

# Post-tuberculosis chronic empyema of the "forty years after"

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**Abstract.** – The authors present 110 cases of patients hospitalized in the last 5 years, with long-term disabling sequelae of pulmonary tuberculosis. Twelve out of them (=10.9%) suffered from post-tuberculous chronic empyema, with an average latency period of 44.83 years between the acute tuberculous illness and the clinical manifestation of the empyema. Nine of the patients had been treated with collapse therapy, induced by artificial intrapleural pneumothorax, 1 with thoracoplasty, and 2 only with late and inadequate anti-mycobacterial chemotherapy. Eleven patients (91.6%) also had a cutaneous fistula (7 cases) and/or a bronchopleural fistula (4 cases).

The authors show how the issue of tuberculous sequelae is a significant not only from the numerical standpoint, but also for the seriousness of the caused pathological conditions, often posing problems for differential diagnosis. Moreover, they stress how tuberculosis should never be neglected or considered last in the differential diagnosis of empyema and pyopneumothorax.

Key Words

Thoracic empyema, Collapse therapy, Artificial pneumothorax, Tuberculous sequelae.

## Introduction

In the pre-antibiotic age, artificial intrapleural pneumothorax was for almost fifty years the main treatment method used for the lung's phtisis, as it showed to be able to control the course of illness and, in a high percentage of cases, to lead to the healing of cavitory lesions. In fact, based on the underlying assumption that the lung affected by tuberculosis should be subtracted from respira-

tory trauma which favours the disease, the method was proposed by James Carson (1772-1843) in 1821<sup>4,5</sup>, and it was later supported by Forlanini since 1882<sup>2,14</sup>.

Early in the century, the new therapeutic method was received with mild hostility. However, due to the excellent results obtained with artificial intrapleural pneumothorax in patients also showing fairly advanced forms of tuberculosis, Forlanini's method was widely adopted in the entire world from 1912 on, with a progressive increase of its indications. For about 40 years, meaning until 1944 (the year of discovery of the first drug with anti-mycobacterial action, streptomycin), pneumothorax was the most effective way to treat pulmonary tuberculosis. Dumarest in France, Saugman in Scandinavia, Brauer in Germany, Spengler in Switzerland, and Eugenio Morelli, Forlanini's pupil, in Italy contributed to spread Forlanini's method<sup>9,10</sup>.

Therapeutic pneumothorax was used less frequently to treat tuberculosis after the development of anti-mycobacterial drugs, and later, due to the great advancement of methods for pulmonary surgical exeresis, it was practically abandoned. In our country, phthiologists maintained an eclectic attitude, and in 1947, the year of introduction into therapy of the first effective antituberculous antibiotic, streptomycin, Omodei Zorini sustained the useful and necessary combination of collapse therapy with chemo-antibiotics. A decade later, after a large clinico-statistical research project carried out by Fegiz and Lucchesi at the "C. Forlanini" Hospital in Rome, he demonstrated that relapses of tuberculosis were less frequent in patients treated simultaneously with the two above methods (5.8% instead of 8.5%)<sup>13</sup>.

Among the most frequent complications of collapse therapy, the formation of “*ex vacuo*” discharge and empyema are well known.

*Biologically encapsulated empyemas*, described by Monaldi in 1935<sup>12</sup>, originate from the transformation of pleural exudate, simple or with corpuscles, formed after therapeutic pneumothorax and ignored in their development.

The term “encapsulation” has only a biological significance for these phenomena, indicating that the pleural serous membrane gradually lost its exchange ability for substances, especially for those with a complex structure.

The primary cause of encapsulation was identified by Monaldi with the reduction of the pH to the range of 6.8-5.7, which decreases the electric charge on the surface of colloidal micellae of empyema, producing the phenomenon of flocculation, associated with the precipitation of calcium salts and the alteration of protein molecules, with consequent hypoproteinemia.

This final alteration causes reduction of the hydrophilia of the empyemic mass, with reabsorption of large amounts of fluid and, later, accumulation of the exudate and the decomposition of the precipitate on the wall of the pleural cavity, which forms “pseudocuticles” (thick layers of material). Germs that may be present in this environment having such an altered metabolism and rich with catabolites, lose their virulence although true self-sterilization is not obtained.

By remaining in this state, empyemas can be considered atoxic, since they cannot interact with the organism. Nevertheless, a slow and silent intoxication can occur, with the typical consequences of chronic, non-eliminated suppuration (renal and hepatic functional disorders, amyloidosis).

Instead, seriously toxic conditions develop when a true interchange between the pleural cavity and the organism is established both spontaneously, due to the slow burrowing of puruloid fluid toward the lung or toward the thoracic wall “*Empiema Necessitatis*”, and because of the formation of fistulous passages caused by surgical operations, which determine voluntarily or accidentally their opening.

In biologically encapsulated empyemas, the inflammatory process can be considered resolved, and the true pathological condition is the empyemic sac, which deforms the underlying lung, not allowing it to expand. Such

empyemas come to medical attention many years after their formation, because of their intrinsic biological delimitation and their low toxicity.

## Clinical Cases

The study was performed on patients hospitalized in the 2<sup>nd</sup> Department of Pneumology at the University of Rome “La Sapienza,” in the “C. Forlanini” Hospital, during the last five years (1992-1996). Out of the total number of hospitalized patients (4604), we took into consideration the ones who showed long-term, more or less disabling consequences of pulmonary tuberculosis (110 patients equal to 2.4% of all hospitalized cases).

Of these 110 patients, 67 (61%) were males, and 43 (39%) females, with a 1.5 M:F ratio.

The mean age was 63.5 years (range 18-90), distributed as following: mean age for males = 63.3 (range 18-86), mean age for females = 63.6 (range 24-90).

The most represented age group ranged between 61 and 70 years, with an incidence equal to 33.6% (37 cases), followed by 24.5% (27 cases) of the age group ranging between 71 and 80 years, and 20.9% (23 cases) of the age group ranging between 51 and 60 years.

Regarding the time that elapsed from the primary tuberculosis and the clinical manifestation of tuberculous sequelae, the average latency period was 34 years (range 1-64 years), with a clear difference between patients treated with surgical therapy, whose average latency period was 43 years (range 20-64), and patients treated only with medical therapy, whose average latency period was 18 years (range 1-40). Such difference is connected to the fact that antituberculous chemotherapy became the first choice therapy only after the 1960s.

With reference to the therapy for pulmonary tuberculosis administered in the past to the patients, 65 patients (59%) had been treated with surgical therapy, 36 (32.7%) with medical therapy, 2 (1.8%) with surgical and medical therapy, and 7 (6.3%) declared never to have been treated with any antituberculous therapy. We wish to specify that we included artificial intrapleural pneumothorax within surgical therapy, although it is usually

included within the category of medical therapy, because it is an instrumental method, barely invasive, whose complications and results are different from the ones of chemotherapy, having instead many analogies with the ones determined by surgical therapy. In 80% of the cases, surgical therapy consisted of artificial pneumothorax, in 15.4% of thoracoplasty, in 3% of phrenicoexeresis, in 1.5% of Jacobaeus operation and endocavitary aspiration.

The most significant sequelae (Table I) were in decreasing order: fibrothorax = 64 cases (58.2%) 8 of which associated with consequences of thoracoplasty; more or less extended fibrosis = 39 cases (35.4%); bronchiectasis = 24 cases (21.8%); parafibrotic emphysema = 14 cases (12.7%); empyema = 12 cases (10.9%) 11 of which with a cutaneous fistula (7 cases) and/or bronchopleural fistula (4 cases); cancer on a scar = 4 cases (3.6%); destroyed lung = 3 cases (2.7%).

The 12 patients (10.9%) with post-tuberculous chronic empyema consisted of 9 males and 3 females. Their mean age was 63.11 years for males (range 47-75) and 72.33 years for females (range 65-77).

Regarding the time that elapsed between the primary tuberculous illness and the clinical appearance of post-tuberculous empyema, we calculated that the average latency period was 44.83 years (range 30-55).

Nine patients had been treated with collapse therapy induced by artificial intrapleural pneumothorax (later two were also treated with medical therapy), one with thoracoplasty, and two only with late and inadequate anti-mycobacterial therapy. As mentioned above, 11 patients (91.6%) had a cutaneous fistula (7 cases) and/or a bronchopleural fistula (4 cases) (Figures 1 and 2).

## Discussion

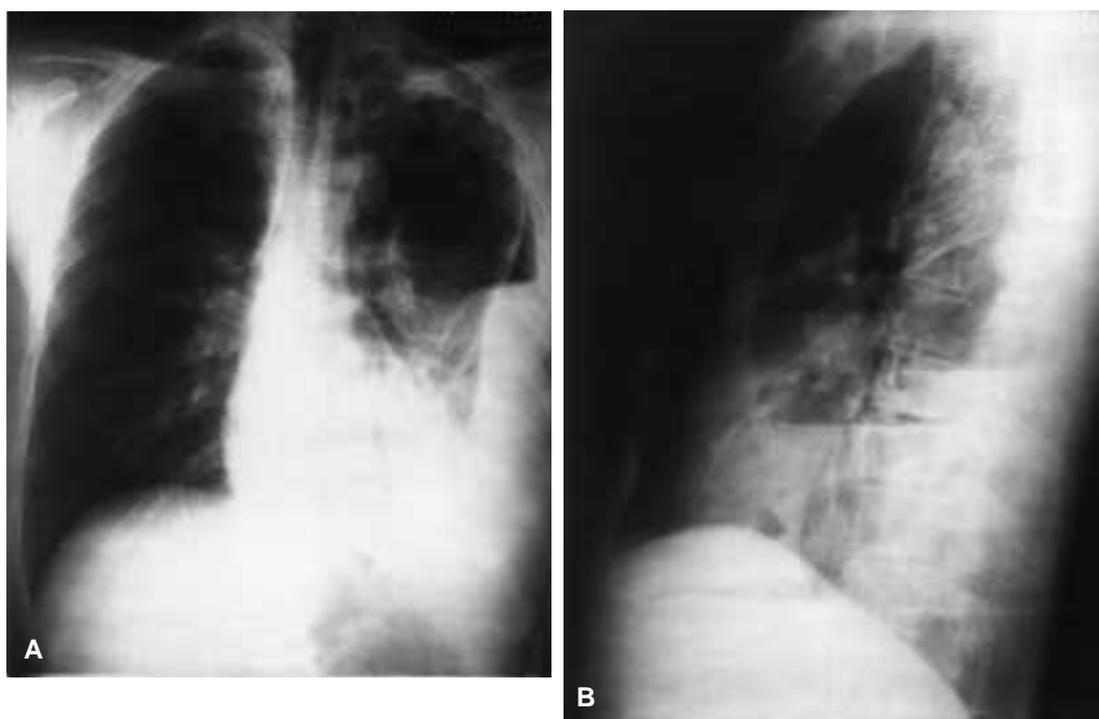
Most authors believe that sequelae of pulmonary tuberculosis are an exceptional medical find, the heritage of a distant past, when collapse therapy was the only effective means, available to physicians, to treat pulmonary tuberculosis. According to most authors, the development of chemo-antibiotic therapy for tuberculosis made the clinical observation of such anatomo-functional alterations and of their related illnesses a "rare" occurrence<sup>17</sup>.

In reality, the observation of tuberculous sequelae is not so unusual in a hospital specialized for lung diseases. The examined cases consist of 110 out of 4604 patients, equal to 2.4% of total hospitalizations in the same period. In literature, few and limited cases of empyema<sup>11</sup> or pyopneumothorax are described as exceptional occurrences, worthy of attention, and tuberculosis is regarded in relation to them as an obsolete and unjustly neglected etiology<sup>7</sup>. Such statements are in contrast with the clinical and epidemiological reality observed by us, which shows how the problem of tuberculous sequelae is significant from the numerical standpoint, and for the seriousness of the caused pathological conditions<sup>1</sup>.

A possible explanation of such viewpoint may be the low acceptance of collapse therapy techniques for the treatment of tuberculosis in Anglo-Saxon countries, and in particular in the United States, at the time when they were largely employed in Italy and in a few North European countries. Collapse therapy was so well perfected and codified by Italian physicians that it was still widely used after the appearance of specific chemotherapeutic drugs, and up to very recent decades. We should not ignore the fact that the disastrous economic conditions of our country in the post-war period greatly slowed down the es-

**Table I.** Incidence of various tuberculous sequelae observed.

Sequelae	Cases	Percentage
Fibrothorax	56	50.9 %
Fibrosis	39	35.4 %
Bronchiectasis	24	21.8 %
Parafibrotic Emphysema	14	12.7 %
Empyema + Fistula	11	10.0 %
Fibrothorax + Thoracoplasty	8	7.3 %
Cancer on a scar	4	3.6 %
Destroyed Lung	3	2.7 %
Megamycetoma	2	1.8 %
Empyema	1	0.9 %
Asthma	1	0.9 %
Bronchial Stenosis	1	0.9 %
Adeno-bronchial syndrome	1	0.9 %
Cleaned cavitation	1	0.9 %
Pneumothorax	1	0.9 %



**Figure 1** (A, B). Chest X-ray in P-A and lateral projection. Fibrocalcified remains in the left apical region; omolateral empyema, multilevelled for the presence of a bronchopleural fistula.

establishment, undisputed today, of the pharmacological therapy over the surgical one for tuberculosis. The excellent organization of a wide network of specialized hospitals and clinics, managed by INPS (National Institute for Social Security) allowed instead the application of such techniques to numerous patients, thus increasing the number of recoveries, but also of tuberculous sequelae.

On the basis of such considerations, tuberculosis should never be neglected or considered the last in the differential diagnosis of empyema and pyopneumothorax. In our cases, empyema was often the initial symptom of a tuberculous sequela or a tuberculous reinfection, silent or oligosymptomatic. Patients noticed a progressive swelling on the thoracic wall, which sometime evolved into an external fistula draining purulent material (“*empiema necessitatis*”). It is unrealistic to accept that a secondary pharmacological prophylaxis of tuberculosis, could be protracted for twenty years or longer, as proposed by some authors<sup>8</sup>. Instead, we must carefully question the real efficacy of short course chemotherapy, sustained especially by Americans. It has

been widely demonstrated that even after a specific antibiotic therapy, tuberculous mycobacteria remain latent in the organism for many years (“buried alive”), in a condition of almost “immune segregation”. It has been shown that intercurrent states of even mild immunosuppression can destroy the balance between mycobacteria and immune system of the host, causing a relapse of tuberculosis. There are many iatrogenic occasions of immunosuppression, due to prolonged cortisone or antibiotic therapies, or, more simply, due to the elongation of the average life span of the general population.

Today we observe patients with consequences of pulmonary tuberculosis, treated with artificial pneumothorax and surgically about 30 to 50 years ago<sup>3,6,15,16</sup>.

Often the long latency period between tuberculosis, possibly treated with collapse therapy or surgery, and the appearance of sequelae, tends to mislead us in our diagnosis, to make us neglect the tuberculous etiology of empyema, and to make us interpret incorrectly the anatomo-functional alterations of the thorax, especially when the first episode

of tuberculosis was ignored or forgotten by the patient. When confronted with pyopneumothorax, associated or not with pulmonary fibrosis, many physicians immediately think of immune etiologies (sarcoidosis, collagen diseases, immunologic deficiencies etc.), disregarding tuberculosis, which is not taken into consideration or is placed among the "rare" causes of differential diagnosis. This approach, undoubtedly determined by the physicians' excessive specialization, and by the excessive attention given to some biological discoveries, also originates from the incorrect belief, widely advertised in recent years, that tuberculosis is an illness almost eradicated by anti-mycobacterial chemotherapy. We observed that epidemiology disclaims these illusions; also clinical practice forcefully recalls the past: if we want to be truly modern in our approach to differential diagnosis of pulmonary diseases, we must restore tuberculosis to its foremost position of a non-rare etiology of pleural empyemas.

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