UNIVERSITY OF TORONTO

Department of Nutritional Sciences

Mid-Term Examination 2008

November 6, 2008

Advanced Nutrition

NFS 484H1 F/ 1484H1 F

Duration – 2 hours

General Instructions:

1. This is an open book examination; therefore students may use any aids that have been brought into the examination room.

2. The examination will be marked out of 50; however, it will constitute only 25% of your final grade.

3. Students must answer all questions in all parts of the examination.

4. All answers should be clearly written in the answer booklets provided. Please provide your answer on the right-hand side of the page only. It will be assumed that the left-hand side of the page is used for note making purposes only and material appearing on this side of the page will not be read or graded.

Good luck

Study 1 (Value: 17/50)

Background

Epidemiological studies have shown that individuals who are physically active have a lower risk of developing type 2 diabetes. Epidemiological studies have also revealed that there is a relationship between low birthweight and the subsequent development of insulin resistance and type 2 diabetes in a range of populations worldwide. However, the mechanistic basis of this relationship is not known and the relative roles played by genetic and environmental factors, and the importance of the interaction between the two, remain the subject of much debate.

Study 1 Protocol

The objective of this study was to investigate the effects of endurance exercise on insulin action in healthy female rats. Adult rats were acclimatized for one week on chow and water ad libitum, then randomly assigned to one of the following groups: sedentary control (n=12) or exercise trained (n=8). Animals in the exercise-trained groups were run on a motorized rodent treadmill for 6 weeks at gradually increasing intensity over the study period.

At the end of the 6-week exercise program, fasting plasma glucose and insulin levels were measured and no differences were observed between sedentary and exercise-trained rats. Muscle biopsies were obtained to measure muscle levels of GLUT-4 protein (Figure 1), hexokinase and citrate synthase enzyme activity levels (Table 1), as well as insulin-stimulated glucose transport activity using 2-deoxyglucose (2-DG) uptake (Figure 2). A standardized high carbohydrate meal was then given to all rats and post-prandial glucose was measured (Figure 3).

Questions:

1. Describe the effects of exercise-training on skeletal muscle GLUT-4 levels (Figure 1), total hexokinase and citrate synthase activities (Table 1), and glucose transport activity (Figure 2) in isolated skeletal muscles. (Value 3/17)

2. Describe the effects of exercise-training on post-prandial plasma glucose (Figure 3). (Value 2/17)

3. Using the data provided in this study, discuss whether hepatic glucose output and muscle glucose utilization would differ during an acute bout of exercise in the trained and sedentary rats. (Value 4/17)

4. Based on the data, discuss why chronic exercise training may be protective against the development of type 2 diabetes. (Value 8/17)

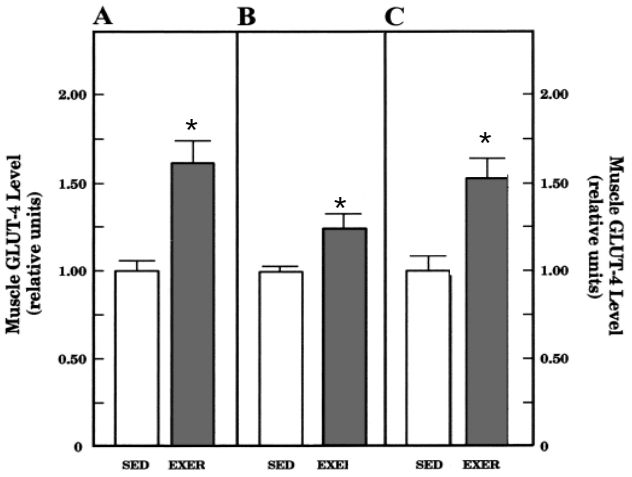

Figure 1. Effect of chronic treatment with exercise training on whole muscle levels of GLUT-4 protein in epitrochlearis (A), soleus (B) and plantaris (C) muscle preparations from lean rats. *p<0.05 vs sedentary group.

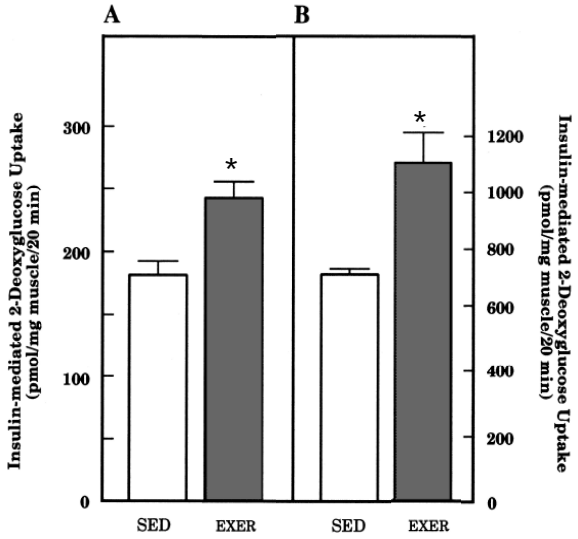

Figure 2. Effect of chronic treatment with exercise training on insulin-stimulated skeletal muscle glucose transport activity in epitrochlearis (A) and soleus (B) muscle preparations from lean rats. *p<0.05 vs sedentary group.

Table 1 Total hexokinase and citrate synthase activities in skeletal muscle of lean rats after the 6 week intervention periods

	Epitrochlearis	Soleus
Total hexokinase		
Sedentary	7.0 ± 0.2	11.4 ± 0.6
Exercise Trained	8.7 ± 0.5*	13.2 ± 0.8*
Citrate synthase		
Sedentary	58 ± 4	118 ± 3
Exercise Trained	74 ± 2*	170 ± 5*

Values are means ± SEM in nmol/mg protein/min for 8-12 animals/group. *p<0.05 compared to sedentary group.

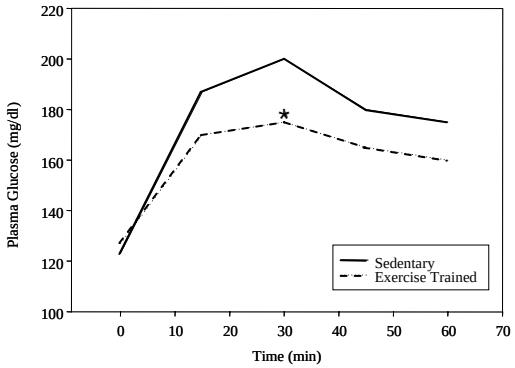

Figure 3: Plasma glucose responses to a standardized high carbohydrate meal in sedentary or exercise-trained rats. Values are means ± SEM. (*) p<0.05 versus sedentary group.

Study 2 (Value: 33/50)

Study 2 Protocol

The objective of this study was to determine the effects of a high carbohydrate, low glycemic index (GI) diet on glucose tolerance in moderately obese men who were born with either low or normal birthweights. 40 men were selected according to birthweight, with 20 of them having birthweights below the 10^{th} percentile and 20 having birthweights in the 50-75^{th} percentile. At entry into the study (baseline), all subjects had been weight stable for at least 6 months and there was no difference in average daily caloric intake between groups. All subjects consumed a high carbohydrate, low GI diet for 4 weeks. Baseline fasting plasma glucose and insulin levels (Table 2) were measured in all participants. Muscle biopsies were taken from the vastus lateralis at baseline and post-intervention to measure the expression of various proteins involved in the insulin signalling pathway (PKC zeta, p85, and p110 beta) as well as total GLUT4 protein levels (Figure 4). Forearm glucose uptake, under basal and insulin-stimulated conditions (after 20 minutes of insulin infusion), was also measured at baseline and post-intervention.(Figure 5).

Questions:

5. Describe the baseline characteristics of the study subjects (Table 2). (Value 2/33)

6. Describe the differences in insulin-signalling protein expression between normal and low birthweight individuals at baseline (Figure 4A) and after the dietary intervention (Figure 4B). (Value 4/33)

7. Using the data from this study, discuss whether you expect to see differences in muscle glucose use between the normal and low birthweight individuals following a high carbohydrate meal at baseline? (Value 4/33)

8. Describe forearm glucose uptake in study subjects at baseline and after 4 weeks of a high carbohydrate, low GI diet (Figure 5). Make sure to include comparisons of differences observed pre- and post-dietary intervention. (Value 5/33)

9. a) Using the data from this study, discuss a mechanism for the changes observed in insulin-stimulated glucose uptake in the low-birthweight group. (Value 3/33)
   b) What specific cellular measure(s)/phenomenon would you measure to confirm this mechanism? (Value 3/33)

10. Is a chronic low GI diet adequate to prevent type 2 diabetes in low-birthweight individuals relative to those with a normal birthweight? (Use data from this study to answer this question) (Value 4/33)

11. Using all the data from both studies and concepts covered in course lectures, discuss what lifestyle factor(s) you would recommend to people who were small at birth for reducing the risk of Type 2 diabetes. Be clear in explaining why you have made specific recommendations, and if people with low birthweights are better off modifying one or multiple lifestyle factors. (Value 8/33)

Table 2 Characteristics of normal and low birthweight men at baseline

	Normal Birthweight	Low Birthweight
Fat mass (kg)	15.6 ± 1.5	15.6 ± 1.5
Lean body mass (kg)	56.9 ± 1.6	54.9 ± 1.0
Fasting plasma glucose (mmol/L)	5.4 ± 0.1	6.2 ± 0.1*
Fasting plasma insulin (pmol/L)	41.3 ± 2.2	53.2 ± 3.7*

* $p<0.05$

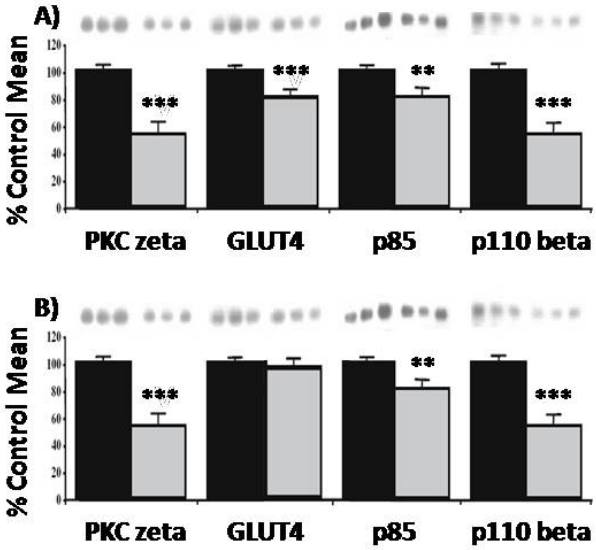

Figure 4: Total cellular protein expression in normal and low birthweight men at **A)** baseline and **B)** after 4 weeks high carbohydrate, low GI diet. Black bars, normal birthweight group; grey bars, low birthweight group. Results are expressed as means ± SEM. **p<0.01, ***p<0.001

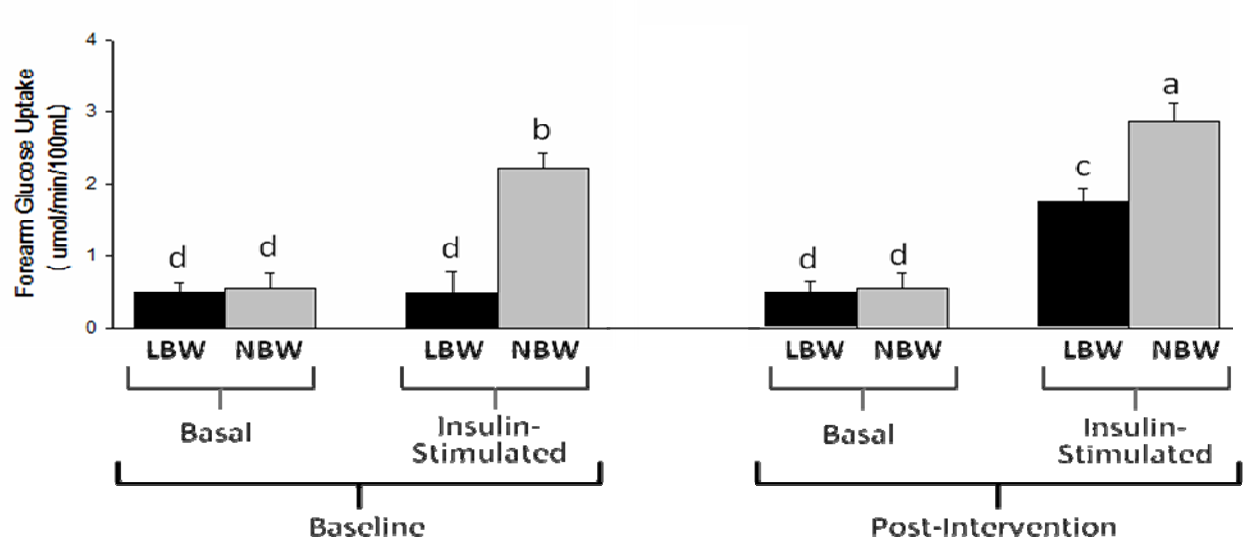

Figure 5 Forearm glucose uptake at baseline and following a 4 week high carbohydrate, low GI diet. Glucose uptake was measured under basal conditions (saline infusion) and after 20 minutes of insulin infusion. Glucose uptake is given as micromoles glucose per minute per 100 ml of forearm tissue. Results are expressed as means ± SEM. Bars with different letters are significantly different from eachother ($p<0.001$). LBW= Low Bodyweight, NBW= Normal Bodyweight