## Hyperbaric exposure with high oxygen concentration inhibits growth-associated increase in the glucose level of diabetic Goto-Kakizaki rats

We have specially designed a hyperbaric chamber for animal experiments, which is an oxygen tank with an oxygen concentrator and an air compressor [1]. This hyperbaric chamber is designed to automatically maintain the elevated atmospheric pressure and oxygen concentration. Increased atmospheric pressure enhances the partial pressure of oxygen and causes more oxygen to dissolve into the blood and plasma. We postulated that the increased availability of oxygen induced by hyperbaric exposure with high oxygen concentration might have a beneficial impact on glucose metabolism. Therefore, we tested this hypothesis by exposing type 2 diabetic Goto-Kakizaki (GK) rats to hyperbaric exposure with high oxygen concentration.

GK rats are non-obese models of type 2 diabetes mellitus, developed by selective breeding of an outbred colony of Wistar rats with high glucose levels as measured by the oral glucose tolerance test [2]. Ten 5-week-old male GK rats were randomly assigned to the control (n = 5) or hyperbaric (n = 5) group. All rats were individually housed in cages of the same size. Rats in the hyperbaric group were exposed to an atmospheric pressure of 1.25 atm with an oxygen concentration of 35.0% automatically maintained by a computer-assisted system. The chamber was 180 cm long and 70 cm in diameter, making it large enough to house a number of rats (up to 20 cages) simultaneously. The rats in the hyperbaric group were exposed to the hyperbaric environment for 6 h (10:00-16:00) daily for 4 weeks. Food and water were provided ad libitum for both groups. All rats were kept in a controlled environment with fixed 12 : 12 h light : dark cycles (lights off from 19 : 00 to 07 : 00) and room temperature maintained at 22  $\pm$  2 °C. After the rats were anaesthetized with an intraperitoneal injection of sodium pentobarbital (50 mg/kg), blood was sampled. Plasma obtained by centrifugation was used for measurement of glucose level. Plasma glucose was determined by a glucose-oxidative method [3].

The glucose levels were significantly lower in the hyperbaric group at 7 and 9 weeks than in the control group (figure 1).

Exercise is known to be effective for preventing and improving impaired glucose tolerance in type 2 diabetes mellitus. Previous studies demonstrated that voluntary running exercise is effective in preventing insulin resistance in

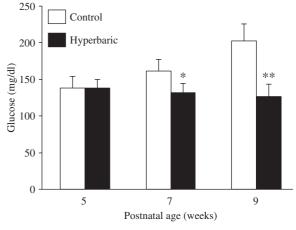


Fig. 1 Glucose levels of diabetic Goto-Kakizaki rats. Values are expressed as mean  $\pm$  standard deviation (n = 5). \*p < 0.01 and \*\*p < 0.001 compared with the control value.

streptozotocin-induced diabetic (impaired insulin secretion model) [4] and Otsuka Long-Evans Tokushima Fatty (OLETF) (insulin resistant model) [5–7] rats.

Previous studies observed that both non-obese GK [8] and obese OLETF [9] rats showed a growth-associated increase in the glucose level. Consistent with our hypothesis that the increased availability of oxygen induced by hyperbaric exposure with high oxygen concentration would have a beneficial impact on glucose metabolism, we observed that the growth-associated increase in the glucose level was completely inhibited by hyperbaric exposure with high oxygen concentration (figure 1). Hyperbaric exposure with high oxygen concentration might therefore provide a new approach to improve impaired glucose tolerance without exercise, food restriction, or drug, e.g. insulin treatment.

## K. Yasuda, N. Aoki

Department of Endocrinology, Metabolism and Diabetes Mellitus, Kinki University School of Medicine, Osaka-Sayama, Japan **T. Adachi, G. Tsujimoto** Department of Genomic Drug Discovery Science, Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan N. Gu, T. Matsunaga, N. Kikuchi, K. Tsuda

Laboratory of Metabolism, Graduate School of Human and Environmental Studies, Kyoto University, Kyoto, Japan

and A. Ishihara

Laboratory of Neurochemistry, Graduate School of Human and Environmental Studies, Kyoto University, Kyoto, Japan

## References

- 1 Ishihara A, Kawano F, Okiura T, Morimatsu F, Ohira Y. Hyperbaric exposure with high oxygen concentration enhances oxidative capacity of neuromuscular units. Neurosci Res 2005; **52**: 146–152.
- 2 Goto Y, Suzuki K, Ono T, Sasaki M, Toyota T. Development of diabetes in the non-obese NIDDM rat (GK rat). Adv Exp Med Biol 1988; **246**: 29–31.
- 3 Marks V, Lloyd K. Preservation of blood sample for glucose analysis by glucose oxidase. Clin Chim Acta 1963; 8: 326.
- 4 Reaven GM, Chang F. Effect of exercise-training on the metabolic manifestations of streptozotocin-induced diabetes in the rat. Diabetologia 1981; **21**: 415–417.

- 5 Shima K, Shi K, Sano T, Iwai T, Mizuno A, Noma Y. Is exercise training effective in preventing diabetes mellitus in the Otsuka-Long-Evans-Tokushima Fatty rat, a model of spontaneous noninsulin-dependent diabetes mellitus? Metabolism 1993; 42: 971-977.
- 6 Shima K, Shi K, Mizuno A, Sano T, Ishida K, Noma Y. Exercise training has a long-lasting effect on prevention of non-insulin-dependent diabetes mellitus in Otsuka-Long-Evans-Tokushima Fatty rats. Metabolism 1996; 45: 475–480.
- 7 Yasuda K, Adachi T, Kikuchi N et al. Effects of running exercise on fiber type distribution of soleus and plantaris muscles in diabetic Otsuka Long-Evans Tokushima Fatty rats. Diabetes Obes Metab 2005 Published Online Early: doi: 10.1111/j.1463-1326.-2005.00507.
- 8 Yasuda K, Nishikawa W, Iwanaka N *et al.* Abnormality in fibre type distribution of soleus and plantaris muscles in non-obese diabetic Goto-Kakizaki rats. Clin Exp Pharmacol Physiol 2002; **29**: 1001–1008.
- 9 Yasuda K, Ishihara A, Adachi T, Shihara N, Seino Y, Tsuda K. Growth-related changes in skeletal muscle fiber type and insulin resistance in diabetic Otsuka Long-Evans Tokushima Fatty rats. Acta Histochem Cytochem 2001; **34**: 371–382.