Studies on Human Postprandial Thermogenesis

Andrzej Wojciech Ziemba¹, Agnieszka Kozacz¹, Marta Steczkowska¹

1 Introduction

Human energy demand is composed of three factors: basal (resting) metabolic rate (65–70%), physical activity (approx. 20%) and heat-generating (thermogenic) effect of a meal (approx. 10%) also referred to as postprandial thermogenesis. (Delany and Lovejoy, 1996). A large body of research have already assessed the impact of various factors on postprandial thermogenesis and these involved hormonal and neurohormonal indices (insulin, adrenaline and noradrenaline) as well as biological factors (age, body weight, physical capacity). Although all of them are highly complex and interdependent, they have so far been analyzed and estimated independently. The present study concentrates on complexity and interactions of major factors affecting an increase in metabolic rate triggered by food intake.

Food consumption leads to an increase in the metabolic rate. In literature the phenomenon is referred to by a range of terms: post-prandial thermogenesis (PPT) diet-induced thermogenesis (DIT), specific dynamic action of food (SDA), thermic effect of meal (TEM), thermic caloric response to food (TRF) (Houde-Nadeau et al., 1995; Glick, 1990; McCarter, 1995). Thermogenic effect of glucose (TEG) seems to be as adequate a term because human body response to glucose intake was a frequent subject of numerous previous studies in this scientific area.

Metabolic rate increase after a single meal typically remains for several hours (Schutz et al., 1985; Blaxter, 1989). The metabolic rate rises with the amount of energy content of food but it increases to a different degree depending on food constituents. The fastest increase is triggered by carbohydrates consumption whereas protein intake causes the effect to last longest. The strongest thermal effect is produced by proteins, followed by carbohydrates and fats (Johnston et al. 2002, Westerterp, 2004). Resting metabolic rate in people on a high-

¹ Department of Applied Physiology, Mossakowski Medical Research Center, Polish Academy of Sciences, Poland
protein diet is by 6% higher than in people on low-protein diet.

According to classical views, postprandial thermogenesis is composed of two elements:

1. Obligatory thermogenesis – the energy expenditure involved in food absorption, digestion, metabolic processes and nutrients storage as glycogen and lipids (Keller, 1996).


Leblanc and Labrie (1997) complement facultative thermogenesis with a “preabsorption stage” (prior to food intake) which results from the sympathetic system stimulation as a response to taste and smell of a meal.

On the other hand, Simonsen et al., 1992 stated that adrenaline- and glucose-induced thermogenesis occurs in skeletal muscles, which is highly likely as that is where the substrate cycle occurs and these involve simultaneous catabolic and anabolic processes e.g. glycogen breakdown and synthesis (McCarter, 1995).

So far only several factors determining facultative thermogenesis have been recognized and these include obesity degree and the degree-dependent insulinemia. Similarly to insulin which has both direct and indirect impact on thermogenesis, overconsumption of carbohydrates can intensify thermogenesis indirectly by insulin or directly by sympathetic part of the autonomic nervous system.

It has been demonstrated that the sympathetic nervous system activation, expressed by elevated noradrenaline (NA) plasma concentration, is highest after glucose intake and moderate after a mixed meal, whereas after sole protein or fat intake no activation is detected (Welle et al., 1981). According to Kim et al. (1994), consumption of a single protein meal stimulates the sympathetic nervous system via α-1 adrenergic receptor, while glucose, fructose and saccharose affect the system through β-1 receptors. Although the influence of pharmacological adrenaline doses on thermogenesis has been the subject of discussion for nearly 100 years (Griffith, 1951), the impact that the hormone has on the control of postprandial thermogenesis is yet to be demonstrated (Müller et al., 1992, Cryer, 1993).

The research conducted so far confirmed that β-1 and β-2 receptors are involved in the control of thermogenesis (Blaak et al., 1993). The results suggest that skeletal muscles, provided mainly with β-2 receptors, play a significant role in thermogenic processes. Pancreatic islet β cells are stimulated through neuronal and hormonal pathways in response to food intake, which increases insulin secretion. The research on glucose impact on thermogenesis can be divided in three groups: 1) analysis of the relation between glucose concentration and thermogenesis magnitude, 2) measurement of thermogenesis and energetic balance with reference to emergency or chronic insulin administration, 3) assessment of postprandial thermogenesis impact on insulin sensitivity. Although the extensive available literature in animal research could be easily systematized in congruence with the above division, scares literature reporting research on humans makes the obtained results inconclusive. In the innumerable available studies on humans, a considerable part of the research involves the role of insulin in obesity pathogenesis. Some authors, who applied metabolic
clamp method with glucose and insulin infusions, indicate insulin participation in thermogenesis control. Landsberg (1990) asserts explicitly that insulin resistance is the mechanism which stabilizes body weight and prevents further weight gain in obesity. One of the ways of stimulating insulin secretion involves the activation of parasympathetic fibers of the vagus nerve innervating the pancreas. However, research with the infusion of glucose and atropine (muscarinic receptors antagonist) administered to obese subjects and to normal-weight people lead to the following conclusions: 1. glucose-induced hyperinsulinemia is independent of parasympathetic system stimulation and 2. Parasympathetic system inhibition does not affect the thermogenic effect of glucose (Schneeberger et al., 1991).

The picture of ‘the hormonal play’ in question is further complicated if we take into account the adrenaline influence on insulin secretion, as then, part of the observed effects may result from the interaction of both hormones or/and the usage or mobilization of the energetic materials that the hormones are affected by. People with insulinemia who fasted for 48 hours were found to demonstrate an increased thermogenic response to adrenaline (Mansell et al., 1990). Müller et al. (1992) propose that adrenaline thermogenic activity is partly inhibited by basal insulin concentration. Selberg et al. (1991) in turn, concluded that while in normoinsulinemia adrenaline increases metabolic rate by 12.9%, in hyperinsulinemia the effect is only slightly limited (8.9%). Hyperinsulinemia may therefore reduce the thermogenic effect of adrenaline.

The role of thyroid hormones in postprandial thermogenesis remains unexplained. Reduced heat-producing effect of food intake was demonstrated in rats with hypothyroidism (Iossa et al., 1996) whereas in hyperthyroid subjects the value of postprandial thermogenesis was reported to be similar to the values in healthy subjects (Randin et al. 1986).

The major factors affecting postprandial thermogenesis have already been analyzed individually and selectively and the analyses have been reported in numerous studies.

1.1 Age

Mixed diets have been observed to diminish postprandial thermogenesis (Schwartz et al., 1990; Thörne & Wahren, 1990b). The relation between thermogenesis decrease and reduced activity of the sympathetic nervous system in the elderly was confirmed by Schwartz et al. (1990). Kerckhoffss et al. also demonstrated that the process of aging is linked to decreased activity of β-adrenergic receptors in thermogenesis.

1.2 Body Weight/Obesity

The higher the degree of obesity, the more significant the reduction of postprandial thermogenesis. After a single meal or glucose intake the termogenic effect was reported to be smaller than (Katch et al., 1992), or similar to (Vernet 1986, the effect degree observed in slim subjects. In fact, the body of research demonstrating similar thermogenic response in obese as well as in normal body weight subjects is as extensive as the research reporting diminished response in obesity subjects. Valensi et al. (1998) interpret the obtained results by claiming that glucose slows fats oxidation rate in obese females with the autonomic nervous system dysfunction despite a similar thermogenic response to glucose in comparison with
adequately matched subjects with normal functioning of the autonomic system. The authors suggest that what is likely to account for this phenomenon is reduced activity of the sympathetic part of the system.

De Jonge and Bray (1997) stated that postprandial thermogenesis reduction in obese subjects is connected with changes of insulin resistance and low activity of the sympathetic system. Varied degree of insulin resistance in obesity can account for discrepancies in findings reported by various researchers. Since insulin secretion and glucose metabolism may be associated with sympathetic nervous system stimulation, alterations in insulin resistance in obesity may also lead to decrease in the sympathetic nervous system response to food intake (Cooney & Storlien, 1994).

According to Van Gaal et al. (1994) higher TEG in obese women is significantly correlated with WHR index but no such correlation with BMI has been identified. In turn, on the basis of multivariate regression analysis Camasatra et al. (1999) claim, that in healthy subjects the independent factors which affect thermogenesis include age, BMI and RQ, while major factors which modulate TEG include insulin sensitivity and, to a lesser degree, abdominal obesity.

### 1.3 Physical Activity

The role of physical activity in postprandial thermogenesis regulation remains a controversial issue. A number of studies suggest that preprandial single exercise session results in increased thermogenesis. Post-exercise thermogenesis increase was identified in slim subjects, whereas no such increase or significantly lower increase was demonstrated by obesity subjects; some researchers, however, did not find any impact of physical exercise on postprandial thermogenesis (Segal et al., 1990, 1992a, 1992b; Barneys et al., 1993). The dissimilarities of findings may stem from various energetic values, food constituents, the diet the subjects adhered to prior to research participation, time span between exercise and food intake, as well as the exercise duration and intensity and the degree of insulin resistance. Obnaka et al. (1998) propose that physical activity impact on the extent of theromgenesis results from the correlation between the rate of muscle glycogen synthesis and insulin secretion.

### 1.4 Hormonal Status

Thyroid hormone plays a key role in regulation of the basal metabolic rate, however, its impact on postprandial thermogenesis is still poorly understood (Randin et al., 1986; Al-Adsani et al., 1997; Acheson et al., 1984). Thyroid hormone is an important determinant of glucose homeostasis. Disorders of carbohydrate metabolism, closely associated with overt forms of thyroid dysfunction, are manifested by impaired glucose tolerance. Both hypothyroidism and hyperthyroidism affect insulin sensitivity (Dimitriadis et al., 2006a; Dimitriadis et al., 2006b; Maratou et al., 2009; Maratou et al., 2010; Dubaniewicz et al., 1989). Thyroid hormone is essential in maximizing the responsiveness to catecholamines at adrenergic receptor level as well as at several post-receptor steps in the catecholamine signaling pathways.
(particularly those initiated in the β-adrenergic receptors) (Wahrenberg et al., 1994; Hellström et al., 1997; Martin et al., 1992).

2 Methodology

The aim of the study was 1) to assess the role of biological and metabolic factors in the glucose-induced thermogenesis in males and females of different age, body weight and physical capacity, 2) to evaluate glucose-induced postprandial thermogenesis in hypothyroid patients in comparison with healthy people.

2.1 Study Populations

Five research series were conducted. Each series was approved of by the Local Ethics Committee.

The subjects had been recruited from free-living population by advertisement and final study group were consisted of non-smoking and non-alcohol drinking subjects of varied intensity of habitual physical activity at various sex, age and body weight. Unless stated otherwise, the exclusion criteria were as follows: diabetes mellitus, hypertension, ischemic heart disease or other clinically significant diseases in history.

Series 1. The aim of the series was to understand which of the analyzed biological factors (gender, age and exercise capacity), anthropometric factors (weight and body composition) and metabolic and neurohormonal indices have the most significant impact on thermogenic effect of glucose. 247 subjects: 112 males and 135 females were included in the study. The whole study group provided the basis for selection of the subjects analyzed in series 2, 3, 4 and 5. The subjects’ characteristics are presented in Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Age (years)</th>
<th>BMI (kg/m²)</th>
<th>VO2ₘₐₓ (l/min)</th>
<th>F% (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>31±1</td>
<td>25.2±0.4</td>
<td>2.3±0.1</td>
<td>21.0±1.4</td>
</tr>
<tr>
<td></td>
<td>(18–68)</td>
<td>(18.8–40.8)</td>
<td>(1.12–3.64)</td>
<td>(4.6–37.4)</td>
</tr>
<tr>
<td>Females</td>
<td>43.7±1.4**</td>
<td>2.5±0.6**</td>
<td>1.83±0.12**</td>
<td>27.6±1.6*</td>
</tr>
<tr>
<td></td>
<td>(16–79)</td>
<td>(17.0–43.3)</td>
<td>(0.77–3.16)</td>
<td>(8.9–44.9)</td>
</tr>
</tbody>
</table>

Table 1: The characteristics of the subjects participating in series 1 of the study. The table presents mean values with standard error (±SE) of: age, Body Mass Index (BMI), maximal oxygen consumption (VO2 max) and percentage of fat in body weight (F%). The significance of differences between males and females is marked with asterisks (*p<0.005, **p<0.0001)

Series 2. The aim of the series was to assess thermogenic effect of glucose and metabolic and neurohormonal modifications induced by oral glucose load in women of various age and similar body mass index. The research involved 22 clinically healthy, non-smoking
elderly women (group A) and 41 middle-aged women of comparable BMI (group B) who constituted control group. Table 2 presents the characteristics of the analyzed subjects.

<table>
<thead>
<tr>
<th>Females</th>
<th>Age (years)</th>
<th>Body weight (kg)</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (n=22)</td>
<td>72±1 (60–88)</td>
<td>66.7±2.4 (48.0–92.0)</td>
<td>26.3±09 (19.2–36.8)</td>
</tr>
<tr>
<td>Group B (n=41)</td>
<td>47.1±0.7** (40–57)</td>
<td>70.7±2.5 (46.0–108.0)</td>
<td>26.2±0.8 (26.2–37.5)</td>
</tr>
</tbody>
</table>

Table 2: The characteristics of the subjects participating in series 2 of the study. The table presents mean values (±SE) and value range of age, body weight and BMI. The significance of differences between groups is marked with asterisks **p<0.0001.

Series 3. The aim of the series was to compare thermogenic response to oral glucose load in sedentary lifestyle girls and physically active girls of a ballet school. The series included 13 girls, secondary school students with sedentary lifestyle (group A) and 12 ballet school girl-students (group B). Between 7 and 13 day of their menstruation cycle, all the subjects underwent oral glucose tolerance test (OGTT). Table 3 shows the girls’ characteristics.

<table>
<thead>
<tr>
<th>Indices</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>17.3±0.5</td>
<td>16.6±0.2</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>54.8±1.6</td>
<td>54.1±13</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>20.2±0.6</td>
<td>19.2±0.3</td>
</tr>
<tr>
<td>Fat (%)</td>
<td>27.5±2.5</td>
<td>16.94±1.6 *</td>
</tr>
<tr>
<td>Fat (kg)</td>
<td>15.4±1.4</td>
<td>9.2±0.9 **</td>
</tr>
<tr>
<td>Lean body mass (LBM) (%)</td>
<td>72.5±2.5</td>
<td>83.1±1.6 *</td>
</tr>
<tr>
<td>Lean body mass (LBM) (kg)</td>
<td>39.5±2.0</td>
<td>44.9±1.3 *</td>
</tr>
</tbody>
</table>

Table 3: The characteristics of the subjects participating in Series 3 of the study. The table presents mean values (±SE). The significance of differences between groups is marked with asterisks * p<0.05 **p<0.001, respectively.

Series 4. The aim of the last series was to assess the impact of body mass reduction on glucose-induced thermogenesis. Series 4 research involved 15 women, aged 31–46 (mean age 38±2) before and after 8-week weight-reducing program. Prior to the treatment, their base body mass amounted to 91.7±3.7 kg (77.5–115.5 kg) and their BMI 33.9±1.2 kg/m² (28.6±33.3 kg/m²). Weight-reducing program. The subjects were recommended to adhere to a diet of 1000 kcal (4.2 MJ) total energy value. To control their dietary compliance, the subjects kept written records of their quantity and quality of food intake. Physiological indices
were measured and tested in the 4th week of the program and on the program completion i.e. in the 8th week.

Series 5. The aim of the series was to explain whether glucose-induced postprandial thermogenesis is different in hypothyroid patients than in healthy subjects. The study population consisted of 32 women (mean age 38.5±2.38 years; mean BMI 28.9±0.91 kg/m²) with newly diagnosed and never treated hypothyroidism who were consecutively included in the study. The subjects’ hypothyroidism varied in etiology and included e.g. iodine deficiency, infections, thyroiditis (including postpartum, subacute, silence thyroiditis and Hashimoto’s) and so on. The diagnoses were based on: 1) medical history identifying among others: rapid weight gain, oedema, fatigue, mood deterioration, constipation, skin dryness and discoloration around elbows and knees; 2) TSH, fT3, fT4 determination also antibodies against specific thyroid antigens; 3) thyroid ultrasonography. The control group consisted of 34 healthy women without any thyroid disorders (mean age 38.1±1.85 years; mean BMI 27.7±0.86 kg/m²) matched for age and BMI. Subjects were excluded from the study if they had serious metabolic diseases and dysfunctions that could affect the test results (diseases that affect the basic energy expenditure, such as diabetes, serious heart disease and liver failure).

2.2 Research Procedures

Anthropometric measurements. Body fat percentage (%) was calculated by measuring four skinfold sites: biceps, triceps, subscapular and suprailiac using Durnin and Womersley formula (1974) where the equations allow for age and gender.

The assessment of glucose tolerance and neurohormonal response to oral glucose load. The subjects reported to the laboratory at 8.30–9.00 am. following an overnight fasting. The ambient temperature of the research room was kept at 22–24°C. After inserting the catheter into the basilic vein and leaving the subjects for 30-minute rest in supine position, their blood samples were taken for the measurement of basal concentration of glucose, insulin and catecholamines: adrenaline (A) and noradrenaline (NA). Oral Glucose Tolerance Test (OGTT) was then performed (75g of glucose in 200ml of water). In the 30th, 60th and 90th minute after glucose administration blood samples were taken for the concentration of glucose and insulin to be measured. Blood samples for the measurement of plasma catecholamine concentration were taken in the 90th and 120th minute after glucose intake. The measurement points were selected on the basis of the results obtained by Mathias et al. (1989), who demonstrated that the highest blood noradrenaline level occurs in the second hour of the test. During OGTT the subjects remained in a supine position throughout the whole test.

The assessment of resting metabolic rate and thermogenic effect of glucose (TEG). In all the study series, after 30-minute rest in a supine position, the subjects had their oxygen uptake (VO2) and carbon dioxide production (VCO2) measured for 20 minutes prior to glucose loading and for the last 5 minutes of each quarter of OGTT by means of SensorMedics (USA). Metabolic rate was measured every 15 minutes for 2 hours without glucose load in randomly chosen group of 10 people (control group).

Exercise capacity assessment. Maximal oxygen consumption (VO2 max) was used to assess exercise capacity. VO2 max was measured in 53 males and 42 females who performed
a graded exercise test on a cycle ergometer with the load increased every 3 minutes to volitional exhaustion. Respiratory minute ventilation and gas composition were analyzed during the 3rd minute of each load by means of SensorMedics (USA) gas analyzer.

### 2.3 Biochemical Analyses

Enzymatic blood glucose determination was performed with a commercial reagent kit (method error 1.8%) (Boehringer, Mannheim, Germany). Plasma insulin was assessed by radioimmunoassay with a reagent kit MI-130 (method error 2.1%) made by Research and Development Centre of Isotopes POLATOM (Świerk, Poland); plasma adrenaline and noradrenaline levels were determined by radioenzymatic method by Da Prada and Zurcher (1979) with Catechola reagent kit produced by Immunotech (Prague, The Czech Republic). Method error for noradrenaline and adrenaline determinations amounted to 6.8% and 4.7% respectively.

### 2.4 Calculations

For total assessment of blood glucose and insulin alterations after glucose loading the areas under the curve of glucose and insulin (BGauc and IRIauc) changes for 2 hours during OGTT were calculated (subtracting appropriate baseline values). Moreover, BGaus/IRIauc ratio was calculated. Fasting glucose and insulin concentration was used to calculate insulin resistance index (HOMA) according to the following formula:

$$\text{HOMA} = \frac{[\text{IRI}-0] \cdot [\text{BG}-0]}{22.5};$$

Energy expenditure (EE) in kJ·min⁻¹ was calculated using the obtained values of expired VO₂ and VCO₂. The value of fasting energy expenditure before glucose administration was subtracted from each E value determined after glucose loading. Overall thermogenic effect of glucose (TEG) was calculated as the area under the curve obtained during the 2-hour period following glucose load.

### 2.5 Statistical Analysis

All the collected figures are presented as mean values with standard error (±SE). To assess the normality of variables the Shapiro-Wilk test was used. Student t-test was applied to compare mean values in two analyzed groups, while the comparison of several mean values of physiological indices was made using the analysis of variance. Pearson correlation coefficients (r) were calculated in Series 1 of the study. On the basis of correlation analysis, multiple linear regression model was adopted for the relationship between BGauc and TEGauc (dependent variables) and independent (predictor, explanatory) variables divided into biological (age, gender, BMI, VO2max, %F) and hormonal & metabolic (A, NA, IRIauc, BGauc, BGauc/IRIauc) indices. −1 is the value designated for men, −0 for women. In accordance with the assumptions and indices division, the following linear regression equations were considered:

$$\text{TEG} = b + a1 \text{ GENDER} + a2 \text{ AGE} + a3 \text{ BMI} + a4 \text{ V02max},$$
where b designates the estimated intercept in the regression equations and a1, a2, a7 designate regression coefficient. In multiple regression analysis, apart from the standard analysis, stepwise regression, forward or backward, was done. Stepwise regression analysis allowed for the selection of the indices which proved to have the most significant impact on BGauc and IRIauc. In standard regression analysis two simple regression models were considered: with or without intercept (b=0). While estimating the model parameters, linear regression equation was put in the regression tables, then further values were added: standard error (SE), significance level (P), standardized coefficients BETA (which are standardized parameters of regression). For the estimate, the following values were also included: the coefficient of multiple correlation, denoted R, (designating the degree of correlation between the dependent variable and all the independent variables; it takes values between zero and one), coefficient of determination $R^2$, (measuring how much of the total variation of the dependent variable is explained by the linear regression), significance level in regression analysis P and standard error of the estimate (SEE) (depicting the average amount of variation/dispersion of the dependent variable value and the values computed from the model).

In all the analyses P values of 0.05 or less ($p<0.05$) were considered as statistically significant. Statistical analyses were made using Statistica 6 PL by StatSoft.

### 3 Results

#### Series 1. Changes of the analyzed indices in males and females during oral glucose tolerance test (OGTT).

Mean basal glucose concentration equaled 4.69±0.05 mmol/l and 4.71±0.04 mmol/l ($p>0.05$) in males and females respectively. After glucose intake the values rose significantly to reach the top level in the 60th minute of OGTT and they amounted to 7.04±0.13 mmol/l in males and 7.44±0.14 mmol/l in females ($p<0.0001$). In 120th minute of OGTT glucose concentration level remained insignificantly elevated in comparison to baseline values and equaled 5.49±0.1 mmol/l in males and 5.39±0.1 mmol/l in females respectively. The analysis of variance did not reveal any significant differences between men and women.

On the basis of glycemia curves, Bgauc in males was calculated at the mean value of 196.3±8.7 mmol·l⁻¹·min. In females the value was slightly higher and amounted to 212.4±9.6 mmol·l⁻¹·min. The difference between the values was statistically insignificant.

10.1±0.6 µU/ml and 12.3±0.7 µU/ml in males and females respectively were the baseline values of blood IRI concentrations. After glucose intake IRI concentrations rose in both genders, however, significantly higher IRI levels were identified in females than in males.
The most elevated IRI values were observed in the 60th minute of OGTT (61.9±3.1 µU/ml in males; 79.2±4.5 µU/ml in females, p<0.01). Compared to baseline values, on completion of OGTT (in 120th minute after glucose intake) insulin concentration remained elevated (it amounted to 49.5±3.0 µU/ml in males and was significantly lower than in females 70.3±4.0 µU/ml (p<0.0001).

4854±227 µU·ml⁻¹·min in males and 5611±292 µU·ml⁻¹·min in females (p<0.05) were the mean values of the area under the curve of insulin changes during glucose tolerance test (IRIauc).

Insulin resistance index HOMA calculated on the basis of fasting glucose and insulin values equaled 2.67±0.17 in males and 3.00±0.19 in females (p>0.05).

Mean resting metabolic rate in males i.e. 4.6±0.2 kJ/min was significantly higher than in females – 3.8±0.1 kJ/min (p<0.0001). After glucose administration the energy expenditure increased and remained elevated until 120th minute of the test, however, value EE in all time points proved to be significantly higher in males. TEG value in males was 54.9±4.8 kJ, while in females 36.4±2.3 kJ (p<0.0001) (Fig. 1).

![Figure 1](image-url)  
*Figure 1*: Mean values of resting metabolic rates (RMR) and energy expenditure (EE) during 120-minute OGTT in females and males. Asterisks denote statistically significant differences between men and women at particular curve points (**p<0.01, ***p<0.001).

There were no significant differences of resting adrenaline rates between males and females (0.23±0.02 nmol/l vs. 0.22±0.02 nmol/l). Glucose intake caused a significant increase of the hormone blood concentration in both genders, yet maximal A concentration was significantly higher in males (0.38±0.03 nmol/l) than in females (0.30±0.02 nmol/l) (p<0.05). Mean baseline values of basal noradrenaline level were significantly higher in females (1.40±0.09 nmol/l) than in males (0.96±0.05 nmol/l) (p<0.001).
Control studies were conducted in a group of 10 randomly chosen subjects who were
not administered glucose. As shown in Table 4, a tendency to metabolic rate decrease was
found, while glucose concentration appeared to maintain the same level for 120 minutes of
measurements.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>0</th>
<th>15</th>
<th>30</th>
<th>45</th>
<th>60</th>
<th>75</th>
<th>90</th>
<th>105</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG (mmol/l)</td>
<td>4.7±0.2</td>
<td>4.7±0.1</td>
<td>4.6±0.1</td>
<td>4.5±0.1</td>
<td>4.7±0.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EE (kJ/min)</td>
<td>4.3±0.4</td>
<td>4.0±0.4</td>
<td>3.7±0.3</td>
<td>3.8±0.2</td>
<td>4.1±0.6</td>
<td>4.0±0.7</td>
<td>3.7±0.6</td>
<td>4.5±0.6</td>
<td>4.0±0.4</td>
</tr>
</tbody>
</table>

Table 4: Mean values (±SE) of blood glucose concentration (BG) and energy expenditure in control group within 120 minutes of resting. Energy expenditure at time point 0 denotes resting metabolic rate.

Relationship, between analyzed indices. Correlation analysis indicated that BMI of the study population increased with age: $r=0.35$ ($p<0.0001$) in males and $r=0.19$ ($p<0.05$) in females. A significant correlation was also discovered between age and body fat percentage (F%): $r=0.65$, $p<0.0001$ in males and $r=0.64$ ($p<0.005$) in females. BMI in both genders was highly positively correlated with body fat % (males: $r=0.86$ and females: $r=0.65$ in, $p<0.0001$).

Physical capacity assessed on the basis of VO2max was negatively correlated with: age (males: $r=0.47$, females: $r=0.85$, $p<0.0001$), with BMI ($r=0.46$ in males, $r=0.66$ in females, $p<0.0001$) and with F% (females: $r=0.71$, $p<0.0001$, males: $r=0.97$, $p<0.05$).

Resting metabolic rate was negatively correlated with age only in males ($r=−0.38$, $p<0.05$), whereas in both genders significant positive correlation was identified between resting metabolic rate and BMI (males: $r=0.56$, $p<0.005$; females: $r=0.61$, $p<0.0001$).

Basal plasma adrenaline concentration (A–0) in males showed a correlation exclusively with age ($r=0.26$, $p<0.05$), while basal noradrenaline concentration (NA–0) was positively correlated with age ($r=0.37$, $p<0.0001$), BMI ($r=0.24$, $p<0.05$), F% ($r=0.48$, $p<0.005$) and A–0 ($r=0.57$, $p<0.0001$). In female subjects there were no significant correlations between A–0 and analyzed indices, a correlation was found, however, between NA–0 and BMI ($r=0.31$, $p<0.005$) and F% ($r=0.41$, $p<0.05$). Female subjects also demonstrated a negative correlation of NA–0 with VO2 max ($r=−0.40$, $p<0.05$) and positive correlation with RMR ($r=0.32$, $p<0.005$) as well as with A–0 ($r=0.61$, $p<0.0001$).

The area under the curve of the changes of blood glucose concentrations (Bgauc) during OGTT in males demonstrated weak positive correlation only with IRIauc ($r=0.21$, $p<0.05$). In females positive correlations with BMI ($r=0.28$, $p<0.005$), with F% ($r=0.41$, $p<0.005$), and RMR ($r=0.30$, $p<0.0001$) were identified, and a decrease of this index with the rise in VO2max was observed ($r=−0.45$, $p<0.05$). Furthermore, in females Bgauc was positively correlated with IRIauc ($r=0.23$, $p<0.05$), with NA–0 ($r=0.39$, $p<0.0001$) and with NAmax in OGTT ($r=0.41$, $p<0.0001$).

The area under the curve of plasma insulin concentration in OGTT (IRIauc) was related to BMI in both genders (males: $r=0.27$, $p<0.005$ and females: $r=0.37$, $p<0.0001$). Positive correlation between IRIauc a RMR was found in females ($r=0.25$, $p<0.05$). Moreover, there
was a significant positive correlation between IRIauc and HOMA (males: \( r=0.37, p<0.0001 \), females: \( r=0.22, p<0.05 \)).

Maximal plasma adrenaline concentration after glucose intake was related to the baseline value of the hormone in both genders (males: \( r=0.50, p<0.0001 \) and to maximal NAmax in females (\( r=0.24, p<0.05 \)). In males Amax was also negatively correlated with baseline insulin concentration (\( r=-0.28, p<0.005 \)).

In both genders a significant positive correlation was observed between maximal plasma noradrenaline concentration (NAmax) during OGTT and the hormone baseline value (males: \( r=0.62, \) females: \( r=0.69, p<0.0001 \)). In males there was also a significant positive correlation between Namax and baseline IRI-0 (\( r=0.23, p<0.05 \)) and HOMA index (\( r=0.25, p<0.05 \)). In females NAmax was correlated with age (\( r=0.28, p<0.05 \)), BMI (\( r=0.25, p<0.05 \)), RMR (\( r=0.27, p<0.01 \)), and BGauc (\( r=0.41, p<0.0001 \)).

In both genders TEG values diminished with age (\( r=-0.30, p<0.05 \)) and BMI (males: \( r=-0.35, p<0.05 \)). In both genders too TEG rose with physical capacity level VO2max (males: \( r=0.35, p<0.05 \)). In males TEG was negatively correlated with %F (\( r=-0.80, p<0.0005 \)). Moreover, a significant negative correlation was found between TEG and IRIauc (males: \( r=-0.43, \) females: \( r=-0.32, p<0.005 \)), and positive correlation between TEG and BGauc/IRIauc (males: \( r=0.46, p<0.005 \), females: \( r=0.42, p<0.0001 \)). Women were the only subjects where a significant correlation between TEGauc and Bgauc was identified (\( r=0.30, p<0.005 \)). A correlation between TEG and NAmax was observed both in males and females (\( r=0.42, p=0.29 \), respectively; \( p<0.05 \)).

Multiple regression results for thermogenic effect of glucose (TEG). The computations including TEG as a variable dependent on gender, age, BMI and VO2max proved physical capacity to be the only one to have the strongest significant impact on thermogenesis (multiple correlation coefficient \( R=0.59, p<0.0001 \)).

\[
\text{TEG} = 19.4 \text{VO2max} \pm 25.4;
\]

In the dependance of TEG on gender, NAmax, Bgauc and IRIauc, the level of significance was high (\( p<0.0001 \)), which indicates a significant correlation of TEG with these indices. In this case, what significantly affected TEG was subjects’ gender (\( p=0.002 \)), Bgauc (\( p=0.008 \)) and IRIauc (\( p<0.002 \)). The correlations were confirmed by the stepwise regression (\( p<0.0001 \)) and thus the obtained equations were as follows:

for males: \( \text{TEG} = 0.09 \text{Bgauc} - 0.004 \text{IRIauc} + 56.2 \pm 23.5 \);

for females: \( \text{TEG} = 0.09 \text{Bgauc} - 0.004 \text{IRIauc} + 39.1 \pm 23.5 \);

In further regression analysis Bgauc was replaced with Bgauc/IRIauc. The estimated equation was statistically significant (\( p<0.0001, R=0.60, R^2 = 0.35 \)), and what attained significance was regression coefficients for the analyzed factors i.e. gender (\( p<0.0002 \)), NAmax (\( p<0.035 \)) and Bgauc/IRIauc (\( p<0.0001 \)). Since the standard analysis proved all the indices significant, stepwise regression analysis appeared to be unnecessary. The following equations were obtained:

for males: \( \text{TEG} = 5.1 \text{NAmax} - 351.3 \text{Bgauc/IRIauc} + 29.0 \pm 22.9 \);

for females: \( \text{TEG} = 5.1 \text{NAmax} - 351.3 \text{Bgauc/IRIauc} + 7.5 \pm 22.9 \);
The estimated regression equation for TEG as a variable dependent on all the investigated indices: gender, age, physical capacity, metabolic and hormonal response to glucose load attained high statistical significance ($p<0.0001$, $R^2=0.47$, $R=0.69$). Except for age and BMI, the other factors play a substantial role in TEG formation: VO2max ($p<0.0001$), NAmax ($p<0.02$), Bgau ($p<0.004$) and IRIauc ($p<0.02$). Stepwise regression analysis demonstrated that from the above factors, TEG was significantly affected by: gender ($p<0.04$, VO2max ($p<0.0001$) NAmax ($p<0.02$), BGauc ($p<0.004$) and IRIauc ($p<0.02$).

The estimated equations for both genders are as follows:

For males: $\text{TEG}= 16.4 \text{VO2max} + 6.7 \text{NAmax} + 0.08 \text{BGauc} – 0.003 \text{IRIauc} \pm 21.7$;

For females: $\text{TEG}=16.4 \text{VO2max} + 6.7 \text{NAmax} + 0.08 \text{BGauc} – 0.003 \text{IRIauc} – 12.7 \pm 21.7$;

Likewise, the replacement of Baus and IRIauc indices with Baus / IRIauc ratio and then estimated linear regression equation also proved to be of high statistical significance ($p<0.0001$, $R^2=0.47$). According to stepwise analysis, a substantial role in TEG was played by: VO2max ($p<0.0001$), NAmax ($p<0.01$) and BGauc/IRIauc ($p<0.0005$).

For males: $\text{TEG}= 11.7 \text{VO2max} + 6.5 \text{NAmax} + 304 \text{BGauc/IRIauc} \pm 21.5$.

For females: $\text{TEG}=11.7 \text{VO2max} + 6.5 \text{NAmax} + 304\text{BGauc/IRIauc} – 16.1 \pm 21.5$.

Series 2. Thermogenic effect of glucose, in females of various age and comparable body mass index. Resting metabolic rate in the elderly subjects equaled 3.36±0.2 KJ/min and was significantly lower than the value observed in the middle-aged group i.e. 4.1±0.2 KJ/min ($p<0.05$). After expression of REE in KJ per kg of body weight the obtained values equaled 0.052±0.003 KJ/min/kg bw and 0.053±0.002 KJ/min/kg/ bw respectively. The values of RMR per kg were not statistically significant. Glucose load did not induce metabolic rate increase in elderly subject, but in fact their metabolic rate decrease was noted. A significant rise in metabolic rate, however, was found in females in Group B. Overall metabolic rate changes after glucose load expressed as TEG amounted to –12.0±0.55kJ in elderly females, and –46.1±0.74 ($p<0.001$) in younger women.

Series 3. Thermogenic effect of glucose, in sedentary lifestyle girls and ballet schoolgirls. Resting metabolic rate and energy expenditure after glucose intake did not differ significantly between both groups, however, physically active girls tended to show higher values of energy expenditure. After conversion of resting metabolic rate to lean body mass no differences were found between the two groups. Thermogenic effect of glucose calculated as the area under the curve (TEG) was significantly higher in ballet schoolgirls (40.35±6.27 vs 21.4±4.85 KJ-min-1, $p<0.02$). Mean energy expenditure increase after glucose intake by ballet dancers equaled 11.46% of resting metabolic rate (about 5.1% of the energy contained in the administered glucose). In the group of the sedentary lifestyle girls their mean energy expenditure increase after glucose consumption amounted to 6.4% (which is an equivalent of 2.7% of the administered glucose energy).

Series 4. Body mass reduction impact, on TEG in middle-aged women. The adherence to 1000 kcal/24h led to body mass reduction by 5.4 kg ($p<0.001$) after 4 weeks and by 9.14 kg ($p<0.01$) after 8 weeks. BMI after 8 weeks dropped significantly from 33.9 to 30.7 kg/m², $p<0.001$).
RMR tended to fall from 5.84±0.25 kJ·min⁻¹ prior to the program commencement to 5.24±0.31 and 5.12±0.28 kJ·min⁻¹ in 4th and 6th week respectively (p>0.05).

During the body mass-reduction program a tendency for TEG to decrease was observed (from the before-program value of 40.2±7.98 kJ to 31.6±3.83 kJ after 4 weeks of the program and 28.8±4.94 kJ on its completion). The differences were not statistically significant (p>0.05).

Series 5. Thermogenic effect of glucose in hypothyroid subjects (Kozacz et al. 2014).

Resting Metabolic Rate, and changes in energy expenditure during a 2 hours period after glucose ingestion. Two-way analysis of variance demonstrated significant hypothyroid or healthy group effects (p<0.0001), the time factor (p<0.0001) and the interaction of these two factors (p<0.0002). Average value of the RMR was lower in hypothyroid patients than in the control group (p<0.0001). After glucose ingestion energy expenditure (Figure 2) increased in both groups and remained elevated throughout the duration of the test. However, in healthy women fast significant increase in metabolic rate occurred in the first 15min (p<0.0001) and maintained significantly elevated until the end of the experiment. By contrast, in the group of patients with hypothyroidism, there was only a slight increase in energy expenditure which was statistically insignificant except for the maximum level appearing at 105th min (p<0.003). The maximum value of energy expenditure in the group of healthy individuals was achieved 1 h after administration of glucose, while in the group with hypothyroidism it occurred only at 105th min of the test and was significantly lower (p<0.0001) than in the control group. The values of energy expenditure during all measurements were significantly lower in women with hypothyroidism (p<0.0001).

![Figure 2](image.png)

**Figure 2**: Mean values±SE of RMR and changes in energy expenditure during 2 h OGTT in the group of hypothyroid (o) and healthy women (Δ). Asterisks denote differences between these groups; *p<0.0001.
Consequently, a small increase in energy expenditure of hypothyroid women caused the value of TEG to be more than twice as low in hypothyroid group 19.68±3.90 kJ than in control group 55.40±7.32 kJ \((p<0.0004)\).

Blood glucose and plasma insulin responses to the glucose load. There were no statistically significant differences in fasting blood glucose and fasting insulin between the groups. Oral administration of glucose in both groups caused expected fluctuations in blood glucose and insulin (Figure 3). Blood glucose in both groups rose rapidly and was significantly higher in the first measurement \((p<0.0001)\) than in fasting state. The maximal level of blood glucose was reached 1 hour after administration of glucose in both groups and it was significantly higher in women with thyroid disorder \((p<0.005)\). Subsequently, the glucose level dropped, however, after 2 h of the test it was still higher than in the fasting state in both healthy women \((p<0.003)\) and hypothyroid patients \((p<0.0001)\).

Plasma insulin levels during the test tended to be higher in women with hypothyroidism than in the healthy subjects until the end of the test but the differences were not significant. As in the case of glucose, insulin rose rapidly; the level of insulin in the first measurement was statistically different from fasting state \((p<0.0001)\) in both groups. Maximal values of plasma insulin did not differ between the groups; however, they were achieved more rapidly by healthy women (at 60th minute of the test) than by women with hypothyroidism (90th min). In fact, insulin levels even increased in the group with hypothyroidism when in the control group it had already fallen. At the end of the OGTT insulin levels remained significantly elevated in both groups compared to baseline values \((p<0.0001)\). Calculated areas under the curves of blood glucose and plasma insulin in the OGTT were significantly higher in women with hypothyroidism than in women without thyroid hormone deficiency.

**Figure 3:** Mean values±SE of fasting blood glucose and insulin and their postprandial changes in the group of hypothyroid (o) and healthy women (A). Asterisks denote differences between these groups; *\(p<0.005\); **\(p<0.0001\)

Calculated indicators of insulin resistance were not significantly different between groups (Table 5) and were on the verge of defining insulin or indicated insulin resistance for both groups.
Plasma catecholamine responses to the glucose load. Both the initial concentrations of catecholamines in plasma and those measured after ingestion of glucose were significantly higher in women with hypothyroidism than in healthy women (Figure 4). Glucose injection caused statistically significant changes in the levels of plasma A and NA concentration in both groups. After 90 min of OGTT there was a significant increase ($p<0.03$) in the level of A in hypothyroid group, whereas in healthy group there was a decrease in the level of A ($p<0.03$) compared to baseline values. In both groups there were statistically significant increases in the level of NA after 90 min but they were considerably greater in hypothyroid group ($p<0.001$) than in healthy group ($p<0.05$). Moreover, the level of NA at the end of OGTT in both groups remained elevated compared to baseline – at the border of significance in hypothyroid group ($p=0.055$) and significantly higher in healthy group ($p<0.02$). However, the level of A returned to baseline after 120 min in both groups. The maximal levels of A and NA in hypothyroid women were significantly higher than in control group ($p<0.0001$ and $p<0.0001$ respectively).

Table 5: Comparison of insulin resistant indicators in healthy and hypothyroid females.

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Healthy subjects</th>
<th>Hypothyroid patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRI₀</td>
<td>9.34±0.59</td>
<td>10.54±1.04</td>
<td>NS</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.89±0.13</td>
<td>2.22±0.24</td>
<td>NS</td>
</tr>
<tr>
<td>QUICKI</td>
<td>0.35±0.01</td>
<td>0.35±0.01</td>
<td>NS</td>
</tr>
<tr>
<td>Matsuda index</td>
<td>5.28±0.38</td>
<td>4.58±0.45</td>
<td>NS</td>
</tr>
</tbody>
</table>

Figure 4: Mean values±SE of fasting blood adrenaline and noradrenaline and their post-glucose levels in the group of hypothyroid (○) and healthy women (△). Asterisks denote differences between these groups; *$p<0.0002$. 
4 Discussion

The 70’s and 80’s of the previous century brought a large number of publications concerning thermogenic effect of glucose and other carbohydrates. Later on, however, the body of research on the subject inexplicably decreased although the problem was not sufficiently described. The approach in currently conducted research differs from the previous studies, which is manifested in the following features:

1. Unlike previous studies, current research has been conducted on a relatively large number of subjects of both genders, different ages, varied body weight and exercise capacity i.e. the factors which so far have been independently considered as significant in postprandial thermogenesis.

2. This study represents the scarce research which discusses the simultaneous influence of all the above factors (age, body weight, exercise capacity) with hormonal and neurohormonal indices.

3. The available literature does not provide any analysis which applied statistical methods (multiple regression analysis) to assess the correlation between factors responsible for thermogenic effect of glucose.

The impact of age, body weight and physical capacity on thermogenesis is difficult to assess because in aging process it is typical for body weight to increase and for physical capacity to decrease (Muller et al., 1995). Resting metabolic rate and physical activity also decline with age and when these are not accompanied by consumption reduction, this contributes to maintenance of positive energy balance (Elahi, 2000b). Using two-factor regression analysis in males and females, thermogenic effect of glucose reduction with age and BMI was demonstrated both in men and women, however, in males the reduction was also correlated with fat percentage. On the other hand, though, both men and women showed glucose-induced thermogenesis increase with a rise of physical activity. Multivariate regression analysis which evaluated simultaneous impact of gender, age, body weight and exercise capacity on thermogenic effect of glucose indicated a significant influence solely of the last of them.

The limitation of the present study is insufficient number of measured variables which may be involved in building the magnitude of thermogenic response (leptin, ghrelin, glucagon etc.).

4.1 The Role of Age in Thermogenic Effect of Glucose

As already mentioned, multivariate regression analysis used in Series 1 of the study did not show a direct correlation of thermogenic effect of glucose with the subjects age. Series 2, which included elderly women, however, demonstrated distinct inhibition of thermogenesis after glucose ingestion, compared with middle-aged women. Extensive literature on the impact of age on thermogenesis induced by mixed meals reports inconsistent findings (de Jonge & Bray, 1997). TEG reduction with age was interpreted as an additive factor contributing to a decrease of overall energy demand in the elderly, thus, lower energy value of food
should be recommended (1990b). The study by Vissera et al. (1995) reported lower postpran-
dial thermogenesis in the elderly, however, the difference between elderly and younger sub-
jects faded out once body composition factor was included. The review of available litera-
ture presented by de Jonge and Bray (1997) may indirectly lead to similar conclusions. On
the basis of 49 publications, the authors concluded that the age of obesity or obesity-free
subjects did not diversify the thermal effect of food.

The hypothesis that age-related reduction of glucose-induced thermogenesis is linked
to changes of body composition is contradicted by the findings of Series 2 of our study.
When comparing two groups of women of identical BMI, similar body weight but different
age, no heat-producing effect of glucose in the elderly females was found. A question arises,
then, what is the mechanism of reduction or even elimination of thermogenic effect of glu-
cose or meal in elderly subjects.

In light of the controversies over heat-generating effect of mixed meals in people of
various age, Melanson et al. (1998) conducted research whose results suggest that aging pro-
cess has no impact on food thermogenic effect as long as people are not hypothyroid or
reduced glucose tolerance patients. The results presented in this study are again contradic-
tory as all the study subjects were clinically healthy. In global consideration of daily energy
expenditure compounds (including the one connected with postprandial thermogenesis) in
the elderly, it is important to note that over 60% of people aged over 75 years suffer from
chronic diseases (Elia et al., 2000). Wilson and Morley (2003) point to yet another aspect of
energy balance in the elderly: they emphasize body weight decrease in people over 70 years
of age. According to the authors, this may be ascribed to so called physiologic anorexia (al-
terations in the hedonic qualities of food – age-related decline in taste and smell), low fat-
free mass, but less prominently with a decrease in fat mass. The decline in the daily energy
expenditure may be supported by a range of factors, such as decrease of Na/K ATPases,
reduced metabolism of muscle proteins or simply lower intensity of physical activity.

4.2 Body Weight/Obesity and Thermogenic Effect of Glucose

As it was the case with age, the prominent role of BMI in thermogenic effect of glucose was
not confirmed either by multivariate regression analysis where BMI was included along
with other biological factors. De Jonge and Bray (1997) performed critical analysis of the
literature on the thermogenic effect of glucose or a meal in obesity. The authors investigat-
ed 49% of the papers published since 1976 which compared thermogenic response in obese and
in slim subjects. 29 publications analyzing obese or normal-weight subjects at similar age
were then selected. A significant thermogenesis reduction in obesity subjects was reported
in 22 of the analyzed articles. Another review by Granat and Brandon (2002) covered 50
publications which discussed thermogenic effect of a meal in obese subjects. The authors
point out the differences in the research methods applied which potentially account for the
inconsistency of the results. Previous TEG analyses involved the comparisons of two groups
of considerably different body weight (slim and obese), whereas in this study (Series 1) glu-
cose-induced thermogenesis was analyzed in subjects of a wide range of body weight: from
slim to obese (BMI ranging from 17.0 to 43.3 kg/m²).

The results of our study suggest that body weight, at least within a certain range,
plays a secondary role in heat-generating effect of glucose. The tendency of TEG decrease which accompanied weight loss resulting from an 8-week low-calorie diet, which was demonstrated in the women in Series 4, proved to be insignificant. The problem requires further research involving a larger population of subjects on a slimming diet. Possibly, varied degree of metabolic and neurohormonal disorders in obesity may possibly have as diverse impact on the results in this type of research, particularly conducted in a small group of randomly chosen subjects.

4.3 The Impact of Physical Activity on the Thermogenic Effect of Glucose

Series 1 of our study demonstrated positive correlation between maximal oxygen consumption (VO2 max) and thermogenic effect of glucose both in men and women. Furthermore, using multivariate analysis and VO2 max as an indicator of exercise capacity, was proven to be the factor that affected TEG more significantly than BMI. The existing literature provides diverse views on the influence that exercise capacity or intensive physical activity have on postprandial thermogenesis. Some authors reported no difference in postprandial thermogenesis between active and non-active subjects (Horton et al., 1994; Tremblay et al., 1983; Burke et al., 1993). On the other hand, however, it was also demonstrated that physical activity may increase the thermogenic effect of glucose or meal (Burkhard-Jagodzinska, 1999; Lopez et al., 2000). Lopez et al. (2000) evidenced a positive correlation between postprandial thermogenesis and VO2 max. In our study, in the analysis of sedentary lifestyle girls and physically active ballet schoolgirls, higher values of TEG were identified in the latter group. The findings confirm previous observations that physical activity does contribute to a rise in postprandial thermogenesis. The effect can be attributed to increased muscle insulin sensitivity (Henriksson, 1995). Smaller insulin increase during OGTT was recorded in the analyzed ballet schoolgirls compared to the inactive girls, with glucose changes being similar in both groups, which may be interpreted as the indication of the ballet dancers increased insulin sensitivity.

What cannot be omitted in the postprandial thermogenesis formation in people of diverse physical activity and exercise capacity is the role of the sympathetic nervous system. The study by Smorawiński et al. (2000) shows that blood adrenaline increase in athletes is larger in comparison with sedentary young males. Similarly, our study did not demonstrate differences in noradrenaline concentrations in OGTT between active and sedentary girls, whereas, adrenaline increase was markedly larger in the physically active subjects. It is not clear whether the adrenaline rise in ballet schoolgirls results from their heightened emotional sensitivity (Neumarker et al., 2000) or from increased long training-related secretory capacity of the adrenal medulla (Kjaer et al., 1998).

4.4 Regulatory Role of Insulin in Thermogenic Effect of Glucose

In Series 1 of the presented study in both genders negative correlation was found between TEG and the area under the curve of insulinemia (IRIauc) and positive correlation between
TEG and BGauc/IRIauc index. Positive correlation between the area under the curve of insulinemia (IRIauc) and body weight expressed by BMI was also identified. Multiple regression analysis in our study indicates a predominant role of insulinemia (IRIauc) and BGauc/IRIauc index in the thermogenic effect of glucose.

Although insulin is regarded as an anabolic hormone, its function in glucose-induced thermogenesis in slim subjects has not been unequivocally and directly defined. While a vast majority of studies on thermogenic effect of insulin was conducted on animals, the research on humans focused mainly on the role of insulin in thermogenesis in obese subjects. Postprandial thermogenesis in obesity subjects may be disturbed due to tissue resistance to insulin and decreased activity of the sympathetic nervous system (de Jonge and Bray, 1997). While reviewing studies on the problem of diminished thermogenesis in obesity, Tappy et al. (1991) demonstrated gradual reduction of heat-producing response in obese subjects with normal glucose tolerance, reduced glucose tolerance and finally in non-insulin-dependent diabetes mellitus patients with hyper- and hypoinsulinemia. Contrastive results were obtained by Laville et al. (1993), who compared a group of initial-stage obesity women with long-term obesity subjects. They identified a comparable thermogenic response in standard glucose tolerance test in both groups whereas hyperinsulinemia and reduced glucose tolerance were observed only in the latter. Vassant et al. (1992) obtained diminished thermogenic effect of glucose in diabetes patients regardless of their body weight, in obesity patients; however, TEG was significantly correlated with the degree of glucose tolerance disturbance.

On the basis of the population research known as “The Horn Study” carried out in Holland (Grootehuis, 2000), a new model of human body reactions was suggested and then complemented by the author of this study (complementary element in bold):


4.5 The Role of The Sympathetic Nervous System in Thermogenic Effect of Glucose

In this study a considerable increase in plasma adrenaline (A) and noradrenaline (NA) after glucose intake was identified in both genders. Furthermore, positive correlation between TEG and maximal NA concentration achieved in OGTT was demonstrated, but no correlation was found between TEG and maximal A concentration. Multiple regression analysis of the data also demonstrated that maximal NA concentration taken into account with gender, age, BMI, VO2 max and alterations in insulinemia and glycemia has a significant impact on glucose-induced thermogenesis. The analysis did not confirm, however, adrenaline influence on TEG formation. Numerous studies regarding the role of the sympathetic nervous system in postprandial thermogenesis were conducted on animals, mainly on rats. The research indicate the significance of brown adipose tissue stimulation by noradrenaline (Cannon & Nedergaard, 2004). In research on humans particular attention was drawn to the relation between diminished heat-generating effect of glucose or meal and the sympathetic nervous system reactivity in obesity subjects. Astrup et al. (1990) demonstrated that arterial
blood noradrenalin increase after glucose intake was slighter in obesity patients than in normal body weight subjects. Valensi et al. (1998), however, identified merely a tendency for glucose-induced thermogenesis to decrease in obese women with the sympathetic nervous system dysfunction.

The presented study did not include a comparison of catecholamine concentrations in obese and slim subjects but it analyzed a correlation between maximal catecholamines concentration in OGTT and body weight, BMI and body fat percentage in a wide range of these indices. Positive correlation between maximal NA concentration and BMI was found exclusively in women. Therefore the negative correlation between BMI and TEG was not caused by weight gain-related decrease in the sympathetic nervous system activity. It’s noteworthy that obesity may also be accompanied by diminished metabolic response to catecholamines.

4.6 Body Weight Reduction Impact on Thermogenic Effect of Glucose

The study weight-reduction program involving 8-week low-calorie mixed diet led to a significant reduction of body weight and BMI and thermogenic effect of glucose tended to decrease. What we observed in our study i.e. the tendency for TEG to diminish and the lack of changes in maximal catecholamines concentration after glucose load during weight-reduction program is the observation consistent with the findings reported by Astrup et al. (1990). The authors compared thermogenic effect of glucose and catecholamines concentration in obesity subjects before and after body weight reduction. After body weight decrease in the analyzed obese subjects thermogenic effect of glucose and catecholamines increase after glucose intake did not alter. The tendencies for TEG and noradrenaline to alter described in the present study as well as the results reported by Astrup (1990) may suggest that decreased thermogenic effect of glucose which continues in obese subjects after their body weight reduction is an indication of the reduction or the lack of facultative thermogenesis induced by disturbed reactivity of the sympathetic nervous system.

4.7 Lack of Thermogenic Response to Glucose Intake

What also deserves consideration is the fact, a number of analyzed subjects do not demonstrate the thermogenic effect after glucose intake. Increased metabolic rate after oral glucose administration was not found in 4% of the subjects analyzed in Series 1 of this study and in 15 (out of 22) elderly women (aged 68–88) participating in Series 2. Like in the control group without glucose intake, in some of the subjects showing no thermogenic effect a decrease in metabolic rate was observed. This can be ascribed to both physical and mental relaxation during OGTT as silence and full comfort of the subjects were ensured for the duration of the test. Such conditions caused a considerable part of the subjects to doze off and they were woken up only for the necessary study procedures. Thus, the lack of TEG can hardly be accounted for by carelessness in careful following of the procedures which were to lead the subjects to basal state. In Series 1 of this study the males who did not show any thermogenic response to glucose were all middle-aged or elderly subjects with overweight or obesity (BMI ranging from 27.1 to 37.4), whereas lack of thermogenesis after glucose intake occurred
both in young, slim females (age 16 years, BMI=19.7) and in middle-aged, overweight women (age 60 years, BMI=29.7) as well as in women over 68 years of age (Series 2). It is extremely interesting that the group without thermogenic response to glucose comprised both overweight and slim subjects. The assumption is that the lack of thermogenesis in slim subjects (BMI<22 kg/m²) reflects the compensatory mechanisms which prevent their energy loss (it should be noted here that this does not refer to the girls analyzed in Series 3). We may hypothesize that what occurs in young highly physically active females is metabolic adaptation leading to “energy saving” which is what happens in hunger or low-calorie diet adherence in weight-reduction. The cases identified in this study provide the ground to presume that the mechanism may refer to some very slim, inactive and some obese people, as it was the case in elderly subjects. In elderly as well as in obese people the lack of thermogenic effect of glucose may stem from the disturbance in the mechanisms controlling body energy balance. We cannot omit to mention, however, one more aspect of this issue which was emphasized by Bouchard et al. (1999). The authors postulate that genotype-dependent differences may to a large extent underlie interindividual variability of thermogenic response to glucose. The role of genetic factors in resting and general energy expenditure were also pointed out by other authors (Amatruda et al., 1993). Thus, a similar hypothesis about genetic impairment of postprandial thermogenesis is not groundless.

On the other hand resting metabolic rate is significantly higher in obese diabetic patients compared to obese non-diabetics, especially in those with poor glycaemic control (Alawad et al. 2013, Amatruda et al., 1993) which may inhibits further increase of energy expenditure after ingestion of a meal.

The principal finding of the last series of the study is that thermogenic response to the glucose ingestion in patients with hypothyroidism was much lower than in healthy subjects. This was demonstrated for the first time. The existing results concerning TEG in thyroid dysfunction are equivocal (Randin et al. 1986; Acheson et al. 1984; Al-Adsani et al. 1997). Both Acheson et al. (Acheson et al. 1984) and Radin et al. (Randin et al. 1986) observed significant increases in RMR in hyperthyroid state compared with healthy subjects but did not report any significant changes in TEG. Radin et al. showed that glucose-induced thermogenesis tended to be reduced after treatment of hyperthyroid patients when euthyroid state was achieved. Al-Adsani et al. (Al-Adsani et al. 1997) observed that slight changes in thyroid hormone levels affected the RMR but not the TEG. However, Ulas et al (Ulas et al. 2012) showed that energy expenditure during sleep was similar between hypothyroid and healthy subjects. Our studies have clearly showed that hypothyroidism associated with reduction in energy expenditure occurs not only in the case of RMR but also by reducing TEG.

The study also demonstrates that thyroid hormone deficiency impairs glucose tolerance, which is in agreement with previous reports (Dimitriadis et al. 2006a; Maratou et al. 2009; Rochon et al. 2003; Kosovskii et al. 1992). Despite much larger amount of insulin released into the blood after glucose ingestion (IRIauc) in women with hypothyroidism, the glucose concentration in blood was high. The differences between the shape of the curves and the areas under the curves suggest postprandial insulin resistance related to hypothyroid state. Interestingly, none of the insulin resistant indicators differed between groups. They revealed insulin resistant state in both groups (potentially due to the relatively high BMI in both studied groups of subjects). However, the calculated indicators were unable to
reflect the above-mentioned differences in the curves between groups.

Insulin appears to play an important role as the link between dietary intake and sympathetic nervous system (SNS) activity by its action in the brain ventromedial hypothalamus (Landsberg, 1990; Sauter et al. 1983). It was also reported that not only obese insulin-resistant subjects display a blunted sympathetic neural response to glucose ingestion compared with insulin-sensitive individuals (Straznicky et al. 2009a also Straznicky et al. 2009b). This was not confirmed by the present results but it should be noted that our study was conducted in subjects with more complex endocrine disorder.

In agreement with previous studies (Nedvidkova et al. 2004; Polikar et al. 1990) the basal plasma levels of adrenaline and noradrenaline were much higher in hypothyroid than in healthy women. Also the amount of noradrenaline released during OGTT was much greater in hypothyroid subjects than in healthy controls. This difference may result from stronger activation of sympathetic nervous system or/and decreased plasma noradrenaline clearance. Nedvidkova et al. (Nedvidkova et al. 2004) demonstrated that hypothyroid subjects have a weaker response to lipolytic stimulations of β-adrenoceptors. Increased sympathetic activity may be a compensatory mechanism to achieve an appropriate level of response tissues to stimulation. Thus, hypothyroidism is related to high activity of the sympathetic nervous system and with desensitization of adrenergic receptors (Wahrenberg et al. 1994; Hellström et al. 1997; Martin et al. 1992; Rubio et al. 1995a; Rubio et al. 1995b).

In present study the plasma level of adrenaline in healthy women decreased in response to glucose and/or insulin elevation as compared to baseline just as it was found in previous studies (Penev et al. 2005; Trunet et al. 1984) whilst in hypothyroid group it showed an increase at the 90th minute of the test. Adrenaline is a hormone with a potent thermogenic effect. It is possible that weak thermal response to the intake of glucose in women with hypothyroidism causes increased secretion of adrenaline in order to enhance thermogenesis. Again, it may be a compensatory mechanism by which adrenaline has to compensate the reduced postprandial metabolic rate. On the other hand, despite the fact that we studied the metabolism of carbohydrates, we cannot exclude the role of lipid metabolism in this metabolic play and its relationship with adrenergic activity.

Nevertheless, even significantly stronger adrenergic activation in women with hypothyroidism is not sufficient to compensate for the “catecholamine specific resistance” with diminished response of tissues to stimulation of β-receptors. The “catecholamine resistance” may be responsible for the reduction of the sympathetic nervous component of TEG. In addition, other factors such as glucagon, glucocorticoids, leptin (Silva, 2006), ghrelin or obestatin (Gurgul et al. 2012) that could influence thermogenesis may also be modulated by thyroid hormone.

It can be concluded that in thyroid patients TEG is diminished and glucose tolerance is decreased while the adrenergic response to glucose administration is markedly greater. It can be speculated that these changes are related to decreased insulin sensitivity and responsiveness to catecholamine action.

References


Landsberg L. (1990) “Insulin resistance, energy balance and sympathetic nervous system activity,” Clinical and...


