### Challenges of Field Medicine from Japan to The "Himalaya Model of Lifestyle-Related Diseases"

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## Field medicine-comprehensive geriatric assessments for the elderly from Japan to highlands

Human aging is universal and inevitable, but there is diversity in aging phenomena that are associated with genetic, cultural and environmental factors. We have conducted comprehensive assessments of the medical functions of community-dwelling elderly, provided effective educational guidance to promote healthy lifestyles in the elderly in Japan, and then compared these with data from other Asian and South American countries. As a result, diseases and frailty in community-dwelling elderly people were found to be influenced by ecologic differences such as the natural environment, historical background, lifestyles, personal habits, religion, and health promotion policies in the particular area. The effects of globalization on highlander's lifestyles was examined with special reference to lifestyle-related diseases, and human aging phenomena through "Comprehensive Assessment," which involves evaluations of the physical, psychosocial, and environmental factors impacting the well-being of older individuals.<sup>1)</sup>

Our medical team has carried out assessing the comprehensive geriatric functions of the community-dwelling elderly and providing efficient education to promote health state of the elderly population in Japan. Adding to the longitudinal geriatric intervention study in Japan, we also investigated older subjects living in other Asian countries.

Longitudinal cohort survey was carried out in Kahoku town (1991 ~ 2005) and in Tosa town (2004 ~ present) in Kochi, Japan. A U-shaped association was found out between home systolic blood pressure and four-year mortality in community-dwelling older men.<sup>2)</sup> J-curve relation was also found out between blood pressure and decline in cognitive function in older people living in community, Japan.<sup>3)</sup> The timed "Up and Go" test and manual button score were shown to be useful predictors of fall and functional decline in basic and instrumental ADL in community-dwelling older people.<sup>4)</sup> Effects of exercise was shown on neurobehavioral function in community- dwelling older people more than 75 years of age.<sup>5)</sup> Effects of

long-term exercise class were also shown on prevention of falls in community-dwelling elderly: Kahoku Longitudinal Aging Study. Effects of group work programs were shown on community-dwelling elderly people with age-associated cognitive decline and/or mild depressive moods: A Kahoku Longitudinal Aging Study. Those community-based geriatric assessment and preventive intervention lowered medical expenses for the elderly.

In our community-based elderly care in Japan there were many achievements recently. Annual mean blood pressure of participants decreased and prevalence of hypertension(BP>140/90)decreased (70% → 44%) from 2004 to 2012. J curve association was shown between economic status and diabetes independently of functional disability in Japanese elderly. We showed prevention of disability and depression in people with impaired glucose tolerance in the 5-year follow-up survey. Those community-based geriatric assessment and preventive intervention elongated not only total lifespan but also lifespan without disability in both kahoku and Tosa town.<sup>9)</sup>

We intended to explore new perspectives regarding how people live in high-altitude environments where oxygen levels are low and natural resources are limited. We focused on aging problems and lifestyle-related diseases because we regard these as manifestations of global environmental issues in the human body. We aimed to clarify "highland civilization" as defined by ecological and cultural adaptations to high-altitude environments, physiological adaptations, and how recent changes in lifestyle have affected quality of life (QOL) among the elderly. We would also propose a model of human-nature interactions in "highland civilization." Study sites were selected from four areas in the Himalaya-Tibet region, the Ladakh region in India, 10) the Arunachal Pradesh State in India, 11) Khaling in Bhutan, 12) and the Qinghai Province in China, 13~16) and each of which has distinct ecological and socioeconomic conditions.

Ecological and cultural adaptation in highlands was characterized as maximal and sustainable utilization of limited but diversified natural resources, flexible management for disasters notwithstanding

those vulnerability, 17) and a simple life with modest virtues. In high-altitude project the human-environment relationships were studied in three ecologically distinct zones in Himalaya-Tibet region: a forest in Arunachal Pradesh and Bhutan, the Ladakh oasis, and the grasslands of Qinghai. For example, in Arunachal Pradesh, distribution of vegetation, ethnic groups, patterns of subsistence-related lifestyle and its recent change, and alien plant invasion were described from 200 to 4000 m of altitude. 11) Survey on rural-urban migration suggested that local residents were increasingly seeking for better education and medical service as well as for non-agricultural activities with the higher cash income. This change in humanenvironment relationship caused by various factors from local to global context uniformly resulted in the rise in lifestyle-related disease such as hypertension and diabetes. 1,10,14~16,18)

The rate of old people in the total population is increasing most rapidly in Japan (23% in 2010、40% in 2060). People with disability, dementia or depression with poor quality of life are also increasing. Not only health promotion but also prevention of disability is the most important and challenging issue. We should carry out check-ups of not only lifestyle-related diseases (Diabetes, hypertension and so on), but also activities of daily living, depression and subjective quality of life in community-dwelling people.

# Effect of early diagnosis of glucose intolerance and lifestyle-modification in community-dwelling old people from Japan, Asian country to highlands

Diabetes is increasing worldwide not only in developed countries but also in developing countries. Our medical team has carried out assessing the comprehensive geriatric functions of the community-dwelling elderly including checking-up of glucose intolerance and providing efficient education to promote health state of the elderly population in Japan. Adding to the longitudinal geriatric intervention study in Japan, we also investigated older subjects living in other Asian countries.

We examined the association among glucose

intolerance (diabetes and impaired glucose tolerance), disabilities and economic status cross-sectionally and longitudinally. We further examine the effects of checking of glucose intolerance and education of lifestyle change to the improvement of glucose intolerance and prevention of disabilities longitudinally.

Longitudinal cohort survey of about 300-400 community-dwelling people was carried out in Tosa town (2004  $\sim$  present) in Kochi, Japan, in Savannakhet, Laos (2004-2006), and in high-altitude area, Ladakh in India (2009-2011).

Using the criteria of the World Health Organization, diabetes, impaired glucose tolerance (IGT), and normal glucose tolerance (NGT) were determined using 75-g oral glucose tolerance test.

The effects of globalization on lifestyles was examined with special reference to lifestyle-related diseases, and human aging phenomena through "Comprehensive Geriatric Assessment," which involves evaluations of the physical, psychosocial, and environmental factors impacting the well-being of individuals. Low functional ability of instrumental activities of daily livings (I-ADL) was defined as a total score of 4 or less in five items of self maintenance (the ability to use public transport, buy daily necessities, prepare a meal, pay bills, handle banking matters, rated on a yes/no basis, full score of 5) in the Tokyo Metropolitan Institute of Gerontology Index of Competence. Depressive state was defined as a Geriatric Depression Scale (GDS-15) score of 10 or more, and depressive tendency was defined as GDS-15 score of 6 or more.

Diabetes, IGT and NGT were determined and I-ADLs and depressive status and serum lipid levels were examined in 258 community-dwelling Japanese elderly aged 60 years (male/female: 120/138,73.4 years) in Tosa, Japan, in 2006. People with diabetes had lower instrumental activities of daily livings (I-ADL) and higher prevalence of depressive feelings. The economic status was classified into low (n = 64), moderate (n = 133) and high (n = 61) according to monthly income by the lower 25th percentile of 65 000 and the upper 25th percentile of 150 000 Japanese yen. The low and high economic groups were associated

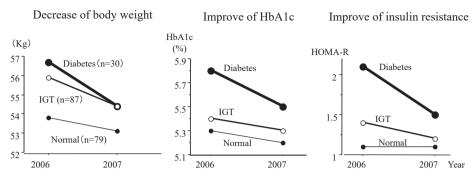


Figure 1 Lifestyle changes after oral glucose tolerance test improve glucose intolerance in Tosa, Japan (Okumiya K et al: JAGS 2008)

with diabetes independently with low functional ability (first model), depressive state (second model) or dyslipidemia (third model) by multiple logistic regression adjusted for age, sex and obesity.<sup>19</sup>)

In 2006 in Tosa, OGTTs were conducted in 418 community-dwelling elderly Japanese aged 60 or more (174 men and 244 women, mean age 73.0) to detect early DM or IGT. Fifty elderly people were found to have DM and 135 IGT at the first time, and 233 NGT. The 185 people with DM or IGT were individually contacted, lifestyle changes of dieting and exercise were recommended, and their family doctors were informed of the results of their OGTT. Body weight, HbA1c, fasting blood sugar, fasting insulin, and homeostasis model assessment ratio (HOMA-R) improved in the follow-up survey after one year. Lifestyle changes after oral glucose tolerance test improved glucose intolerance in community-dwelling elderly people after 1 year (Figure 1).200 We showed prevention of disability in I-ADL in people with impaired glucose tolerance in the 5-year follow-up survey in Tosa, Japan. 21,22)

We also investigated older subjects living in other Asian countries and compared with those in Japan. High prevalence of diabetes mellitus was disclosed in older people in a rural area in Laos in spite of low prevalence of obesity.<sup>23)</sup> There the close association was seen between low economic status and glucose intolerance in elderly subjects. <sup>24)</sup> Fragility to rapid lifestyle change was suggested as the trade off of adaptation to low Calorie diet. Improvement in obesity

and glucose tolerance was shown in elderly people after lifestyle changes 1 year after an oral glucose tolerance test in a rural area in Lao People's Democratic Republic.<sup>25)</sup>

Highlands are the places where people have built specific means of livelihood and unique cultures to survive in challenging environment with thin air and limited ecological resources over the generations. Life. aging, disease and death are closely linked to lifestyle and environmental condition in the Himalaya/Tibet. Communities in the highlands have kept the interaction with those in lowlands in balance. However, in recent years, the wave of globalization has rushed over highlands and urbanization and environment destruction are expanding. Lifestyle-related diseases, such as diabetes and hypertension, are increasing quickly with the elongation of longevity and changes in lifestyle worldwide. Highlands may be fragile, and are possibly the area most susceptible to the effects of globalization. The effects have also reached living environments of highlanders, such as migration to cities from village communities, decrease in physical activity due to spread of motorbikes and drastic decline in forest and grass cover. As a result of extended life spans and change in lifestyle, the number of so-called civilization diseases such as hypertension and diabetes may be increasing. There is a possibility that highlanders are vulnerable to aging and lifestyle related diseases by the change of lifestyles because of hypoxic stress, high levels of ultraviolet radiation or high oxidative stress or others. On the other hand, there

remains the local knowledge like spirit of cooperation within communities and healing of mind through the network of religious activities in highlands.

The change in human-environment relationship caused by various factors from local to global context uniformly resulted in the rise in lifestyle-related disease such as hypertension and diabetes in highlands.

The "Himalaya model of lifestyle-related diseases" and "Diabetes acceleration model "was developed (Figure 2).<sup>26-28)</sup> The background of the association of diabetes with high hemoglobin and oxidative stress was considered as trade-off of hypoxic adaptation with aging process.<sup>15)</sup> People with glucose intolerance had lower I-ADL, but lower prevalence of depressive feelings and higher subjective quality of life in Ladakh, India.

The traditional lifestyle of highlanders was preventable of diabetes. But there was the vulnerability to diabetes by quick lifestyle change in highlanders by the effect of epigenetics. Insulin secretion was lower in Ladakh than in Japan, <sup>29)</sup> though Japanese was known to have lower insulin secretion than the other countries.<sup>30)</sup> The low insulin secretion in Ladakhy farmer may be associated with most limited availability of food resource in dry highland in the childhood of old people, i.e. the effect of epigenetics. While Tibetan urban dweller in Yushu had higher insulin secretion because of livestock farming previously, but they had much higher insulin resistance with higher prevalence of obesity than in Japan and in Ladakh.<sup>29)</sup>

We recommended lifestyle changes to people with diabetes, impaired glucose tolerance or hypertension in Ladakh (Photo 1). Their body weight, walking meter and blood pressure were checked every two weeks in local health clinics. Those 170 people were followed up during one to two years and their fasting blood sugar, HbA1c and blood pressure were improved after follow-up. Lifestyle changes after oral glucose tolerance test improved glucose intolerance in community-dwelling elderly people after 1-2 years also in Ladakh (Figure 3). People with hypertension were also followed up and their blood pressure was also improved by lifestyle change and by low amount of anti-hypertensive medicine (Figure 4). "Diabetes

acceleration model" implies not only fragility to diabetes by lifestyle change but also improvement of impaired glucose tolerance by lifestyle modification in highlanders.

In conclusion we showed the close association among glucose intolerance, disabilities and economic status. We further showed the effects of checking of glucose intolerance and education of lifestyle modification to the improvement of glucose intolerance and prevention of disabilities longitudinally in community-dwelling people in both lowlanders and highlanders. Prevention of lifestyle-related diseases and health education should be advocated, especially in high altitude dwellers, with rapidly prevailing socioeconomic globalisation.

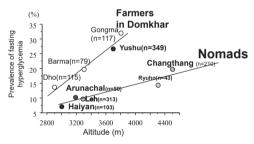


Figure 2 Association between high altitude and glucose intolerance in nomads and farmers (Okumiya K et al: BMJ open 2015)



Photo 1 Lecture on lifestyle-modification for communitydwelling old people in Domkhar village, Ladalh, India

#### Fasting blood sugar mg/dl 140 DM 135 P<0.05 130 125 120 115 **IGT** 110 P<0.05 105 Normal 100 95 2009/10 2010/11 Year

# Hemoglobin A1c 7.6 7.4 7.2 7 6.8 6.6 6.4 6.2 6.2 6.3 8 1GT Normal 9 < 0.01 9 < 0.01 1 Year

Figure 3 Improve of glucose intolerance in Domkhar, Ladakh
Diabetes (DM) (n=16 including 8 people with anti DM medicine)
Impaired glucose tolerance (IGT) (n=49)
Normal (n=97)

### Systolic blood pressure

### mm Hg 155] Hypertension 150 145 P<0.01 140 135 130 Normal 125 P<0.01 120 115 2009/10 2010/11 Year

### Diastolic blood pressure

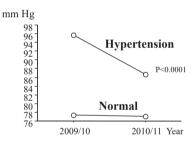


Figure 4 Improve of hypertension in Domkhar, Ladakh
Hypertension (n=89 including starting antihypertensive medicine)
Normal (n=73)

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