

Tuberculous Peritonitis:

43 Years' Experience in Diagnosis and Treatment

PETER DINEEN, M.D., WILLIAM P. HOMAN, M.D., WILLIAM R. GRAFE, M.D.

The clinical course of 70 patients with tuberculous peritonitis seen over a 43 year period has been reviewed. Thirty-seven patients were diagnosed prior to the advent of anti-tuberculous chemotherapy and 33 after. Clinical manifestations remained unchanged over the period of study. Abdominal pain (93%), fever (63%), gastrointestinal upset (60%), weight loss (60%), and ascites (59%) continue to be the most common findings. Females outnumbered males 2:1. In 89% of patients the duration of symptoms prior to diagnosis was a week or longer, and in 47% it was longer than a month. Diagnosis was confirmed by histologic examination of intra-abdominal tissue in 44% of cases, by clinical suspicion with an extraperitoneal site of tuberculosis in 29%, by bacteriology of peritoneal fluid in 24%, and by autopsy alone in 3%. An extraperitoneal site of tuberculosis was present in 83% of patients. The importance of obtaining a definitive diagnosis, and of instituting immediate antimicrobial therapy is emphasized by the mortality of 49% in the pre-antibiotic era, and of 7% in patients receiving antimicrobial therapy. The conclusions from this review are that: 1) with suggestive clinical manifestations and bacteriologic proof of active tuberculosis anywhere in the patient, operation is not mandated; 2) in the presence of the above clinical manifestations, and in the absence of definitive bacteriologic proof, exploratory laparotomy is indicated for diagnostic purposes; 3) antituberculous chemotherapy is highly effective, and is the treatment of choice.

MAN'S LONG ENCOUNTER with tuberculosis has extended as far back as Neolithic times as indicated from skeletal remains. Despite this association the relationship between pulmonary disease and extrapulmonary tuberculosis was not appreciated until Laennec in 1804 postulated their common basis. The realization of the infective nature of tuberculosis awaited the latter

From The Department of Surgery, The New York Hospital-Cornell Medical Center, New York, N.Y. 10021

portion of the 19th century, and the work by Vellemin and Koch.

Shortly after the term tuberculosis was introduced in 1839, the first well documented case of "tubercular peritonitis" was cared for at The New York Hospital in 1843. The case is presented as illustrative of tuberculous peritonitis in the pre-antibiotic era. The outcome was all too typical, although the clinical presentation is not different from that seen today.

Wm. Henry Johnson. 40. Seaman. W. Indies About a month ago began to complain of want of appetite, occasional nausea and some pain about umbilical region: took salts and Senna and was freely purged. Pain in the abdomen became increased and has continued since, with . . . some heat of skin and slight fever. Has had slight cough for a long time. Not troubling him and not attended with loss of flesh and strength until within 4 weeks. Has had occasional night sweats.

The patient was treated with mustard plasters and tincture of opium applied to the abdomen, purgatives, ipecac, and quinine for fever, with brandy and wine. He died seven weeks following admission after a slow down-hill course. Post-mortem examination revealed:

Cadaver exceedingly emaciated. Lungs small and tubercles infiltrating throughout both . . . The peritoneum was found everywhere thickly studded with tubercles . . . Mesentery was thickened and hard . . . A few tubercles beneath the capsule of the liver.

Despite the widespread impression that tuberculous peritonitis is rare today, it continues to be seen with

TABLE 1. *Method of Establishing Diagnosis of Tuberculosis Peritonitis*

Examination of intra-abdominal tissue	31 (44%)
Clinically suspected with TB elsewhere	20 (29%)
Bacteriology of peritoneal fluid	17 (24%)
Autopsy only	2 (3%)
	70 (100%)

regularity on the surgical services of our institution, including two cases in the past year. Consequently a review was undertaken to study our experience in diagnosis and treatment of this disease, with particular regard to the role of surgery, and to the impact of anti-tuberculous chemotherapy upon the disease.

Materials

From 1932 through 1975, 70 cases of tuberculous peritonitis were diagnosed and treated at The New York Hospital-Cornell Medical Center. On January 1, 1946 the first patient with tuberculosis was treated with streptomycin at this Center. Thirty-three patients were seen following the introduction here of streptomycin in 1946, and 37 patients were seen prior to this date. Of the 48 patients who survived to leave the hospital 40 (83%) received follow-up for at least a year. The mean duration of follow-up for all patients was 7.3 years.

Results

Diagnosis. The definitive diagnosis of tuberculous peritonitis is based upon bacteriologic or pathologic proof of tuberculosis within the peritoneal cavity, or upon

suggestive clinical manifestations and bacteriologic proof of tuberculosis outside the peritoneal cavity. In 31 patients (44%) the diagnosis was established by pathologic examination of intraabdominal tissue obtained at exploratory laparotomy with the characteristic findings of caseating granulomata, with Langhan's giant cells, and acid-fast organisms.

In 20 patients (29%) diagnosis of tuberculous peritonitis was established on clinical grounds with the additional finding of a bacteriologically proved tuberculous focus elsewhere in the body. In 12 of these 20 patients proof of extraperitoneal involvement was obtained from the sputa; in 6 from examination of peripheral lymph nodes; in 5 from urine examinations; and in one from microscopic examination of involved bone.

In 17 of the 70 patients (24%) the diagnosis of tuberculous peritonitis was established by bacteriologic examination of peritoneal fluid obtained by paracentesis. In 7 of these the guinea pig inoculation was positive, the culture was positive in 5, and the acid fast examination in 5. Thus, of 37 paracenteses 46% resulted in a diagnosis, but only 5 (14%) resulted immediately in the definitive diagnosis required for institution of anti-tuberculous chemotherapy.

In two patients (3%) the diagnosis of tuberculous peritonitis was made only at autopsy. Summary of the means of diagnosis of tuberculous peritonitis in this series is given in Table 1.

In all, 58 patients (83%) had at least one possible extraperitoneal site of tuberculosis documented. Tabulation of the data is given in Table 2.

Material

Fifty Caucasians, 17 Negroes, and three Orientals comprised this series. The age range was from 8 months to 75 years, with a mean of 35.5 years. Distribution by age is summarized in Fig. 1. There were 45 females (64%), and 25 males (36%). Thirty-eight patients (54%) were born in the United States, while 32 (46%) were foreign-born. Twenty were from Europe, 9 were from North America exclusive of the U.S., and three were from Asia. Fifteen patients (21%) gave a history of exposure to tuberculosis, and in 11 of these the contact was with one or more members of the immediate family (mother 4; father 1; sibling 9; spouse 1).

The distribution of tuberculous peritonitis seen at The New York Hospital-Cornell Medical Center by year is given in Figure 2. Of interest was the general downward trend in the early sixties (with no cases from 1960-1964) and an increase in frequency since 1964.

Clinical Features

Throughout the 43-year period of this study the clinical presentation of tuberculous peritonitis has re-

TABLE 2. *Extraperitoneal Sites of Tuberculosis in Patients with Tuberculous Peritonitis*

No other site of tuberculosis	12 Patients (17%)
Extraperitoneal site of TB	58 Patients (83%)
Inactive TB On Chest Film	15
Active Pulmonary TB	15
Pleural Effusion on Chest Film	14
Renal Tuberculosis	10
Tuberculous Enteritis	9
Tuberculous Salpingitis	8
Scrofula	8
TB Mesenteric Adenitis	8
TB Osteomyelitis	4
TB Pericarditis	2
Military TB	2
TB Empyema	2
TB Arthritis	2
TB Hepatitis	2
TB Splenitis	2
TB Meningitis	1
TB Thyroiditis	1
TB Laryngitis	1
TB Tracheitis	1
TB Of Adrenal	1
TB Pleuritis	1
TB Prostatitis	1
TB Cystitis	1

mained unchanged (Table 3). Abdominal pain has been the most common clinical manifestation, occurring in 65 patients (93%). In 35 patients the pain was said to be generalized. Of the remaining 30, with abdominal pain that was localized, 25 (83%) had pain in the right or left iliac, or hypogastric region of the abdomen.

Forty-four patients (63%) manifested fever greater than 37.5°. In only 9 was the temperature above 39.0°.

Forty-two patients (60%) also complained of loss of weight, often despite the presence of ascites. Three patients had weight loss of less than 10 lb; in 24 the weight loss was from 10–20 lb; in 8 from 21–50 lb; in 4 more than 50 lb; and in three cases weight loss was present, but not quantitated.

Forty-one patients (59%) had ascites. In 36 cases it was noted clinically, while in the remainder it was appreciated only at exploratory surgery.

Less commonly recorded findings were night sweats (26 patients; 37%), chills (12 patients; 17%), and distinct abdominal mass (18 patients; 26%). In the majority of the latter the mass was located in the right or left iliac region (11 patients).

Duration of Symptoms

Summary of duration of symptoms prior to diagnosis is given in Table 4. Of note has been the comparatively long course of the disease before diagnosis was made. In 89 per cent of patients the delay was a week or greater, while in 47 per cent it was longer than a month.

Laboratory Data

Of the 67 patients who had an appropriate test, 32 (48%) were anemic as defined by a hemoglobin of less

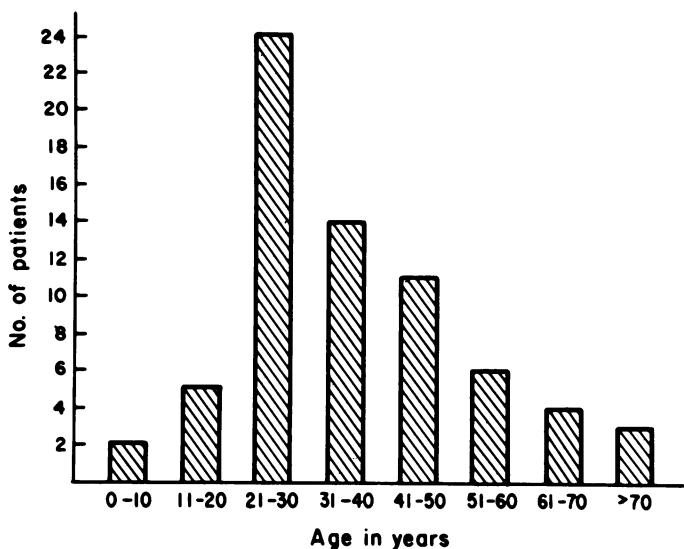


FIG. 1. Distribution by age of 70 patients with tuberculous peritonitis.



FIG. 2. Year of diagnosis of 70 patients with tuberculous peritonitis seen at New York Hospital-Cornell Medical Center.

than 12g%, or a red blood cell count less than 4.2 million/mm³. Of the 69 patients receiving a white blood cell count, 20 (29%) were elevated above 10,000/mm³. Sixty-six patients had differential counts, and in 13 (20%) the lymphocytes were abnormally elevated (23%). Twenty-seven patients had intradermal injections of OT or PPD, and in 24 (89%) the test was positive. Five patients had ascitic fluid subjected to analysis for protein and in each the value was greater than or equal to 3.5g%. Ten patients had cell counts on peritoneal fluid with a range of 100 to 4000/mm³, and a mean of 1990/mm³. Lymphocyte differential on peritoneal fluid was performed 9 times. In three cases the value was less than 70%, and in 6 cases the value was greater than 70%.

Abdominal Surgery in Tuberculous Peritonitis

Thirty-six patients, or 51% of the total, had abdominal operations related to tuberculous peritonitis. One patient had two operations. The indications for these 37 operations are summarized in Table 5. In 20 cases (54%) the true diagnosis was unsuspected prior to the operation. Eighteen of the operations were performed in the pre-streptomycin era and 19 after.

TABLE 3. Clinical Manifestations of Tuberculous Peritonitis in 70 Patients

Mainfestation	Number of Patients (%)
Abdominal pain	65 (93%)
Fever	44 (63%)
Gastrointestinal upset	42 (60%)
Weight loss	42 (60%)
Ascites	41 (59%)
Anemia	32 (48%)
Night sweats	26 (37%)
Abdominal mass	18 (26%)
Chills	12 (17%)

TABLE 4. Duration of Symptoms Prior to Diagnosis of Tuberculous Peritonitis in 70 Patients

Duration of Symptoms	Number of Patients (%)
1 Week	7 (11%)
1 Month	28 (42%)
6 Months	21 (31.5%)
1 Year	7 (10.5%)
5 Years	2 (3%)
Unknown	2
Diagnosis at autopsy only	2

The most commonly performed operation was exploratory laparotomy with omental biopsy (23 cases), followed in frequency by exploratory laparotomy with resection of female genital organs (four cases) and exploratory laparotomy alone (3 cases). There were two cases each of laparotomy with appendectomy, and with diverting colostomy. There was one case each of laparotomy with drainage of a tuberculous abscess, with cholecystectomy or with cholecystostomy.

Postoperative complications were confined to two cases of fecal fistula (5%), and to two postoperative deaths (5%) within one month of surgery. Both deaths occurred before 1946. One was due to the effects of widespread tuberculosis, the other to acute generalized bacterial peritonitis from a ruptured tuberculous urinary bladder.

Medical Therapy

Prior to the introduction of streptomycin at this hospital in 1946, treatment revolved about general supportive care, artificial heliotherapy, and transferral to a sanatorium. Following the introduction of streptomycin, the emphasis of treatment shifted to the use of chemotherapy in the treatment of tuberculous peritonitis. Of the 31 patients who received antituberculous chemotherapy, streptomycin was used in 18 (58%), INH in 20 (65%), PAS in 6 (19%), rifampin in 6 (19%), ethionamide in 2 (6%), and cycloserine and ethambutol in one each (3%).

Results of Therapy

From 1932 to 1946 there were 16 in-hospital deaths from tuberculosis and two deaths in the followup period among 37 patients. This amounts to a 49% mortality rate.

Following the introduction of streptomycin in 1946 there were four hospital deaths from tuberculosis and one death in the period of followup among 33 patients. Since 1946 the mortality rate for patients with tuberculous peritonitis at this institution has therefore been 15%. The difference is statistically significant ($P < 0.01$) when compared to the pre-antibiotic era. Three of the patients

who died in the post-antibiotic era, however, were the only patients of the 33 who did not receive antituberculous chemotherapy because of error in diagnosis. Thus, of the patients receiving antituberculous chemotherapy, the mortality was two of 30 or 7% ($P < 0.005$).

Effect of Laparotomy on the Outcome of Tuberculous Peritonitis

Osler⁹ originally believed that merely opening the abdominal cavity had a beneficial effect upon tuberculous peritonitis, and this belief was carried into the 1940's.³ Although the significance of our data is open to question because of its retrospective nature, it is interesting to observe that in the pre-antibiotic era three of the 18 patients who underwent laparotomy subsequently died, while 15 of 19 patients who did not undergo laparotomy went on to die of tuberculosis.

Case Reports

Case 1. A 75-year-old Caucasian man was admitted November 1957 because of malaise and anemia. Following a "virus attack" 8 months previously he had continued to feel poorly and, because of anemia and guaiac positive stools, admission was advised. Physical examination revealed moderate tenderness to palpation in the right upper quadrant of the abdomen. The stool guaiacs $\times 3$ were negative and there was 1+ pitting ankle edema bilaterally. The blood pressure was 170/85, and the remainder of the history and physical exam was normal, including no history of exposure to tuberculosis.

Laboratory examination showed a blood hemoglobin of 7.0g%; white blood cell count 7,900/mm³ (10% lymphocytes); urinalysis 100wbc/hpf, 0 rbc/hpf, and 1+ protein. Because the BUN was 136mg% a diagnosis of chronic renal failure was made. Despite fluid and electrolyte restrictions, and dietary control the patient expired two weeks following admission. Tuberculosis was not suspected.

Autopsy disclosed fibrocaceous pulmonary tuberculosis, and diffuse tuberculous peritonitis. In addition there was active tuberculous prostatitis, chronic pyelonephritis, and diverticulosis coli.

Comment

This patient died with active tuberculosis, but without the benefit of antituberculous chemotherapy. The out-

TABLE 5. Indications for Surgery in Patients With Tuberculous Peritonitis

Indication	Number of Patients
Suspected TB peritonitis	13
Intra-abdominal mass	6
Suspected appendicitis	6
Unexplained abdominal pain	6
Suspected cholecystitis	2
Colocutaneous fistula	2
Unsatisfactory response to chemotherapy	1
Duodenocolic fistula	1
Sigmoid stricture	1
	38

come, had the diagnosis been made antemortem, and the role tuberculous peritonitis played in this patient's demise are problematic. The case, however, serves to emphasize the difficulty in diagnosing tuberculous peritonitis which, because of its often subtle manifestations, may easily be overlooked and treatment omitted.⁴

Case 2. A 26-year-old Negro woman was admitted March 1975 with a two week history of vague right upper quadrant abdominal pain, weight loss of 5 pounds, fever to 40°, night sweats and shaking chills. Admission chest film revealed a soft infiltrate in the right upper lobe. The leukocyte count was 4,000/mm³; hematocrit 34%; 1st strength PPD negative. Sputum smear was negative for acid fast bacilli.

Over the next 2 days of hospitalization, her abdominal symptoms and signs worsened, with severe pain, localization of tenderness to the right lower quadrant with rebound tenderness. She developed signs of ascites. The leukocyte count remained at 4,000/mm³.

A diagnosis of tuberculous peritonitis was entertained, and exploratory laparotomy was performed. The peritoneal cavity contained 1,500 cc of turbid ascitic fluid with extensive fine nodularity of all the serous surfaces. The greater omentum was markedly thickened and there was extensive adhesion formation among the loops of intestine. A biopsy of the greater omentum showed, by frozen section, granulomata with caseation necrosis, and acid-fast bacilli were identified on smear. Cultures of the biopsied material eventually grew *Mycobacterium tuberculosis*. Following immediate postoperative initiation of treatment with streptomycin and INH, the temperature returned to normal within one week, and she was discharged in two weeks on long term isoniazid and rifampin therapy.

Comment

This patient did well because a high index of suspicion allowed the correct diagnosis to be considered and pursued. The findings at laparotomy are representative of tuberculous peritonitis. Prompt therapy resulted in dramatic improvement.

Discussion

The route of infection of the peritoneum by the tubercle bacillus is varied. Infection may occur: 1) by reactivation of a long-latent tuberculous focus in the peritoneum; 2) from a primary focus in the lung or elsewhere; 3) from infected mesenteric lymph nodes; 4) from contamination from tuberculous enteritis; and 5) from infection of the peritoneum from tuberculous salpingitis in the female. In the present study a probable extraperitoneal site of tuberculosis could be identified in 83% of patients indicating a possible source of spread. Similarly, in an autopsy series 97% of patients had a primary focus of the disease demonstrated.¹¹ Tuberculous peritonitis is virtually always associated with an extraperitoneal focus of disease.

In our series, as in most reports, the ratio of females to males approached 2:1. Unlike others, however, Caucasians significantly outnumbered Negroes (50 to 17) in

our patients. This is attributed to the fact that this Hospital, for much of its history, has had a predominantly Caucasian population. Most patients seen here (24) were in the third decade of life, although no age group was exempt from the disease. The youngest patient was 8 months, and the oldest 75 years.

The incidence of tuberculous peritonitis in this country is difficult to determine accurately. There were 33,000 new cases of tuberculosis reported in 1975.¹⁴ Large series have estimated the frequency of tuberculous peritonitis to range from 0.1%^{7,8} to 0.7%^{6,12} of all cases of tuberculosis. This would place the incidence of tuberculous peritonitis in the United States at between 33 and 230 cases for 1975. From the New York Hospital-Cornell Medical Center experience it is believed that the latter figure is probably more representative. This series shows a downward trend in the number of cases of tuberculous peritonitis seen at The New York Hospital since 1935, which is in agreement with the accepted trend for tuberculosis nationwide. The rise in the number of cases of tuberculous peritonitis since 1965 may be due to sampling error, since there has been no corresponding rise in tuberculosis documented nationally.

In relatively few other diseases does the welfare of the patient depend to such a large extent upon the diagnostic acumen of the physician, and upon the institution of appropriate therapy. In patients in this series tuberculous peritonitis was associated with a 49% mortality in the pre-drug era, and a 7% mortality in patients receiving antituberculous chemotherapy. These figures are consistent with those reported by others.^{8,13,15} In addition, since 1946 all three patients in whom the diagnosis was not made, and in whom drug therapy was therefore omitted, died.

The correct diagnosis of tuberculous peritonitis depends primarily upon an appreciation of the manifold clinical manifestations of the disease and upon bacteriologic proof of tuberculosis somewhere in the body. Generally, the patient presents with abdominal symptoms of a week or longer. Half of the patients will have had symptoms for longer than a month when the diagnosis is made. Occasionally, however, a patient will present with abdominal symptoms of acute onset suggesting acute appendicitis or acute cholecystitis. In these the diagnosis is first suspected only at laparotomy.

Clinical manifestations—abdominal pain, fever, gastrointestinal upset, weight loss, ascites—are usually nonspecific and may suggest an occult malignancy or cirrhosis with ascites. Although the correct diagnosis may be entertained, differentiation from these other disorders is usually impossible without further investigation.

In this regard the unequivocal demonstration of a

tuberculous focus somewhere in the body is paramount, and allows chemotherapy to be instituted on a rational basis. The usual techniques of culturing may require several weeks to obtain a definitive result, and may be negative especially when an aliquot of ascitic fluid is used.² While sputum smear for acid-fast bacilli may be helpful if the patient has concurrent pulmonary tuberculosis, microscopic examination of fluid obtained by paracentesis is often fruitless. If biopsy and pathologic examination of an extraperitoneal site of tuberculosis is not possible, it is often imperative to perform exploratory laparotomy to obtain tissue to support a clinical diagnosis before instituting therapy. Since 1946 there have been no operative deaths associated with laparotomy for tuberculous peritonitis at this institution. Interestingly, in the pre-antibiotic era laparotomy was thought to have a favorable effect upon the outcome of tuberculous peritonitis.³ If necessary laparotomy can be carried out under local anesthesia with small risk. The use of percutaneous needle biopsy has been proposed,¹¹ but it is our opinion that its associated morbidity and mortality is higher than that of laparotomy. In addition diagnosis is established only 64% of the time.

The danger of relying solely upon a clinical diagnosis is illustrated by a patient seen here who was treated for a prolonged period with a diagnosis of tuberculous peritonitis, while at autopsy he was found to have had an unsuspected retroperitoneal lipofibrosarcoma. Had more aggressive attempts been made to establish the diagnosis the outcome might have been more favorable.

With the exceptions of pathology and microbiology, laboratory examinations are seldom specific enough to allow for a definitive diagnosis. If diagnosis is uncertain little time should be spent pursuing these tests. In the majority of the cases in this series the O.T. or PPD skin tests were positive (89%). Likewise, anemia was common (48%) and was usually of the type associated with chronic illness. A relative lymphocytosis has been stressed, but was present in only 20% of patients in this series. Examination of the peritoneal fluid always revealed a protein content equal to or greater than 3.5g% indicating the presence of an exudate. The cell count was variable (100–4000/mm³) with lymphocytes usually constituting 70% of the cells.

When the peritoneal cavity is explored, the diagnosis of tuberculous peritonitis should rarely be in doubt. Typically there are small granulomata studding the serous surfaces and extensive plastic adhesions among loops of intestine with thickening and shrinkage of the omentum and varying amounts of cloudy ascitic fluid. In most instances laparotomy should be accompanied by biopsy of intra-abdominal tissue (usually omentum) to allow an immediate definitive diagnosis to be made. Less com-

monly it may be advisable to remove the female genital organs which, if grossly infected, serve as a continuing focus of tuberculosis. A localized tuberculous abscess, if found, should be evacuated. Drainage is not recommended.

The treatment of tuberculous peritonitis is based upon specific antituberculous chemotherapy, and is highly effective. Only two deaths occurred in this series in patients on antibiotic therapy. In both cases far advanced tuberculosis was being treated only with streptomycin. There were no deaths from tuberculous peritonitis in patients correctly diagnosed antemortem subsequent to the availability of multiple drug therapy. Although some authors prefer the use of INH alone in the treatment of tuberculous peritonitis, all our patients were treated with combination drug therapy following the availability of INH and have done well. We presently prefer the use of INH and rifampin in combination for two years following the diagnosis of tuberculous peritonitis.^{10,15}

In none of the patients reported here treated by drug therapy was there subsequent evidence of pericarditis or intestinal obstruction. This raises the question of the advisability of using corticosteroids as proposed by some,¹¹ but which in itself is not innocuous.

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