

## HISTORY OF ONCOLOGY

# Arsenic powder in the treatment of cancer: the invention of French physician Pierre Alliot (1610-1685)

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## Summary

Throughout history arsenic had a dual role as an ideal poison and as a remedy. Derived from the Greek word “arsenikón” meaning masculine or valiant, referring to its powerful activity, arsenic was prescribed since antiquity in mixtures and it was applied topically to treat cancer. In the 17<sup>th</sup> century, the French physician Pierre Alliot (1610-1685) proposed a secret remedy for cancer treatment. His invention, known as Alliot’s powder, gained popularity and it was also prescribed

to queen mother Anne of Austria (1601-1666) who was suffering from breast cancer, without any effectiveness. Despite the result, Alliot became famous and arsenic-based formulas were introduced in medicine to treat malignancies, mainly acute promyelocytic leukemia, till nowadays.

**Key words:** Pierre Alliot, realgar, arsenic, breast cancer, history of oncology

## Introduction

Found in air, food, water and soil, arsenic influenced humanity since antiquity more than any element or toxic compound. Derived from the Greek word “arsenikón” meaning masculine or valiant referring to the powerful activity of the sulfide which was applied, arsenic had a dual role as an ideal poison and as a remedy [1]. It seems that the earliest known forms of arsenic were the red and yellow sulphides, As<sub>4</sub>S<sub>4</sub>-realgar and As<sub>2</sub>S<sub>3</sub>-orpiment respectively [1]. Hippocrates (460-377 BC) mentioned pastes of realgar and orpiment for the treatment of ulcers [2], while Aristotle (384-322 BC) recognized its toxic properties stating: “the horse, and every other beast of burden, is destroyed by the poison of sandarach (arsenic)” [3]. The red and yellow sulphides of arsenic were also mentioned by Theophrastus (c.371-c. 287 BC) in his treatise *On Stones* as well as by Dioscorides (40-90) who suggested

them as a remedy for coughs and asthma, burned in combination with resin and inhaled through a tube [4,5]. In the 11<sup>th</sup> century, Avicenna (980-1037) recommended also arsenic for asthma treatment. *Liber servitoris*, a treatise written by the prominent physician Abulcassis (936-1013) was recommending sublimed arsenic as a septic and pungent capable to remove the “fungous flesh” of ulcers as well as a depilatory [6]. In Chinese pharmacopoeia arsenic was proposed to treat carbuncles and abscesses when applied to the skin but it was also worn as an amulet against dangerous animals [7,8]. Furthermore, drinking realgar wine was part of the Chinese dragon festival as it was supposed that arsenic could banish all diseases, fade scars, regenerate the lost teeth and turn the grey hair into black [8]. During the 15<sup>th</sup> and 16<sup>th</sup> century, arsenic was widely used as a poison in royal and ecclesiastic cycles and it

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was the main ingredient of cantarella, the poison weapon of Borgias family [9]. At the beginning of the 16<sup>th</sup> century, the distinguished physician and alchemist Paracelsus (1493-1541) designated arsenic, along with opium, mercury, lead, and copper sulfate, as part of the “modern” pharmacopoeia of that era. According to his alchemical theory, cancer corresponded to arsenic in the macrocosm, it was a “morbus arsenicalis” and arsenic itself could cure it [10]. Almost a century later, the French physician Pierre Alliot (1610-1685) introduced an arsenic-based powder for the treatment of cancer which became very popular, keeping its formula secret [11] (Figure 1).

### Pierre Alliot's life and work

Pierre Alliot was born in the commune of Bar-le-Duc, the historic capital of the Duchy of Bar in Lorraine, France, of a noble but derogated family of Florence origin [11,12].

Alliot studied medicine in the University of Pont-à-Mousson, a Jesuit ruled institution founded in 1572 by the duke of Lorraine Charles III (1543-1608) [13]. During his studies, he became close to Professor Jean Levrechon (?-1635) and in 1638, after Levrechon's death, he succeeded him in the

direction of Maison Dieu, a hospital in Bar-le-Duc [13]. Alliot became famous for his abilities and he was called to the bedside of Prince Ferdinand (1639-1659), nephew of Duke of Lorraine Charles IV (1604-1675). The prince underwent a lithotomy and Alliot followed his convalesce. Despite the death of Prince Ferdinand after the operation, the Duke acknowledged Alliot's endeavors and named him Physician-in-Ordinary in 1661 [11]. Three years later he published a treatise on the treatment of cancer without surgery and cautery iron (*Nuntius profligati sine ferro et igne carcinomatosis, missus, ducibus itineris Hippocrato et Galeno, ad chirurgiae studiosos*) in which he proposed to cure cancer by the application of a specific powder, keeping secret its composition as well as “Letters on apparent cancers” (*Epistola D.D. Petri Alliot ad D. B. de cancro apparente*) [14,15]. In 1665 Alliot gained such a reputation that he was called to treat the queen mother Anne of Austria (1601-1666) who was suffering from breast cancer (Figure 2) [16]. The treatment failed and Anne died one year later, in 1666. The failure of Alliot's powder did not affect his reputation; he was awarded by a liberal pension from the King Louis XIV (1636-1715) and became physician to the Grand Duchess of Tuscany Marguerite-Louise (1645-1721) [13].



**Figure 1.** Pierre Alliot (1610-1685), physician and inventor of the famous powder [Source: <http://www.professeurs-medecine-nancy.fr>].



**Figure 2.** Portrait of Anna of Austria by Peter-Paul Rubens, ca 1622-1625.



After a journey in royal courts, Pierre Alliot returned to Bar-le-Duc and continued with success to prescribe his remedy. In his private life, he married Bonne de Mussey, and their children followed medical, political and religious orientation: Jean Baptiste (1640-1729), Physician-in-Ordinary to the King Louis XIV and to the Duke of Lorraine Leopold (1679-1729); Pierre (?- 1715), Abbot of Senones; Hyacinthe (?- 1705), Abbot of Moyanmoutier; and François, advisor to the Chamber of Accounts in Bar-le-Duc. In 1698, the Duke Leopold (1679-1729) rehabilitated the nobility titles of Bonne de Mussey and provided also a letter of nobility to Jean-Baptiste Alliot as a gesture of gratitude for his and his father Pierre services [11,12].

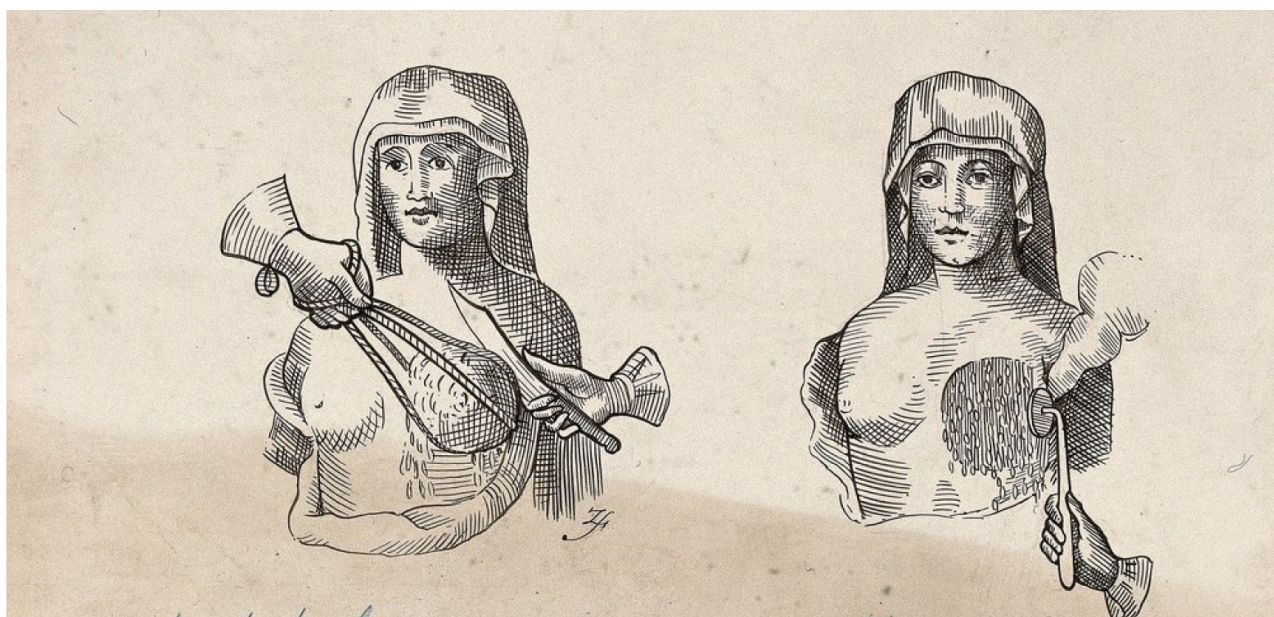
### The arsenic powder of Alliot: a promising cure or charlatan formula?

Throughout centuries, physicians attempted to cure cancer employing mainly cautery iron, surgical excision and topical application of caustic substances such as arsenic, corrosive sublimate, caustic potash, nitrate of silver, chloride of zinc etc. Recommended by physicians and charlatans, these substances enjoyed more or less reputation for their effects in cancerous lesions. Of all these substances, arsenic attracted the attention of physicians since antiquity and acquired the highest and most extensive reputation, forming the basis of almost all the secret remedies for cancer which have at any time been prescribed externally or internally [17].

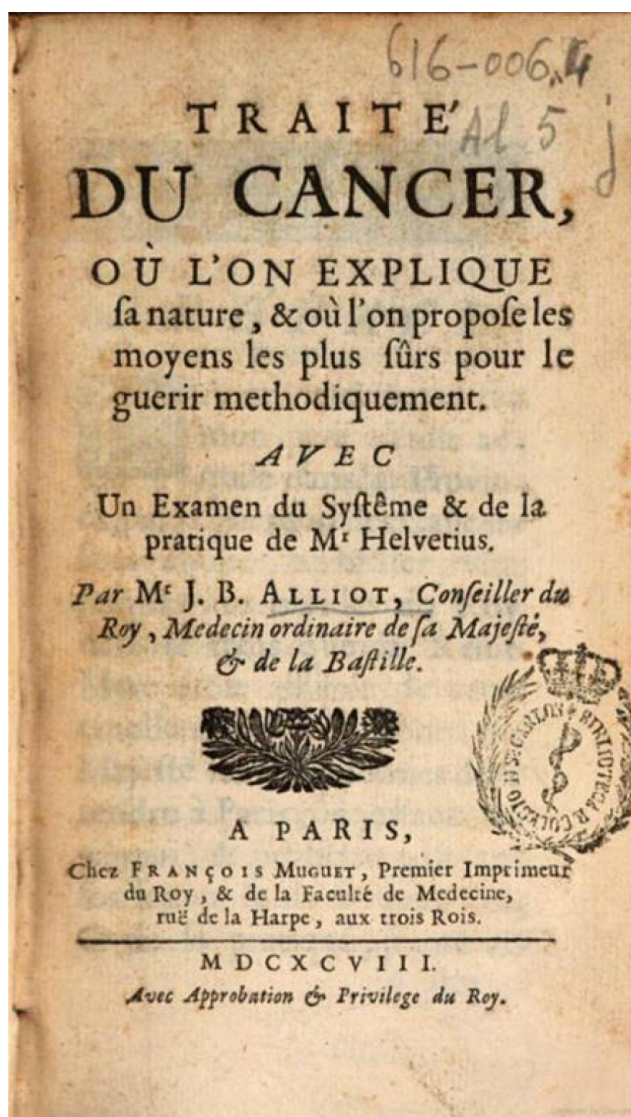
In Roman period, Scribonius Largus (c. 1-c. 50), court physician to the Emperor Claudius (10-54) provided in his work *On the composition of medicines* (*De compositione medicamentorum liber*) an effective recipe for cancer treatment containing arsenic, copper, cucumber and ashes of burnt paper [18,19]. In medieval period, Henri de Mondeville (1260-1320), the first French surgeon who wrote a treatise on surgery entitled *Surgery* (*Cyrurgia*) sustained that excision could provide the best therapeutic result [19]. However, in cases that the tumour could not be totally extirpated, arsenic was suggested as it was considered the best cauterant. In the 16<sup>th</sup> century, the German physician and botanist Leonhart Fuchs (1501-1566), author of a book about plants and their uses as medicines, mentioned the use of arsenic with mistletoe as effective remedy against all tumours [20].

Nevertheless, certain physicians were deciding to keep secret the composition of their mixtures. The presence of secret remedies goes back to antiquity. The first “discoverers” of mixtures were trying to keep secret their formula, passing it from generation to generation in their family, monopolizing thus the treatment [17]. In France, before 1728, it does not seem to have existed legislation about the secret drugs but we find some actions taken from the state to protect the people against the remedies of charlatans; the drugs provided by pharmacists without medical prescription; and the drugs prescribed by priests and monks [17].

Certain secret remedies were receiving patents and they were approved by the King. That was also



**Figure 3.** Picture illustrating how to perform a mastectomy and cauterize the wound, ca 1603 [Source: Wellcome Library, London].



**Figure 4.** Frontispiece of Jean-Baptiste Alliot's treatise on cancer, 1698.

the case of Alliot's powder. On May 1664, the queen mother Anne of Austria palpated a mass in her left breast but she did not pay attention and even ignored it. On October, the mass became painful and one month later she experienced pain, fatigue and a waxy complexion. The court physicians examined her and diagnosed breast cancer [21]. At that time, no effective treatment existed for breast cancer; physicians were practising bloodletting and enemas to restore the equilibrium of bodily humours. Excessive yellow bile explained her skin colour and excessive black bile was the cause of cancer. Despite the medical literature of the time which, in scarce references, suggested removal of the breast (without anesthesia or asepsia), operation was rarely practised and none of the physicians dared to propose such a treatment to Anne (Figure 3) [16]. Initially, Anne's personal physician Claude Seguin

(1596-1681) suggested bloodletting but his method failed to decrease her pain. Antoine Vallot (1595-1671), Louis XIV's physician, proposed to apply hemlock plaster to the tumor without a result; her health status aggravated. Then, Louis XIV decided to call the priest and physician François Gendron (1618-1688), who was known to possess an effective substance for the treatment of cancer that he invented during his stay in New France [21]. In the Lake Erie, in Ontario, Gendron found some stones, known as "Erie stones" (pierres ériennes), ground them into powder and prepared an ointment [22]. It was believed that his mixture was miraculous and could treat a variety of diseases including cancer; however, in the case of Queen Mother, Gendron's drug failed [21]. Physicians, charlatans, even witches attempted to treat Anne without any success. Daniel Morel, secretary of the King recommended Pierre Alliot who had invented a powder against cancer [11]. On April 1665, Pierre Alliot followed by his son Jean-Baptiste came in Paris. His arrival raised a polemic in medical circles; he was considered a "foreigner" as at that time Lorraine was not part of the French Kingdom. Moreover, he did not have the right to exercise throughout the kingdom as he was not a graduate from the Faculty of Paris and Montpellier [21]. Guy Patin (1601-1672), the dean of the Faculty of Medicine in Paris, supporter of Galenic theories and opponent to every new idea in medicine, in his letters, considered Alliot a charlatan, expressing in a way his disappointment as he was not called to treat the queen mother [23]. Anne's treatment started on August 1665. Alliot's caustic powder was applied on the cancerous mass; a severe burn occurred and the necrotic tissue was daily cut-off in the presence of the royal family, the physicians and surgeons of the court. Alliot was stopping the excision only when a living tissue was appearing, an evidence of drug effectiveness. It seems that Anne had a slight improvement but after a short interval, her health deteriorated; severe pain and fever appeared [11,16]. At the beginning of January 1666, Anne presented fever and erysipelas and her physicians discontinued the administration of Alliot's powder. However, it was too late; she died few days later, on January 20<sup>th</sup> at the age of 65 years [11].

Despite the ineffectiveness, Alliot received a pension and honours for the administration of his secret drug and returned to his hometown. His son Jean-Baptiste, much appreciated by the King Louis XIV, remained in Paris and became his personal physician and counselor. It was under the King's suggestion that he published in 1698, thirteen years after the death of his father, a treatise on cancer (*Traité du cancer*) (Figure 4) in which he



revealed the composition of the famous powder: “realgar was repeatedly digested in strong alkaline solutions, and when it was nearly all dissolved, the solutions were filtered and the arsenic was precipitated from them by acetate of lead. After frequent washings with tepid water, and burning alcohol several times upon it, the precipitate was finely pulverized, and in this state was sprinkled upon the surface of the ulcer” [25,26]. The secret was revealed and the famous powder was containing arsenic, an old remedy which fitted in a new theory of cancer pathogenesis. According to Pierre Alliot and several other physicians of that period, cancer was not just the result of humoral imbalance but it was appearing due to an increased acidity in the human body [19]. In order to decrease the acidity and destroy the tumour, Alliot prescribed alkaline arsenic. Answering the initial question, if the powder was a promising cure or charlatanism, we could sustain that Alliot’s invention neither could cure cancer, nor was based on charlatans’ theories; it was the result of an erroneous medical opinion of that time about cancer’s pathophysiology.

## Conclusion

Pierre Alliot became famous in the 17<sup>th</sup> century thanks to the invention of his arsenic based powder. At the end of the 18<sup>th</sup> century, the physician and pharmacist Thomas Fowler (1736–1801) developed and patented a formulation of potassium arsenite which became widely known as Fowler’s solution, used in various affections such as epilepsy, depression, dropsy, malaria, syphilis, cancer and dyspepsia. In 1865, Fowler’s solution was administered as a tonic to patients suffering from leukemia and an improvement of their condition was reported [8]. In 1931, the solution was prescribed in myeloid leukemia, in combination with irradiation and in 1970’s, in China, started the experimentation of arsenic trioxide in cases of acute promyelocytic leukemia (APL), the results of which were published almost 20 years later [27-29]. Currently arsenic trioxide is part of APL chemotherapy, accelerating the death of leukemic cells and stimulating normal blood cells to develop properly. Arsenic traced a long history in cancer treatment and it still continues to surprise us.

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