

## Department of Laboratory Medicine

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Masato Suzuki, *Professor*  
Sadayori Hoshina, *Associate Professor*  
Hironari Sue, *Associate Professor*  
Kenichi Sugimoto, *Associate Professor*  
Hashizume Toshihiko, *Assistant Professor*

Akihiro Ohnishi, *Associate Professor*  
Ken Kaito, *Associate Professor*  
Hiroshi Yoshida, *Associate Professor*  
Tomokazu Matsuura, *Assistant Professor*

### General Summary

Research projects in our department in 2007 were concerned with clinical physiology, clinical microbiology, clinical chemistry, clinical biochemistry, hematology, cardiology, clinical cell biology, and clinical psychiatry. Research achievements in each division are described below.

### Research Activities

#### *Clinical physiology*

The present study investigated the effects of acid-base disturbance on blood lactate kinetics, the onset of blood lactate accumulation (OBLA), the lactate threshold (LT), and the ventilation threshold (VT) during incremental cycle exercise. Nine healthy male volunteers participated in this study. Subjects were orally given  $\text{NH}_4\text{Cl}$ ,  $\text{NaHCO}_3$ , and  $\text{NaCl}$  at doses of 1.87 mM/kg body weight. Exercise was started at a load of 80 W and was subsequently increased by 10 W per minute using the ramp method until voluntary exhaustion 60 minutes after  $\text{NH}_4\text{Cl}$ ,  $\text{NaHCO}_3$ , and  $\text{NaCl}$  were administered. Both LT and OBLA were significantly higher in subjects who received acidotic treatment and were lower in subjects who received alkalotic treatment than in subjects who received control treatment. Acid-base disturbance induced differences in the blood lactate response to the same exercise load and affected LT, OBLA, and VT. Care must be taken when using LT, OBLA, and VT as indices of aerobic capacity in some patients with acid-base disorders, such as those who are undergoing hemodialysis, are obese, or have diabetes.

#### *Clinical microbiology*

The DNA diagnosis of clinical fungal infection was established with mycotic universal sequencing and applied to tissues of patient with mycosis. The minimum inhibitory concentration of fosfomycin with ciprofloxacin for multidrug-resistant *Pseudomonas aeruginosa* was measured with an oxygen potential electrode system and applied to the patient. The dioxin chemical structure was proposed for anti-inflammatory, antiproliferative agents versus the resistance mechanisms of the thermophilic bacterium *Bacillus midousuji*.

#### *Clinical chemistry*

To investigate how liver disease alters serum glycosylated proteins as markers of diabetic

control, we studied serum glycated albumin (GA), hemoglobin A1c (A1c), and, especially, the GA/A1c ratio in 255 patients with an alanine aminotransferase level greater than 35 IU/L in comparison with those in 829 patients with type 2 diabetes mellitus in a cross-sectional manner. The 255 patients with liver disease were divided into groups of 69 patients with biopsy-proven liver cirrhosis, 66 patients with chronic hepatitis, and 120 patients with fatty liver diagnosed with abdominal echography. The mean GA/A1c ratio ( $\pm$ SD) was significantly higher ( $p < 0.0001$ ) in patients with cirrhosis ( $3.71 \pm 1.03$ ) than in patients with hepatitis ( $3.03 \pm 0.45$ ) or diabetes ( $3.05 \pm 0.42$ ), whereas the mean GA/A1c ratio in patients with fatty liver ( $2.74 \pm 0.31$ ) was significantly lower ( $p < 0.0001$ ) than that in patients with diabetes. In patients with cirrhosis the GA/A1c ratio increased significantly depending upon reductions in the serum albumin level or the platelet count or both. The GA/A1c ratio was significantly correlated with other laboratory variables, such as serum levels of albumin, cholinesterase, and total cholesterol, and was weakly correlated with the blood hemoglobin level. We also followed the serum levels of GA and A1c and the GA/A1c ratio for 13 months (blood was collected 5 times) in 18 patients enrolled in this study. The coefficient of variation of the GA/A1c ratio was smaller than that of GA or A1c. The receiver operating characteristic curve of the GA/A1c ratio for patients with cirrhosis versus those with fatty liver was the most reliable between the 4 groups, and the cut-off value for patients with cirrhosis versus those with fatty liver was 2.94. These results suggest that the GA/A1c ratio could be a useful marker for the differential diagnosis of patients with abnormal serum levels of alanine aminotransferase.

#### *Clinical biochemistry*

We performed several research studies and obtained the following results.

1. Current issues of low-density lipoprotein homogenous assay were highlighted by lipoprotein analysis with a method of high-performance liquid chromatography we developed.
2. Supervised, regular exercise training for 4 months can increase adiponectin levels, but exercise for 2 months produces less significant increases.
3. Evaluation of very low density lipoprotein cholesterol is useful for monitoring lipoprotein amelioration.
4. Subanalysis of the Japanese Investigation of Kinetic Evaluation in Hypertensive Event And Remodeling Treatment Study showed that treatment with an angiotensin II receptor antagonist can prevent cardiovascular events in Japanese women.

#### *Hematology*

Abnormal chromosome patterns in multiple myeloma were compared according to gender and age. The hypodiploid pattern was most frequently found and was followed by hyper, pseudo, and tri/tetra patterns. The hypodiploid pattern was commonly found in younger patients, whereas the hyperdiploid pattern was frequently detected in older patients. In older patients, changes of +15 and -13 were most common and were followed by +11, +19, and +3 in both genders and in older patients. Deletion of a sex chromosome was found in 56% of men and 40% of women and was common

in younger patients. Band 14q32 was most common and was followed by 11q13, 1p22, and 8q24. There were many characteristics of gender and age, such as band 11q13 in men, and band 8p11 in younger patients. These results indicate several characteristics in modal number, imbalance, complexity, and breakpoints that were related to the gender and age of patients. These characteristics should be recognized when the karyotype of multiple myeloma is evaluated.

### *Cardiology*

We are studying catheter intervention for atrial fibrillation. To eliminate atrial fibrillation, segmental ostial catheter ablation (SOCA) was performed to electrically isolate the pulmonary veins from the left atrium. Our aim is to improve the method of SOCA. This year we showed the efficacy of 2 new methods of SOCA. One method is segmental pulmonary vein antrum isolation using the large lasso catheter, and the other method is reducing the recurrence of atrial fibrillation by eliminating ATP-induced transient venous conduction.

### *Clinical cell biology*

1. Immunohistochemical study of lecithin retinol acyltransferase in hepatic stellate cells in liver diseases
2. Examinations of hepatic metabolism and the toxicity of drugs by means of a mini-bioartificial liver and stable isotope compounds
3. Development of an implant-type bioartificial liver
4. <sup>13</sup>C-glucose breath test for diagnosis of insulin resistance
5. Ultrasound molecular imaging for diagnosing small cancers
6. Plasma examination for the transforming growth factor  $\beta$  activating reaction to diagnose liver damage

### *Clinical psychiatry*

We reported on the effects of psychotropic drugs (antidepressants or antipsychotics) on electroencephalography (EEG) from the viewpoint of the radioreceptor binding (histamine H1) profile.

A retrospective study is under way to clarify the clinical significance of the 6-Hz spike and wave on EEG. We have continued to investigate epileptic seizures and chronological EEG changes in mentally handicapped patients. We reported on a patient with epilepsy and a psychiatric disorder who underwent temporal lobectomy and was successfully treated and reported on a patient with abnormal behavior during sleep who likely had epilepsy. Moreover, we examined premonitory signs and symptoms as epileptic prodromes.

### **Publications**

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