

# Glucose Pulse

## A simple method to estimate the amount of glucose oxidized during exercise in type 1 diabetic patients

MARIA PIA FRANCESCATO, MD<sup>1,2</sup>  
 LUIGI CATTIN, MD<sup>3</sup>  
 MARIO GEAT, MD<sup>3</sup>  
 ELENA TOSORATTI, MD<sup>1,2</sup>

STEFANO LAZZER, PHD<sup>1,2</sup>  
 CLAUDIO NOACCO, MD<sup>4</sup>  
 PIETRO ENRICO DI PRAMPERO, MD<sup>1,2</sup>

In type 1 diabetic patients, exercise contributes to enhance insulin sensitivity (1,2) and may help, together with diet and insulin therapy, to achieve and maintain better metabolic control (3,4). However, lack of insulin regulation during exercise leads to frequent metabolic imbalances (5). Fat and carbohydrates are the main substrates for energy production in skeletal muscle during aerobic exercise in well-fed humans (6), with their relative contribution to total energy production being a function of exercise intensity (7–10). Below the anaerobic threshold, both oxygen consumption and heart rate during exercise increase linearly as a function of exercise intensity (6). On the basis of these relationships, the aim of the present study was to verify the possibility of using heart rate to estimate the amount of glucose oxidized during exercise in type 1 diabetic patients as well as in a control group of healthy subjects.

### RESEARCH DESIGN AND METHODS

Fifteen type 1 diabetic patients (9 men, 6 women, HbA<sub>1c</sub> [A1C]  $6 \pm 1.2\%$ , reference values 4–6%) (11) aged 18–45 years (average  $38 \pm 6$ ) and 15 healthy subjects (9 men, 6 women,  $34 \pm 7$  years) gave their voluntary consent to participate after being informed on the nature, purpose, and possible risks.

Duration of diabetes and mean insulin dose were  $17 \pm 8$  years and  $0.52 \pm 0.1$  IU  $\cdot$  kg<sup>-1</sup>  $\cdot$  day<sup>-1</sup>, respectively. Average body weight and height were  $71 \pm 9$  kg and  $175 \pm 9$  cm in diabetic patients vs.  $70 \pm 9$  kg and  $175 \pm 8$  cm in healthy volunteers (BMI  $23 \pm 2$  vs.  $23 \pm 2$  kg/m<sup>2</sup>). The study was approved by the local ethical committee and was conducted according to the Declaration of Helsinki.

Inclusion criteria were no clinical evidence of chronic complications (albumin excretion rate, eye examination, deep breathing heart rate variability, Valsalva ratio, tilt test ratio), no medication other than insulin, and self-management to maintain a good metabolic balance.

Patients were asked to maintain their usual diet and insulin dose and to control their blood glucose levels according to the self-management procedures. According to their self-reported physical activity habits, volunteers were subdivided into groups as “aerobically trained” (eight patients, seven healthy), who exercised regularly at least 30 min for 3 days/week, and “sedentary” (seven patients, eight healthy), who exercised occasionally (12). The experimental sessions were performed  $3 \pm 1$  h postprandial.

Thirty minutes before the start, an extra amount of carbohydrates (mainly sugar, sugar drops, or crackers) was given

to the diabetic patients (13). Other carbohydrates (5 g each time) were given during the exercise to prevent falling of glycemia below 6 mmol/l. On average, a total amount of  $19.6 \pm 11.6$  g carbohydrates were given before and/or during the trial. No carbohydrates were given to healthy subjects.

The experiment consisted of four exercises performed on a cycloergometer (Ergomed 839E; Monark, Vansbro, Sweden) lasting 10 min each (total duration of 40 min) of increasing intensity corresponding to 0.7, 1.0, 1.5, and 2.0 W/kg body mass and 0.7, 0.95, 1.25, and 1.75 W/kg body mass in men and women, respectively.

Oxygen consumption (V<sub>O<sub>2</sub></sub>), carbon dioxide production (V<sub>CO<sub>2</sub></sub>), and heart rate were measured every 15 s using a metabolic unit (K4; Cosmed, Rome, Italy) at rest and during the last 5 min of each exercise intensity (14) and averaged over the last 2 min. Glycemia was tested before and every 5 min during exercise with reactive strips (Glucotrend; Roche Diagnostics, Basel, Switzerland). Three minutes after the end of the trial, a capillary blood sample was taken to determine lactate concentration using reactive strips (Accusport; Boehringer, Mannheim, Germany).

Respiratory quotient, assumed to be equal to the respiratory exchange ratio (RER), was calculated as the ratio between V<sub>O<sub>2</sub></sub> and V<sub>CO<sub>2</sub></sub> (12). Assuming that net protein utilization did not contribute to any significant extent to energy production during exercise (6), glucose oxidation rates (GLU<sub>ox</sub>) were calculated applying common equations (15). The following regressions were calculated for each subject: heart rate vs. V<sub>O<sub>2</sub></sub>, V<sub>O<sub>2</sub></sub> vs. RER, RER vs. GLU<sub>ox</sub>, and heart rate vs. GLU<sub>ox</sub>. For the last two regressions, the values corresponding to the highest exercise intensity were discarded when the postexercise blood lactate concentration exceeded 4 mmol/l, which is considered as anaerobic threshold. All of the glucose pulse, i.e., the ratios between GLU<sub>ox</sub> expressed per unit body weight and heart

From the <sup>1</sup>Department of Biomedical Sciences and Technologies, University of Udine, Udine, Italy; the <sup>2</sup>M.A.T.I. Centre of Excellence, University of Udine, Udine, Italy; the <sup>3</sup>Department of Clinical, Morphological and Technological Sciences, University of Trieste, Trieste, Italy; and the <sup>4</sup>Diabetologic Unit, Hospital S. Maria della Misericordia, Udine, Italy.

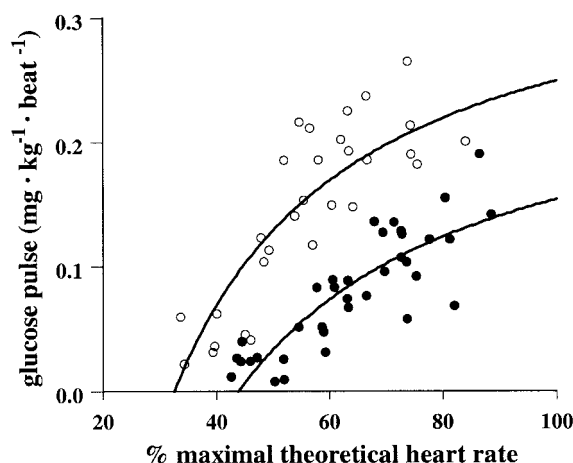
Address correspondence and reprint requests to Maria Pia Francescato, Department of Biomedical Sciences and Technologies, University of Udine, P.le Kolbe 4, 33100 - UDINE, ITALY. E-mail: mfrancescato@mail.dstb.uniud.it.

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**Abbreviations:** RER, respiratory exchange ratio.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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**Figure 1**—Glucose pulse ( $\text{mg} \cdot \text{kg}^{-1} \cdot \text{beat}^{-1}$ ) as a function of the percentage of maximal heart rate (average of eight measurements during the last 2 min of exercise). The aerobically trained type 1 diabetic patients (●) show lower values compared with the sedentary patients (○). Regression equations are as follows: glucose pulse =  $(0.504 \times \% \text{HR}_{\text{max}} - 22.11)/\text{actual heart rate}$ ; and glucose pulse =  $(0.679 \times \% \text{HR}_{\text{max}} - 22.05)/\text{actual heart rate}$  for a 36-year-old trained or sedentary patient, respectively (see text for details).

rate expressed as percentage of maximal theoretical heart rate ( $\text{HR}_{\text{max}} = 220 - \text{age}$ ) (12) were calculated.

ANCOVA was applied to investigate differences between groups. A value of  $P < 0.05$  was assumed as statistically significant.

**RESULTS**— The heart rate vs.  $\text{VO}_2$ ,  $\text{VO}_2$  vs. RER, RER vs.  $\text{GLU}_{\text{ox}}$ , and heart rate vs.  $\text{GLU}_{\text{ox}}$  relationships were statistically significant ( $R > 0.90$ ;  $P < 0.05$ ) for all of the volunteers, type 1 diabetic or healthy subjects.

No significant differences for  $\text{GLU}_{\text{ox}}$  were found between males and females ( $F = 0.07$ , NS) or between diabetic and healthy subjects ( $F = 0.06$ , NS), whereas self-reported training habits had a significant effect ( $F = 9.3$ ,  $P < 0.005$ ), with  $\text{GLU}_{\text{ox}}$  higher in sedentary subjects.

The glucose pulse of the sedentary and trained diabetic patients is plotted in Fig. 1 as a function of the percentage of  $\text{HR}_{\text{max}}$ . The two lines represent the glucose pulse that can be estimated from the relationship between  $\text{GLU}_{\text{ox}}$  and percentage  $\text{HR}_{\text{max}}$  in aerobically trained or sedentary patients.

**CONCLUSIONS**— This study shows that heart rate can be a useful physiological parameter to be used to estimate the amount of glucose oxidized during exercise. The correlation coefficients between

heart rate and  $\text{GLU}_{\text{ox}}$  were greater than 0.95 in all volunteers, both healthy and type 1 diabetic subjects, indicating a highly significant correlation between the two variables. This relationship is the basis of the “glucose pulse” concept, defined as the  $\text{GLU}_{\text{ox}}$  expressed per unit of heart rate. Endurance training leads to a lower  $\text{GLU}_{\text{ox}}$  (16,17), which was also observed in the present study with a lower glucose pulse in aerobically trained patients. The relationship between the glucose pulse and the percentage of maximal theoretical heart rate is not linear. Nevertheless, if only a heart rate below 70% of maximal is considered, the following linear equations apply:

$$\text{trained} = 0.00353 \pm 0.0023 \times \% \text{HR}_{\text{max}} - 0.1428 \pm 0.1328 \quad (n = 23, R = 0.846)$$

$$\text{and} \\ \text{sedentary} = 0.00597 \pm 0.0035 \times \% \text{HR}_{\text{max}} - 0.1801 \pm 0.1891 \quad (n = 24, R = 0.869).$$

In nonobese type 1 diabetic individuals without autonomic neuropathy, the current equations can be used to calculate glucose oxidation during exercise based on easily measurable heart rate. From these concepts, it is possible to use simple tables matching heart rate, glucose oxidation, and dietary equivalents to be ingested, thus providing a potential clinical tool for prevention of exercise-related hypoglycemia.

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