

The “100 Days Cough” Was Not Originally Whooping Cough

We read with great interest the article by Liang et al [1]. We have recently published the earliest known case of whooping cough that occurred during the first pandemic [2], and in that publication we postulated that the likely source of whooping cough was the Far East, after which it was introduced to Persia (1484–1495) and then to Europe. This new article sheds light on the term “100 days cough”, which has been attributed in this article and other works as being synonymous with whooping cough [3, 4], because the entire disease can last approximately 3 months (hence the term “100 days cough”).

The authors translate the relevant section as follows: “if the back [of the child] is cold, there would be a cough. [If] it is not cured within a month and there is a cough within a hundred days, only one or two out of ten will recover.” After tentatively claiming that this could be whooping cough, the authors pose the following question: “Does the above passage in this monumental Chinese medical Treatise truly represent clinical pertussis observed as a pediatric condition with prolonged cough?” The authors are unsure, it seems, because of the brevity of the passage. We believe that the 100 days cough as described by the translation of Liang et al [1] is not whooping cough.

In our recently published work, we used what is known about the natural history, epidemiology, and immunology of the disease to come to the conclusion that the records we examined were indeed documenting the first human pandemic [2]. When we applied the same methodology to this text, we came up with a different conclusion than the authors. If we examine the description of the 100 days cough in *Zhubing yuanshou lun*, we see that it describes an illness in children that is marked by a chronic cough and high mortality. At first glance, this seems to

be supported by the epidemiologic fact that children are affected and that the mortality is high. Epidemiologically, we run into a problem, because this would mean the disease was already endemic. Thus, we would have to explain a scenario in which a highly contagious and recognizable endemic disease was isolated to China for almost a millennia, even though there was significant contact with Persia and the rest of the world. Furthermore, whooping cough is suspected when a cough of 14 days exists with paroxysmal cough, inspiratory whoop, or posttussive vomiting [3, 5]. None of these classic symptoms are mentioned. The mortality mentioned in the text is 80%–90%, if we equate never recovering with death as the authors have also done. This far exceeds what is reported for whooping cough (up to 6% in nonimmune populations) [6]. In addition, the mortality is stated to have occurred after the first month. This would mean the mortality would have occurred in the second and third month of the disease, which most closely matches the convalescent stage of whooping cough, when the patient is improving. It is widely known that the mortality occurs during the paroxysmal stage, when active whoops are associated with the complications of pneumonia, cyanosis, syncope, hemorrhage, and seizures [7, 8]. The paroxysmal stage lasts 1–6 weeks, although in most cases this stage ends by the first month or into the fifth week [6]. Moreover, the paroxysmal phase is not static; there is a period when the cough worsens and then starts to get better before transitioning to the convalescent phase. Complications such as pneumonia occur at the height of the paroxysmal stage [6], which would be before the total time given for the paroxysmal period. Even if we add to the duration of cough the 1–2 weeks of coughs present with a host of other symptoms in the catarrhal stage to the maximum for the

paroxysmal stage, we cannot go beyond 2 months. Can one find cases of paroxysmal cough later than 6 weeks? Of course, but then we are dealing with rarities, upon which generalizations such as the one presented in the *Zhubing yuanshou lun* cannot be built. These crucial but overlooked points make it unlikely that the 100 days cough in the *Zhubing yuanshou lun* was referring to whooping cough.

It is far more likely the chronic cough with mortality that increases as the duration of cough increases is associated with other infectious conditions such as a complication of a bacterial pneumonia (such as lung abscess), of which there are many causes. We do think this article is important in that it sheds a light on the origins of the 100 days cough. It could be that this term never had anything to do with whooping cough, or perhaps it later changed meaning and became used for whooping cough. In either case, it seems that more work needs to be done on the 100 days cough.

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