10 years after abdominal surgery (8 patients).
+ mean±S.D. ; *p<0.05 ; **p<0.01

Table 1. Comparison of Drug Tolerance Coefficients

Drug/Group	I	II	IIa	IIb
INH	14/53(26.4)*	8/21(38.1)	5/13(38.5)	3/8(37.5)
RFP	2/53 (3.8)	0/21(0)	0/13(0)	0/8(0)
SM	3/20 (15.0)	2/6 (33.3)	2/5 (40.0)	0/1(0)
EB	2/36 (5.6)	4/16(25.0)	2/9 (22.2)	2/7(28.6)

*Number of cases with complete tolerance/number of cases using (%). Tolerance concentrations (μg/ml) were 0.1 for INH, 50 for RFP, 20 for SM, and 5 for EB.

months in Group II, 3.5±2.5 months in group IIa, and 1.5±0.8 months in Group IIb, with group IIa showing a significantly longer time than Groups I and IIb (both $p<0.05$).

7. Comparison of drug tolerance coefficient (Table 1)

All 74 patients were treated with either the combination INH, RFP and SM, or INH, RFP and EB. In a comparison among groups of the tolerance coefficient for these four drugs, no significant difference among groups was found.

8. Breakdown of surgical histories (Table 2)

In Group IIa, 5 were operated on for gastric ulcer, 3 for duodenal ulcer, 2 for stomach cancer, 1 for rectal cancer, 1 for cholelithiasis, and 1 for ureterolithiasis. In Group IIb, 4 were operated on for gastric ulcer, 1 for uterine cancer, 1 for cholelithiasis, 1 for ectopic pregnancy, and 1 for abdominal injury (surgery two times for ileus). No differences were observed in the incidence of any disease between the two groups.

9. Incidence of abdominal surgery

Of the 74 patients under treatment for the first time for active pulmonary tuberculosis, 21, or 28.4%, had a history of abdominal surgery.

Table 2. Breakdown of Abdominal Surgery Histories

Diagnosis	IIa(13)	IIb(8)	Significant difference
Gastric ulcer	5	4	N. S.
Duodenal ulcer	3	0	N. S.
Stomach cancer	2	0	N. S.
Rectal cancer	1	0	N. S.
Uterine cancer	0	1	N. S.
Cholelithiasis	1	1	N. S.
Ureterolithiasis	1	0	N. S.
Ectopic pregnancy	0	1	N. S.
Abdominal injury (surgery two times for ileus)	0	1	N. S.

DISCUSSION

In the times when tuberculosis was widespread, a person often acquired it with his or her first exposure.[6)] Even today when the chance for exposure is greatly reduced due to BCG inoculations, a survey of infantile tuberculosis[7)] showed a source of infection in 61.4% of the cases, thus indicating that initial exposure is an important factor in the development of tuberculosis. However, among abults only 3.7% of those who contracted tuberculosis had contact with a tuberculosis patient in the previous 3 years,[8)] thus showing that many patients contract the disease a long time after exposure.

These infected people are thought to carry the tubercle bacillus for a long time and then for some reason acquire the disease,[9)] but the mechanism of its development has not yet been clarified. One possibility is that lowered resistance in the host may make it easier for the disease to develop. Many factors can be given as reasons for the development of the disease in infected people. Aoki[8)] studied 1,217 patients being treated for the first time and giving a positive reaction for tubercle bacilli. Of these, he reported that diabetes was a possible factor facilitating development of the disease in 8.0% of the patients and adrenocortical hormones in only 1.8%. The incidence of hemodialysis, renal insufficiency, alcoholism, pneumoconiosis, gastrectomy, and other conditions as factors was very low. Aoki thus claimed that these conditions are not considered to be factors in 90% of those with adult tuberculosis.

Mikami et al.[4)] studied these unidentified factors of disease promotion from the standpoint of the daily life of the tuberculosis patient. Their results showed that daily life factors were seen in 81% of the cases of infectious pulmonary tuberculosis. Physical and heart strain played an important role. Diseases, mainly diabetes, were a factor in 29% of the cases, and insufficient weight was involved in 15% of the cases.

We thought that by comparing the background and examination results of a group with a history of abdominal surgery with those of a group without such a history, we could demonstrate new factors in the development of the disease. However, the scope of our study led us to the conclusion that a low nutritional condition, long considered a factor in the development of disease, was the primary cause since it was so marked in Group IIa.

Both absolutely insufficient nutritional intake and hypermetabolism due to chronic infectious diseases are considered to be the cause of the underweight condition often seen in tuberculosis.[10)] The principal cause for reduction of weight is known to be closely related to the reduction of lipids in the body.[11)] Our study did not comare patients with a control group as did Mikami et al.,[4)] but as shown in Fig. 1 in which the degree of obesity of patient groups is tabulated, each of the groups showed an underweight trend of -7% to -11%, with Group IIa being the lowest. Again, we did not compare these results with a healthy control group, but of the average values for serum total protein, albumin, and the A/G ratio, Group IIa was the lowest. Total cholesterol, too, was significantly lower in Group IIa than in Group I.

In Group IIa, pulmonary tuberculosis developed an average of 4.0 years after abdominal surgery, and the group showed a tendency to be underweight with an average degree of obesity of -10.9% and a definitely low total cholesterol level, which, when compared with Group I, were most likely influenced by abdominal surgery. Group IIb, which developed pulmonary tuberculosis at an average of 24.5 years after abdominal surgery, was probably able to avoid falling into a low nutritional or underweight condition after surgery. Even though group IIb was definitely older than Group I (Fig. 1), the former showed no difference from Group I in total cholesterol (Fig. 3), extent of lesions in chest X-rays (Fig. 5), and the time required until bacterial drainage became negative (Fig. 6). In contrast, Group IIb required less time than Group IIa until bacterial drainage became negative (Fig.6).

These results indicate that when a patient undergoes surgery for the intraperitoneal diseases shown in Table 2, the patient is more likely to suffer a low nutritional, underweight condition, thus enhancing the risk of pulmonary tuberculosis. It is known that underweight people develop pulmonary tuberculosis, more easily,[1-4] that their underweight condition correlates significantly with a lowered cellular immunity as indicated by an immunological skin reaction,[12] and that they show more incidences of the spread of tuberculous lesions in chest X-rays.[12,13]

Gastric ulcer[4] or surgery for gastric ulcer[6] has been designated as a factor in the development of pulmonary tuberculosis, but based on the results shown in Table 2, nonrecurring cancer, cholelithiasis, and ureterolithiasis are also factors. Furthermore, not only disease, but also daily life factors, as pointed out by Mikami et al.,[4] are likely to be important in patients with a history of abdominal surgery. Whether or not it is all right to consider tuberculosis only from the standpoint of nutrition will have to be determined through further study, and the method and scope of the surgery and post-operational therapy and nutritional management will have to be compared between pulmonary tuberculosis patients and healthy patients in order to clarify the truly important factors in the development of tuberculosis.

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