

**Rôle of Lipophilia in the Etiology of Obesity.\***

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Bergmann<sup>1</sup> suggested that the adipose cells of the obese possess a quality which permits them to seize an abnormally large amount of circulating fat and to hold this fat in the storage depots when the normal individual would release it as a source of energy. By this mechanism neither ingested nor stored fat is available for energy in the obese individual, thus rationalizing the increased food intake.

The only experimental data to support this concept has been supplied by Hetenyi,<sup>2</sup> who found that the total blood lipids of obese subjects decreased during undernutrition, but remained constant in individuals of normal weight. Hetenyi interpreted this fall in total blood lipids as indicating that the fat could not be mobilized for heat production. This was felt to be direct evidence that lipophilia actually is a determining factor in causing obesity.

Since in each instance Hetenyi's subject lost at least one kilo of body weight during the period of undernutrition, his interpretation could have been readily evaluated by nitrogen balance studies in obese individuals during undernutrition, but no such data were published. It is well known that the glycogen stores in the animal organism are rapidly depleted during 2 to 3 days of undernutrition so that after this preliminary period there remains only fat and protein in the body to be utilized for heat production. If fat stores can not be mobilized and so utilized as is postulated by the theory of lipophilia, a negative nitrogen balance should rapidly ensue, or weight should remain constant. Even though Strang<sup>3</sup> previously demonstrated that obese individuals remain in nitrogen balance during severe undernutrition as long as the protein intake remains one gram per kilo of ideal body weight or higher, nevertheless it was felt that similar nitrogen balance studies over a comparatively long period of

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<sup>1</sup> v. Bergmann, G., *Oppenheimer Handbuch der Biochemie*, 1910, **4** (Teil 2), 212.

<sup>2</sup> Hetenyi, Geza, *Deutsch. Arch. f. klin. Med.*, 1936, **179**, 134.

<sup>3</sup> Strang, J. M., McClugage, H. B., and Evans, F. A., *Am. J. Med. Sc.*, 1931, **181**, 336.

time in conjunction with the determination of total blood lipids would help in evaluating the theory of lipophilia.

*Procedure.* Three obese female subjects and 3 female controls of normal weight were given constant daily diets of known nitrogen content. Total daily protein intake was always higher than one gram per kilo of ideal body weight. The initial caloric value of the diet was approximately 80% of the basal requirement for the individual. This was decreased 20% at weekly intervals so that by the fourth week the caloric value of the diet was only 20% of the basal requirement. Daily 24-hour urinary nitrogen excretion was determined by the macro-Kjeldahl method and total post-absorptive blood serum lipids were determined by the micro-oxidative procedure of Boyd<sup>4</sup> at weekly intervals. Total heat production of each obese individual was measured by the determination of insensible loss of weight<sup>5</sup> on at least 6 successive days and the average of all daily values was assumed to be the average daily heat production of the individual for the entire experimental period.

*Results and Discussion.* Table I shows the data for the obese subjects. In each instance (with one exception) positive nitrogen balance was maintained throughout the entire period of observation. Blood lipids varied considerably with some tendency to rise during the early days of undernutrition but to fall later to nearly their initial values. In the control subjects (Table II) there was some tendency for a negative nitrogen balance to occur, but the blood lipids varied essentially in the same direction as for the obese subjects. Thus from our data we could find no evidence that obese subjects were oxidizing their body protein and were forced to the conclusion that they were utilizing their own body fat. The latter appeared to be as easily available for heat production as in the normal individual. Likewise we were unable to confirm Hetenyi's contention that there is a difference in the response of the total serum lipids in obese and normal subjects to underfeeding. We can not interpret the variations in blood lipids. We feel that these variations are not associated with any intrinsic abnormality of the adipose tissue cell. The lipemia during fasting in mice found by MacLachlan<sup>6</sup> in contrast to the slight fall of blood lipids found by Chaikoff, *et al.*,<sup>7</sup> in both normal and obese dogs during undernutrition indicates at least one other factor, a species variability.

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<sup>4</sup> Boyd, E. M., *J. Lab. and Clin. Med.*, 1936, **22**, 956.

<sup>5</sup> Newburgh, L. H., Johnston, M. W., Lashmet, F. H., and Sheldon, J. M., *J. Nutrition*, 1937, **13**, 203.

<sup>6</sup> MacLachlan, P. L., *Proc. Soc. Exp. Biol. and Med.*, 1941, **48**, 411.

<sup>7</sup> Entenman, C., and Chaikoff, I. L., *J. Biol. Chem.*, 1942, **142**, 129.

TABLE I.  
Nitrogen Balance, Total Serum Lipids and Weight Loss of Obese Subjects During Undernutrition.

Subject	Diet	Days of diet	*Nitrogen balance, g	Total serum lipids, mg%	Avg 24-hr heat production	†Wt loss (lbs)	
						Actual	Predicted
B.B.	<i>Ad lib.</i>			699.9			
Ht. 5'6½"	80% basal	7	+1.61	807.7			
Wt. 281	60% "	7	+0.87	868.1	2932	19.75	19.6
	40% "	7	+0.40	910.0			
	20% "	11	-0.37	710.0			
	20% "	7	-0.37	493.0			
L.W.	<i>Ad lib.</i>			540.7			
Ht. 5'7¼"	80% basal	7	+1.21	574.4			
Wt. 248	60% "	7	+4.62	700.0	2409	17.0	17.1
	40% "	7	+3.59	850.0			
	20% "	7	+1.20	950.0			
	20% "	7	+1.20	630.0			
O.P.	<i>Ad lib.</i>			560.0			
Ht. 5'7"	80% basal	7	+1.09	700.0			
Wt. 227	60% "	7	+1.69	856.0	3000	11.0	10.5
	40% "	7	+1.60	610.0			
	20% "	7	+1.70	605.0			

\*First three days on each diet omitted.

†Loss for entire experimental period except for first 3 days.

TABLE II.  
Nitrogen Balance and Total Serum Lipids of Control Subjects During Undernutrition for 7-day Diet.

Subject	Diet	*Nitrogen balance, g	Total serum lipids, mg%
R.P.	<i>Ad lib.</i>		523
Ht. 5'5"	80% basal	-1.12	706
Wt. 124.5	60% "	+0.08	846
	40% "	-1.40	703
L.A.	<i>Ad lib.</i>		610
Ht. 5'4"	80% basal	+1.63	750
Wt. 122½	60% "	+0.76	843
	40% "	+0.26	607
M.M.	<i>Ad lib.</i>		499
Ht. 5'3"	80% basal	+0.21	710
Wt. 113	60% "	+2.21	806
	40% "	+0.82	542

\*Calculated as in Table I.

Table I also shows the actual weight loss of our obese subjects in comparison to their predicted weight loss. In each instance these values are in close agreement. However, our predicted values for weight loss are calculated on the basis of loss of body fat. Were we to assume that body fat can not be mobilized and oxidized the pre-

dicted values for weight loss would have, of necessity, to be calculated on the basis of loss of body protein. In such a case our predicted values would be over twice the actual values. We feel that the agreement in our values (calculated on the basis of fat loss) is very strong evidence in favor of the view that body fat is actually utilized and adds further evidence against the existence of lipophilia.

*Summary.* Three obese subjects remained in positive nitrogen balance during a prolonged period of undernutrition. The blood lipids varied in essentially the same manner as in 3 control subjects. The actual weight loss during undernutrition was in very close agreement with that predicted on the assumption that body fat was utilized for heat production. These results indicated that the concept of the existence of lipophilia in human obesity is untenable.

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