First, Alteration of cardiopulmonary functions along with altitude from 3250m to 4647m

# Subjects

 The neuro-cardio-pulmonary function, including the Kohs block design test, the Up & Go, the Functional Reach and the Button tests, was examined



Ladakhi subjects living at different altitudes
(Phey village, 3250 m: 17 men and 55 women; Chumathang village, 4193 m: 29 men and 47 women; Sumdo village, 4540 m: 38 men and 57 women; and Korzok village, 4647 m: 84 men and 70 women). Result : cardiopulmonary functions among the 5 villages, including Leh at 3524 m

• The average age of residents of both genders decreased with altitude (p<0.0005).

• The average of SpO2 decreased with altitude (p<0.0001).





Result : cardiopulmonary functions among the 5 villages, including Leh at 3524 m

• Diastolic BP increased with altitude. By contrast, systolic BP did not correlate with altitude.



p<0.0001

Result : cardiopulmonary functions among the 5 villages, including Leh at 3524 m

- Hb increased with altitude.
- Height, weight and BMI decreased with altitude in both genders.







### Discussion 5 towns at different altitudes

- Altitude was found to affect neuro-cardiopulmonary functions in Ladakh, India.
- At high altitude, SpO2 decreased, whereas Hb and diastolic BP increased with altitude.
- Residents of both genders were younger and leaner at higher altitude.



Second, Alteration of cardiopulmonary functions between Ladakh (3524m) and Tosa(25m)

# Subjects



- in 40 elderly subjects (19 men and 21 women, mean age: 74.7±3.3 years) in Leh, Ladakh (altitude: 3524 m),
- for comparison with 324 elderly citizens (97 men and 227 women, mean age: 80.7±4.7 years) of Tosa, Japan (altitude: 250 m).

- Oxygen saturation (SpO2), respiration rate at rest and several cardiovascular variables, including BP, HR, conventional 12-lead ECG, and
- PWV was measured between the right arm and ankle in a supine position, using a VaSera CAVI instrument (Fukuda Denshi Co., Ltd., Tokyo, Japan).



 BP was measured 6 times (twice in a sitting, twice in a supine and twice in a standing position).

 The Up & Go test measured, in seconds, the time it took the subject to stand up from a chair, walk a distance of 3 meters, turn, walk back to the chair, and sit down again.



- This test is a simple measure of physical mobility and demonstrates the subject's balance, gait speed, and functional ability.
- A lower time score indicates a better physical mobility.

- Functional Reach, used to evaluate balance, represents the maximal distance a subject can reach forward beyond arm's length while maintaining a fixed base of support in the standing position.
- A higher score indicates a better balance.



- Manual dexterity was assessed using a panel with combinations of 10 hooks, 10 big buttons, and 5 small buttons. There were three discrete measurements of time recorded for each participant (10 "hook-on" s, 10 big "button-on-andoff"s, and 5 small "buttonon-and-off"s).
- The total manual dexterity time in seconds, defined as the button score (Button), was calculated by adding the average times for one hook-on and one big or small button-on-and-off.
- A lower button score indicates a better manual dexterity.

• The Kohs block design test and time estimation test were used to assess the overall cognitive function.





Result : comparison of neuro-cardio-pulmonary function between elderly citizens in high and low altitude towns

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•	All 6 measurements 01		Leh	Tosa	p-value
	the 6 HR	Age	74.7	80.7	<0.0001
	measurements were	BMI	23.8	24.4	N.S.
	statistically significantly higher in Leh than in Tosa.	SBP S1	155.7	153.4	N.S.
		DBP S1	91.0	87.3	0.05
		Pulse S1	76.4	70.4	<0.005
		HR with stand	13.8	9.9	<0.001
•	Changes in HR from the supine to the standing position were larger in Leh than in Tosa (13.8 $\pm$ 8.1 bpm vs. 9.9 $\pm$ 6.7 bpm, p<0.001).	Up & Go	15.0	17.6	N.S.
		Kohs	9.0	16.4	<0.0001
		TE10-1	8.5	11.5	<0.005
		TE10-2	7.9	10.0	<0.01
		<b>TE60-1</b>	42.7	57.1	<0.0005
		<b>TE60-2</b>	38.3	55.4	<0.0001
		SpO2	88.0	96.6	<0.0001
		Respiration	21.1	17.8	<0.0001

Result : comparison of neuro-cardio-pulmonary function between elderly citizens in high and low altitude towns

 In Leh at 3524 m. elderly residents had a lower SpO2 and a higher respiration rate than elderly Japanese residents in Tosa (SpO2: 88.0 ± 4.3 % vs. 96.6 ± 1.2 %, p<0.0001; RR: 21.1 ± 4.2 vs. 17.8 ± 4.2, p<0.0001).





Several reasons may account for the difference.

- First, at higher altitude, atmospheric oxygen is lower; hypoxemia stimulates sympathetic nerve activity, which is associated with an increase in BP and HR.
- Second, Ladakh is a cold desert and its environmental temperature drops as low as -45°C in winter, whereas in summer, the temperature reaches up to 27°C, a factor that will also stimulate sympathetic activity and increase BP.

Third, it has been reported that salt intake in Ladakh people is larger than in Japanese, which may result in an exaggerated increase in syst. and diast. BP with age, compared to Japanese people.

(A report lists urinary sodium values (in nmol/24h) of 209.1 and 198.2 for males and females in Ladakh, as compared to 191.0 and 145.6 for males and female in Osaka.)

- Fourth, ACE (angiotensin-converting-enzyme) gene I/D polymorphism is reportedly associated with high-altitude disorders. It is also speculated that this polymorphism may be related to the larger increase in BP with age observed herein.
- Fifth, medical services are only now developing in Ladakh, and citizens do not have sufficient access to medicines.
- Sixth, poverty in Ladakh people is such that delivery of electric power is insufficient.

Lastly, Leh, the capital of Ladakh, was once the central meeting-point for trade caravans from Central Asia and the plains of India. The main religion is Tibetan Buddhism and many monks practice it in its original form. Cultural differences between Ladakh and Japan may also contribute to the differences in the effect of aging on BP.

# **SpO2 & BP**

#### Ladakh citizens at high altitude

Relationship
 between SpO2 & BP
 in citizens, at high
 altitude of 3524 m, in
 Ladakh

 Citizens of the lower SpO2 show higher systolic BP. SBP



# SpO2 & PWV (CAVI) Ladakh citizens



Citizens of the lower SpO2 show the larger PWV.

Chronic hypoxia induces elevated BP, and advanced atherosclerosis.

y = 16.2 - 0.093x(n = 197, r = -0.293,p<0.0005)

# **Conclusion & Discussion**

- Adaptation to high altitude was confirmed in the thorough investigation in Leh.
- Diastolic, but not systolic, BP was higher, and the increase in HR with postural change from the supine to the standing position was higher in Leh than in Tosa.
- The present study also showed that the cognitive function (estimated by the Kohs block design test) and ADL functions (scored by the Functional Reach and Button tests) were worse at high than at low altitude.

# Space & Life

# Health Watch

Predicting predictability

Complexity & Field Medicine Molecular Biology & Medicine Key words for citizens in High-altitude area: (1) Hypoxemia 低酸素血症 (2) **BP**, especially Distolic **BP** (3) Orthostatic Tachycardia (4) Congitive Impairment (5) **Depressive mood** 抑うつ (6) Biological Clock 体内時計 (7) Female 女性 (8) Arterial stiffness 動脈硬化

#### In conclusion, <u>Comprehensive Cardiovascular</u> <u>Assessment</u> is needed to achieve better Dx for a more fruitful Tx.

#### Specifically,

the effect of different environmental factors such as

(1) the weather, (2) inside and outside temperatures, (3) sunshine duration, (4) geomagnetic latitude and (5) geographical altitude, the effect of <u>lifestyle features</u> such as

6 body weight, 7 salt intake, 8 fruit and vegetable intake, 9 alcohol consumption, 10 smoking, 11 physical activity and 12 duration of sleep, as well as of 13 depression and 14 QOL scores (healthiness, mood, family relationship, financial satisfaction, life satisfaction and sense of happiness), and

the effect of neurobehavioral functions

needs to be assessed together with <u>BP changes</u>, including circadian (24-hour), circasemiseptan (3.5-day) and circaseptan (7-day) characteristics such as amplitudes (swinging), day-night ratios (dipping), morning surge and complexity of BP variability.

# What is Life ? Biological Clock and its Clinical Use

Today' topics are

- Recent progress in chronobiology
  Chronomics
- > Ecological medicine in the field
- Chronoastobiology

# Astrobiology and Chronomedicine Prof. Franz Halberg in 2007



## Chronoastrobiology

is depending a philosophy of

"Early organisms on Earth have developed and adapted oneself to the surrounding cycles on cosmos"

# Hints of nature and rules of procedure in mapping chronomes

生体リズム追求の法則

Hint 1 When we have analyzed a data series and found a new periodicity, we have to search for a near-match in the natural physical environment.

生体情報に新しい周期性を発見したとき、注意深く自 然界の counterpartを見出す努力を惜しむな。同じ周期 を自然界に確認してこそ、真実となる。

Halberg F,

Neuroendocrinol Lett, 2001

#### Repeated ambulatory monitoring reveals a Monday morning surge in blood pressure in a communitydwelling population



Murakami S, Otsuka K et al., Am J Hypertens 2004, 17 : 1179-1183.

#### LEAST-SQUARES SPECTRUM OF Kp\* (1932 - 1990)\*\*



## Hints of nature and rules of procedure in mapping chronomes 生体リズム追求の法則

Hint 2 Any old or newly observed periodicity in physics should prompt the search for something equivalent in biology.

自然界に存在する周期性は、全て生物界にも存在すると考えよ。



# Tree Ring of Sequoia



# Tree Ring of Sequoia



It seems of interest to look for a proxy marker of solar activity in tree ring widths that cover the past 2000 years or more. We have analyzed 11 sequoias and had found a period of 534 years as the most prominent feature.

#### Spectrum of original average 11 tree rings' width



#### CIRCASEMIMILLENNIAL CYCLES IN THE EMERGENCE OF PROMINENT PERSONALITIES AND IN THEIR ENVIRONMENT



A similar cycle was found in the spectrum of international battles (in log-transformed data) with a period of 499 years, as also found in human creative cultural growth.

# What is Life ? Biological Clock and its Clinical Use

## In conclusion,

- Recent progress in chronobiology
   Chronomics
- > Ecological medicine in the field
- Chronoastobiology

# Prehabilitation =未病 黄帝内経素問(約2000年前後漢)

# Restoring Full Life Chronomics REHABILITATION Recover Ability Ability

We have to try to do "prehabilitation", by using Chronomes and Chronomics.

Many Thanks, Prof. Masatoshi MURASE and his Organizing Committee of Nishinomiya-Yukawa Symposium 2007

What is Life ? The Next 100 Years of Yukawa's Dream