Dose-response relations between incidence rates of cancers of all sites combined, as well as those of the lung and bladder, and cumulative arsenic exposure were also observed in a cohort follow-up study.[19] Because only a few wells were shared by residents living in villages of the southwestern arseniasis-endemic area in Taiwan, median arsenic levels in well water of study villages were used to derive individual exposure to ingested inorganic arsenic in those studies. In other words, the cumulative arsenic exposure was estimated in a less precise way, which may have resulted in a non-differential misclassification of individual exposure. In the arseniasis-endemic area in northeastern Taiwan, each household had its own well for drinking water. Because arsenic contents in wells among villages showed striking variations, even though residents living in the same village had very similar socioeconomic status, lifestyles, and medical care facilities, significant differences in exposure to ingested inorganic arsenic occurred through consumption of well water. These natural experimental circumstances were considered most appropriate for the assessment of cancer risk associated with ingested inorganic arsenic. In a previous study carried out in the northeastern arseniasis-endemic area, we found a significantly increased risk of developing cancers at all sites combined, as well as those of the colon, rectum, skin, and urinary organs. These findings are consistent with those reported previously in the southwestern arseniasis endemic area.[16,18,19,26,27]

Arsenic is a well-documented human carcinogen of the skin and several internal organs. However, there is only limited evidence showing the carcinogenicity of inorganic arsenic in experimental animals.[28-30] In addition, arsenic is inactive or extremely weak in inducing genetic mutations at specific loci.[4,31] The possible modes of action for inorganic arsenic carcinogenicity might include induction of chromosome abnormalities, inhibition of DNA repair, induction of oxidative stress, and increase of cell proliferation.[32] The genotoxicity of arsenic includes changes in chromosome structure and number, increases in sister chromatid exchanges and micronuclei, gene amplification, cell transformation, and aneuploidy.[15,31-35] The role of inorganic arsenic in carcinogenesis has been hypothesized as that of a co-carcinogen such as a promoter or progressor rather than as an initiator.[30,31]

Because the evidence was far from adequate to draw definite conclusions on the exact mechanism by which inorganic arsenic induces various cancers in humans, we essentially reevaluated the carcinogenic effects of arsenic. This study aimed to assess the synergistic interactions between many elements and arsenic in well water. These elements include Zn, Na, Ca, Cu, Fe, Mn, Mg, Cr, Sr, Ba, Cd, Be, and B. Some elements such as Cd, Be, Cr, Fe, and Ni, are well-documented human carcinogens for specific chemical forms.[4] However, other elements, including Zn, Mn, and Cu, have been recognized as essential trace elements of antioxidant enzyme-superoxide dismutase (SOD) and also as being involved in the antioxidant process.[20,21] The prevalence of cerebrovascular diseases among residents in the Lanyang Basin is higher than that of the general population in Taiwan, and Na seemed to be a risk factor for these diseases.[23] Mg, Sr, B, and Ba may have toxic effects on enzymatic function, and skeletal and blood vessel systems.[36] Our study found that there were seven elements significantly correlated with arsenic in well water. However, only Mn had significant protective effects on the development of cancer. In addition, the synergistic interaction between Mn and As was not observed in this study. According to our findings, arsenic exposure through water consumption should be the major risk factor of developing various cancers among residents in the Lanyang Basin.

ACKNOWLEDGEMENTS

This study was supported by grants (NSC-86-2314-B-002-336, NSC-87-2314-B-002-005, NSC-87-2314-B-038-035) from the National Science Council, Republic of China.

REFERENCES

1. WHO. Environmental Health Criteria 18 Arsenic; World Health Organization: Geneva (1981).
2. USPHS. Toxicological profile for arsenic; Public Health