Even before vaccination has completely stopped the transmission of coronavirus disease 2019, the monkeypox virus has started to spread. In light of this situation, it would be worthwhile to review the development and introduction of variolation to Korea.

DEVELOPMENT OF VARIOLATION IN CHINA

In China, a method of acquiring immunity from smallpox by collecting biological samples from smallpox patients was developed relatively early in history. Although it is believed that the variolation method was introduced from India to China in the 11th century [1], *Douzhen Xinfa* (Essential knowledge and secrets of pox diseases), which Manjeon published in 1549, is believed to be the oldest record of the variolation method in China. During the Ming Dynasty (Longqing, 1567–1572), the variolation method was further developed in Huangshan City, and this area became the center of variolation in China [2].

According to the *Yizong Jinjian* (The golden mirror of medicine), an inoculation document published in 1749 (the 14th year of Qianlong) at the command of Emperor Qianlong, inoculation methods included *douyifa* (variolation through clothing), *doujiangfa* (wet variolation), *hanmiaofa* (dry variolation), and *shuimiaofa* (water variolation). The terms *miao* and *doumiao* referred to the smallpox vaccine. *Douyifa* was a method of putting the clothes worn by a smallpox patient on a child who had not yet contracted smallpox. *Doujiangfa* was a method in which a smallpox patient’s pus (*doujiang*) was dissolved in water, moistened with a fabric, and put directly into the nose. In *hanmiaoafa*, a smallpox virus-containing scab (*doujia*) was powdered and blown into the nose through a tube (Fig. 1). In China, *doujiangfa* and *hanmiaoafa* were mainly used.

Doctors who specialized in inoculation hid their secrets from others in order to monopolize vaccination. They found that if the virus was preserved in a *doujia* state, the activity of the virus was maintained for a long period of time. Variolation was carried out relatively safely using matured miao, with its toxicity weakened by refining seven times. The amount of antigen was reduced to re-
duce the possibility of infection while maintaining antigenicity [2].

In Japan, a Chinese inoculator, Li Jen-Shan, proposed the method of Chinese-style variolation after a severe smallpox outbreak in Nagasaki in 1744, but it was not popular except in some areas.

EUROPEAN SPREAD OF THE CHINESE METHOD OF VARIOLATION

Starting around the 17th century, the Chinese method of variolation spread to Russia, Central Asia, Turkey, Japan, and Joseon-era Korea. After signing the Treaty of Nerchinsk, Russia sent envoys to the Qing Dynasty in 1689 (the 28th year of Kangxi) to learn "vaccine medicine" [3], a concept that included both treatment and prevention (variolation) methods. Although variolation was introduced to many European countries through the reports sent from Jesuit missionaries in Beijing in 1726, it was not widely accepted [4].

Mary Wortley Montagu (1690–1762), the wife of the British ambassador to the Ottoman Empire, played a very important role in proving the efficacy of variolation. In 1721, she administered variolation to her daughter in front of doctors dispatched by the Royal College of Physicians. Thereafter, the effectiveness of variolation became accepted among English intellectuals. Starting in the following year, the British royal family received variolation. The Turkish inoculation method she implemented was a method of injecting pus collected from smallpox patients into small wounds made on the skin of the person to be vaccinated. Most of those vaccinated experienced only mild symptoms, such as a slight rash, and were able to gain immunity. However, in rare cases, smallpox developed, and death ensued after vaccination. This method was spread throughout England in the 1740s, and after the 1770s, it was implemented even in small villages in the countryside [5]. Subsequently, Edward Jenner implemented variolation and modified it to vaccination for the first time in 1796 [6,7].

VARIOLATION TO JOSEON

In Korea, in the late 18th and early 19th centuries, Jeong Yak-Yong (1762–1836) and Lee Jong-In first recognized that smallpox is infectious and can be prevented by vaccination. However, vaccinations against smallpox were not carried out among members of the public until 1880.

In 1798, Lee Jong-In, a doctor who was active in Pocheon, collaborated with Park Jae-Ga (1750–1805) to inoculate scholars north of Hanyang and south of Pocheon. In 1798 (22nd year of King Jeongjo), he first saw the Jongduseo (Book on variolation) from Park Jae-Ga, and he also referred to Yizong Jinjian, Lantai Guifan (Standard criteria of the orchid dais) and Zhongdou Xinshu (New book on variolation), and other sources. He achieved effective results in his practice. He reviewed the Douzen Dinglan (Decisive discussion on smallpox) written by Zhu Chungu, who was an imperial doctor in the Kangxi era (1662–1722) of the Qing Dynasty. Lee Jong-In finally compiled a medical book called Sijongtongpyeon (Compendium of vaccination) and disseminated variolation among the civilian population.

Jeong Yak-Yong edited two books, Zhengshi Zhongdoufang (Formulas for smallpox vaccination) written by Zheng Wangyi and Youke Zhongdou Xinfa Yaozhi (Pediatric variolation essentials) in a book entitled Yizong Jinjian and bound them into one volume named Jongdusimbupyoji (Medical treatise on smallpox vaccination). He included the edited volume, Comprehensive Treatise on Measles, as an appendix (1800).

The development of marine transportation spread the vaccination method, helping it to become more widespread than variolation. The delivery of fresh vaccines is the key to vaccination. When transportation was not sufficiently developed, only variolation was feasible; however, vaccination became more popular as the transport of fresh vaccines became possible. The spread of the inoculation method in Joseon-era Korea was made possible by the editing and publication of Chinese versions of books on variolation or vaccination.
NOTES

**Ethical statements**
Not applicable.

**Conflicts of interest**
The author has no conflict of interest to declare.

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