

## Department of Public Health and Environmental Medicine

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Hiroyuki Yanagisawa, *Professor*  
Shingo Yogosawa, *Assistant Professor*

Machi Suka, *Associate Professor*

### General Summary

1. Our major research projects in the 2013 academic year focused on; 1) the effects of zinc-excess ingestion on blood coagulation in Sprague-Dawley rats; 2) potential mechanisms responsible for tubulointerstitial nephropathy induced by fluoride in rats with unilateral ureteral obstruction; 3) transgenerational effects of maternal arsenic exposure; 4) molecular approaches to cancer chemoprevention with food factors; 5) platelet count and bubble formation after hyperbaric exposure; 6) development of a 14-item health literacy scale; 7) a questionnaire survey of health checkup reports; 8) a questionnaire survey on the quality of life (QOL) of menopausal women; 9) ecological studies of suicide mortality in Japan; 10) the effects of L-carnosine and its zinc complex polaprezinc on pressure ulcer healing; 11) visit-to-visit variability in systolic blood pressure predicts development and progression of diabetic nephropathy, but not retinopathy, in patients with type 2 diabetes; and 12) mental health in the workplace.

### Research Activities

#### *Experimental Medicine*

1. Effects of zinc-excess ingestion on blood coagulation in Sprague-Dawley rats  
Humans are in a zinc-subdeficient state in Japan. Therefore, zinc supplements are commercially available. However, only a few reports of the toxicity of zinc excess have been published. In our previous studies, a hemorrhagic tendency was observed in rats fed a high-zinc diet. Therefore, we focused on blood coagulation observed in rats fed a high-zinc diet.
2. Potential mechanisms responsible for tubulointerstitial nephropathy induced by fluoride in rats with unilateral ureteral obstruction  
Fluoride, an environmental pollutant, is excreted from the kidney. The toxic effects of fluoride may cause renal function to deteriorate further in animals with impaired renal function. In our previous animal experiments, ICR-derived glomerulonephritis mice, which have impaired renal function, were more severely affected by fluoride. In the present study, we used rats with unilateral ureteral obstruction causing tubulointerstitial fibrosis. We examined whether fluoride exacerbates tubulointerstitial nephropathy in rats with unilateral ureteral obstruction.
3. Transgenerational effects of maternal arsenic exposure  
Arsenic is a carcinogen in humans. Our recent study has shown that arsenic exposure of maternal C3H mice increases hepatic tumors in male offspring (F1) and grandchildren (F2). Using this model, we investigated the effects of arsenic on the target organs of arsenic, such as the lung, kidney, bladder, and testis.

#### 4. Molecular approaches to cancer chemoprevention with food factors

Carcinogenesis is closely related to lifestyle, including eating habits. For this reason we have tried to develop a preventive approach to cancer using food factors, including phytochemicals and trace elements. We have analyzed the inhibitory effects on the growth of cancer cells and its molecular mechanism. Now, we are focusing on signal transduction pathways related to carcinogenesis, such as mitogen-activated protein kinase/extracellular signal regulated kinase and phosphatidylinositol 3-kinase/Akt pathways. To establish an evidence-based cancer prevention method, we are trying to identify anticancer ingredients in foods, working alone or in combination, and to elucidate their mechanisms of action.

#### 5. Platelet count and bubble formation after hyperbaric exposure

The platelet count is related to the risk of decompression sickness. Several studies have found a decrease in platelet count after decompression. We investigated Doppler bubble detection and platelet count after hyperbaric exposure. The low bubble grade did not change with the platelet count. Our results suggest that the change in platelet count is related to the severity of decompression sickness, not the risk of decompression sickness.

#### *Epidemiology, evidence-based medicine, investigation, and medical informatics*

##### 1. Development of a 14-item health literacy scale

We developed a generic health literacy measure for Japanese adults which consists of 5 items for functional literacy, 5 items for communicative literacy, and 4 items for critical literacy.

##### 2. A questionnaire survey on health checkup reports

A Web-based survey was conducted among men and women aged 35 to 59 years (n = 424). We evaluated 5 different types of health checkup reports for understanding consumer preferences.

##### 3. A questionnaire survey of quality of life in menopausal women

A Web-based survey was conducted among women aged 45 to 59 years (n = 510). We elucidated the determinants of quality of life in middle-aged Japanese women.

##### 4. Ecological studies of suicide mortality in Japan

We described geographical variations in suicide mortality in Japan and identified, through multilevel analysis, the prefectures and areas that had significant negative and positive contextual effects on suicide risk.

##### 5. Effects of L-carnosine and its zinc complex polaprezinc on the healing of pressure ulcers

We determined the effects of L-carnosine and its zinc complex polaprezinc on the healing of pressure ulcers. The results suggest that L-carnosine and polaprezinc accelerate the healing of pressure ulcers to a similar degree over 4 weeks and that polaprezinc is effective and well tolerated in an 8-week treatment of pressure ulcers.

##### 6. Visit-to-visit variability in systolic blood pressure predicts the development and progression of diabetic nephropathy, but not retinopathy, in patients with type 2 diabetes

We performed a retrospective cohort study and analyzed whether visit-to-visit variability in systolic blood pressure can predict the development and progression of nephropathy and retinopathy independently of mean systolic blood pressure in patients with type 2 dia-

betes.

#### 7. Mental health in the workplace

Mental health in the workplace is increasingly recognized as a serious problem. Several questionnaires have been used in attempts to prevent mental illness in Japan. Concrete questions in questionnaires are important for managing stress in the workplace. The objective of this study was to analyze the association of workers' mental health with job stress and character traits.

#### Publications

**Sakae K, Agata T, Kamide R, Yanagisawa H.** Effects of L-carnosine and its zinc complex (Polaprezinc) on pressure ulcer healing. *Nutr Clin Pract.* 2013; **28**: 609-16.

**Kajihara C, Itoh K, Agata T, Suka M, Yanagisawa H.** Mental health, job stress, and character traits in Japanese male workers. *Jikeikai Medical Journal.* 2013; **60**: 55-63.

**Suka M, Odajima T, Kasai M, Igarashi A, Ishikawa H, Kusama M, Nakayama T, Sumitani M, Sugimori H.** The 14-item health literacy scale for Japanese adults (HLS-14). *Environ Health Prev Med.* 2013; **18**: 407-15.

**Yanagisawa H, Kawashima T, Furuta S, Shibasaki Y, Yotsuya O.** Plasma zinc disposition in subjects with low zinc levels following administration of Polaprezinc (zinc L-carnosin complex). *Biomedical Research on Trace Elements.* 2013; **24**: 185-9.

**Suka M, Yamauchi T, Tachimori H, Takeshima T.** Suicide trends and geographical variations in Japan. Proceedings of Joint Meeting of the IASC Satellite Conference for the 59th ISI WSC and the 8th Conference of the Asian Regional Section of the IASC; 2013 Aug 22-23; Seoul, Korea. Seoul: IASC; 2013. p. 249-55.