



## K-Dramas vs

# Arsenic Poisoning Today

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Historical Korean dramas (K-dramas for short) are exciting, enticing and captivating. As viewers, our attention are drawn to moments of tension and suspense, usually centred around something that is sinister and imminent.

[Spoiler alert] *Empress Ki*, episode 51 (available on Netflix): Eunuch Golta tests a tray of food with a silver needle. All clear. He proceeds to serve the dish to Emperor Ta-Hwan who gobbles it down, smiling. Moments later, the emperor violently coughs up bright red blood and collapses to the ground.

Assassination scenes are a staple to almost all period dramas. It is not housewives alone who succumb to the addictive nature of dopamine; doctors do too. We might attribute the appeal of K-dramas to the actors' attractive looks, romanticism and the bygone lifestyle, but it really is dopamine.

So, does testing for poison with a silver needle really work?

### Origin of poison testing

During the Joseon dynasty in Korea, arsenic-sulphur compounds were used as a major ingredient of *sayak*.<sup>1</sup> *Sayak* was the poison used mainly as an execution method reserved for the royals and elites during that period.<sup>2,3</sup> It was also an ideal secret weapon for homicidal purposes, given its colourless, odourless and tasteless properties.<sup>4</sup> Arsenic can be administered in a series of small doses, with symptoms going unnoticed for a long period of time.<sup>5</sup> It is speculated that silver chopsticks were invented in Korea around 523 AD, with the intention to detect arsenic poison during meals,<sup>6</sup> after royalty in the ancient Korean kingdom became aware that silver reacts with sulphides and sulphur-based poisons, tarnishing it by forming an insoluble black deposit.

This method of poison testing is flawed, however, as it would take a significant amount of time for the arsenic sulphide in food to discolour silver. Non-sulphur-containing arsenic compounds like arsenic trioxide would also not react and thus escape detection. Furthermore, with the invention of more accurate laboratory detection tests for the poison, the need to test food with silver needles or chopsticks is now completely obsolete.

### Is arsenic poisoning still relevant today?

Arsenic is a metalloid that exists in multiple forms: elemental, gaseous (arsine), organic (arsenobetaine) and inorganic (trivalent or pentavalent arsenic). Contaminated soil, water and food are the primary sources of arsenic exposure in the general population. The World Health Organization recommends a maximum concentration of 10 parts per billion or 10 mcg/L of arsenic in drinking water. According to the Food and Agriculture Organization of the United Nations, climate change will cause more arsenic and other heavy metals from mining sites to circulate in our environment, threatening our food security.<sup>7</sup> Locally, the Singapore Food Agency (SFA) has in place regulatory requirements that involve testing of food products to ensure that maximum limits of arsenic contamination are not exceeded. For instance, the limit of inorganic arsenic is set at 0.2 parts per million for polished rice.<sup>8</sup> SFA reports that our seafood and rice products are not excluded from these tests as heavy metals are naturally occurring contaminants, though it is impossible to eliminate them entirely from our food supply.

In industry, arsenic is used to manufacture paints, fungicides and pesticides, and it is a by-product of smelting and semiconductor manufacturing. It has therapeutic uses as well. Traditionally, arsenic was used widely in the 19th century in the form of Fowler's solution to treat a range of conditions including leukaemia, syphilis, psoriasis and eczema. Arsenic trioxide is still used today to treat acute promyelocytic leukaemia, leveraging its mechanism as an inducer of apoptosis.

Though arsenic continues to be an ingredient in many non-Western traditional medicinal and homeopathic products, it is more likely an unintended contaminant. There have been health alerts published by the Health Sciences Authority in recent years to warn the public against purchasing and using unlicensed health and cosmetic products found to contain high levels of arsenic (eg, Euzema Confidence Revival Cream and TCM Recipe

Licozen Ointment). Both were advertised on online platforms, claiming to be steroid-free, 100% safe and natural treatments for eczema.

### The real symptoms of arsenic poisoning

Arsenic poisoning may be acute or chronic. Arsenic toxicity occurs from inhalation, dermal exposure and primarily by ingestion. Organic arsenic (arsenobetaine) found in seafood and fish is non-toxic whereas inorganic arsenic is toxic. Trivalent arsenic or arsenite (As[III]) is 60 times more toxic than pentavalent arsenic or arsenate (As[V]). Clinical manifestations are a result of inactivation of enzymes required in cellular energy pathways and DNA replication.

Acute arsenic poisoning occurs from accidental ingestion or deliberate self-harm. The most visible and earliest manifestation of toxicity are gastrointestinal symptoms of nausea, vomiting, abdominal pain and diarrhoea.<sup>5</sup> Vomiting of blood or losing consciousness is certainly not an instant response, and would take minimally 30 minutes to several hours for the effects to kick in at a lethal level.<sup>9</sup> Profuse diarrhoea is characteristic and the term "bloody rice water" diarrhoea has been used. Shock and cardiovascular collapse may result from massive intravascular volume depletion and blood loss. Other complications include seizures, acute encephalopathy, cardiomyopathy, prolonged QT and hepatitis.

Chronic arsenic toxicity affects virtually all body systems, with the most serious consequence being an increase in malignancies, particularly bladder and skin cancers. Clinical features vary significantly as it is dependent on the dose, form, route and duration of arsenic exposure. Non-specific abdominal pain and diarrhoea may occur. The skin is highly susceptible to the toxic effects of arsenic. Hyperpigmentation in the face, trunk or extremities occurs first, accompanied by palmar and solar keratosis. Arsenic deposits in keratin-rich tissue (ie, hair and nails) can be visible as prominent transverse white lines in the nails, also called Mees' lines. Peripheral neuropathy can develop,

together with encephalopathy and cognitive impairment. Cardiovascular complications include cardiomyopathy and blackfoot disease, which is an obliterative peripheral vascular disease of the lower limbs that was reported in Taiwan.<sup>10</sup>

A review of 17 cases of chronic arsenic toxicity in Singapore found that 14 patients (or 82% of cases) with cutaneous lesions were secondary to arsenic from Chinese proprietary medicines while the remaining three consumed well water.<sup>11</sup> In another report of three patients presenting with ulcerated skin lesions and with advanced neoplastic disease, the possibility of chronic arsenic poisoning went undetected until a history of traditional Chinese medicine use was traced.<sup>12</sup>

Arsenic concentrations should be measured if a potential source of exposure is identified with clinical features suggestive of either acute or chronic poisoning. The diagnosis of arsenic poisoning is established with an elevated urinary arsenic concentration. Blood concentrations are of limited utility as arsenic is rapidly distributed into tissues, while hair and nail samples are unreliable due to the risk of external contamination. However, as urinary arsenic tests measure both inorganic and organic arsenic forms, seafood and seaweed must be omitted from the diet for at least five days before the test is performed.<sup>13</sup>

Management of patients with suspected arsenic toxicity should be discussed with a clinical toxicologist. Acutely poisoned patients would require haemodynamic stabilisation and electrolyte replacement, likely in an intensive care setting. Removing the source of exposure is crucial. Chelating agents such as dimercapto-succinic acid (eg, Succimer) and dimercaptopropanesulphonic acid (eg, dimercaptopropane sulfonate) can enhance urinary arsenic excretion and would have a role in the management of acute toxicity. Its efficacy in chronic poisoning is not well established.

K-dramas can create a dramatic illusion of what arsenic poisoning looks like. In reality, symptoms are typically non-specific in subacute and chronic presentations. Obtaining the patient's occupational history and use of traditional and herbal medications or supplements as potential sources of arsenic exposure is crucial for early detection. Hyperpigmentation and keratotic papules are sufficient indicators of dermatological manifestations of chronic toxicity. More awareness is needed for physicians to have a high index of suspicion for early diagnosis and treatment to prevent downstream complications.

And for those wondering what happened in *Empress Ki*, the rim of the cup was poisoned, escaping the silver needle's poison detection. ♦

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