

# Chloroquine in the COVID-19 pandemics and quinine in the cattle plague epidemics in the eighteenth century: déjà vu all over again

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**Abstract.** Drug treatment of diseases is not a usual task for occupational and environmental physicians. However, these professionals should be aware that some concerns on treatment during an epidemic were raised centuries ago. This commentary discusses Bernardino Ramazzini's remarks made during a cattle plague epidemic occurring four centuries before the current COVID-19 emergency; he emphasised that prescription of some drugs usually given against every kind of fever deserved careful attention. Ramazzini's contribution can be regarded as an early example of attention to evaluating the benefits and harmful effects of taking new drugs and witnesses the scientists' continuous effort to tackle new and unexpected health challenges.

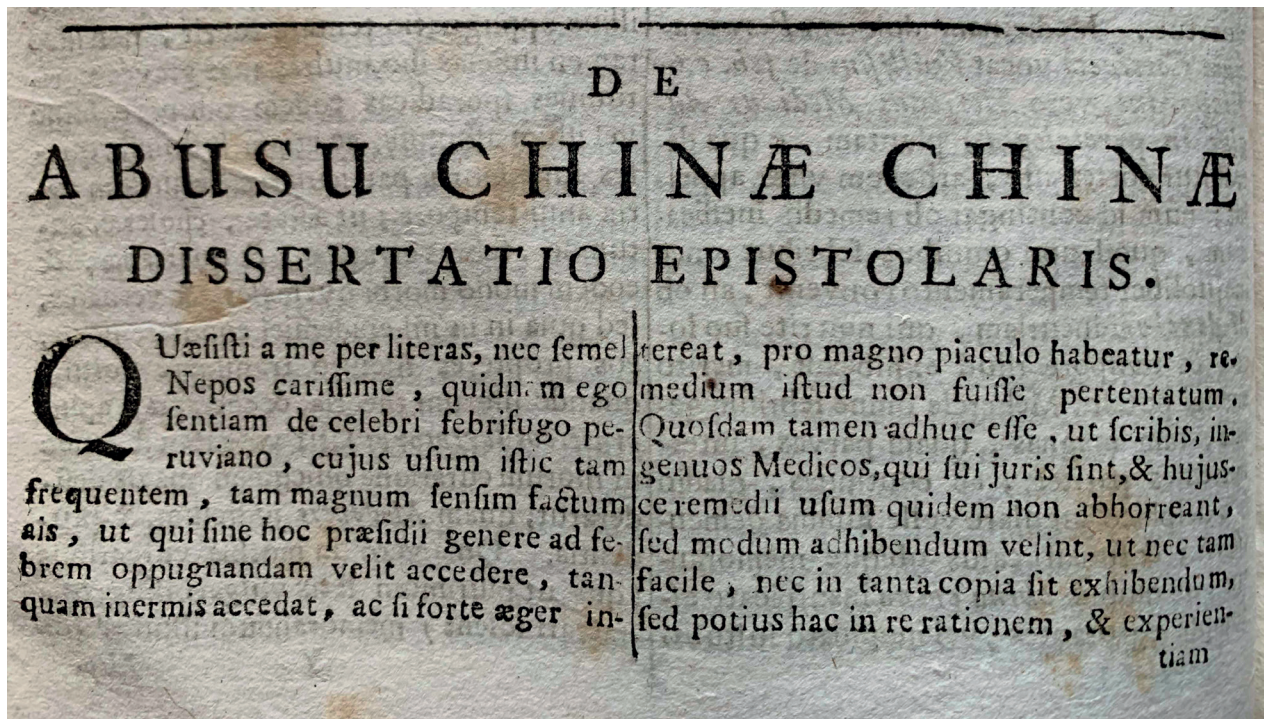
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Even in the time of an epidemic, every measure should be based on a scientific approach in guiding public, occupational and environmental health strategies based on surveillance, risk mitigation and containment of transmission (Collegium Ramazzini, 2020). Although drug treatment of diseases is not a usual and specific task of occupational and environmental health physicians and is not crucial for their health practice, the therapy of coronavirus disease (COVID-19) is of indisputable interest.

The increasing amount of data and the sometimes contradictory results on the use of hydroxychloroquine and chloroquine for the treatment of COVID-19 pandemics (Hernandez et al., 2020, Rome and Avorn, 2020) prompted me to address some concerns raised centuries ago on this issue. It is worth mentioning some remarks by Bernardino Ramazzini —better known for his commitment towards workers' health (Franco, 1999)— *on the fight against a cattle plague epidemics occurring centuries before the current COVID-19 emergency.*

On the occasion of a rinderpest epidemic devastating the Italian peninsula at the beginning of the eighteenth century, Ramazzini was leading a group of experts established to study the issue (Franco, 2020, Ramazzini, 1739b). Since the contagion was rapidly propagating in closed spaces affecting both people and cattles, he suggested the lockdown of infected animals and other measures. Consequently, the authorities limited livestock businesses and freedom of movement of the people who had been in contact with infected animals.

As for the treatment of cattle plague, Ramazzini suggested treatment with Cinchona bark (*cortex peruvianus, vulgo Chinae Chinae*) —its active principle quinine would have been isolated after several decades; chloroquine and hydroxychloroquine, which share with quinine the quinoline ring system, would have been synthesized and used as antimalarials after more than 2 centuries. In his iv oration on the theory and practice of fevers given in 1702, he already had recognised that this remedy was widely used for the treatment of fever and acknowledged that, other than its proven



**Figure 1.** Title page of Ramazzini's work *De abusu Chinae Chinae dissertatio epistularis*. (From: *Opera Omnia*. 1739).

effectiveness, nothing was known (Ramazzini, 1739a). Ramazzini revived what Hippocrates argued, namely that the task of science was to uncover the unknown. Wondering whether the Cinchona bark could be used to fight the malignant fever occurring in cattle disease, he suggested investigating the strength of the substance. After a few years, however, he realized that the bark was being used indiscriminately for all causes of fever, thus involving a serious misuse. In his "*De abusu Chinae Chinae dissertatio epistularis*", first published in 1714 (Ramazzini, 1739c), he reported that the bark caused marked complications in patients taking it, especially over a long period (Figure 1). Because continuous use of Cinchona bark usually entailed adverse effects, he warned that prescription of the drug deserved careful attention.

In the light of the contradictory results observed in current studies about COVID 19 treatment (Hernandez et al., 2020, Rome and Avorn, 2020), Ramazzini's contribution can be regarded as an early example of the attention paid to evaluating the benefits and

harmful effects of taking new drugs and witnesses the scientists' continuous effort to tackle new and unexpected health challenges.

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