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Fasting biochemical parameters and their relationship to anthropometric measurements in childhood obesity

by

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Fasting plasma immunoreactive insulin, triglyceride, free fatty acid, cholesterol, glycerol, blood glucose, lactate, pyruvate level, and lactate/pyruvate ratio were measured and an intravenous glucose tolerance test was done in obese and control children. The levels of most of the metabolites and the glucose tolerance were similar in the two groups except for the higher immunoreactive insulin and triglyceride levels in the obese group. Further metabolic alterations could be detected when the obese children were divided into subgroups on the basis of fasting insulin and triglyceride levels, and of glucose tolerance. Only three significant correlations were found between metabolic parameters and anthropometric measurements when the obese group was treated as a whole, but numerous other positive and negative correlations were detected in the subgroups. The most striking and unexpected finding was the negative correlation between cholesterol and free fatty acids and some indices of fatness in the whole obese group and in some subgroups. It is concluded that obese children ("exogenous obesity") cannot be regarded as a metabolically homogeneous group and the correlations between anthropometric parameters and plasma metabolites remain to be controversial.

The hormonal and metabolic abnormalities have been widely investigated in "exogenous obesity". It is generally associated with fasting and reactive hyperinsulinaemia [27, 26, 11, 4, 9, 10] as well as with an abnormal pattern of growth hormone secretory response during glucose tolerance test [26, 35], insulin-induced hypoglycaemia [7], arginine infusion [26, 7, 11] and exercise [38]. As to the plasma lipid concentration, the most common abnormality is an increase in the concentration of plasma triglycerides [1, 32, 25, 37].

Concerning the relationship between body composition and plasma hormonal and nutrient levels, contradictory observations have been reported. Besides negative results [30, 23], some authors observed a positive correlation between body fat mass, adipose cell size and fasting insulin level [13, 34, 31]. Such a relationship between circulating insulin and total body fat has also been found by

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Parra et al. [26] in obese children. In contrast with the significant positive correlation between plasma triglyceride, cholesterol and fatness, Thomas and Garn [36] were not able to show such a relationship. Blood glucose and anthropometric indicators (skinfold thickness, weight and height) turned out to correlate directly [18] in a population aged from 5 to 80 years.

In view of these inconsistent observations the present study was undertaken to investigate the relationship between anthropometric measurements and plasma metabolites and hormonal levels in different subgroups of obese children.

Materials and Methods

The investigations were carried out in 24 non-obese and 35 obese children with body weights more than 20% in excess of the ideal body weight, as given in the tables of Maaser [21]. In children whose height exceeded 160 cm, the ideal body weight was calculated according to the formula (height-100)$\times$0.9. Skinfold measurements were performed at 4 sites (biceps, triceps, subscapular, suprailiacal) with Herpenden caliper according to Durnin and Rahaman [12]. Body fat per cent of weight was calculated using the formula $\left(\frac{4.95}{\text{body density}} - 4.5\right) \times 100$ [33]. The formulas given by Brook [5] were used for the determination of body density. Lean body mass and theoretical body water were calculated with the help of the formulas total body weight minus body fat mass and lean body mass $\times 0.73$, respectively. The indices of relative weight, the ponderal index $\left(\frac{\text{weight}^{-3}}{\text{height}}\right)$ and the body mass index $\left(\frac{\text{weight}}{\text{height}}\,2\right)$ were used for further characterization of obesity.

Blood samples for biochemical determinations were taken on two different days after an overnight fast and the mean of the two values were used for the calculations. To perform an intravenous glucose tolerance test, 0.5 g/kg glucose was injected into a cubital vein in two minutes using a 40% solution. Blood samples were drawn from the other arm just before and 10, 20, 40, 60, 90 and 120 minutes after the glucose load. K_G was calculated according to the formula $\ln 2/t_{1/2} \times 100$, where $t_{1/2}$ was assessed by the usual graphic method on semilogarithmic paper.

Blood glucose concentration was estimated by the glucose oxidase method. Plasma triglyceride and glycerol levels were determined with full enzymatic method using Boehringer kit. Plasma FFA was measured according to Laurell and Tibbling [20]. Plasma lactate and pyruvate determinations were performed with the enzymatic assay of Hajivassilion and Rieder [1]. Immunoreactive insulin (IRI) and growth hormone (GH) levels were measured with double antibody radioimmunoassay method using commercially available kits of Radiochemical Centre Amersham for IRI and of Biodata for GH determination.

The mean, standard error and the correlation coefficient were calculated with standard methods. Statistical significance of the difference between the means of various groups was evaluated according to Student's t-test.

Results

Fasting metabolite and hormone levels

IRI and triglyceride concentrations were significantly increased in the obese children (Fig. 1). Other bio-

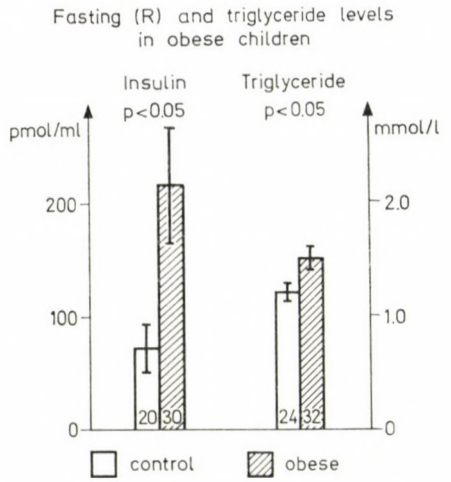

FIG. 1. Fasting IRI and triglyceride levels in obese children

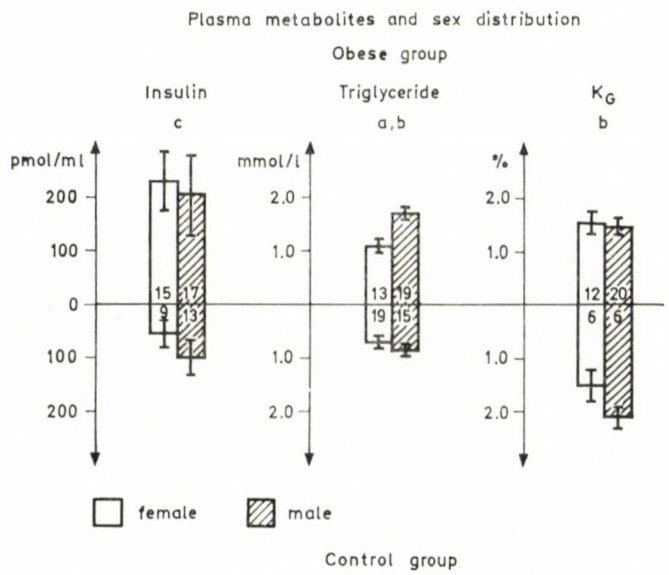

FIG. 2. Effect of sex distribution on plasma metabolites. a) $p < 0.05$ obese female — obese male; b) $p < 0.05$ control male — obese male; c) $p < 0.05$ control female — obese female

chemical parameters such as blood glucose, FFA, cholesterol, glycerol, lactate, pyruvate, lactate/pyruvate ratio and K_G were similar in the obese and control groups.

Both obese and control children were divided into male and female subgroups and the metabolite levels of the subgroups were compared within the control and obese group.

Furthermore, comparisons were made between obese and control female and obese and control male children, respectively. Metabolites with significant differences within or between the groups are shown in Fig. 2.

No significant sex difference could be detected in the baseline levels of the control children. Fasting metabolite and hormone levels of the obese girls and boys were similar except the significantly higher triglyceride levels in the obese boys. Fasting IRI was higher in the obese females, triglyceride higher and K_G lower in the obese males, compared to the control females and males, respectively.

The male and female obese children were further divided into the following subgroups. (1) Hypertriglyceridaemic (HT) and non-hypertriglycerid-

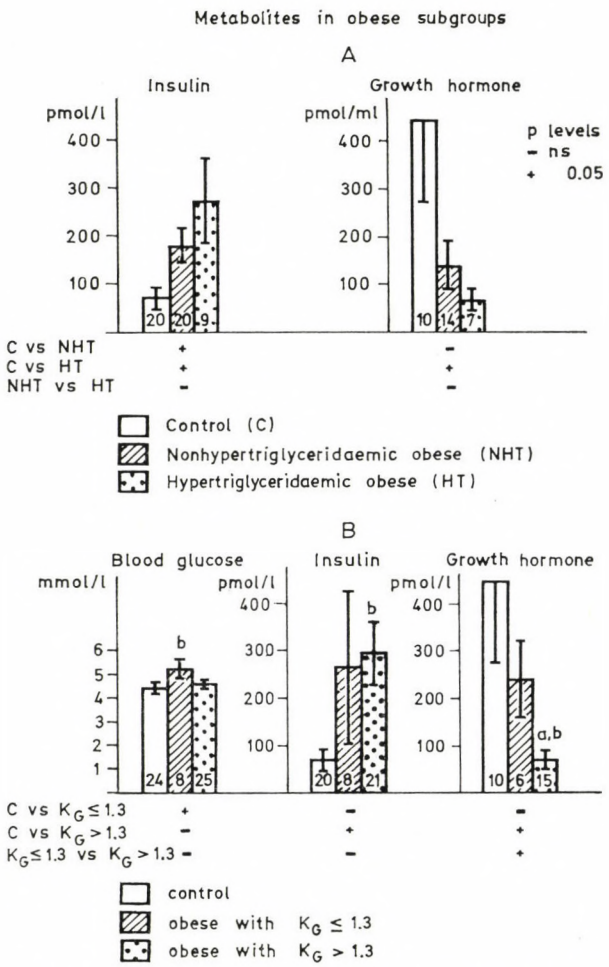

FIG. 3. Metabolite levels in the obese subgroups

TABLE I

Anthropometric values in obese and control children (M ± SE)

	Control	Obese	p
Age, years	10.6	10.7	ns
Weight, Kp	32.9±2.2	60.8±3.3	<0.001
Height, cm	142.7±3	149.4±2.6	ns
Triceps, mm	10.0±0.7	28.9±1.0	<0.001
Biceps, mm	5.6±0.4	15.6±0.9	<0.001
Subscapular, mm	8.3±0.7	31.5±1.0	<0.001
Suprailiacal, mm	9.4±0.8	27.7±1.6	<0.001
Sum of skinfolds, mm	33.3±2.41	104.7±3.6	<0.001
Body fat, per cent of weight	20.0±1.3	40.5±0.8	<0.001
Lean body mass, Kp	26.2±1.6	37.1±2.3	<0.001
Theoretical body water, per cent	59.0±1.1	43.8±0.6	<0.001
Relative body weight, per cent	89.9±2.5	148.9±3.8	<0.001
Body mass index (weight Kp/height cm^2)×10^3	1.6±0.1	2.7±0.1	<0.001
Ponderal index (weight Kp^{-3}/height cm)×10^2	2.2±0.1	2.6±0.1	<0.001

aemic (NHT) children with a fasting triglyceride value above or below 1.7 mmol. (2) Hyperinsulinaemic (HI) and non-hyperinsulinaemic (NHI) subgroups were based on the mean value of the glucose induced insulin response. A value exceeding 956 pmol/l was regarded as hyperinsulinaemic. (3) A K_G value below or above 1.3 was used in forming the subgroup of normal and impaired glucose tolerance, respectively (NK_G and IK_G groups).

Both hypertriglyceridaemic and non-hypertriglyceridaemic children had significantly higher fasting insulin levels than controls, but the difference between the two subgroups was not significant (Fig. 3a). Both subgroups had considerably lower fasting GH values; especially low levels were observed in hypertriglyceridaemic children (Fig. 3a).

None of the measured metabolites differed significantly in the hyperinsulaemic and non-hyperinsulinaemic subgroups.

Obese children with normal K_G had fasting blood glucose similar to controls, but fasting blood glucose was significantly higher in the "impaired K_G" subgroup (Fig. 3b).

Anthropometric measurements

All the anthropometric parameters used to measure the degree of fatness showed a considerable and significant increment (Table I). Not only body

fat, but the lean body mass was also increased in overweight children, while their height remained in the normal range. Theoretical body water was significantly decreased in obese children.

There was no significant difference between the anthropometric parameters of control boys and girls and obese boys and girls. Body fat and lean body mass were in excess in obese males as compared to control males, while the lean body mass was nearly the same in obese females as in control females.

Hypertriglyceridaemic children were significantly taller and had lower relative body weight and ponderal index than children in the non-hypertriglyceridaemic subgroup (Fig. 4a).

Anthropometric parameters were similar in the hyperinsulinaemic and non-hyperinsulinaemic subgroups.

Children in the "impaired K_G" subgroup were on the average 2 years older and nearly 20 Kp heavier than children in the normal KG subgroup. They were also significantly taller, had an increased lean body mass and thicker biceps skinfold (Fig. 4b).

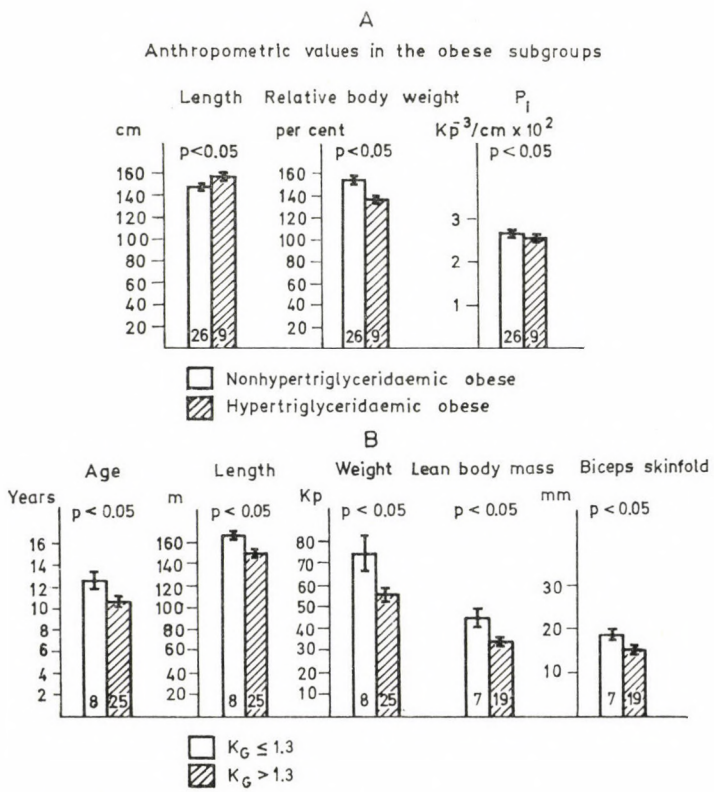

FIG. 4. Anthropometric values in the obese subgroups

TABLE II

Significant correlations between biochemical and anthropometric parameters in control and obese children and in obese subgroups

	Control		Obese		Hyperinsulinaemic obese		Non-hyperinsulinaemic obese	
K_G	weight	−0.798+	weight	−0.629++	height	−0.596+	weight	−0.593+
Insulin pM/ml	triceps skf	0.478+			body fat	0.734++		
	suprail. skf	0.432+			body water	−0.726++		
FFA uM/l	biceps	−0.467+			suprail. skf	−0.612+		
	W/H²	−0.540+						
Cholesterol mM/l			biceps skf	−0.485+	biceps skf	−0.601+		
			sum of skf	−0.364+				
Triglyceride mM/l	weight	0.424+						
	biceps skf	0.713++						
	subscap. skf	0.596++						
	suprail. skf	0.632++						
	sum of skf	0.583++						
	body water	−0.493+						
	rel. weight	0.598++						
Glycerol mM/l							biceps skf	−0.746+
							subscap. skf	−0.599+
							sum of skf	−0.689+
							weight	−0.533+

p levels: + < 0.05
++ < 0.01

Correlation between biochemical parameters and anthropometric measurements
Control and obese group

K_G correlated negatively with body weight in both control and obese children (Table II). Insulin and two skinfolds (triceps and suprailiacal) correlated positively and significantly in control but not in obese children. FFA levels showed a negative correlation with biceps skinfold and with body mass index, but only in the control group. Cholesterol also correlated negatively with biceps skinfold and with the sum of skinfolds, but only in the obese group. Plasma triglycerides correlated with a number of anthropometric measurements listed in Table II.

Obese subgroups

The hyperinsulinaemic subgroup had some further correlations not observed in the obese group as a whole (Table III). Insulin had a strong significant correlation with body fat and a negative one with body water. FFA and suprailiacal skinfold, cholesterol and biceps skinfold also correlated negatively. Interestingly enough a number of skinfolds and weight showed negative correlation with glycerol, but only in the non-hyperinsulinaemic subgroup.

Some of the anthropometric data of the hypertriglyceridaemic obese children correlated with K_G and FFA. Non-hypertriglyceridaemic children had a greater number of significant correlations between their metabolite levels and anthropometric data.

Only few significant correlations were found in the normal and "impaired" K_G subgroups.

Discussion

In agreement with previous reports [1, 4, 9, 10, 11, 25–27, 34, 37] the two metabolic characteristics of obese children were hyperinsulinaemia and hypertriglyceridaemia. Fasting FFA, glycerol and cholesterol levels remained in the normal range.

Further metabolic alterations could be detected when the obese children were divided into subgroups on the basis of fasting insulin and triglyceride levels and that of glucose tolerance. Decreased basal growth hormone levels were found in the HT, NHI and NK_G subgroups. Plasma cholesterol was increased in the NHI and IK_G groups. Hypertriglyceridaemia was a characteristic feature of a small subgroup of obese children, mainly of males. Eight of the nine hypertriglyceridaemic children were boys.

Impaired glucose tolerance (IK_G) was found in eight children. Lactate was decreased in the NHT group only. On the basis of these observations we may conclude that some of the biochemical alterations are not characteristic of obese children as a whole, so they cannot be regarded as a homogeneous group.

Correlations between anthropometric parameters and biochemical alter-

TABLE III

Significant correlations between biochemical and anthropometric parameters in obese subgroups

	Hypertriglyceridaemic obese		Non-hypertriglyceridaemic obese		K_G 1.3 obese		K_G 1.3 obese	
K_G	sum of skf	−0.752	weight	−0.613	suprail. skf	−0.558		
			height	−0.604				
Insulin, pmol/l			triceps skf	0.560				
			biceps skf	0.738				
			subscap. skf	0.478				
			sum of skf	0.611				
			rel. weight	0.434				
			body water	−0.647				
FFA, μmol/l	rel. weight	0.794			height	−0.452	height	−0.737
	P_i	0.703						
Cholesterol, mmol/l			weight	−0.466				
			biceps skf	−0.569				
			subscap. skf	−0.546				

p levels: + < 0.05
++ < 0.01

ation may help to identify obese subgroups of liability to later risks by simple anthropometric measurements. Several authors [6, 29, 31] have demonstrated an inverse correlation between body fat mass and glucose tolerance. A similar negative correlation between K_G and weight was observed in our study.

Positive correlation between fasting insulin level and the degree of fatness was observed only in the controls, in the hyperinsulinaemic and non-hypertriglyceridaemic obese subgroups.

It is noteworthy that we found a positive correlation between plasma triglyceride levels and the degree of fatness in control but not in obese children. Earlier studies reporting a positive correlation of plasma triglyceride with fatness were performed on a random population including lean and obese individuals [14, 17, 3, 18].

FFA showed negative correlation with some anthropometric data, such as biceps skinfold, body mass index in controls, HI, IK_G and NK_G subgroups, while these correlations were positive in the Hi subgroup. Plasma glycerol also showed a negative correlation with biceps, subscapular skinfolds and with the sum of the 4 skinfolds and weight in NHI children. The unexpected negative correlation of FFA and glycerol in some subgroups can be explained with impaired FFA mobilization from adipose tissue [19]. Rath and Petrasek [30] reported a significantly lower fatty acid release from subcutaneous adipose tissue in obese women with one or both obese parents as compared with obese subjects with nonobese parents. A low order negative correlation between in vitro FFA release and the degree of fatness has also been reported [30]. A decreased release of fatty acids from adipose tissue was found in genetically obese animals [22]. Other authors, however, could not confirm these observations [24, 16, 8]. Our results also suggest the possibility of decreased lipolysis in certain obese subgroups.

The correlation between plasma cholesterol and anthropometric parameters is controversial. Thomas and Garn [36] found no significant correlation, but subsequent investigators did in fact find a direct relationship [14, 17, 3, 18]. On the other hand, our data in agreement with recent reports [23, 28] show a significant negative correlation between plasma cholesterol and anthropometric parameters (biceps, subscapular skinfold and the sum of 4 skinfolds and weight) in the whole obese group, and the HI and NHT subgroups.

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