

Adipose cell size in obese Africans: evidence against the existence of insulin resistance in some patients

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SUMMARY Aspects of adipose tissue cellularity were examined in 15 non-diabetic premenopausal African women with simple obesity living in Johannesburg. A smaller group of six non-obese Black women served as controls. Adipose tissue was obtained by biopsy from the deltoid, gluteal, and abdominal regions, and the mean fat cell size for each site was determined. Fasting plasma glucose, insulin, and lipid levels, and the glucose and insulin responses to a 100 g oral glucose load, in these subjects provided metabolic data for correlative analyses.

As expected, the overall mean and regional adipocyte sizes were significantly larger in the overweight subjects. Significant regional variations in fat cell size were also seen, the gluteal region adipocytes being larger than those of other sites in both obese and non-obese women. A significant positive correlation was found between fat cell size and the percentage of ideal body weight. There was no significant relationship between adipocyte size, however, and any of the metabolic variables measured—notably basal or stimulated plasma insulin. Nearly half of the overweight women showed large adipocytes with normal plasma insulin concentrations.

A proportion of African women with hypertrophic obesity do not appear to demonstrate any classical metabolic features of insulin resistance; this may be related partly to their high carbohydrate intake and unusual degree of physical activity. Our results do not, however, indicate that hyperinsulinaemia is completely absent in obese Black women.

In previous metabolic studies of obese Africans living in Johannesburg some distinctive features were found, notably with respect to endogenous insulin secretion (Joffe *et al.*, 1975, 1976). A substantial proportion of non-diabetic subjects did not show hyperinsulinaemia, which evoked the speculation that some overweight Black patients lack insulin resistance—the endocrine hall-mark of obesity in most populations (Sims *et al.*, 1973). However, no documentation of adipose cell size has yet been made in these subjects, and the present investigation was focused on this important aspect.

Subjects and methods

We examined 15 non-diabetic, premenopausal African women with simple obesity residing in Johannesburg. A smaller group of six non-obese Black women with minor or inactive medical and surgical conditions served as controls. Various

pertinent clinical features of these two populations are included in Table 1.

The overweight patients had all become fat during adulthood and were relatively stable; they were in domestic or commercial employment and consequently fairly active. Their diet was 'western' in type except for their carbohydrate intake (maize, bread, potatoes, beans, and sugar), which was excessive. Neither they nor the controls were taking drugs known to affect carbohydrate or lipid metabolism, and no dietary restrictions were imposed for several days before investigation. All participating subjects gave their informed consent to the study, which was approved by the University Ethical Committee.

Tests were performed after a 10-hour overnight fast. (Supervision during this period was undertaken in hospital inpatients and arranged in outpatients through prior contact with employers.) Basal plasma samples were taken for the estimation of glucose (Auto Analyzer), immunoreactive insulin (Welborn and Fraser, 1965), and triglyceride and cholesterol (Technicon, 1970). The plasma glucose and insulin

Table 1 Pertinent clinical and plasma biochemical data (mean \pm SE of mean) in obese and non-obese Black women

	% Ideal body weight*	Age (yr)	Skinfold thickness† (mm)	Fasting glucose (mmol/l)	Glucose area‡	Fasting insulin (mU/l)	Insulin area‡	Fasting triglyceride (mmol/l)	Fasting cholesterol (mmol/l)
Obese (n = 15)	185 \pm 9	42 \pm 2	41 \pm 2	5.11 \pm 0.22	16.39 \pm 1.56	19 \pm 5	92 \pm 18	1.07 \pm 0.09	5.65 \pm 0.36
Non-obese (n = 6)	102 \pm 4	39 \pm 6	15 \pm 3	5.22 \pm 0.39	14.06 \pm 1.83	14 \pm 2	58 \pm 11	0.98 \pm 0.31	4.20 \pm 0.39
Significance	p < 0.0005	NS	p < 0.0005	NS	NS	NS	NS	NS	p < 0.05

*Based on Metropolitan Life Insurance Co Tables, 1959.

†Mean of deltoid and abdominal wall.

‡Arbitrary units.

Conversion: SI to traditional units—Glucose: 1 mmol/l \approx 18 mg/100 ml.
Triglyceride: 1 mmol/l \approx 88.5 mg/100 ml.
Cholesterol: 1 mmol/l \approx 38.6 mg/100 ml.

responses to a 100 g oral glucose load were then determined over 2 hours, and the areas circumscribed by the glucose and insulin curves were calculated (Spitz *et al.*, 1970). On the same morning adipose tissue was obtained by percutaneous needle biopsies from the deltoid, gluteal, and abdominal wall regions of each subject. The samples were immediately placed in chilled physiological saline, and the mean fat cell size for each site was determined by a modification of the direct microscope technique discussed by Sjöström (1977). The 'overall mean fat cell size' was derived from an average of the three sites and expressed as the triglyceride content per cell. Results were analysed for significance by paired and unpaired *t* tests and linear correlation coefficients (Bradford Hill, 1966).

Results

Table 1 summarises the biochemical findings in the two groups. A tendency to hyperinsulinaemia and hypercholesterolaemia was noted in the obese population.

The overall mean and regional fat cell sizes of the obese and non-obese subjects are depicted in Figure 1. As expected, mean and regional adipocyte sizes were all significantly larger in the overweight patients. Significant regional variations in fat cell size were also seen, the gluteal region adipocytes being larger than those of other sites in both obese and non-obese women.

Correlations of fat cell size with other clinical and metabolic variables were examined. A significant positive correlation emerged between the overall mean fat cell size and the percentage ideal body weight (IBW) (Fig. 2). Individual sites showed a similar relationship to % IBW, closest for the gluteal region ($r = 0.70$). On the other hand, there was no significant correlation between adipocyte size (either the overall mean or from individual sites) and any of the metabolic variables measured—notably basal plasma insulin, insulin area, triglyceride or fasting

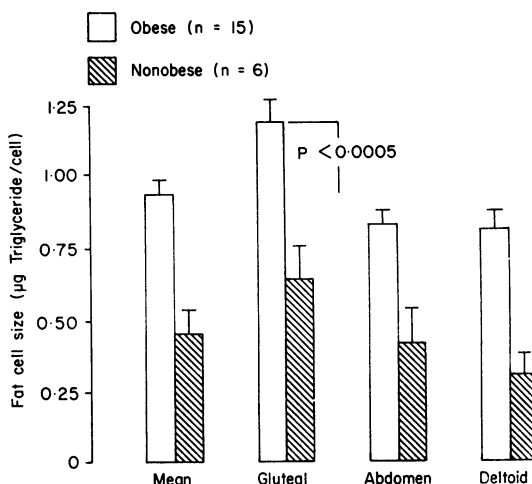


Fig. 1 Overall mean and regional adipocyte sizes of obese and non-obese African women. Differences between obese and non-obese groups are all statistically significant ($p < 0.001$). Gluteal region fat cells are larger than those of other sites, particularly in obese subjects.

glucose (Table 2). This held true if the obese patients were analysed separately as well as for the pooled data. To calculate the proportion of overweight subjects with large adipocytes who had normal or low insulin levels, we selected those with basal insulin concentrations below 15 mU/l and mean triglyceride contents exceeding 0.70 $\mu\text{g}/\text{fat cell}$. Six of the 15 (40%) obese patients showed this combination.

Discussion

At a morphological level the pattern of adipose tissue cellularity in African women is similar to that reported in other studies on normal subjects and hypertrophic obesity (Björntorp *et al.*, 1975; Krotkiewski *et al.*, 1975). Thus adipocytes of obese

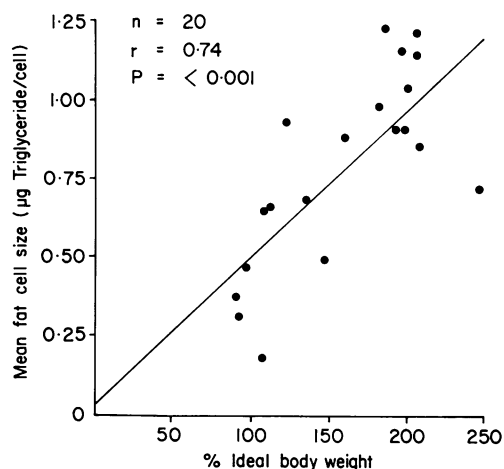


Fig. 2 Correlation between overall mean adipocyte size and per cent ideal body weight in obese and non-obese African women. (One obese patient has been omitted because of uncertain weight documentation.)

Table 2 Correlation coefficients between overall mean and regional adipocyte sizes and some metabolic variables in obese and non-obese Black women (pooled data)

Adipocyte size	Fasting glucose	Fasting insulin	Insulin area	Fasting triglyceride	Fasting cholesterol
Mean	0.13	0.15	0.24	0.23	0.20
Gluteal	0.18	0.12	0.10	-0.28	—
Abdominal	0.15	0.08	0.13	0.02	—
Deltoid	0.25	0.22	0.43	0.01	—

All r values are non-significant ($p > 0.05$).

subjects were greater than those of the non-obese, there was a significant regional variation, gluteal fat cells being the largest, and positive correlations were noted with the degree of body weight. We have not assessed the total number of fat cells present, but a recent publication casts doubt on the reliability of this measurement (Jung *et al.*, 1978).

Of greater interest was the lack of correlation between fat cell size and plasma insulin levels in the non-diabetic, obese patients, an observation previously reported in overweight subjects living in Sweden and the USA (Björntorp and Sjöström, 1971; Stern *et al.*, 1972). This and the fact that in many instances the large adipocytes were not accompanied by hyperinsulinaemia suggests that insulin resistance was commonly not associated with these adipocytes. In terms of modern concepts, the concentration or affinity of insulin receptors seems to be normal on these cells and not decreased

(Archer *et al.*, 1975), but further investigations along these lines are warranted. Our results do not imply that insulin resistance is totally lacking in obese Black women since some subjects with large adipocytes showed undoubted hyperinsulinaemia. Reasons for the absence of insulin resistance in a proportion of overweight African patients are speculative but may be related partly to such factors as their high carbohydrate intake (Lerner *et al.*, 1971) and their unusual degree of physical activity (Björntorp *et al.*, 1970).

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References

- Archer, J. A., Gorden, P., and Roth, J. (1975). Defect in insulin binding to receptors in obese man: amelioration with calorie restriction. *Journal of Clinical Investigation*, **55**, 166-174.
- Björntorp, P., Carlgren, G., Isaksson, B., Krotkiewski, M., Larsson, B., and Sjöström, L. (1975). Effect of an energy-reduced dietary regimen in relation to adipose tissue cellularity in obese women. *American Journal of Clinical Nutrition*, **28**, 445-452.
- Björntorp, P., De Jonghe, K., Sjöström, L., and Sullivan, L. (1970). The effect of physical training on insulin production in obesity. *Metabolism*, **19**, 631-638.
- Björntorp, P., and Sjöström, L. (1971). Number and size of adipose tissue fat cells in relation to metabolism in human obesity. *Metabolism*, **20**, 703-713.
- Bradford Hill, A. (1966). *Principles of Medical Statistics*, 8th edition. Lancet, London.
- Joffe, B. I., Goldberg, R. B., and Seftel, H. C. (1976). In *Current Topics in Diabetes Research* (International Congress Series, 400), edited by J. S. Bajaj, p. 166. Excerpta Medica, Amsterdam.
- Joffe, B. I., Goldberg, R. B., Seftel, H. C., and Distiller, L. A. (1975). Insulin, glucose and triglyceride relationships in obese African subjects. *American Journal of Clinical Nutrition*, **28**, 616-620.
- Jung, R. T., Gurr, M. I., Robinson, M. P., and James, W. P. T. (1978). Does adipocyte hypercellularity in obesity exist? *British Medical Journal*, **2**, 319-321.
- Krotkiewski, M., Sjöström, L., Björntorp, P., and Smith, U. (1975). Regional adipose tissue cellularity in relation to metabolism in young and middle-aged women. *Metabolism*, **24**, 703-710.
- Lerner, R. L., Brunzell, J. D., Hazzard, W. R., Porte, D., Jr., and Bierman, E. L. (1971). Mechanism of improved glucose tolerance on high carbohydrate diets in normals and mild diabetics (Abstract). *Diabetes*, **20**, 342-343.
- Sims, E. A. H., Danforth, E., Jr., Horton, E. S., Bray,

- G. A., Glennon, J. A., and Salans, L. B. (1973). Endocrine and metabolic effects of experimental obesity in man. *Recent Progress in Hormone Research*, **29**, 457-496.
- Sjöström, L. (1977). Comments on adipocyte sizing. *Clinica Chimica Acta*, **74**, 89-91.
- Spitz, I. M., Rubenstein, A. H., Bersohn, I., Abrahams, C., and Lowy, C. (1970). Carbohydrate metabolism in renal disease. *Quarterly Journal of Medicine*, **39**, 201-226.
- Stern, J. S., Batchelor, B. R., Hollander, N., Cohn, C. K. and Hirsch, J. (1972). Adipose-cell size and immunoreactive insulin levels in obese and normal-weight adults. *Lancet*, **2**, 948-951.
- Technicon (1970). Simultaneous measurements of cholesterol and triglycerides. In *Auto Analyzer Manual AA 11*. Technicon, Tarrytown, N.Y.
- Welborn, T. A., and Fraser, T. R. (1965). The double antibody immunoassay of insulin. *Diabetologia*, **1**, 211-218.

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