Therapeutic Pneumothorax and the Nobel Prize

Nils Hansson, PhD, and Igor J. Polianski, PhD

Department of History of Medicine and Medical Ethics, Cologne University Hospital, Cologne; and Institute of the History, Philosophy and Ethics of Medicine, Ulm University, Ulm, Germany

At the turn of the 20th century, the epidemic proportions of tuberculosis puzzled great parts the scientific community. Thus it is not surprising that well-known scholars who worked on particularly promising solutions to fight the disease were nominated for the Nobel Prize for Physiology or Medicine, perhaps the most prestigious benchmark of scientific excellence. The authors have gathered files on the Italian phtisiologist Carlo Forlanini (1847 to 1918) at the Nobel Prize archive for Physiology or Medicine in Solna, Sweden. Drawing on these files and contemporary publications, the authors discuss the origin of artificial pneumothorax for treating pulmonary tuberculosis, show how it became an international gold standard operation, and trace why the Nobel committee finally chose not to award Forlanini. Twenty Nobel Prize nominations for Forlanini were submitted from 1912 to 1919 exclusively by Italian scholars. In 1913 and 1914, Forlanini was on the shortlist of the Nobel Committee and thus one of the prime candidates for the prestigious prize. Important aspects of the rise, fall, and revival of the artificial pneumothorax from 1815 to 2015 are highlighted along with its benefits and risks.

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At the turn of the 20th century, the artificial pneumothorax (abbreviated PNX) became the treatment of choice in most severe cases of pulmonary tuberculosis. Also known as lung collapse therapy and therapeutic pneumothorax, PNX was unable to cure the disease completely, but it intervened in the disease process, slowing down its progression. However, from its inception collapse therapy was highly controversial due to the frequent complications associated with its use. On the one hand this "great benefit to mankind" (Nobel Archive [NA], nomination for Carlo Forlanini by Camillo Golgi in 1914) was put forward on multiple occasions for the Nobel Prize for Physiology or Medicine. On the other hand the pneumothorax needle was called "the most dangerous weapon ever placed in the hands of a physician" [1]. In the pre-antibiotic era there was no satisfactory alternative. In addition to the infamous spittoon, called "Blue Heinrich," the pneumothorax device became a distinctive signature of medical culture and everyday life of the early 20th century. In Thomas Mann's novel "Magic Mountain," for example, a group of patients at a sanatorium in Davos, Switzerland, referred to themselves ironically as "fraction of half lungs" because they were being treated with PNX and whistling from their pneumothorax hole [2]. However, after the discovery of specific chemotherapy artificial pneumothorax fell into disuse, and by the beginning of the 1960s the method was seen as obsolete [3].

But there is life in the old dog yet. Although statistics show that tuberculosis (TB) prevalence and mortality rates are slowly declining each year, it remains one of the world's deadliest communicable diseases. According to WHO [the World Health Organization] one third of the world's population is infected with Mycobacterium tuberculosis and about 1.5 million people died from TB in 2013 worldwide. For developed countries the anti-tuberculosis drug resistance might become a major public health problem in the near future. The WHO estimates that there were 480,000 new multidrug-resistant tuberculosis cases in the world in 2013 [4]. A recent case report suggests that the therapeutic pneumothorax provides promising results in cases of multiple-drug-resistant TB at least as an adjuvant to antimycobacterials [5]. In addition, there are some further lung surgery procedures where application of the lung collapse might be useful; however, not related to TB treatment [6, 7]. The irony of the story: It was not the first time when PNX first fell into disgrace and was rehabilitated later. In this historical vignette, we will take a closer look at the rise of the PNX with particular focus on the Nobel Prize candidacy of the Italian dermatologist and phthisiologist Carlo Forlanini (1847 to 1918). Although more than 130 years have passed since Forlanini's original paper on PNX was published, it is still cited on a regular basis [8]. Drawing on contemporary publications and archive files at the Nobel Archive in Sweden, we will discuss the origin of PNX, how it became an international gold standard, and trace why the Nobel committee finally chose not to award Forlanini.

Background

Tuberculosis was still a common cause of death among adults during the early 20th century. On the eve of World War I, the proportion of tuberculosis in the overall mortality rate reached, for example, for the City of Vienna, 20% to 25% [9]. In 1914, the pulmonary tuberculosis

Address correspondence to Dr Hansson, Department of History of Medicine and Medical Ethics, Cologne University Hospital, Joseph-Stelzmann-Str 20, Geb. 42, 50931 Cologne, Germany; e-mail: nils.hansson@uk-koeln.de.

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mortality rate was approximately 10 per 10,000 in Great Britain [10]. The corresponding numbers were 16 in Germany and 23 in France [11]. After the outbreak of World War I it increased even more dramatically [12]. Thus it is not surprising that well-known scholars who worked on particularly promising solutions were nominated for the Nobel Prize for Physiology or Medicine, perhaps the most prestigious benchmark of scientific excellence. For example, Robert Koch (1843 to 1910) had been a nominee more than 50 times before he was awarded the Nobel Prize in 1905 for his investigations and discoveries in relation to tuberculosis.

As hinted above, Forlanini was another strong candidate for the Nobel Prize due to his work on artificial pneumothorax. To conduct PNX, Forlanini pumped filtered compressed air into the pleural space. The procedure reminds of thoracentesis, with the difference that no fluid is removed. This mechanical approach allowed further progression of tuberculosis lesions to be prevented in certain circumstances.

Various hypotheses have been offered as to the causes of this favorable effect. Some believed that the temporary immobilization of the lung and mechanical pressure permitted the draining and closure of tuberculosis cavities. Other proposed mechanisms included the reduced absorption of toxic metabolites of the pathogen and an increase in the body's defenses through the stimulation of lymphocytosis [13]. To penetrate and introduce air into the pleural space a "pneumo device" was used, which consisted of a hollow needle, hydraulic pump, and pressure gauge.

Forlanini first tested the method in a clinical experiment in 1888 [14]. The reports of the first successful treatments followed in 1894 and on a more representative and international scale in 1906 [15]. General disappointment about the failure of tuberculin as a cure for tuberculosis provided a boost to the development of Forlanini's method at the beginning of the 20th century. Forlanini achieved a breakthrough in 1912, when his report at the Seventh International Congress in Rome was followed by frenetic applause [14]. The very same year he attained his first nomination for the Nobel Prize for Physiology or Medicine.

Nobel Prize Nominations for Forlanini

From 1912 to 1919, Forlanini was nominated at least 20 times for the Nobel Prize. The historian Elisabeth Crawford has called candidates who attract many votes from one specific country "favourite sons" [16]. That label can be attached to Forlanini, as all of his nominators were Italian professors of medicine. They put forward several arguments to try to convince the prize jury why Forlanini should be seen as "the person who shall have made the most important discovery within the domain of physiology or medicine" (Will of Alfred Nobel, 1895) [17].

Three of the nominations for Forlanini were submitted by his close friend Camillo Golgi (1843 to 1926) from Pavia, who, as a former Nobel Laureate (1906) had the right to propose a candidate each year (NA, yearbooks of 1912, 1917, 1919). In his nominations, Golgi argued that Forlanini's PNX method had been of "great benefit to mankind," another phrase that Alfred Nobel had used in his will.

A. de Giovanni from Padua stressed in his nomination letter of 1913 that Forlanini had opened up a new scientific avenue (NA, Giovanni 1913). Because at least some members of the Nobel committee saw great potential in PNX, Forlanini was viewed as one of the prime Nobel Prize candidates during 1913 and 1914. Why did he not receive the Prize?

Evaluations by the Nobel Committee

In 1913, Johan Gustaf Edgren (1849 to 1929), professor of internal medicine at the Karolinska Institute Sweden was chosen as Nobel committee evaluator of Forlanini, probably because pulmonary tuberculosis was one of his main scientific interests. Edgren's key arguments for Forlanini were that the method had significant theoretical weight, probably based on earlier observations that spontaneous pneumothorax could promote healing, and sound practical evidence. "Thanks to Forlanini's treatment, a substantial number of hopeless patients have regained their health and their working ability. With more experience and an improved technique, even better results are to expect" (NA, Evaluation of Forlanini by Edgren in 1913).

Edgren concluded that Forlanini was prize-worthy, but the other members of the prize jury voted in favor of other candidates. Significant for the non-awarding apparently was a reference to the current debate and confusion about the risks of therapy in the report. Edgren was not as overwhelmed as Forlanini's nominators or other commentators, who proposed that PNX should be considered even for healthy patients to prevent tuberculosis [18]. He pointed out that the method was tricky, and that it even might be harmful in some cases. Although PNX was associated with a high percentage of favorable outcomes (eg, substantial improvement of symptoms could often be observed within a few days of treatment), frequent complications frustrated its general acceptance. The German phthisiologist Karl Mosheim stated in 1905 that "disparate views" circulate in this question and the "positions are in a state of fermentation" [19]. Finally, the pneumothorax itself was regarded as a severe complication of tuberculosis. Thus it was no wonder that most doctors hesitated. During the 1910s in Germany and the United Kingdom, many experts only recommended the so-called gas chest treatment "as a last resort in apparently hopeless cases" after all alternatives had been exhausted [20–22].

When performed on elderly patients or those with large chest cavities, artificial pneumothorax was associated with a worsening of symptoms. If the lung did not release from the pleura, pleural ruptures and dangerous infections would occur [23]. Pneumopleuritis was most feared, which, if it became septic, claimed patients' lives. Initially, there was no clear understanding of the frequency of pleuritis (10% to 70%, according to different observers), its cause, or its prognosis. Most