

QUININE.

BY QUARTERMASTER-SERJEANT ERIC F. SMITH.

Royal Army Medical Corps.

THE daily dose of quinine is familiar to many of us on duty in tropical climates, but few realize the fascinating and romantic history of quinine and its relation to cinchona.

Quinine itself is an alkaloidal product from the bark of the cinchona tree, and was first isolated in the year 1849 by the French chemists, Pelletier and Caventon, and for their labours they were awarded 10,000 francs by the French Government.

As early as 1746 French chemists were endeavouring to obtain a crystalline substance from cinchona bark with a view to its employment in the treatment of fevers. In 1792, one Fourcroy, at Paris, obtained slight results, but he lived in troublous times and was not able to pursue his investigations. He did, however, place on record a prophecy which was remarkably true. "These researches," he wrote, "will no doubt lead to the discovery one day of an anti-periodic febrifuge, which once known may be extracted from various plants."

The cinchona tree is a native of Peru. It takes its name from Countess Ann of Chinchon, wife of the Spanish Viceroy of Peru, who, so far back as 1638, was cured of a fever, probably malaria, after taking an infusion of the bark. So enthusiastic was this lady over her cure that, on her return to Spain in 1640, she recommended it to her friends for divers ills, and did her best to popularize the bark. Its use medicinally was probably known to the Peruvians years before the Countess was cured of her malady, and the story runs that its efficacy was first discovered as the result of an earthquake which caused a number of cinchona trees to fall into a lake. A native, suffering from the violent thirst consequent on a high fever, drank of the waters of this lake and found himself shortly afterwards cured of his ailment. In consequence this lake near Loxa was for a time credited with miraculous healing properties, until the reasons for its curative powers were discovered. Charles Lamb's history of the origin of roast pork is almost a parallel, although in this instance earthquakes could not be made to order like the Chinaman's houses on fire.

The Count and Countess of Chinchon brought with them, on their return to Spain, their personal physician, one Juan del Vego, who afterwards took up his residence at Seville, and having obtained a considerable quantity of the bark, sold it as a secret remedy at one hundred reals per pound. The silver real being worth about eightpence in our money, the wily physician must have netted a handsome fortune. His success created

a considerable amount of jealousy and controversy until the remedy remained no longer a secret.

It is more than probable that the Jesuit Missionary Fathers in Peru knew of the virtues of this bark before the Countess had them introduced to her. They attempted to keep their knowledge a secret, and some of them, on their return to Europe, introduced the powdered bark to the Jesuit College at Rome, and explained its use in the treatment of fevers and agues, with a view to profiting the coffers of Mother Church. The Procurator General of the Order, afterwards Cardinal de Lugo, on a visit to Paris in 1649, cured Louis XIV of a fever after administering the powdered bark. This royal cure was a gigantic advertisement, and the Jesuit fathers, anxious to propitiate "le grand monarque," took care that they themselves obtained all the credit for the discovery of the remedy. It ultimately became known as Jesuit's bark or Cardinal's powder, and was in great demand, but could only be obtained through the medium of the followers of Ignatius Loyala. So popular, indeed, did it become, that imitations, containing no cinchona but possessing the necessary appearance and taste, were made up by unscrupulous physicians. The necessary bitter taste was simulated by the addition of aloes. These concoctions were advertised by the then known mediums of advertisement, and it is clear that "cure alls" and secret remedy merchants are not modern innovations. They certainly lacked the press columns, with publication of "unsolicited" testimonials, but dupes were to be had for the asking, then as now. Strange to say, the very title, "Jesuit's Bark," drove cinchona out of fashion. Early in 1700 there was an outcry against the Order, and its enemies made it easy to turn the masses against any cures for which the members of the Order had made themselves responsible.

It was left to an Englishman to bring finally to the fore the value of cinchona as a specific for agues. Robert Talbor, an apothecary's assistant at Cambridge, was a student at the University in 1663. He has been accused of many acts of roguery, but seems to have been possessed of a high degree of intelligence, and had what we should call a good "bedside manner."

He wrote a book on the cure and cause of agues, and prescribed therein numerous secret remedies of his own, but amongst other things he brought to notice the therapeutic value of Peruvian bark (the name he adopted for cinchona). He cured the daughter of Lady Mordaunt, and Charles II himself, when those personages were stricken with fever. The "merry monarch," always prolific with his honours, knighted Talbor, appointed him one of his physicians and gave him a salary of £100 per annum. Charles so far interested himself in his new doctor that Talbor persuaded him to write to the College of Physicians, ordering that august body to refrain from interfering with Talbor's practice. What the present Royal College of Physicians would have said to such a royal command can only be left to the imagination. The next we hear of this persuasive medico is

in Paris, where he quickly attained popularity, and came under the notice of Madame de Sévigné, whose letters are world-famous. In one of these epistles she writes (in 1680): "The Englishman has promised on his head to cure Monseigneur (the Dauphin) in four days. If he fails I believe that he will be thrown out of the window." Talbor did cure his illustrious patient, and woman-like, Madame chronicles with malicious joy the embarrassment of Antoin d'Aquin, Louis XIV's head physician.

D'Aquin, to justify his existence and professional ability, published an angry attack on his English confrère, and said amongst other things that in curing the Dauphin of one disorder Talbor gave him a worse complaint. Talbor obtained 2,000 guineas from his royal patron, and a pension of £100 for the prescription, which, when published after his death at the age of 41, in 1681, gave the composition as follows: Infusion of rose leaves, and parsley in water, with lemon juice, added to which was a strong infusion of Peruvian (cinchona) bark. Talbor's detractors said that opium was another ingredient, but as Wootton, in his "Chronicles of Pharmacy" adds, "if he did he invented a valuable combination."

In the British Museum Library there is an interesting collection of quack advertisements, dated 1675 *et seq.* Amongst these pamphlets is one issued by a Dr. Charles Goodall, "at the Coach and Horses, near Physician's Colledge, Warwick Lane." He advertises "for the public good a very superior sort of Jesuit's Bark ready powdered and papered into doses" at 4s. the ounce.

Nearly all the quinine used by the world nowadays is obtained from cinchona trees grown in Dutch Java. The trees are tended scientifically with the object of producing bark rich in quinine, the most important of the many chemical substances found in the bark.

Cinchona flourishes well in India, but little of the world's supplies of quinine are now obtained from that continent, and it is to be deplored that in the country where quinine is in such great demand greater efforts are not made to cultivate it extensively and so capture the world's market.

The tree was first introduced in India for cultivation through the efforts of Sir Clements Markham, the famous explorer, and one time President of the Royal Geographical Society. Markham tried to insist on the adoption of the name "chinchona" instead of "cinchona," in justice to the name of the lady who first introduced the bark into Europe. He writes of the Countess as "one of the most noble benefactors of the human race," somewhat extravagant praise which calls to mind De Quincey's "unconscious minister of divine pleasures" regarding the chemist who first sold him opium.

In 1859, Markham was commissioned by the Indian Government to proceed to South America to obtain seeds for the cultivation of the tree in India, but lack of enthusiasm on the part of the authorities, and their parsimony in meeting the expenses of the pioneers, all but wrecked a scheme which might have been of great advantage to the Empire, both

humanely and financially. Markham himself gave his whole time and efforts in an attempt to bring to the notice of the authorities the value of the cinchona cultivation in India, and he was so far successful in planting the first trees in that country.

His coadjutors, some of whom were crippled in health as a result of their labours in a fever-ridden country, received a mere pittance, and barely a recognition. After Markham, the world is indebted to Charles Ledger for the finest cinchona seed. Ledger was employed from 1841 to 1858 by the New South Wales Government in South America buying alpacas. During his travels a Spanish-American servant, Manuel Manami, introduced to him some seed of excellent strain. Ledger sent these seeds to his brother in England with the intention of offering them to the British Government for trial in India. After months of negotiations the offer was refused, and the Dutch Government on being approached bought them for £33, thus laying the foundation of the present large cinchona cultivation areas in their Java possessions, and incidentally depriving the British market of a valuable commodity. Ledger has been called the "Cinchona Pioneer," and the trees which yield the majority of the world's supplies are named after him (*Cinchona Ledgeriana*). The Dutch were so pleased with the results that they paid Ledger the sum of £100 for his efforts. The "Ledger" cinchona was introduced into India, and produced such excellent results that Markham himself, always an unselfish investigator, requested the authorities to make some substantial mark of recognition to the man who had done so much towards obtaining the perfected tree. The Government, however, refused to untie its purse strings, and Ledger was too modest to bring himself to the fore.

Professor H. G. Greenish, Dean of the School of Pharmacy, in an interview reported by the *Indian and Eastern Druggist*, stated that he remembered well "the day when cinchona was sent in such quantities to London that at the London Docks there used to be special floors devoted entirely to the reception of cinchona bark, the major share of which came from India. At the present time comparatively small quantities of cinchona are introduced in London, and most of the bark that does reach the Thames comes from South America or Dutch Java, India's quota having entirely disappeared."

The *Pharmaceutical Journal*, in 1923, gives the statistics of production of cinchona bark as summarized in the "Bulletin of the Imperial Institute" as follows: "Java, 228,880,000 pounds; India, 2,000,000 pounds; other countries, 440,000 pounds.

Before the Great War the Amani Institute, in German East Africa, specialized in the cultivation of cinchona trees for quinine production. During the war the Amani Institute passed into British hands. A recent analysis of the Amani bark proved that it contained nearly twice as much quinine as the Dutch "Ledger" bark. The future of the Amani cultivation is watched with interest, and it would seem that the seeds from Africa

could be introduced into India, and an attempt made to recapture the world's quinine trade for the Empire which uses most of this valuable medicine.

The value of quinine as a specific for malaria was summed up in the "Medical History of the War," vol. ii, p. 217, etc., as follows:—

"In spite of much and varied experimentation, no drug has been found to have any specific action on malaria except quinine. No method of administration, other than the long-recognized oral exhibition of the drug, has been proved to be of superior value in the routine treatment of malaria. . . . The early or immediate and prompt treatment of malaria by quinine in doses of ten grains three times a day quickly cures the disease in a large proportion of the cases." The tincture cinchona co. of the B.P. (sometimes called Huxham's tincture of bark) was originally prescribed by Dr. John Huxham, and published as a specific in his "Essay on Fevers," in the year 1785. Huxham was considered to be rather a prosy prescriber, even by his contemporaries in a day when it was believed that the more complicated a prescription the better the results. One of Huxham's published prescriptions contained more than 400 ingredients. Fortunately for Part B Dispensers, this prescription has no place in the B.P. and Whittle is silent regarding it.

Huxham's original prescription for tinct. cinchona co. should be interesting to both Part A and B candidates:—

Cort. peruv. opt. pulv.	2 oz.
Flor. aurant. hispan.	1 "
Rad. serpent. virgin.	3 "
Croci anglic.	4 sc.
Coccol	2 "
Vini gallici	20 oz.

F. Infusio clausa per dies aliquot (tres saltem quatuorve).

JRAMC

Quinine

Eric F. Smith

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