

Prof. Chiho Watanabe

○アブストラクトデータ

Relationship between Hg and Se levels in Taiji inhabitants

Seafood is a potential source of methylmercury (MeHg) and selenium (Se) in many coastal populations across the world. While Japan is known as one of high fish-eating populations, the consumption is not homogenous across the country; some of the coastal communities consumed much more seafood than the average Japanese, hence higher exposure to MeHg. Consuming seafood would lead not only to high mercury intake but also to high intake of several nutrients including essential trace elements as well as PUFA, and the net health impact would be the sum of these negative and positive factors.

Among other nutrients, potential role of selenium (Se) in modifying MeHg toxicity has been demonstrated by many experimental studies, but the findings from epidemiological studies have generated mixed results. This might be due to the fact that Se is not existing in one single form in the human body (as well as in mammalian body), and the physiological/toxicological roles of this element varies with the chemical form, hence, measurement of the total Se may provide insufficient information regarding the potential interaction with MeHg. In this presentation, data from a small whale-consuming population in Japan will be presented with regard to their mercury consumption as well as selenium nutrition. Blood samples were obtained from the adult of this population (n=111); total Hg in blood and total Se in plasma were determined with AAS and ICP-MS.

The geometric means for whole blood Hg and plasma Se were 34.2 $\mu\text{g/L}$ and 142.3 $\mu\text{g/L}$, respectively, indicating higher exposure to MeHg (than average Japanese population). A strong positive correlation existed between the whole blood Hg and whole blood as well as plasma Se concentrations. The strong correlation ($r = 0.408$) with the latter (plasma) may suggest the interrelation may not be limited to direct chemical binding. In addition to these findings, chemical speciation of plasma Se has been conducted using HPLC-ICP-MS to examine if the level of specific component of Se changes with the exposure to MeHg. Result of this evaluation will be reported, and discussion will be given in terms of comparison to the existing findings from various populations across the world.

○発表データ



Background (2)

- **Se in plasma**
 - selenoproteins Se exists as selenocystein selenoprotein P (SePP) extracellular glutathione peroxidase (exGPx)
 - albumin: Se exists as selenomethionine
- **Se speciation in fish-eating population**
 - Latvian: exGPx and SePP positively correlated with RBC-Hg (*Hagmar et al., 1998*)
 - Swedish: exGPx and SePP did not correlate with p-Se nor with fish consumption (*Huan, 1995*)
 - cf. Brazilian Amazon: B-Hg and p-Se positively correlated (*Lemire et al., 2011*)
 - Choi et al.

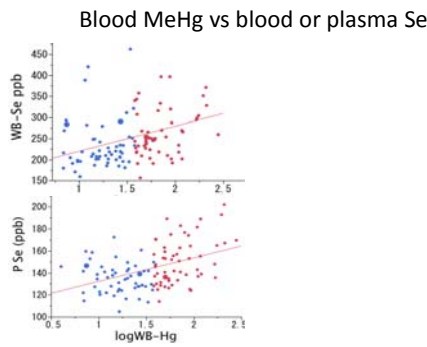
ICMGP2013 Aug 2, 2013@Edinburg

Methods

- **Participants:** inhabitants of T town in West Japan. Age >30 yr invited for a health check up. Questionnaire on basic demographic variables and food consumption pattern. - July 2010. - Blood and hair samples collected; plasma separation *on site*.
- **Lab. Measurements:** Hg – Gold-amalgamation AAS. Se – ICP-MS with collision cell; Speciation of plasma Se – HPLC-ICP-MS. Appropriate Reference Materials (NIES, Seronorm) used for QC.
- **Ethics:** Approved by Ethical committee at Graduate School of Medicine, The University of Tokyo.



ICMGP2013 Aug 2, 2013@Edinburg



ICMGP2013 Aug 2, 2013@Edinburg

Background (1)

- **Nutritional modification of MeHg toxicity;**
 - fish-eating populations - focused on those rich in fish – i.e., PUFA, I, Se
 - *Watanabe(2002)* – probably non-kinetic, inorganic Hg resulting from de-methylation and/or effects on selenoproteins might be important.
 - *Rice (2008)* – modification by “fish eating” is easier to detect than those by specific nutrient like Se, PUFA.....
- **MeHg and Se relationship using bio-indicators**
 - *Chapman (2000)* - blood levels of Hg and Se correlated most of the reviewed reports.
 - Faroe island (infants) *Choi et al. (2008)*
 - cord blood concentrations of Hg and Se positively correlated.
 - No evidence for protective role of Se on MeHg neurotoxicity.

ICMGP2013 Aug 2, 2013@Edinburg

Purpose and objectives

- Clarify the relationship between MeHg exposure and selenium indicators, blood Se plasma Se – SePP, exGPx, and albumin
- Determine if Se metabolism is modified by, or responds to, exposure to MeHg through fish consumption.

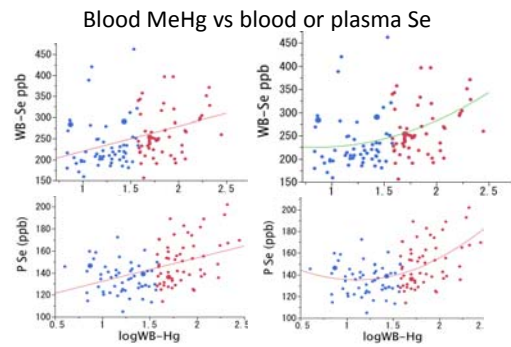
ICMGP2013 Aug 2, 2013@Edinburg

Results – 1. demographic and basic exposure status

	Total (n=111)	Males (n=45)	Females (n=66)	p values
Age (year)	62 (33-83)	64 (37-83)	60 (33-81)	0.05
Hair Hg (µg/g)	9.1 (1.2-72.2)	13.5 (2.7-65.0)	7.2 (1.2-72.2)	<0.01
WB Hg (µg/L)	34.2 (4.0-280.4)	53.1 (7.5-280.4)	25.4 (4.0-212.2)	<0.01
WB Se (µg/L)	244.2 (156.0-495.2)	255.3 (170.5-495.2)	236.8 (156.0-491.5)	0.09
Plasma Se (µg/L)	142.3 (104.7-222.2)	146.4 (113.3-202.0)	139.6 (104.7-222.2)	0.10
WB Se/WB Hg molar ratio	18.1 (2.4-139.9)	12.2 (2.4-96.6)	23.7 (3.9-139.9)	<0.01

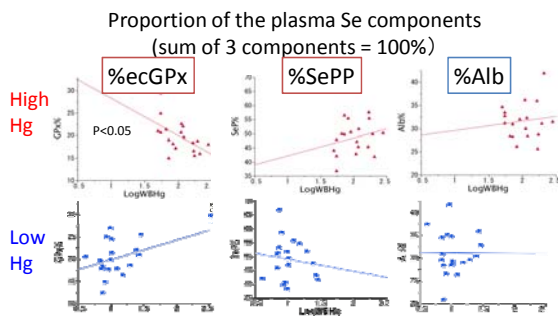
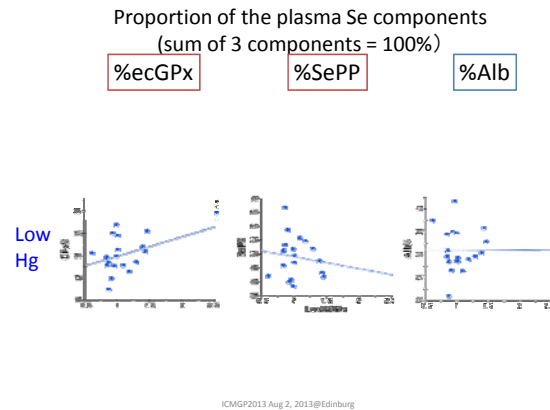
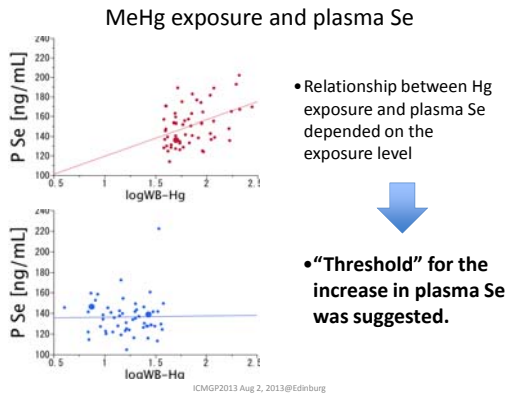
cf. In other speciation studies on fish-eaters;
Latvia RBC-Hg 0.1-44 µg/L; plasma Se 24-123 µg/L
Swedish Hg N.A.; plasma Se 60-120 µg/L

ICMGP2013 Aug 2, 2013@Edinburg



Non-linear relationship is suggested, especially for plasma Se.

ICMGP2013 Aug 2, 2013@Edinburg

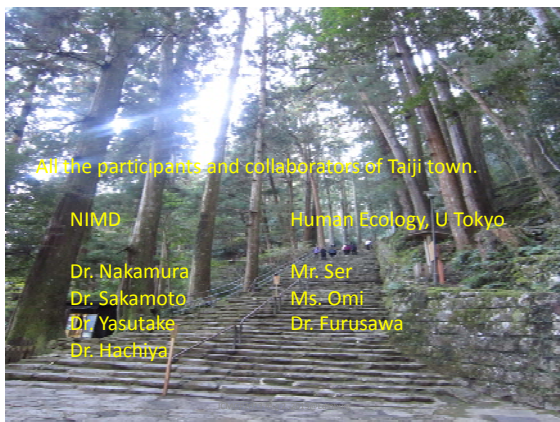


The proportion was related with MeHg exposure only in the ecGPx at higher exposure level.

Discussion 2

- **Levels of plasma Se**
 - are simply the sum of plasma components containing Se, and
 - are the consequence of several factors, mainly synthesis and secretion.
 - “**Albumin-Se**”: Se as selenomethionine, no specific role for Se. No specific mechanism could operate to change the proportion of this component; i.e., Either albumin per se ↑ and/or selenomethionine/methionine ↑
 - **ecGPx and SePP**: Se as selenocystein, specific selenoproteins. The responses would involve alteration in Se metabolism. Potential reasons for “ecGPx ↓ and SePP (↑)”
 - source: ecGPx – kidney, SePP – various (liver is the major one)
 - Functions/effects of the proteins; ecGPx – antioxidant ? SePP – very rapid turnover. Transportation of Se. antioxidant.

ICMGP2013 Aug 2, 2013@Edinburg



Discussion 1

- **Relationship between the plasma Se and MeHg exposure varied by the exposure level;**
 - existence of a “threshold” for increase in plasma Se? → cf. Positive effect of Se on motor functions
 - apparent *only in the groups with high Hg exposure* (through fish consumption) Brazilian Amazon (Lemire et al., 2011)
 - **Relationship between each plasma component of Se and MeHg exposure**
 - non-homogenous among the components;
 - % ecGPx ↓ in High-MeHg
 - % Alb: the “exposure level” dependence was the least noticeable.
- simple “co-intake” from fish may not be the case. MeHg exceeding certain level may act as a trigger for these observations in plasma Se levels.

ICMGP2013 Aug 2, 2013@Edinburg

For summing up

- **Limitations**
 - the HPLC-ICP-MS may not be specific enough to capture the “real” specific proteins.
 - physiological functions of these selenoproteins are still not exactly known.
- **Conclusion**
 - Plasma as well as RBC Se concentration increased presumably when MeHg exposure exceeded certain “threshold”.
 - Both non-specific albumin and specific two selenoproteins showed response to MeHg exposure.
 - The differential response of the two selenoproteins, ecGPx and SePP may suggest the priority of the latter, although this needs to be confirmed in future study along with elucidation of the toxicological relevance of these observations.

ICMGP2013 Aug 2, 2013@Edinburg

