## Precisions on the History of Quinine

**To the Editor**: We read with interest the excellent and entertaining review by Jiménez Palop[1] on the update on the use of antimalarials in rheumatology published recently. However, we allowed ourselves to carry out some observations on the historical aspects mentioned in it. The discovery, the diffusion, and arrival in Europe of this "miraculous" substance are one of the lesser-known aspects in the history of medicine. The discovery of quinine, better known as a "powder or quinine bark," constitutes a transcendent event. Its crushed bark was the only effective remedy against malaria for centuries, until the 19th century when its purified alkaloid was synthesized and baptized as quinine, which in the 20th century was substituted by synthetic compounds (primaquine, cloroquine, hydroxicloroquine).

Carlos Linneo, in his work *Genera Plantarum* (1742), based on descriptions by La Condamine, who studied the plant in the mountains of Loja (present day Ecuador), classified the tree from which the bark of quinine originated in the new genus *Cinchona*. This name was inspired by the "classic" tale of the medic Sebastiano Bado (referred by Antonio Bolli, a merchant from Genoa) in his opus *Anastasis corticis Peruviae seu china china defensio* (Figure 1), who in 1663 described the arrival of the quinine bark to western medicine, produced after the wife of the Count of Chinchón, viceroy of Peru, affected by tertian fever (malaria), was healed in a miraculous way by this remedy (Figure 2).[2]

Romantic legend, name change and a resuscitated vicequeen: the recorded dates for the administration of the Chinchón viceroy in Peru were 1629-1639, which partially match those given by Bado, for when we subtract "30 or 40 years" from 1663, we obtain 1623-1633, leaving barely 4 years (1629-1633) for the date of the supposed healing of the countess. Another chronological inconsistency in his book is that the return of the viceroy to Spain occurred in 1633, they year in which a provision of bark was housed in the Chinchón's residence and that had been brought from Peru, when in reality the former viceroy arrived in Castille in 1641.[3]

Antonio de Suardo, author of the diary of the Vicegovernment of Chinchón (May 1629-May 1639) discovered in 1930 in the Archivo de Indias de Sevilla, was studied and published by Vargas-Ugarte in 1935 and later by Haggis.[4] Suardo does not mention the countess's fever, referred by Bolli to Bado. On the contrary, the diary allows the assumption that, except for minor problems, her health was optimal, with an active agenda in Lima's society; in contrast, there are many references to the counts' and his sons tertian fevers, dates and treatments administered; to top it all off, the latter ones are mostly bloodletting and purging. It strikes as odd, therefore, that the diary refers to fevers that both the viceroy and his son had but fails to mention a medicine that had been successfully used by the countess.


ANASTASIS
CORTICIS PERVVIÆ,
SEV
CHINÆ CHINÆ
DEFENSIO,
SEBASTIANI BADI GENVENSIS
Patrij vtriusque Nosochomij olim Medici,
Et
Publicæ Sanitatis in Ciuitate Consultoris.
Contrà
VENTILATIONES
IOANNIS IACOBI CHIFLETII,
GEMITVSQVE
VOPISCI FORTVNATI PLEMPII,
Illustrium Medicorum.
*Opus in tres libros distinctum, & in eis Documenta Medicinæ, & Philosophiæ.*
ILLVSTRISSIMO D.
IOANNI LVCÆ DVRATIO
GENVÆ, Typis Petri Ioannis Calenzani. M. DC. LXIII.
*Superiorum vestia.*

***Figure 1.*** *Front of the publication by Sebastiano Badi* Anastasis corticis peruviae, seu chinae chinae defensio *or, in Spanish, "Resurrección de la corteza Peruana, defensa de la quina quina" (1663).*

Clements Markham, president of the Royal Geographic Society based in London, in 1874 dedicated a memoir to the countess "Ana de Osorio," wife of the Chinchón viceroy: "…who after returning to Spain was dedicated to curing the ill with the bark that she herself had brought from Peru…" Thanks to Cipriano-Zegarra we know that the countess of Chinchón that was in Peru was not Ana de Osorio, but Francisca Henríquez de Rivera, because the count had been widowed of Mrs Ana and had wed again before being sent to America. If that wasn't enough, Mrs Francisca died in Cartagena de Indias (present day Colombia) on the January 14, 1641, when she and the Chinchón viceroy were to be embarked on their way back to Spain. In reprints of Palma, after 1879, this is excused as a "listening" mistake and Mrs Leonor (Ana de Osorio?) is "renamed" Mrs Francisca.

*"On a June afternoon of the year 1631, the bells of all of the churches of Lima tolled to a funereal tone…" "…Don Luis Fernandez de Cabrera, count of Chinchon, viceroy of these kingdoms of Peru by grace of His Majesty Felipe IV had arrived in Lima in January 1629 with his most beautiful and young wife Doña Leonor, who a short time after felt attacked by these periodic fevers that are designated as tertian and considered by the Incas as endemic to the valley of Rimac…*

*…Save her, oh God! A miracle, lord! A miracle!—The countess will be saved, most excellent sir—answered a voice at the door of the room. The viceroy turned his head surprised. It was a priest, a son of Ignatius of Loyola, who had pronounced such consoling words. The count of Chinchon bowed before the Jesuit. The latter continued: –I wish to see the vicequeen. Your lordship must have faith and God will do the rest. The viceroy led the priest to the bed of the dying queen. One month later, a great party took place in the palace, celebrating the recovery of Doña Leonor. The fever-curing properties of the Cascarilla had been discovered…*

*…Attacked by fevers, an Indian from Loja called Pedro de Leyva drank, in order to quench his thirst, water from a stream, on whose banks grew some quinine trees. Saved in such a manner, he made his experience known, making other persons with the same illness drink from jars of water in which he deposited the roots of Cascarilla. With his discovery he traveled to Lima and communicated it to a Jesuit, who after performing the happy cure of the vicequeen, provided humanity with a better service than the friar who invented gunpowder…[11]."*

***Figure 2.*** *The countess's powders. By Ricardo Palma (1872-1910). (Taken from* El Correo del Perú*, a weekly publication with monthly illustrations, No. XLI, year II, October 19, 1872, p. 323-4.).*

The above mentioned French explorer La Condamine thought he had established 1638 as the year of the cure of the countess and mentioned to the viceroys' medic Juan de Vega as the introducer of quinine into Spain, where apparently he sold it for "a hundred reales the pound." Gaspar Bravo (1669) also mentions this, attributing to de Vega the diffusion of quinine in Spain. However, documents signed by de Vega in the University of Lima until 1659 (Haggis[4] and Jaramillo-Arango[5]) are proof of his permanence in Lima after the Chinchón former viceroy returned to Spain and there is no evidence of any trip of de Vega to Spain during that period. If, as all of the above indicates, the anecdote of the cure of the countess is false, any other related affirmation is difficult to prove, so the "Castilian healings of the Countess" are also a false episode.

Descriptions of quinine in the 16th and 17th centuries: the agustine friar Antonio de La Calancha (1633) and the Jesuit priest Bernabé Cobo (1652), who resided in Peru in the time of Chinchón, were the first to describe the powder in that country; they noted their "miraculous" curative properties and none of them mentions the relationship of the viceregents with quinine. Half a century before, Monardes (1571)[6] and Fragoso (1572)[7] had pointed out to a plant indigenous to the new kingdom (present day Colombia and Ecuador), to which no name was assigned. They described quinines' unmistakable morphologic characteristics and astringent properties, as well as its use in cases of diarrhea, fever and any effusion.[8]

*Diffusion in western medicine and arrival to Europe*: by 1663, when Bado published his book, the application of quinine to patients with fever was the medical eye of the hurricane affecting Spanish, Italian, and Dutch circles, because its acceptance meant a milestone, forcing doctors to modify their "classic dogmas" on the humoral etiology of diseases.

A larger discredit of Dr. de Vega' alleged contribution came when van der Heyden (Gante, 1643) mentioned the use of quinine (*Pulvis indicus* or *P jesuitti*) to fight tertian and quartan fevers, which also indicates that father Bartolomé Tafur (another "accused" of introducing quinine to Spain) didn't introduce quinine to Europe either 1642-1643, because it should have arrived earlier, as pointed out by the fact that in 1639 the professors from Alcalá used it to cure don Miguel de Barreda.

Advantages from quinine were beneficial for religious groups, especially the Jesuits, who possessed the monopoly of this "panacea." Perhaps because of that, this history is not devoid of contraband and deceit, and there is reference of at least one "false Jesuit bark" (*Iva frutescens*), with which unscrupled merchants took advantage of the naïve to sell them false quinine. In fact, though the last word on this has not yet been spoken, there are Jesuit texts that mention that quinine reached Rome in 1632, with the provincial of the Jesuit missions in Peru, father Alonso Messia Venegas, as its introducer, when he brought a sample of the bark to present it as a primacy, and who had left Lima 2 years earlier, because evidence of his stay in Seville 1632 has been registered, publishing one of his books there and following his way to Rome as a procurator.

Finally, there is also confusion as to the origin of the name "quinine," which is the one that has prevailed to designate a tree (or rather, a genus of trees, because there are several *Cinchona* sp. With these qualities in the cloudy Andean forest). In his classic opus, the great botanist Monardes included a chapter on the antithermic properties, as well as those of other nature of the "root from china," Mexican "panacea" plant much used during

the 16th and 17th centuries, better known as zarzaparrilla (*Smilax officinalis*, *S. china*).[9] A third planta which also has antipiretic properties: the Peruvian balsam, origin of the "quinine seeds" and denominated "quinaquina" or "kina-kina" in spanish (*Myroxylon* sp),[10] passes to be "china china" in italian. This would not be of any particular importance if it weren't for the fact that pronunciation of "chi" did not change to "qui" in Italian (and perhaps Latin). And, even though "radice di china," "corteccia di china" and "china-china" are botanically distinct, this distinction is difficult to make if only centered to what is written. Because Latin was the language of science, these confusions have been maintained for 3 centuries.

Therefore, we have the much repeated and "improved" healing of the countess of Chinchón (cured are the vicequeen, the viceroy, and/or their son, Mrs Leonor becomes Mrs Ana, and Mrs Francisca, the viceroys medic turns from Cleto Martínez to Juan de Vega, the marquis de Zárate–best friend of the viceroy–is transmuted into the "marquis de Corpa" and the Indian from Leiva is rebaptized as Pedro de Leyva), seems to be only a romantic tale to promote and validate the use of quinine (a passionate history that deserves a closer analysis), in a baroque Europe where everything that came from America necessarily had an aura of mystery that surrounded it.

Francisco Medina Rodríguez

Enfermedades Autoinmunes,
Centro Médico Nacional Siglo XXI, México DF. México.

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