

On the Inhalation of Cinchonia, and its salts.

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There can be very little doubt that at some future time we shall possess the means of giving to patients many potent remedies in the form of inhalation, rather than in the usual way. This is at least among the hopes of the therapist of the present day. Absorption of medicinal substances by the intestinal mucous surface is but too often uncertain, while the passage to the blood through the lungs seems to be always an open track, when the agent inhaled is in a state of vapor. How desirable it would be to possess the means of inhaling quinine in the congestive fevers of our malarious districts, we can very well conceive. Guided by these ideas, I have sought industriously for some means of attaining this result, and although I have failed, as I shall here show, in evolving any very marked practical benefit from these researches, I have met with certain facts of such interest that I desire to put them on record as indicating a novel direction for medical thought and action.

At one time, the analogy in chemical composition, between certain of the newly formed ethers and quinia itself, seemed to point out these as fit subjects for therapeutic use and trial. The difficulty of procuring them, obliged me, however, to relinquish effort in this direction, and I turned from them to examine anew the alkaloids derived from cinchona bark. While thus engaged, one of my friends, now Dr. Bill, of the army, pointed out to me in Fresenius's Chemistry, his account of cinchonia, which he describes as volatile at high temperatures.

Struck with this, I searched carefully for any account of its inhalation, but as yet have been unable to find in the books on Cinchona any description of inhalation, as a mode of using the alkaloid in question. The last complete work on quinia, by M. Briquet, enumerates many methods of employing the alkaloids and bark, but neither among the means in use, or out of use, is this one alluded to. Occasionally, in disease of the lungs or throat, inhalation of pulverized cinchona bark has been resorted to, and M. Briquet relates,—*"Traité Thérapeutique du Quinquina et de ses préparations,"* p. 118,—that those who work in the storehouses of cinchona bark are sometimes thus cured of malarious fevers. This could only occur through accidental ingestion, and inhalation of the floating particles of bark.

Cinchonia and its salts are the only alkaloids which appear to be volatile by heat. After many experiments, I have finally resorted to the following very simple method of inhaling them:—About forty grains of pure cinchonia, being mixed up with sand, are placed in a capsule, and heated by a spirit-lamp. The sand is useful in diffusing the heat, and preventing too rapid a destruction of the alkaloid. A heat of about 300° melts the particles of cinchonia into a brown fluid, and from this, if the evaporation be carefully managed, the volatilized alkaloid escapes in the form of a gray vapor.

When a microscope glass is held over the capsule, and the heat is too elevated, the cinchonia decomposes, and a dark red gummy-matter, with the odor of burned benzoin, adheres to the glass. A rather lower temperature drives off the cinchonia in a gray vapor, which may be made to redeposit the pure alkaloid upon the interior of a funnel held over it, or upon a microscope slide. The alkaloid thus obtained is in branching needles.

On a number of occasions, I inhaled the vapors of cinchonia, often breathing them for ten or twenty minutes, without much inconvenience, when care was taken to regulate the supply of heat. The brown or reddish volatile substance which is given off when the heat used is too great, so irritates the throat as to cause nausea, and oblige the patient to cease inhaling.

When carefully inhaled, a part of the alkaloid is deposited on the throat and in the mouth, where its sub-bitter taste is soon perceived. To guard against error, which might arise from swallowing these portions of the alkaloid, I refrained from swallowing whilst inhaling, and frequently rinsed the throat with water.

Upon four occasions, I noted the symptoms caused by the cinchonia thus

employed, taking care to allow the excitement of the system produced by the inhalation to pass away before I counted the pulse. In three instances the pulse *fell*, losing from 6 to 10 beats per minute. In the fourth, the pulse remained a few beats above the normal number. The person on whom these experiments were made is liable to still greater depression of cardiac energy, when under the influence of quinia. At first, it was difficult to separate the ordinary signs of cinchonism from the feelings of cerebral confusion, caused by breathing too rapidly. These sensations, however, were evanescent. At the end of a quarter of an hour, or even less, the head was clear, and within half an hour afterwards the patient felt a quickly increasing headache, with giddiness, and sometimes a feeling as though the brain was swelling into monstrous bulk. These sensations passed away within four or five hours, unless the inhalation was renewed.

Still uncertain as to whether or not the alkaloid entered the blood, I caused a healthy adult, æt. twenty-nine years, to inhale the fumes from forty grains of the heated cinchonia four times in one day. Symptoms of cinchonism were felt only after the first inhalation, which was made at 10 A. M.; at 12 M., the second inhalation took place, and at the same time four ounces of clear urine, s. g. 1023, were passed. The other inhalations occurred in the afternoon and evening, but none other of the urine passed was saved, until 7 A. M. next day.

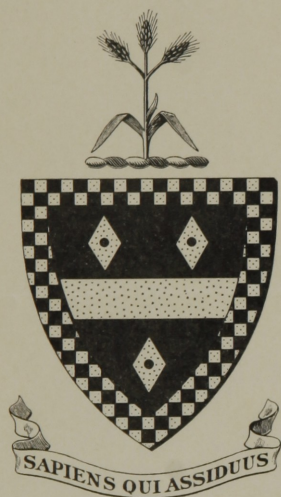
The first specimen was examined by Bouchardat's test, the iodated iodide of potassium. This reagent gave a faint but decisive brown precipitate of iodide of cinchonia, when employed in the usual way; when, however, I placed in a test tube a portion of the test solution, and slowly poured upon it the lighter wine, a profuse deposit of the iodide announced the presence of cinchonia in the urine. In the usual mode of making this test,—although the precipitate is perceptible enough,—it almost immediately redissolves in the urine, which appears to possess a remarkable power of dissolving the iodides of cinchonia and quinia, since when these precipitates are thrown down from an aqueous solution of a salt of either alkaloid, they are found to be very insoluble. The second specimen of urine contained only traces of cinchonia, and twenty-four hours after the last inhalation no evidence of the presence of the alkaloid in the urine could in any way be obtained.

It will be readily seen from what I have said, that I do not anticipate any remarkably valuable practical results from the new mode of administering cinchonia in vapor. The want of therapeutic power in this alkaloid, when compared with quinia,—dose for dose,—the difficulty of regulating the heat so as to volatilize, and yet not decompose it, as well as the unpleasantness of the process of inhalation, combine to deprive these experiments of any great practical utility. In a single case of tertian intermittent fever, I employed the inhalation of cinchonia vapor. The patient had no new attack for one month, although no other ulterior measures were employed. The case was a very irregular and uncertain one, and I therefore attach but little faith to this single therapeutic test. I should add that my patient complained a good deal of the effect of the alkaloid upon his glottis and larynx. For a time it altered the tones of his voice very considerably.

In two cases of chronic bronchitis, of long standing, I also used the fumes of cinchonia; one of these dated his first improvement from the use of these inhalations, in which he persisted every other day, for more than two weeks; no other treatment was used until he had been much aided by the means above described. He learned after a time to employ the cinchonia without my aid. The other patient submitted to one inhalation, but declined any further proceedings of a similar character, declaring that the remedy was worse than the disease, only shorter. When we are successful in volatilizing the alkaloid without decomposition, the process of inhalation is not very disagreeable; but when the heat is too high, and the cinchonia becomes altered, it is extremely difficult to continue to breathe it.

The salts of cinchonia are also volatile by heat, but they offer no advantages which do not equally belong to pure cinchonia. The sulphate is quite inadmissible for inhalation use, since sulphuretted gases are given off in small amounts when the heat is too elevated, and decomposition takes place.





*Weir Mitchell*

