Zeitschrift: Asiatische Studien : Zeitschrift der Schweizerischen Asiengesellschaft = Études asiatiques : revue de la Société Suisse-Asie

Herausgeber: Schweizerische Asiengesellschaft

Band: 69 (2015)

Heft: 3-4

Artikel: Antisyphilitic mercury drugs in early modern China and Japan

Autor: Trambaiolo, Daniel

DOI: https://doi.org/10.5169/seals-696823

Daniel Trambaiolo*

Antisyphilitic Mercury Drugs in Early Modern China and Japan

DOI 10.1515/asia-2015-1044

Abstract: Toxic mercury chloride compounds, including preparations and mixtures of corrosive sublimate ($HgCl_2$) and calomel (Hg_2Cl_2), were widely used in early modern Chinese and Japanese medicine. Some of these drugs had been manufactured in East Asia for more than a thousand years, while others were produced using newer recipes developed in East Asia after the arrival of syphilis or introduced through contact with European medical knowledge. This paper traces the history of the uses and methods of production of sublimated mercury chloride drugs in early modern East Asia, showing how the Chinese doctor Chen Sicheng's invention of the drug *shengshengru* (J. *seiseinyū*) 生生乳 in the seventeenth century exerted a strong influence over eighteenth- and nineteenth-century Japanese doctors' treatment of syphilis. Japanese doctors' efforts to produce and use *seiseinyū* provided a foundation of technical knowledge that was important for their later reception of European-style mercury chloride drugs.

Keywords: East Asian medicine, Tokugawa Japan, pharmaceuticals, syphilis, Dutch studies (rangaku)

1 Introduction

The arrival of syphilis in East Asia during the early sixteenth century presented a new set of challenges to the region's doctors and encouraged experimentation with new forms of therapy. The spread of syphilis[1] thus stimulated a number of

1 My use of the term "syphilis" in this paper is intended as a pragmatic translation for a group of related terms (*yangmeichuang/yōbaisō* 楊梅瘡, *meichuang/baisō* 梅瘡/黴瘡, *meidu/baidoku* 梅毒/黴毒, etc.) referring to a new disease category that emerged in East Asia during the sixteenth century. Many of the patients diagnosed by early modern doctors as suffering from "syphilis" would not have been thus diagnosed according to modern biomedical definitions of the disease. However, there is ample evidence from skeletal remains that syphilitic infection, like other forms of venereal disease, was common in early modern Japan. (See Johnston 2009 for a discussion of the literature on this subject.)

***Corresponding author: Daniel Trambaiolo,** Department of Japanese Studies, The University of Hong Kong, Hong Kong, China, E-mail: trambaio@hku.hk

medical innovations, including a resurgence of interest in the use of mercurial drugs such as corrosive sublimate and calomel. Chinese doctors began to use these drugs to treat syphilis during the sixteenth and early seventeenth centuries, and Japanese doctors soon followed their example. The emergence of new ways of thinking about disease and healing during this period and the introduction of medical ideas and imported pharmaceuticals from Europe stimulated focused investigations into these drugs' natures and uses.

Long before the arrival of syphilis, mercury and its compounds had enjoyed a continuous history of spiritual and medical significance in East Asia. In ancient China, cinnabar and mercury were associated with ideas and practices related to life, death, transformation and healing. Traces of cinnabar have been found in Chinese burial sites from as early as the Shang period (2nd millennium BCE), and although historical accounts referring to "rivers of mercury" flowing through the tomb of the first Qin emperor (260–210 BCE) may have been exaggerated, archaeological surveys have confirmed the presence of elevated levels of mercury in the soil around the tomb site.[2] High levels of mercury were also discovered in the hair and internal organs of a Han-dynasty noblewoman buried at Mawangdui (ca. 168 BCE), most likely as a consequence of cinnabar consumption during her lifetime.[3] A collection of medical recipes in another tomb at Mawangdui included several formulas containing cinnabar or mercury, intended for the treatment of a variety of skin conditions.[4]

Mercury and its compounds played a central role in the development of Daoist traditions of thought and practice between the third and eighth centuries CE.[5] It was not only the mysterious physical properties of the silvery liquid that fascinated the early Daoist alchemists, but also the variety of transformations that it could undergo. Liquid mercury could easily be produced by heating the bright red mineral ore cinnabar (HgS); this mercury could then be further transformed into other visually distinct substances such as the orange-red oxide (HgO) and the white chlorides ($HgCl_2$, Hg_2Cl_2). This diversity of transformative possibilities greatly appealed to the early Daoists, who saw transformation (*hua* 化) as a fundamental principle of the cosmos and thought of the transformations that took place within the alchemical apparatus as manifestations of a broader cosmic order. Their discovery of mercury's capacity for transformation helped reinforce their belief in its spiritual significance and its value as a component in elixirs of longevity or immortality.

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2 Needham 1976: 2–3, Golas 1999: 143; Duan 2011: ch. 6.

3 Changsha Mawangdui yihao Han mu gushi yanjiu weiyuanhui 1980: 215–225.

4 Ma 1992: 434, 556, 578, 589, 596, 613, 642. For translations and discussion, see Harper 1998.

5 Needham 1976: 123–129.

Enthusiasm for the consumption of mercury elixirs declined gradually during the Tang (618–907) and Song (960–1279) periods, when doctors were becoming reluctant to recommend the use of such highly toxic substances.[6] As part of his critique of Daoist practices, the ninth-century Confucian scholar Han Yu 韓愈 wrote a detailed account of the fates of people who had suffered illness or death after consuming mercury or cinnabar elixirs; in the thirteenth century, the doctor Zhang Gao 張杲 collected a series of anecdotes from earlier writers to serve as cautionary tales about mercury and cinnabar poisoning.[7] Even the Daoists of this period were increasingly substituting the methods of "internal alchemy" (*neidan* 內丹) for those of "external alchemy" (*waidan* 外丹), employing meditative techniques to bring about transformations of hidden alchemical essences within the human body rather than performing physical manipulations of material substances.[8] Although the consumption of mercury and cinnabar elixirs persisted into later centuries, such consumption was coming to be seen as excessively risky.

Against this background, the arrival of syphilis in the sixteenth century stimulated a renewed interest in the medicinal uses of toxic mercury-containing substances.[9] In contrast to the rich and varied records concerning the arrival and spread of the "French disease" in Europe, only sparse and ambiguous documentation survives concerning the early spread of syphilis in China and Japan.[10] Nevertheless, various sources attest to the appearance during the early sixteenth century of a new disease that was perceived as having arrived from elsewhere. One Chinese collection of medical anecdotes described the appearance of a new disease called "Guangdong sores" (*guangchuang* 廣瘡) during the final years of the Hongzhi period (1488–1505), and the popular tendency to associate syphilitic symptoms with specific geographic origins proved as attractive in East Asia as it had been in Europe.[11] A new disease that spread through Japan in 1512 was known as "Chinese sores" (*tōgasa* 唐瘡, とうがさ; *tōmo* とうも), later Japanese sources referred to the disease as "Nagasaki sores" (*hizengasa* 肥前瘡) or "European sores" (*nanbangasa* 南蛮瘡), and residents of northeastern Japan talked about "Edo sores" (*edogasa* 江戸瘡).[12] Doctors, however, preferred to use more neutral technical vocabulary: the most common medical

6 Obringer 1997; Obringer 2001.

7 Obringer 1997: 50–51; Zhang 1984 [1224]: 9:15a–23b.

8 Pregadio/Skar 2000.

9 The question of whether or not syphilis was present in Eurasia before the establishment of trans-Atlantic contacts remains controversial, but a recent review has found no indisputable evidence for pre-Columbian syphilis in the Old World and concluded that a New World origin remains the most plausible hypothesis (Harper et al. 2011).

10 On the early history of syphilis in Europe, see Arrizabalaga et al. 1997: 20–37.

11 On early Chinese references to the new disease, see Chen 1994: 206.

12 Dohi 1922: 121–122.

designation for the new disease, "bayberry sores" (C. *yangmei chuang* 楊梅瘡), referred to the physical appearance of patients' skin lesions. Some writers believed that the disease was spread by sexual contact, but others claimed it could arise from lifestyle or environmental causes such as inappropriate diet or atmospheric moisture.

Since the new disease was distinct from any previously described in the East Asian medical tradition, the selection of appropriate methods of pharmacotherapy required a certain amount of improvisation. However, within a few decades after the disease's arrival, Chinese and Japanese doctors had settled on two main types of drug therapy that they continued to use against syphilis until the late nineteenth century: the rhizome of the smilax plant (C. *tufuling*; J. *dobukuryō* 土茯苓 or *sankirai* 山帰来), and mercurial drugs such as corrosive sublimate.

The sixteenth-century Chinese scholar Li Shizhen 李時珍 summarized centuries of accumulated knowledge about the production and medicinal uses of sublimated mercury chlorides in his *Bencao gangmu* 本草綱目 (Systematic Materia Medica, 1596).[13] He listed corrosive sublimate under the heading *shuiyinfen* 水銀粉 rather than the more common *qingfen* (J. *keifun* 輕粉), but his description of its production was similar to descriptions found in other sources. Liquid mercury, alum, and cooking salt were mixed together into a paste and spread onto the bottom of a reaction vessel that was then sealed and heated over a fire while its lid was cooled with water. After breaking open the vessel, the white corrosive sublimate could be scraped off the inner surface of the lid.[14] Calomel (C. *fenshuang*/J. *funsō* 粉霜) was prepared from corrosive sublimate by further rounds of sublimation, sometimes with the inclusion of additional mercury or sulphur in the reaction vessel.[15] Corrosive sublimate and calomel were used for a similar range of medicinal purposes in the treatment of skin infections, syphilitic symptoms, accumulated phlegm, watery swellings, and pediatric conditions.

In Japan, just as in China, the bright red color of cinnabar gave it special social and ritual significance from an early date. The earliest Chinese written account of Japanese customs (ca. 280 CE) noted that Japanese women used cinnabar as a cosmetic to adorn their bodies.[16] Cinnabar was mined at a number of sites, of which Ise was the most prominent.[17] Production of sublimated mercury chlorides in Japan using Chinese techniques and local materials began at least as early as the eighth century.

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13 See Nappi 2009 for discussion of this treatise and its historical context.

14 Li 1982 [1596]: *juan* 9, vol. 1, 527–530.

15 Li 1982 [1596]: *juan* 9, vol. 1, 530–531.

16 Sōda 1965: 3.

17 On the early history of cinnabar mining and mercury production in Japan, see Matsuda 1970 and Matsuda 1987.

As one of the most important sources within Japan of cinnabar and mercury, Ise became a major center for the production of mercury chlorides. Sublimated mercury chloride was manufactured there for use as a whitening cosmetic known as *Ise oshiroi* 伊勢白粉, which was recorded as a tribute item from the province of Ise in a late eighth-century historical chronicle.[18] However, by the seventeenth century the cinnabar mines around Ise were largely exhausted, and Japanese production of sublimated mercury chlorides came to depend on supplies of mercury imported by Chinese or Dutch merchants. This shift in the source of mercury made it easier for producers in the region of Kyoto and Osaka to compete with those in Ise, but producers in Ise continued to enjoy certain advantages, such as their technical knowledge of production methods and their ready access to supplies of clay for making reaction vessels.

Japanese pharmacological literature offered a variety of opinions about which sources of *keifun* were most suitable for medicinal use. In the late seventeenth century, Endō Genri 遠藤元理 included corrosive sublimate (*keifun* 輕粉) in his list of "Japanese medicines for which it is necessary to distinguish between high and low quality"; he claimed that the best came from Kyoto, while that from Ise was somewhat inferior.[19] However, later writers such as Hiraga Gennai 平賀源内 and Ono Ranzan 小野蘭山 asserted that the best *keifun* came from Ise.[20] Japanese doctors also made use of corrosive sublimate imported by Dutch merchants: at the end of the seventeenth century, the German visitor Engelbert Kaempfer noted that "certain Japanese persistently press newly arrived foreigners for sublimate mercury and pay a high price for it."[21] Over the course of the eighteenth century, the increasing use of new Chinese and European mercurial drugs encouraged Japanese doctors to familiarize themselves with the ways these drugs were manufactured.

2 Doctor and patient perspectives on the harshness of mercury chloride drugs

Japanese doctors began to make use of sublimated mercury chlorides as antisyphilitic remedies not long after the arrival of syphilis in their country. Manase

18 Kaibara 1911 [1709]: 84. The historical chronicle cited in this source is the *Shoku Nihongi* 続日本紀 (797 CE).

19 Endō 1681: 1:3a.

20 Hiraga 1763: 2:1b; Ono 1803: 5:3a-b. For further discussion, see Sōda 1980: 10–12.

21 Bodart-Bailey 1999: 63, 209.

Dōsan 曲直瀬道三, the most influential Japanese doctor of the late sixteenth century, used corrosive sublimate (*harayagusuri* はらや薬) to treat "Chinese sores" (*tōgasa* 唐瘡) in the final decades of the sixteenth century.[22] By the end of the eighteenth century, Japanese doctors were treating syphilis using a variety of sublimated mercury chloride drugs: *soppiru* and *karumera* prepared according to European methods, *keifun* and *funsō* prepared according to Chinese methods, and a variant of *keifun* called *seiseinyū* 生生乳.

Japanese doctors in the eighteenth and nineteenth centuries often justified their use of these drugs through the innovative ideas of "Ancient Formulas" (*kohō* 古方) medicine. Advocates of Ancient Formulas claimed that their new style of medicine represented an authentic form of the art that had once flourished in ancient China but had subsequently been lost as later doctors recklessly followed their own arbitrary opinions and departed from the ancient Way. The therapeutic methods of this style of medicine were based on the writings of the third-century doctor Zhang Zhongjing 張仲景, whose *Shanghanlun* 傷寒論 (Discourse on Cold Damage) was the oldest surviving collection of medical formulas in the East Asian tradition and thus an important source of evidence about the practice of medicine in ancient China.

Zhang Zhongjing's formulas did not include corrosive sublimate or any other sublimated mercury drug: the techniques for manufacturing these drugs had not yet been invented at the time he wrote his treatise. Nevertheless, Japanese advocates of Ancient Formulas medicine felt that the harsh effects of these drugs on patients' bodies paralleled the harshness of many of Zhang Zhongjing's formulas and that by using these drugs they were following the spirit of Zhang Zhongjing's style of medical practice. The influential Ancient Formulas doctor Yoshimasu Tōdō 吉益東洞 argued that Zhang Zhongjing's therapeutic style was based on vomiting, sweating and purging therapies because the violent effects of drugs (*menken* 瞑眩) were essential to expel the poison of disease.[23] This idea of *menken* became a central element of Japanese medical discourse on the efficacy of sublimated mercurial drugs.

Kako Kakushū 加古角洲, an early nineteenth-century doctor who based his ideas closely on those of Yoshimasu Tōdō, argued that syphilis needed to be understood in terms of Tōdō's doctrine that "all diseases arise from a single poison" (*manbyō ichidoku* 萬病一毒). He therefore criticized his contemporaries' reliance on specific anti-syphilitic drugs such as smilax rhizome and Five Treasures Elixir (*gohōtan* 五宝丹) and adopted an aggressive approach to treatment based on sweating, vomiting, purging, mercurial, and arsenical formulas.

22 Dohi 1921: 83.

23 Trambaiolo 2014: 94–95.

He understood the efficacy of mercurial drugs in terms of their general ability to "melt and transform deeply buried stiff and stagnant poisons."[24]

Consistent with his belief that the nature of syphilis was not radically different from that of other diseases, Kako Kakushū argued that the use of drugs like *keifun* and *seiseinyū* should not be restricted to syphilis patients alone.[25] His contemporary Ishibashi Masaaki 石橋正炳 similarly argued that *seiseinyū* could be used as an effective treatment for patients suffering from longstanding bodily pain, malignant swellings, or malignant sores that had proven resistant to other forms of treatment: in such cases, he claimed, treatment should be based on the manifest symptoms rather than on speculation about underlying causes, and it was thus needless to discuss whether or not the patient's suffering was truly due to "syphilis".[26] This type of reasoning provided a principled justification for the use of mercurial drugs to treat a wide variety of illnesses.

Nevertheless, the use of these drugs in practice remained closely associated with syphilitic categories of diagnosis. Most patients remained wary of the harsh effects of mercurial drugs, and the understanding of syphilis as a disease whose symptoms were both severe and difficult to treat motivated patients to submit to much harsher courses of therapy than they would otherwise have been willing to accept.

The experience of Japanese syphilis patients is vividly reflected in the following account recorded by the nineteenth-century Osaka doctor Funakoshi Kinkai 船越錦海, who devoted himself to syphilis medicine after his own experience of suffering from the disease:

> My parents also contracted this disease and did not live out their natural span: my father departed this world at the age of twenty-nine and my mother at forty-four. I too suffered from this disease for several years during my youth. I used all sorts of medicines without the slightest success. I therefore described the details of my illness to a doctor and begged him: "Rather than suffering like this for a long time, I would consider a quick death as a blessing. Even the harshest of drugs holds no terrors for me. Please, give me a harsh treatment of the sort that only one in ten people survive."
>
> The doctor replied: "In that case, from among the *keifun* medicines you should use Seven Treasures Pills (*shichihōgan* 七宝丸)." He told me to take one week's worth of pills. By the fourth day, the insides of my mouth were swollen and painful. Thinking it would be difficult to consume the remaining three days' worth of pills with my mouth in pain, I took all the remaining pills on the morning of the fifth day. Beginning that night, my mouth began to fester severely, and each day I spat out two *shō* 升 of saliva. It continued like this

24 Kako 1808: *fugen*, 1b–3a.

25 Kako 1808: *furoku*, 16a; cf. also 6a–7a.

26 Ishibashi 1810: 19a–20a; *furoku*, 2a.

for more than thirty days. My mouth gradually recovered, but the disease poison did not diminish. The doctor said: "This is because the strength of the drugs was insufficient. You should take more Seven Treasures Pills." I therefore attacked the disease from the eleventh month until the sixth month of the following year, all without the slightest success.

By this time my body was debilitated and exhausted, just skin and bones. I ceased to consume drugs and ate meat for about sixty days. My strength recovered and my flesh grew back, but the sores grew increasingly severe. After this I tried inhaling medicines (*kagigusuri* 嗅薬) and after about six or seven days I began to spit out saliva. After more than fifty days, I partly recovered from the poison of the sores. But I did not recover fully, so I stopped this as well. After I ceased treatment, the disease poison gradually increased, and by the third month of the following year my suffering and pain were double what they had been originally.[27]

3 Chen Sicheng 陳司成 and *seiseinyū*

The Chinese treatise that had the greatest influence over eighteenth-century Japanese doctors' use of antisyphilitic mercury chloride compounds was Chen Sicheng's *Meichuang milu* 黴瘡秘錄 (Secret Record of Syphilis, 1636). Chen belonged to a family from Haining that had been practising medicine since the time of his eighth-generation ancestor, a minor official involved in the administration of the government salt monopoly.[28] His interest in syphilis developed after a friend contracted the disease while staying in the town of Hulin for the provincial-level civil service examinations. Later in life, when Chen found himself without the money needed to pursue an official career and decided to devote himself exclusively to the study and practice of medicine, his travels as a doctor provided him with ample opportunities to refine his understanding of syphilis, and his *Meichuang milu* represented the culmination of twenty years of observation and reflection.[29]

Chen Sicheng's treatise was largely forgotten in China after its initial printing, but it was reprinted twice in Japan during the eighteenth century (1725, 1774) and exercised considerable influence over Japanese doctors' treatment of syphilis. Chen's treatise included recipes for several different types of "Poison-Transforming Pill" (*huaduwan* 化毒丸) containing a mercurial drug of his own invention called *shengshengru* 生生乳 that was manufactured by a procedure similar to that for corrosive sublimate but using a number of additional ingredients (most notably the arsenical mineral *yushi* 礜石; on the identity of this

27 Funakoshi 1843, quoted in Dohi 1921: 129.

28 Chen 1994 [1636]: 5.

29 Chen 1994 [1636]: 1.

mineral, see discussion below). Known in Japanese as *seiseinyū*, this drug became one of the most popular antisyphilitic drugs of late eighteenth and early nineteenth-century Japan.

Chen Sicheng claimed that the action of *seiseinyū* was milder than that of corrosive sublimate, but not all Japanese medical writers agreed. In the early nineteenth century, Ishibashi Masaaki, influenced by Ancient Formulas ideas, agreed that *seiseinyū* was a slower and milder drug and argued that corrosive sublimate and *seiseinyū* could each be useful under appropriate circumstances.[30] By contrast, Asai Nankō 淺井南皐, a doctor who opposed Ancient Formulas medicine, had little patience for the idea that the mica and arsenic in *seiseinyū* could disperse the poison of mercury to yield a milder drug; he insinuated that Chen had exaggerated the differences among these drugs as a ploy to extract greater profits from his patients.[31] Hirano Genryō 平野元亮, the author of an early nineteenth-century popular medical manual, was also sceptical about the claims made by advocates of *seiseinyū* for its mildness, arguing that its arsenical content made it too risky to use except by direct application onto sores or by inhalation as a vapour.[32]

Although the harshness of mercurial drugs was thought to be an essential aspect of their efficacy, doctors and patients alike were wary of the risks of causing harm. Hirano Genryō proposed that doctors should seek to bring the disease-poison and drug-poison into a state of balanced conflict (*tsuriai* 對抗), since therapy could fail either by being too mild or by being too harsh.[33] He insisted that it was important to achieve the physiological response of *menken* indicated by stimulation of salivation but criticized the assumption that salivation alone was sufficient to release the poison of syphilis from the body; he warned that patients in the early stages of illness often made the mistake of using remedies that were too mild and later overcompensated for their earlier caution by turning to excessively violent mercurial treatments.[34] Conversely, he also warned that the symptoms of poisoning by mercurial drugs were sufficiently similar to those of syphilis itself that patients often mistook the effects

30 Ishibashi 1810, 1b; Appendix, 1a–b.

31 Asai 1808: 2:19a–20a.

32 Hirano 2006 [1835]: Vol. 2, 17–34.

33 Hirano 2006 [1835]: Vol. 2, 26. Hirano's writing style often juxtaposed Chinese characters with Japanese phonetic glosses (*furigana*) that would normally carry a slightly different meaning, leaving to the reader the task of reconciling the contrasting meanings. In this case, the Chinese characters imply conflict, while the Japanese phonetic gloss implies balance.

34 Hirano 2006 [1835]: Vol. 2, 26, 31. Hirano believed that failure to achieve *menken* could lead to the development of untreatable *mukumi* 腫脹 (dropsy) or *rōsai* 癆瘵 (phthisis). On the history of *rōsai*, a term that later came to mean "tuberculosis," see Johnston 1995: 43–46.

of the drug for the progression of the disease and thus increased their dosage when they should have been decreasing it.[35]

The mercurial remedies that patients used during the later stages of syphilis were colloquially known as "down the hatch medicines" (*nagekomigusuri* 投げ込み薬), as they were swallowed rapidly to reduce direct contact with the membranes of the oral cavity and lessen the associated risk of causing gum decay and loss of teeth. Drug preparations such as Chen Sicheng's Poison-Transforming Pills were coated in a layer of cinnabar that would retain its integrity while being swallowed but disintegrate as it passed through the digestive tract.[36] Japanese doctors adopted a variety of similar means of achieving the same goal. Ishibashi Masaaki recommended that medicines containing *keifun* or *seiseinyū* should be wrapped in a thick coating of gold or silver foil and swallowed without chewing, with special care and attention being necessary when giving these medicines to children younger than six or seven.[37] The eclectic doctor Tachibana Nankei 橘南谿 recommended that such medicines should be swallowed in a single gulp and followed by buns (*manjū* 饅頭) or jellies (*yōkan* 羊羹) to help physically push any remaining traces of the toxic drugs out of the oral cavity and into the stomach.[38]

Other doctors developed supplementary forms of treatment specifically to mitigate the harmful effects of mercurial drugs. Tachibana Nankei listed a number of remedies that could be taken in case the toxicity of the drug proved harsher than expected, ranging from sophisticated formulas containing *Coptis* rhizome (*ōren* 黄連), licorice root, pomegranate skins, and various other herbal ingredients, to a simple paste made from green beans boiled in water, which he recommended should be prepared in advance and kept on hand whenever these drugs were to be used.[39] Kako Kakushū possessed a secret family recipe for moderating the violence of *seiseinyū* or *soppiru*.[40] Ishibashi Masaaki argued that although the violent effect (*menken*) of the mercury drugs was inseparable from their therapeutic value, it also carried the danger of causing further decay of the flesh; he therefore advised patients to alternate mercury drugs with croton or rhubarb-based purgatives. Since it was difficult to predict how these drugs

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35 Hirano 2006 [1835]: Vol. 2, 18–23. According to Genryō, many people afflicted with syphilis misidentified their symptoms in the early stages of the disease as relating to a blood stagnation disorder and therefore relied on topical lotions and oils to "suck out the pus" or on surgical procedures such as scraping out infected material by means of a probe inserted into the male urinary tract.

36 Chen 1994 [1636]: 45–48.

37 Ishibashi 1810: 2a.

38 Tachibana 1797: 107.

39 Tachibana 1797: 111–115.

40 Kako 1808: *furoku*, 9b–10b.

would act in combination, each patient had to be observed individually in order to give the appropriate treatment.[41]

Certain hot springs were also thought to be useful for dispelling the poison of mercurial therapies from the body: since these springs were generally different from those that were used for treating syphilis itself, patients seeking this type of cure often needed to travel extensively between different hot springs and cities.[42] Developing a practical understanding of how to apply antisyphilitic mercurial drugs thus sometimes necessitated finding cures for the effects of the drugs themselves.

4 Manufacturing mercurial medicines

The popularity of Chen Sicheng's book in eighteenth-century Japan led to a demand for *seiseinyū*, but even at the beginning of the nineteenth century there was still little publicly available information about how to produce it.[43] Doctors who knew how to produce *seiseinyū* tended to keep their knowledge secret, and when they passed on their knowledge it was by personal instruction rather than through publication of instruction manuals.[44] Ishibashi Masaaki wrote in 1810 that *keifun* from Ise was inexpensive and widely available in medicine stores, but *seiseinyū* was prohibitively expensive for all but the richest patients. Even for those who could afford it, the commercially available product was uneven in quality. Patients lacked clear knowledge of how to assess the quality of the drugs they were purchasing, and they therefore ran the risk of using drugs that had been improperly prepared. According to Ishibashi, the high prices at which medicine stores were able to sell *seiseinyū* reflected not the cost of its ingredients but rather the limited diffusion of knowledge about how to select these ingredients and transform them into a useable drug.[45]

Chen Sicheng's recipe for *seiseinyū* included a number of further ingredients in addition to the mercury, alum, and cooking salt used for producing *keifun*:

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41 Ishibashi 1810: 1b–2a, 8b, 24b.

42 Suzuki 2005: 90.

43 Ishibashi 1810: *daiji*, 1a. This claim seems to suggest that the earlier printed treatises of Kurosawa Shōeki (1780) and Ōta Shin'an (1784) achieved only a limited diffusion. Ishibashi did not refer explicitly to any of the published Japanese treatises that described the production of *seiseinyū*, noting only that the production method was "described in several books" (Ishibashi 1810: *hanrei*, 1a) and he alluded to Chen Sicheng's treatise only indirectly (Ishibashi 1810: 3a).

44 Ishibashi 1810: preface, 1a–b.

45 Ishibashi 1810: *daiji*, 1a-b; 21a.

niter, green vitriol, mica, green salt, and the arsenic mineral *yoseki* 礜石. Japanese doctors regarded the inclusion of this toxic arsenic mineral as the defining characteristic of *seiseinyū* and debated its significance for the drug's efficacy. It is not clear why Chen Sicheng chose to include an arsenic mineral in his new drug. Some early modern European sources mention an alleged practice of adulterating corrosive sublimate with arsenic, but it is unclear that this practice was ever widespread, and it appears to have been regarded only as an adulteration rather than as a method of conferring desired qualities on a drug.[46] Rather than deriving inspiration from European sources, Chen most likely speculated independently that the poison of arsenic might balance the poison of mercury and reduce the toxicity of *keifun* while maintaining its efficacy against disease.

As eighteenth and nineteenth-century Japanese writers often noted, the production of these drugs could itself be a dangerous procedure. Authors of printed manuals on the preparation of sublimated mercury compounds gave advice on the need to avoid the toxic fumes that might be emitted from the reaction vessel. Ishibashi Masaaki stressed the importance of sealing the vessel tightly, both to prevent loss of product and to minimize exposure to the fumes: "If anybody should encounter its *qi*, they will experience all sorts of violent effects (*menken*)."[47] Ōta Shin'an 大田晋庵 recommended that the procedure should be performed outdoors on a clear and windless day with screens on four sides to shelter the reaction vessel from breezes, that anyone tending to the reaction vessel should cover his mouth and block his nostrils with cloth bundles containing mugwort leaves (*aigyō* 艾葉) and *Coptis* rhizome (*ōren* 黄連), and that particular care was essential to prevent the fumes from coming into contact with the eyes. As a remedy for those who had accidentally come into contact with the "poison of the medicine" (*yakudoku* 藥毒), he recommended treatment with a decoction of *Coptis* rhizome and licorice root (*kanzō* 甘草), *Coptis* Rhizome White Tiger Decoction (*ōren byakko tō* 黄連白虎湯), the juice of a radish (*daikon* 大根), or simply cold water.[48]

Until the end of the eighteenth century, methods for producing *seiseinyū* were often deliberately maintained as lineage secrets and transmitted by individual doctors only to their own direct heirs. One such secret recipe was passed down in the lineage of the Saga doctor Haruhi Gen'an 春日元庵 from his ancestor Haruhi Genryō 春日元亮, who had supposedly obtained the recipe

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46 Barchusen 1698: 194; Barchusen 1718: 209–212; Girtanner 1797: 324. I am grateful to Dagmar Wujastyk for bringing these sources to my attention.

47 Ishibashi 1810: 18b.

48 Ōta 1784: 2:2a–4a; cf. also Hanawa 1766: 33–36.

from a knowledgeable Dutch surgeon while visiting Nagasaki in 1711.[49] Haruhi Gen'an claimed that even the Dutch had treated this recipe as a secret; Haruhi Genryō and his successors had restricted its transmission to a single member of each generation of their own lineage. When Haruhi Gen'an first set eyes on a printed version of Chen Sicheng's treatise, he was shocked to discover that Chen's recipe for *seiseinyū* was strikingly similar to his own family's "secret" recipe. He concluded that the *Meichuang milu* had been falsely attributed to Chen Sicheng and that the Chinese had originally received the recipe from the Dutch.[50] Gen'an's willingness to accept this improbable conclusion highlights the growing importance in Japan of Dutch knowledge concerning antisyphilitic mercurial drugs, a topic explored further below.

Even doctors who possessed a recipe for *seiseinyū* could only make use of it if they were able to obtain starting ingredients of appropriate quality, a problem that was not always easy to solve. According to the Haruhi lineage tradition, the best mica was imported from Europe, while the Korean product was an acceptable but inferior substitute. Niter was sold in medicine shops as "white niter" (*shiro enshō* 白えんしやう), for which the best product came from Ise, or "horse tooth niter" (*baga shō* 馬牙消), for which the best product had a sweet and sharp flavor and came from Etchū or Sanuki; the niter from seaside regions was supposedly inferior. Doctors also needed to exercise great care to obtain genuine green vitriol (*ryokuban* 緑礬) from China, since the Japanese product was toxic and the "Chinese green vitriol" sold by unscrupulous medicine merchants was often in fact blue vitriol (*tanban* 胆礬).[51]

The correct selection of arsenical mineral was widely seen as critical to the quality of the final product. Chen Sicheng's recipe described this mineral as *yushi* (J. *yoseki* 礜石), a term that in China generally referred to the minerals arsenopyrite (FeAsS) and loellingite ($FeAs_2$). However, the same term was also used in Japan as a name for arsenolite (As_2O_3, otherwise known as J. *hiseki*/C. *pishi* 砒石).[52] Hanawa Hironori 塙寛度 listed the different varieties of *yoseki* available, ranging from the high-quality "peach-blossom" variety through

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49 Sōda 1985: 16–20. Sōda's article includes a partial transcription of Haruhi Gen'an 春日元庵, *Oranda shinden yōbaisō chiryōsho* オランダ新伝楊梅瘡治療書 (Book on the Treatment of Syphilis Newly Transmitted from the Dutch; n.d., probably late eighteenth or early nineteenth century). The Dutch doctor, whose name is transcribed in the Japanese text as "Seirukettan," has not been identified.

50 Sōda 1985: 17.

51 Sōda 1985: 18–20. Note that in English, the common names of blue vitriol ($CuSO_4$) and green vitriol ($FeSO_4$) give an exaggerated impression of the difference in color, as green vitriol is in fact bluish-green in color.

52 Sōda 1985: 26.

yellow and white to the low-grade grey variety.[53] Tachibana Nankei noted the availability of arsenic minerals from China and the Japanese varieties obtained as a by-product of the Iwami silver mines; although he understood that the latter was strictly *hiseki* rather than the *yoseki* listed in Chen Sicheng's original recipe, he claimed it was the best product to use as an ingredient for *seiseinyū*.[54] Ishibashi Masaaki likewise recommended using arsenolite from Iwami, noting that it was commercially marketed in Edo as a rat poison.[55]

This type of advice on the selection of ingredients illustrates both the potential and the dangers of the marketplace for Japanese doctors wishing to produce their own drugs in the late eighteenth and early nineteenth centuries. It was possible to purchase materials from the various provinces of Japan, Korea, China, or even Europe, but the ability to select appropriately from among these materials required doctors to make fine distinctions among different versions of the same product and to exercize vigilance against the possible deceptions of merchants.

5 From *seiseinyū* to *soppiru*: European-style mercury drugs in Japan

Just as the reproduction and circulation of Chen Sicheng's treatise in Japan stimulated a growing demand for *seiseinyū*, the translation and circulation of European medical treatises stimulated demand for European-style sublimated mercury drugs. Beginning in the late eighteenth century, translations of European medical treatises allowed a broader range of Japanese doctors to become acquainted with European doctors' uses for corrosive sublimate (*soppiru* [Dutch *sublimaat*] or *mōshōkōtan* 猛升汞丹 ["fierce sublimated mercury elixir"]) and calomel (*karumera*, *dorushisu* [Latin *dulcis*], or *kanshōkōtan* 甘升汞丹 ["sweet sublimated mercury elixir"]). Japanese doctors recognized the similarities between the ingredients and production processes for these drugs and those for the sublimated mercury drugs of the Chinese tradition, but they continued to regard the drugs prepared according to Dutch and Chinese methods as distinct substances.

Reliable knowledge of European methods for producing sublimated mercury chlorides began to circulate more widely through the influence of the Swedish

53 Hanawa 1766: 15–16.
54 Tachibana 1797: 91–92.
55 Ishibashi 1810: 12a.

physician and natural historian Carl Peter Thunberg, who visited Japan and met with the Nagasaki interpreter and physician Yoshio Kōgyū 吉雄耕牛 in 1775–1776. Subsequent *rangaku* scholars translated European pharmacological treatises and put these treatises' recommendations into practice, providing a firmer basis of technical knowledge that by the early nineteenth century enabled Japanese doctors to substitute locally produced versions of these drugs for the expensive products imported from Europe.

Thunberg himself had brought a supply of corrosive sublimate from Holland to Japan, hoping to make a profit by selling it during his visit.[56] However, in contrast to Kaempfer's observation a century previously that the Japanese were always eager to purchase corrosive sublimate, Thunberg was unable to find buyers for his product. He ended up dividing it into small parcels and bestowing it as a gift on Japanese doctors with instructions to administer it as an aqueous solution with syrup, a method of consumption that was unfamiliar in Japan at the time but subsequently became standard among Japanese practitioners of European-style medicine.[57]

Thunberg concluded from his experience that Japanese doctors were "totally ignorant of the use and application of this sure, but at the same time dangerous, medicine"; he claimed that they "had some idea, indeed, of salivation, but thought it too difficult and dangerous."[58] Apparently neither Thunberg nor the Japanese doctors with whom he interacted were able to recognize the underlying similarity between the drug Thunberg had brought with him from Europe and the Chinese-style drugs with which they were familiar. Subsequent generations of Japanese doctors became more aware of the parallels between European and Chinese methods for the sublimation of mercury chlorides, but they hesitated to conclude that the substances prepared according to Dutch and Chinese methods were mere variants of the same drug. Indeed, they sometimes made strong claims of functional difference. Writing in the early nineteenth century, Nakagawa Shūtei 中川修亭 claimed that the corrosive sublimate he produced by European methods was ten times as effective as the *seiseinyū* his Japanese contemporaries produced by Chinese methods. Nakagawa even suggested that European-style corrosive sublimate could be used as a substitute for calomel when the latter was unavailable, implying that he regarded European-style

56 Screech 2005: 35–36, 162–163.

57 Takahashi 2002.

58 Screech 2005: 162. Eighteenth-cenury Japanese doctors were aware that mercurial drugs could induce salivation, but unlike their European contemporaries they did not necessarily view salivation as the primary mechanism of these drugs' efficacy; instead, they saw it as just one of several ways in which the *menken* of mercurial drugs could become apparent.

calomel and corrosive sublimate as more closely equivalent to each other than to the sublimated mercury drugs of the Chinese tradition.[59]

Japanese doctors sometimes found that they needed to modify the procedures described in European pharmacological treatises in order to obtain a satisfactory quality of product using the materials available to them in their own country. Nakagawa Shūtei noted that calomel prepared in Europe was subjected to as many as eight rounds of refinement through sublimation due to the fierce nature of the corrosive sublimate used as starting material; through his own investigations, he had found that the corrosive sublimate available in Japan required only three or four rounds of sublimation to produce calomel of an appropriate quality.[60] On the other hand, he straightforwardly rejected the recipes found in some European treatises for the preparation of calomel through the further sublimation of corrosive sublimate without addition of mercury, which he believed was unlikely to produce a high-quality drug. Like many Japanese doctors of his period, Nakagawa did not simply accept the authority of European medical writings but systematically tested their claims against his own practical experience.

This critical attitude that Nakagawa and other doctors showed in their reception of translated pharmacological knowledge was matched by the caution with which they evaluated imported drug materials. As they could discover by reading European pharmacological treatises, false or adulterated mercury chloride drugs were common even in Europe. It was natural to assume that this problem would only be compounded by the great distance between Europe and Japan, the lack of information about methods of production and evaluation, and the elevated prices that imported drugs could command.[61] The development of more reliable knowledge for the local production of these drugs within Japan thus promised not only a way to obtain these drugs more cheaply, but also a way to reduce the risk of encountering false or adulterated versions of drugs that were highly toxic even in their purest forms.

Yet despite this problem of false and adulterated drugs, imported samples continued to serve as points of reference against which the local product was evaluated. The Hiroshima *rangaku* scholar Nakai Kōtaku 中井厚沢, who had initially learned about Western methods for producing *soppiru* during his studies with Yoshio Kōgyū, noted that although the *soppiru* produced according to Yoshio's method had similar efficacy (*kō* 功) to the imported product, in appearance the local product was "brittle like calomel (*funsō* 粉霜)" while the imported

59 Nakagawa 1980 [1808]: 311.

60 Nakagawa 1980 [1808]: 327–328.

61 Nakagawa 1980 [1808]: 310–311.

product was "hard like a stone and comes in heavy quantities, sometimes even in lumps larger than a chicken's egg."[62] It was only later, after he had acquired sufficient knowledge of Dutch to study a range of European pharmacological treatises, that Nakai was able in his own practical investigations to produce corrosive sublimate that more closely resembled the product imported from Europe. The commercial circulation of European drugs as commodities and the textual circulation of descriptions of these drugs' methods of production were thus complementary aspects of the development of local knowledge of production techniques.

6 Conclusion

From the earliest uses of mercury chloride drugs against syphilis in China to the proliferation of different varieties of these drugs in nineteenth-century Japan, the methods of producing and using sublimated mercury chloride drugs were subject to continual experimentation and modification, as doctors and patients sought to balance the perceived need for highly toxic drugs to eliminate disease from the body against the fear of causing excessive harm. These drugs were substances of intense commercial and intellectual interest, since the circulation of medical treatises recommending the use of particular drugs often preceded these drugs' local availability and thus stimulated demand for their importation or local production. At the same time, these drugs were also an important focus of interaction between the European and Chinese medical traditions in Tokugawa Japan, highlighting the central role of material exchange in the cross-cultural encounters of early modern East Asia.

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62 Nakai 1980 [1806]: 285–286. For a similar visual comparison of locally produced and imported corrosive sublimate, see Nakagawa 1980 [1808]: 320.

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