

Thermic effect of glucose and thermal body insulation in lean and obese subjects: a calorimetric approach

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The fact that many obese subjects have a tendency to gain weight with no real excess of food intake is generally accounted for by a low physical activity (Bullen, Reed & Mayer, 1964). Although a few authors have claimed that the efficiency of energy utilization could be greater in obese than in lean subjects (Galton & Bray, 1967), there is no clear evidence to support this concept.

In a period of weight gain, the positive energy balance in the obese can be explained by a relative excess of energy intake in relation to a decreased energy expenditure. The latter may be due partly to lack of muscular exercise, but other factors may contribute to save energy in the obese such as impairment of glucose oxidation with a low thermic effect (specific dynamic action) or decreased heat losses during cold exposure resulting from an elevated body thermal insulation.

Since this symposium is concerned with 'Applications of human and animal calorimetry', I will briefly describe the methods of direct and indirect human calorimetry used in Lausanne.

Direct calorimetry

We have built a direct calorimeter of low thermal inertia and rapid response time, large enough to accommodate patients (Spinnler, Jéquier, Favre, Dolivo & Vannotti, 1973). Our instrument is a heat-flow calorimeter in which the rate of heat loss by a subject is measured by a gradient layer.

The heat flow through a layer is given by Fourier's law:

$$\dot{Q} = A \frac{\lambda}{D} (T_1 - T_2),$$

where \dot{Q} is the heat flow through the layer, A is the area of the layer, λ is the specific thermal conductivity of the layer, D is the thickness of the layer, and T_1 and T_2 are the temperature of inner and outer surfaces, respectively.

The calorimeter is a small chamber with a volume of 1.56 m³. The inner surface is completely covered with a gradient layer. The gradient layer consists of an epoxy resin 2.4 mm thick with a copper circuit printed on both sides. The electrical resistance of each circuit is dependent on its temperature. The measurement of the heat flowing through the layer is performed by accurate measurements of the difference in temperature between the two surfaces of the layer. The copper

circuits of the inner and outer surfaces of the gradient layer are connected in a Wheatstone bridge. The voltage measured is proportional to the sensible heat flowing through the layer (\dot{Q}). The measurement of detectable heat (radiative plus convective) using a gradient layer requires a constant temperature of the outer surface of the layer. The walls of the chamber are maintained at a constant temperature, within 0.005° of the set temperature, by circulating water through channels in the walls of the chamber.

Evaporative heat losses of the subject are measured through a ventilatory circuit. Outside air is forced through the ventilatory circuit at a flow rate of 1150 l/min. The air is first cooled to a low temperature, T_1 , and completely saturated with water. Before reaching the chamber, it is passed through a heater where it is warmed to the chamber temperature, T_2 . The water vapour lost by the subject increases the water content of the air. Outgoing air from the chamber passes through a heat exchanger (condenser) maintained at the low temperature, T_1 . The water vapour lost by the subject condenses out and gives up its latent heat which is measured by a gradient layer: this corresponds to the evaporative heat losses of the subject. Respiratory heat losses can be measured separately through a respiratory circuit.

Indirect calorimetry

The oxygen consumption ($\dot{V}O_2$) of the subject is measured by an open-circuit system. A transparent plastic, ventilated hood is lowered over the subject's head and secured around his neck with an airtight tissue. A slight negative pressure is maintained in the hood to prevent expired air from leaking out. The air flow at the outlet of the hood is measured using a pneumotachograph and samples of the out-flowing air are continuously passed through a paramagnetic oxygen analyser and an infra-red carbon dioxide analyser. The non-protein respiratory quotient is determined by subtracting the oxygen consumed and carbon dioxide produced by protein utilization assessed from urinary nitrogen excretion. The tables of Lusk (1924) were used to obtain the amount of carbohydrate and lipid oxidized.

Thermometry

Internal temperature is measured using a tympanic thermocouple. Mean skin temperature is calculated by weighting eight individual skin temperatures according to the method of Hardy & Du Bois (1937).

Utilization rate and thermic effect of glucose in lean and obese subjects

Two groups of female subjects who were familiar with the equipment were studied in the direct calorimeter (Pittet, Chappuis, Acheson, de Techtermann & Jéquier, 1976). Group 1 consisted of ten control subjects, aged 24.2 ± 1.7 years with a mean body-weight of 56.6 ± 1.9 kg ($102 \pm 2.0\%$ of ideal weight). Group 2 consisted of eleven obese subjects, with a mean weight of 83.7 ± 4.4 kg ($159.3 \pm 7.9\%$ of ideal weight).

The subjects were introduced into the calorimeter at 28° and 30% relative humidity. After a 40-min period of measurements in the fasting state, an oral dose of 50 g glucose was given and measurements including direct and indirect calorimetry were done during 150 min. Control experiments were done in three control subjects to study the effect of an energy-free meal, 150 ml water+lemon juice. The results are given in Fig. 1.

At 28°, a temperature considered to be near the thermal neutral environment, in the fasting state heat losses expressed in kJ/m² per h were significantly higher in the control subjects (192±5.3) than in the obese (162.6±3.9). Metabolic rate was also more elevated in controls (177.8±8 kJ/m² per h) than in the obese (164.1±4.8) but the difference was not significant.

Simultaneous measurements of metabolic rate (*M*) and heat losses (*H*) allow us to calculate the heat storage (*S*); for a resting subject, $S=M-H$. Hence, at 28°, control subjects were in negative thermal balance ($S = -14.2 \pm 5.0$ kJ/m² per h) whereas the obese were in thermal equilibrium ($S = 1.5 \pm 4.8$ kJ/m² per h).

After the ingestion of glucose, metabolic rate measured over the 150-min period increased in both groups, by 13.0% in the control and 5.2% in the obese. Calculated in terms of specific dynamic action the increase in metabolic rate was 12.0% and 5.2%, respectively, of the energy content of the load. Heat losses did not change significantly during the 150 min after glucose in either group. Thermal balance became positive in both groups, 10.9±5.6 and 10.8±4.8 kJ/m² per h in controls and obese, respectively.

The oxidation rate of the different substrates was calculated. In the fasting state, control subjects oxidized mainly carbohydrate (90.4 mg/min) and less lipid (68.8 mg/min), whereas the main energy substrate utilized by the obese was lipid (103.7 mg/min) and less carbohydrate (50.2 mg/min). After the glucose load, carbohydrate oxidation rate increased in both groups to reach 159 mg/min in controls and 95.6 mg/min in the obese. Lipid oxidation decreased slightly and protein metabolism remained unchanged. The energy-free meal (water+lemon juice) induced no significant change in metabolic rate or heat losses.

The main finding of this study is a lower thermic effect of glucose in obese than in control subjects. The obese had a lower oxidation rate of carbohydrate than controls in both the fasting and postprandial states. This can be explained by the inhibition of carbohydrate oxidation in the presence of elevated plasma free fatty acids (FFA) as described by Gomez, Jéquier, Chabot, Büber & Felber (1972); the entry of FFA into muscle cells is stimulated and their utilization depends mainly on their concentration. In addition, Randle, Hales, Garland & Newsholme (1963) showed that increased fatty acid oxidation leads to inhibition of key enzymes in the glycolytic pathway which decreases the rate of glucose oxidation.

The fact that the obese were in thermal equilibrium at 28° whereas the controls were in negative thermal balance may be related to the differences in thermic effects observed. The increase in metabolic rate after glucose ingestion in the controls may play a thermoregulatory role, whereas there was no need for an extra heat production in the obese subjects.

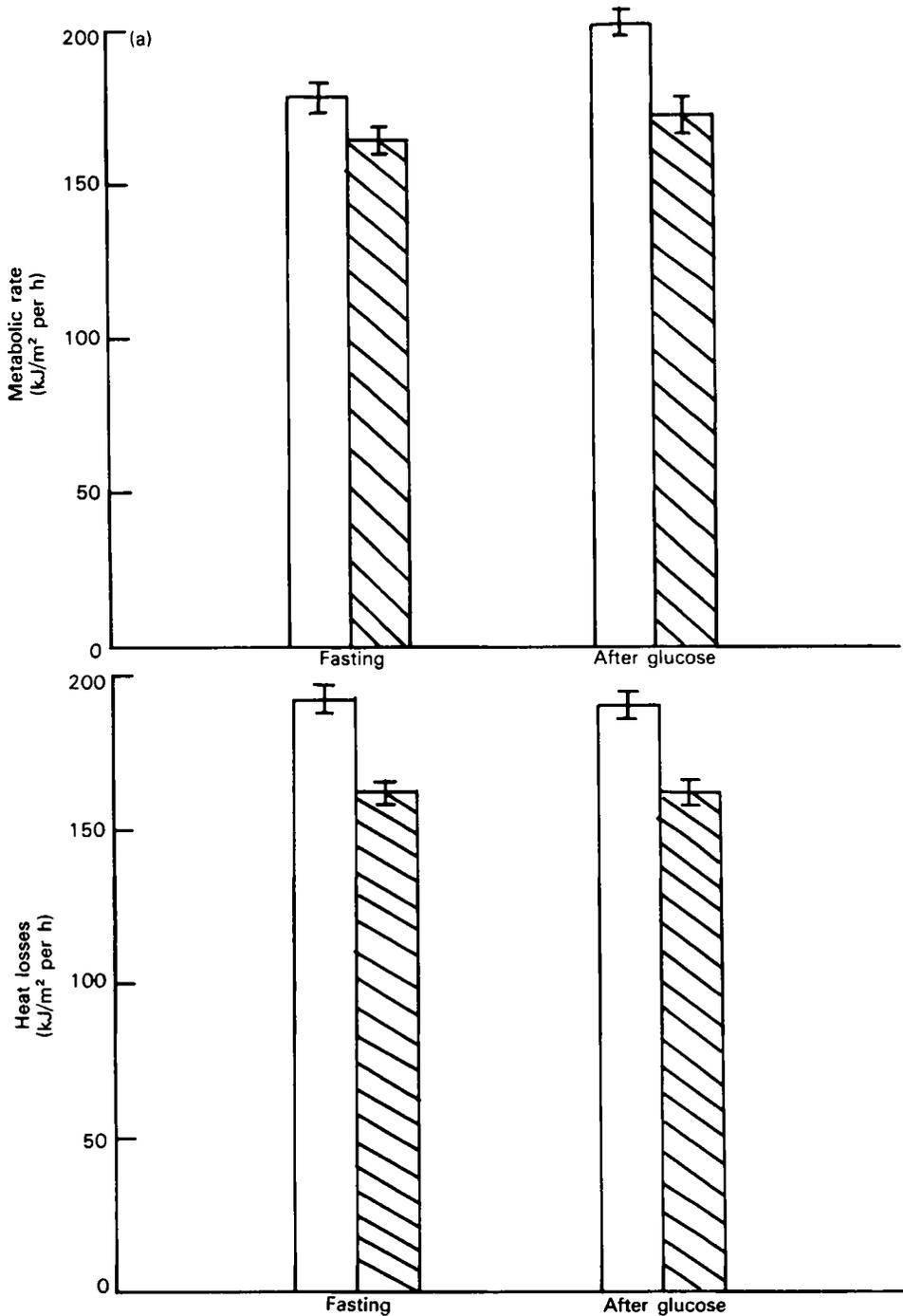


Fig. 1. (a) Metabolic rate (kJ/m^2 per h) during a 40-min control period (fasting) and during 150 min after an oral dose of 50 g glucose for a group of ten female control subjects \square and for a group of eleven female obese subjects \boxtimes . The increase in metabolic rate after the glucose load was statistically significant in the group of control subjects ($P < 0.001$). (b) Heat losses (kJ/m^2 per h) for the same group of subjects. Vertical bars represent the standard errors of the mean values.

Thermal body insulation

It is well established that in thermally comfortable environments, thermal body insulation does not play a role in the regulation of human energy expenditure. However, during cold exposure, the amount of heat lost influences the cooling rate of the body and can elicit metabolic responses. Under these conditions, the degree of thermal body insulation is an important factor; a large insulation can contribute to saving and may lead to an economy of fuels consumed by the body.

Thermal body insulation (I_b) is obtained by the equation:

$$I_b = \frac{(T_{int} - \bar{T}_{sk}) A_b}{\dot{H}_{sk}}$$

where T_{int} is internal (or core) temperature, \bar{T}_{sk} is mean skin temperature, A_b is body surface and \dot{H}_{sk} is total heat losses through the skin. Thermal body insulation depends on the composition and the thickness of subcutaneous tissues as well as on their blood flow (Jéquier, Gyax, Pittet & Vannotti, 1974). The study of thermal body insulation in subjects of widely different body-weight may give some insight into the mechanism of the low energy expenditure observed in obese subjects exposed to cold, or in anorexic patients in a neutral thermal environment.

Subjects

The subjects of this study were women with no evidence of endocrine disease. They were assigned to four groups according to their weight and anamnesis. Fig. 2 shows the weight (in % excess of ideal weight) and the mean thickness of subcutaneous fat of the four groups of subjects.

- (1) *Controls* ($n=27$): women with body-weight within $\pm 10\%$ of ideal weight.
- (2) *Anorexic* ($n=18$): women with body-weight between -10 and -30% of ideal weight, and with an anamnesis of anorexia nervosa.
- (3) *Trend to obesity* ($n=29$): women moderately obese (weight $+10$ to $+35\%$ of ideal weight) and with an anamnesis of easy weight gain.
- (4) *Obese* ($n=34$): women with marked obesity (body-weight in excess of $+50\%$ of ideal weight).

Experiments

Heat losses (in W/m^2) and total body insulation were measured in each group of subjects at an ambient temperature (T_a) of 28° or 20° or both. (Most subjects performed only one test.)

Heat losses

Fig. 3 shows that controls had higher heat losses than the three other groups at 28 or $20^\circ T_a$.

Thermal body insulation

Thermal body insulation was determined as previously described. In addition, the insulation due to the subcutaneous fat was calculated from measurements of subcutaneous fat thickness (Fig. 2) and the coefficient of thermal conductivity of fat ($0.21 W/m$ per deg C) as described by Jéquier *et al.* (1974).

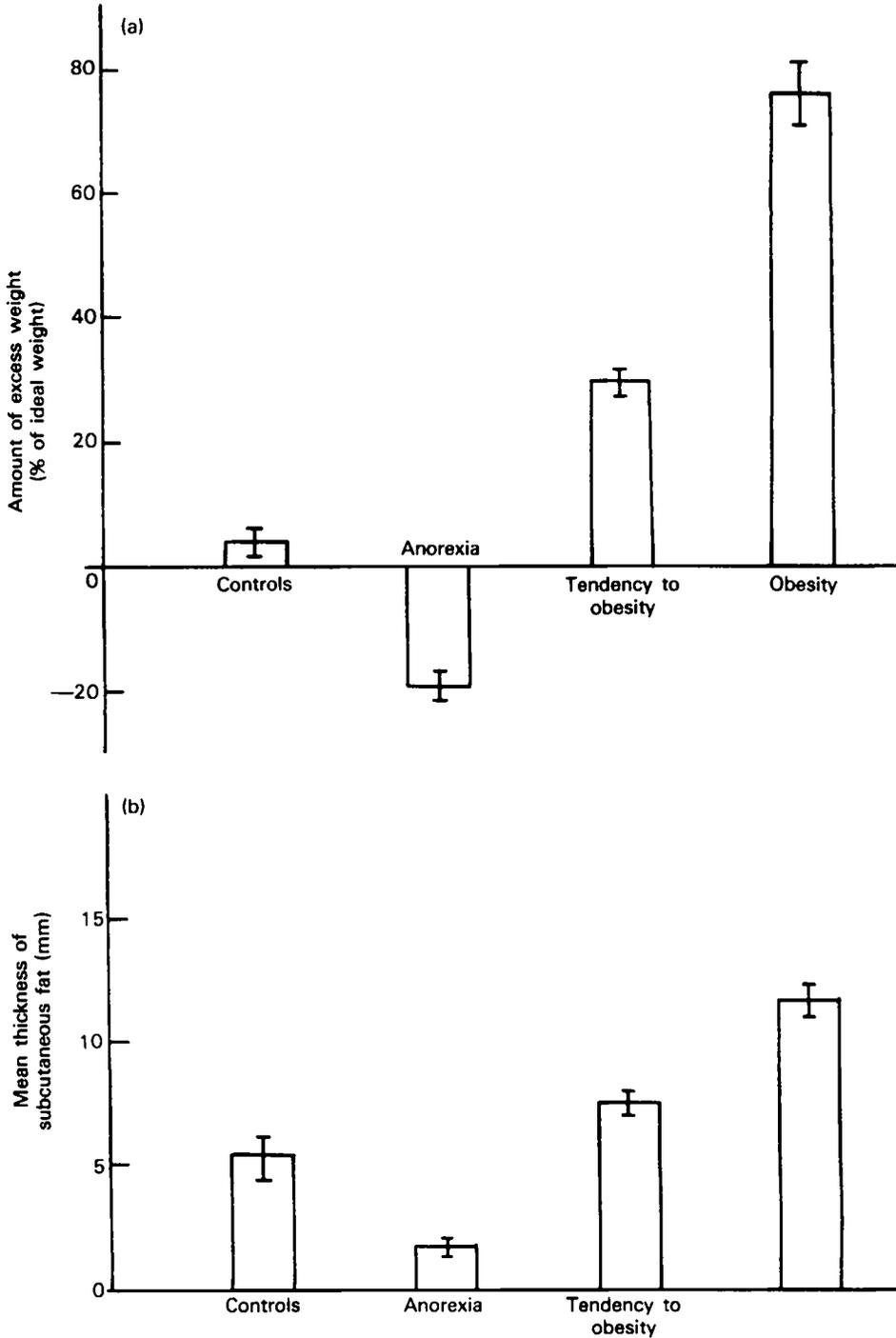


Fig. 2. (a) Excess weight (in % of ideal weight) in four groups of female subjects. (b) Mean thickness of subcutaneous fat (in mm) in the same four groups of female subjects. Vertical bars represent the standard errors of the mean values.

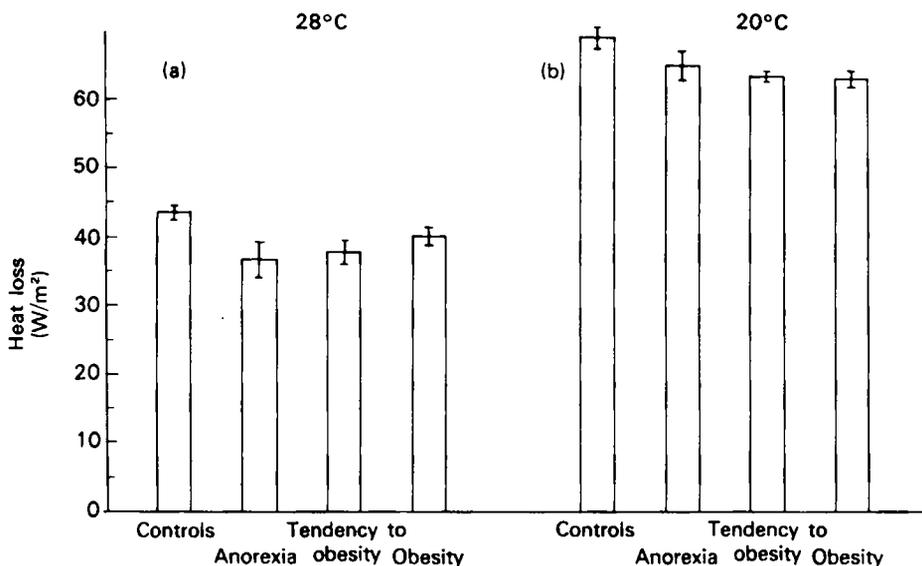


Fig. 3. Heat losses (W/m^2) in four groups of female subjects as in Fig. 2. (a) The measurements were performed by direct calorimetry 30 min after exposure at an ambient temperature of 28° . (b) The measurements were performed 1 h after exposure at an ambient temperature of 20° . Vertical bars represent the standard errors of the mean values.

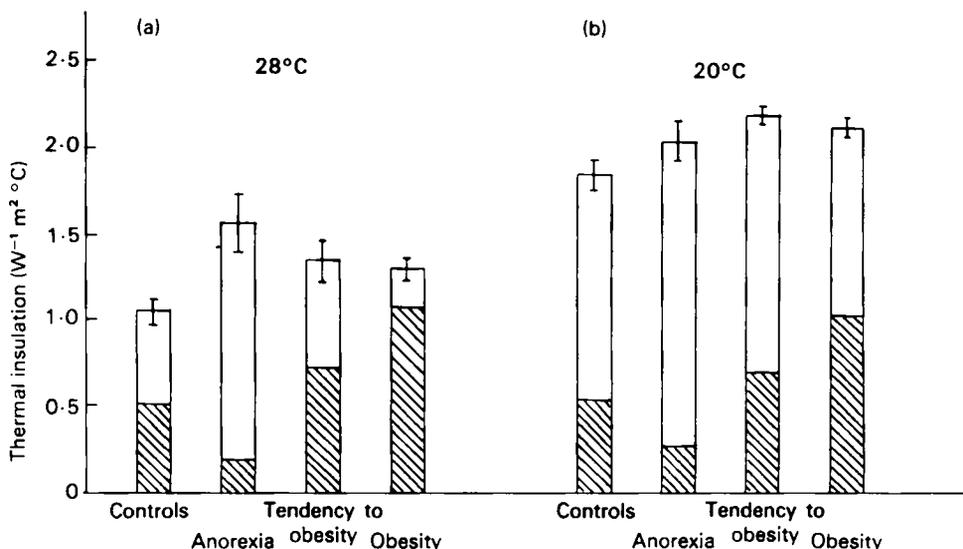


Fig. 4. Thermal body insulation ($W^{-1} m^2 \text{ } ^\circ C$) in the four groups of female subjects as in Fig. 2. (a) 30 min exposure at 28° . (b) 1 h exposure at 20° . \square , represents the insulation due to the subcutaneous fat. \square , represents the insulation due to the tissues underlying the subcutaneous fat, i.e., the insulation related to the decrease of blood flow by vasoconstriction. Vertical bars represent the standard errors of the mean values for total insulation.

Fig. 4 shows that subcutaneous fat insulation depends upon the weight of the subjects (dashed area of the columns). The white part of the columns represents the insulation due to the tissues underlying the subcutaneous fat, i.e., the

insulation related to the decrease of blood flow by vasoconstriction. Subjects with anorexia nervosa had the largest insulation at 28°, thanks to an intense vasoconstriction in subcutaneous tissues. In contrast, the obese had a large 'fat' insulation and a small 'regulatory' insulation.

After 1 h of cold exposure at 20°, body insulation rose in all subjects. The increase in insulation was especially important in the tendency to obesity and obese groups. Subjects with a tendency to obesity presented a large 'regulatory' insulation (white part of the column) which indicates an increased vasoconstriction of subcutaneous vessels with a decreased heat transfer by the blood flow.

Metabolic heat production

The physiological consequence of the large insulation and of the decreased heat loss in the obese groups is a smaller metabolic response to cold. The decrease in skin temperature is a well documented stimulus of metabolic heat production in the cold. Therefore in Fig. 5, the metabolic heat production (\dot{M}) was plotted against mean skin temperature (\bar{T}_{sk}). Controls had higher \dot{M} than the obese (both groups of obese were considered together) and anorexia nervosa subjects. When \bar{T}_{sk} fell below 30°, controls increased \dot{M} (beginning of shivering) while obese or anorexic subjects showed no stimulation of \dot{M} . Hence, the threshold of \bar{T}_{sk} at which \dot{M} is stimulated appeared to be lower in obese and anorexic subjects than in controls. Moreover, the obese and to a lesser extent the anorexic subjects showed the largest thermal insulation which allowed them to save energy by decreasing heat losses. This economy of energy is probably related to the lack of stimulation of thermogenesis during cold exposure.

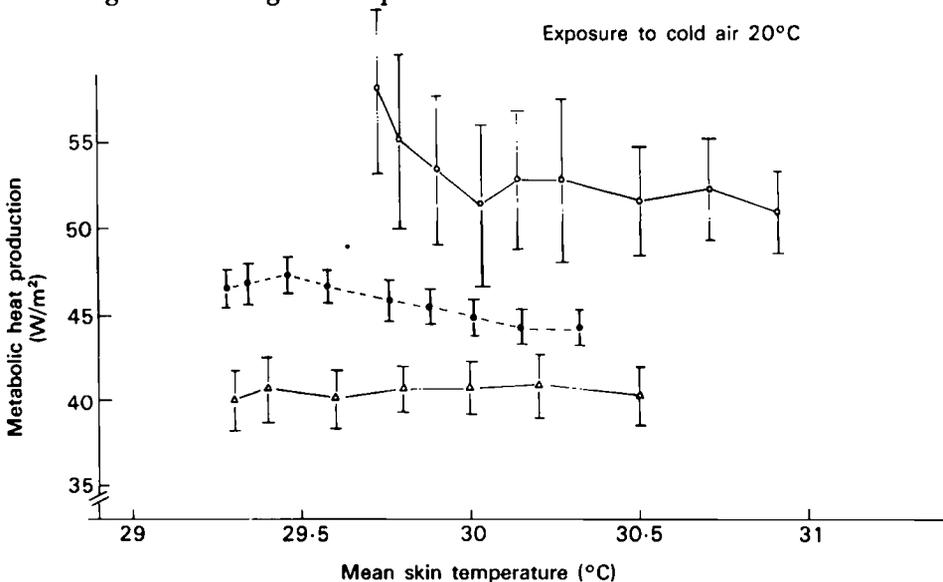


Fig. 5. Relationship between mean skin temperature and metabolic heat production (in W/m^2) in the control group \circ — \circ , the tendency to obesity and the obese groups \bullet — \bullet , and the anorexia nervosa group \triangle — \triangle . The measurements were performed during 1 h exposure at an ambient temperature of 20°.

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