

age, sex, cigarette smoking, and alcohol consumption. No synergistic interactions of Mn and Cu with As on the risk of developing cancer at all sites combined were observed in this study. (2000, volume 2, p 57-65)

## INTRODUCTION

Arsenic is a ubiquitous element widely distributed in nature and mainly transported in the environment by water. Humans are exposed to arsenic through water, air, food, and beverages. Arsenic in seafood is high and predominantly in its organic forms which are considered less toxic than inorganic arsenic. Sources of high exposure to arsenic through ingestion include drinking water with elevated levels of inorganic arsenic, some drugs used to treat leukemia and psoriasis, and arsenic-contaminated wine. Workers from industries such as smelting and refining copper, producing and using arsenic-containing agricultural chemicals, and manufacturing glass, semiconductors, and various pharmaceutical substances may have an increased occupational exposure to air-borne arsenic.<sup>1,2</sup> The maximum contaminant level (MCL) for arsenic in drinking water set by the US Environmental Protection Agency (USEPA) is 50 ug/L.<sup>3</sup> In the US, it has been estimated that about 350,000 people may drink water containing arsenic higher than this level.<sup>4</sup>

Inorganic arsenic has been well documented as a human carcinogen of the skin and lung.<sup>1-3,5</sup> It is also involved in the development of several other cancers in humans without showing any organotropism. Two studies showed an increased mortality from lung cancer due to occupational exposures to airborne arsenic through inhalation among copper smelter workers in Anaconda<sup>6-8</sup> and Tacoma, WA.<sup>9-11</sup> Significant associations between ingested inorganic arsenic and risk from cancers of the lung and bladder have been observed in patients treated with Fowler's solution, in Moselle vintners exposed to arsenic pesticide-contaminated wine, and in persons exposed to inorganic arsenic from artesian well water.<sup>12-16</sup> Inhaled inorganic arsenic has also been found to be associated with increased mortality from bladder cancer among workers in the US and Japan.<sup>12,13</sup> Excess mortality from kidney cancer has

also been observed among copper smelter workers and patients treated with Fowler's solution.<sup>15</sup> A significantly increased mortality from stomach cancer has been reported among Swedish copper smelter workers and Moselle vintners.<sup>15-17</sup> In our previous studies, an increased mortality from cancers of all the sites of lung, liver, bladder, kidney, skin, and prostate gland combined has been observed among residents in the endemic area of blackfoot disease (BFD) in Taiwan.<sup>16-18</sup> A significant dose-response relation between long-term exposure to inorganic arsenic through drinking water and the incidence from cancers of all the sites combined, as well as the lung and bladder has also been reported in our recent cohort follow-up study.<sup>19</sup>

Zn, Cu, and Mn are essential elements which can reduce the carcinogenicity of arsenic through inhibition of free radicals induced by arsenic.<sup>20,21</sup> While some elements, such as Cd, Be, Cr, and Fe, are well-documented human carcinogens for specific chemical forms, the elements whose concentrations we examined in well water were selected based on reasons including carcinogenicity or toxicity of these elements or having synergistic effects with arsenic in developing cancers.

Although a dose-response relationship between arsenic exposure through water consumption and risk of development of various cancers was observed in previous studies carried out in BFD endemic areas and in the Lanyang Basin of northeastern Taiwan, only 1% of study subjects were affected with arsenic-related cancers. In addition, there was no solid evidence from animal experiments to support the carcinogenicity of arsenic. In order to elucidate whether arsenic is the only major exposure source in well water for high-cancer-risk groups of the Lanyang Basin, we aimed to assess the exposure to elements, including Zn, Na, Ca, Cu, Fe, Mn, Mg, Cr, Sr, Ba, Cd, Be, and B, in well water among residents in the Lanyang Basin and to evaluate the synergistic interactions between these elements and ar-