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## STUDIES OF FOOD-INTAKE REGULATION IN MAN

### Responses to Variations in Nutritive Density in Lean and Obese Subjects

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**Abstract** The effect on spontaneous food intake of concealed variations in nutritive density of machine-dispensed liquid diet was studied in five lean and four obese young adults and two obese juvenile subjects. They were unaware of the changes in caloric concentration and that food intake was being monitored.

The lean subjects maintained weight during machine feeding, and when nutritive density was altered, promptly adjusted the volume consumed to maintain near constant energy intake. The obese

adults ingested a small fraction of the calories needed to maintain weight and failed to adapt volume intake to appreciable changes in caloric concentration. The obese juvenile subjects consumed large quantities of formula however, one also failed to adjust volume intake when caloric density was varied.

Lean young adults appear to regulate energy intake at the physiologic level when the nutritive concentration of the diet is altered covertly. Grossly obese adults seem incapable of such regulation.

**B**ECAUSE of the complexity of man's relation to his diet, it is difficult to separate the physiologic substratum of human eating behavior from the enormous overlay of nonphysiologic factors that may influence food intake.<sup>1,2</sup> For this reason, it has been difficult to carry out meaningful studies of food-intake regulation in human subjects, and investigators have usually found it necessary to seek answers to their questions relating to man by observing feeding behavior in laboratory animals. Thus, the effect of varying nutritive density on food intake has been measured in several animal species<sup>3-5</sup> but has not been amenable to systematic study in man.

The recent development of an electronically monitored mechanical feeding device has made it possible to examine more objectively certain aspects of eating behavior in human subjects.<sup>6</sup> This machine permits accurate recording of food intake on a minute-by-minute basis while the subject remains unaware of the composition and caloric content of the liquid diet that is dispensed, and of the fact that intake is being monitored. In this way, many of the variables that complicate the normal eating process are minimized and the chances of obtaining more reliable and reproducible data are improved. In the

present study, we used this apparatus to ascertain the effect of systematic changes in caloric density of the diet on spontaneous food intake in lean subjects and obese patients.

### SUBJECTS AND METHODS

Five healthy male students 20 to 25 years of age served as lean subjects. Six grossly obese patients were studied, two were adolescent boys 13 and 15, and four were women 25 to 30 years of age. None of the obese subjects had impaired glucose tolerance. Height and weight data, including relative weights,<sup>7</sup> on all subjects are given in Table 1.

All subjects were studied on a metabolic research ward and were maintained on light activity. An attempt was made to prevent significant day-to-day variations in energy output, as estimated from energy-expenditure diaries.

The food-dispensing apparatus, described in earlier reports,<sup>6,8</sup> is shown diagrammatically in Figure 1. When the feeding apparatus is in use, the reservoir and pump are covered, and the printing timer that registers the food intake is always kept in a separate room. The subject is unaware of the fact that his intake is being recorded, and can attempt to monitor the quantity consumed only by counting the mouthfuls obtained.

After one to seven days on the standard hospital diet, each subject was placed on machine feeding, receiving all food except water from the dispensing device.

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Table 1. Characteristics of the Experimental Subjects.\*

SUBJECT	AGE (YR)	SEX	HEIGHT (CM)	WEIGHT (KG)	RELATIVE WEIGHT (%)†
Lean adult subjects:					
T.T.	22	M	172	62	91
D.S.	25	M	180	73	100
Y.C.	20	M	176	54	77
C.M.	20	M	163	61	100
G.D.	23	M	173	62	91
Obese adult subjects:					
H.D.	25	F	158	84	160
R.M.	30	F	178	143	210
M.G.	30	F	168	103	172
A.F.	25	F	156	85	165
Obese juvenile subjects:					
A.V.	15	M	165	101	163
W.D.	13	M	180	135	178

\*Data obtained at time of entry into study.

†Relative weight =  $100 \times \text{actual/suggested weight}$ .

The formula diet used in these studies was prepared in the research kitchen by means of a dairy-type Manton-Gaulin pressure homogenizer operating at a pressure of 6000 pounds per square inch. In terms of contribution to total calories, the diet had the following composition: carbohydrate (dextrose and lactose), 45 per cent; protein (a mixture of sodium caseinate and skim-milk protein) 15 per cent; and fat (butterfat and vegetable oil), 40 per cent. Vitamins and trace minerals were added to the formula in amounts adequate for daily maintenance.<sup>7</sup> The diet contained 46 and 34 mEq of sodium and potassium per 1000 kcal respectively.

The concentration of the liquid diet was manipulated by the addition or subtraction of water to create varying nutritive densities ranging from 0.5 to 1.5 kcal per milliliter. Concentration changes were masked by the addition of carrageenin as a thickening agent, and a saccharine solution was used to compensate for changes in sweetness of the mixture. In some cases flavoring agents were added to the formula, but when this was done, the same flavor was used throughout a given experiment.

The subjects were weighed each morning upon arising and after voiding. The dial of the metabolic scale (Toledo, model no. 2181) was reversed, and the subjects remained unaware of measured changes in their weight.

## RESULTS

### Lean Adult Subjects

When the nonobese subjects were changed from a hospital diet of conventional food to liquid-formula intake by machine, there was a small initial drop in body weight. (We have observed this phenomenon previously and attribute it in part to water loss resulting from a diminished sodium intake during formula-diet ingestion.) After the early fall in body weight all the lean subjects were able to maintain



Figure 1. Monitored Food-Dispensing Apparatus.

The formula diet (A) is constantly mixed by a magnetic stirrer (B). Tubing from the reservoir leads to a dispensing syringe-type pump (C), which delivers a bolus of formula through the mouthpiece. The entire dispensing unit is contained within a refrigerator. The pump is adjusted to respond with a single delivery cycle to the signal of an actuating button (D). Whenever the button is pressed, a predetermined volume of homogenized formula is delivered directly into the subject's mouth by the pump. Each delivery is recorded by a printing timer (E) that prints out each event and the date and precise time at which the event occurred. The timer and recorder are in a room remote from the subject, who is kept unaware of their existence. When the apparatus is in use, the reservoir and pump remain covered.

weight within fairly narrow limits (0.6 to 2.3 per cent of initial body weight) by making appropriate adjustments in the calorie intake whenever the nutritive density was varied. Table 2 summarizes calorie and volume intakes of the five nonobese subjects while they were obtaining their diet from the dispensing apparatus.\* It is evident that in all of them, a statistically significant increase in volume intake occurred when the nutritive density of the formula was decreased. Moreover, when the subjects were again offered a more concentrated formula, a statistically significant decrease in mean volume intake occurred. Such adjustments in volume intake were sufficiently compensatory to prevent significant variations in calorie intake in all but two

\*For more extensive tables on the lean and obese adults and the obese adolescent subjects, order NAPS Document 01640 from National Auxiliary Publications Service, c/o CCM Information Corporation, 866 3d Ave., New York, N.Y. 10022; remitting \$2 for each microfiche-copy reproduction or \$5 for each photocopy. Checks or money orders should be made payable to CCM Information Corporation—National Auxiliary Publications Service.

Table 2. Effect of Concealed Variations in Caloric Density of Mean Spontaneous Feed Intake ( $\pm$  Standard Error) of Lean and Obese Adults and Obese Adolescents.\*

SUBJECT		SEQUENCE OF VARIATIONS IN CALORIC CONCENTRATION OF DISPENSED DIET							
		P value		P value		P value		P value	
Lean adults:									
T.T.	kcal/ml		0.75(10)		1.5(13)		0.75(15)		1.5(13)
	Volume		3014 $\pm$ 151	<0.001	1566 $\pm$ 72	<0.001	2617 $\pm$ 97	<0.001	1621 $\pm$ 65
	Calories		2260 $\pm$ 131	NS	2349 $\pm$ 108	<0.05	1962 $\pm$ 73	<0.001	2431 $\pm$ 97
D.S.	kcal/ml	1.5(12)		1.0(12)		1.5(9)			
	Volume	1310 $\pm$ 87	<0.005	1732 $\pm$ 98	<0.01	1274 $\pm$ 117			
	Calories	1965 $\pm$ 131	NS	1732 $\pm$ 98	NS	1911 $\pm$ 176			
Y.C.	kcal/ml	1.0(8)		0.66(6)					
	Volume	1447 $\pm$ 180	<0.01	2285 $\pm$ 159					
	Calories	1447 $\pm$ 180	NS	1570 $\pm$ 105					
C.M.	kcal/ml		0.66(7)		1.0(6)				
	Volume		1990 $\pm$ 107	<0.001	1445 $\pm$ 48				
	Calories		1316 $\pm$ 75	NS	1445 $\pm$ 48				
G.D.	kcal/ml	1.0(5)		0.66(5)					
	Volume	2492 $\pm$ 178	<0.01	4079 $\pm$ 417					
	Calories	2492 $\pm$ 178	NS	2447 $\pm$ 244					
Obese adults:									
H.D.	kcal/ml	0.9(7)		0.7(7)		0.9(6)		0.66(9)	
	Volume	324 $\pm$ 22	NS	237 $\pm$ 46	NS	258 $\pm$ 20	NS	230 $\pm$ 18	
	Calories	291 $\pm$ 19	<0.01	168 $\pm$ 33	NS	232 $\pm$ 18	<0.001	138 $\pm$ 11	
R.M.	kcal/ml	1.5(10)		0.75(10)		1.5(10)		0.5(10)	1.5(13)
	Volume	441 $\pm$ 15	NS	432 $\pm$ 25	NS	356 $\pm$ 33	<0.005	208 $\pm$ 27	NS
	Calories	660 $\pm$ 23	<0.001	322 $\pm$ 18	<0.001	533 $\pm$ 49	<0.001	104 $\pm$ 14	<0.001
M.G.	kcal/ml	1.0(11)		0.66(12)		1.0(12)		0.66(13)	
	Volume	452 $\pm$ 34	NS	543 $\pm$ 57	NS	563 $\pm$ 42	<0.005	244 $\pm$ 27	
	Calories	452 $\pm$ 34	NS	358 $\pm$ 37	<0.025	563 $\pm$ 42	<0.001	161 $\pm$ 18	
A.F.	kcal/ml	0.9(7)		0.7(7)		0.9(7)			
	Volume	328 $\pm$ 59	NS	193 $\pm$ 39	NS	159 $\pm$ 25			
	Calories	295 $\pm$ 53	<0.025	135 $\pm$ 27	NS	143 $\pm$ 23			
Obese adolescents:									
A.V.	kcal/ml	1.0(6)		0.66(18)		1.0(13)			
	Volume	3978 $\pm$ 243	NS	4161 $\pm$ 195	NS	4049 $\pm$ 186			
	Calories	3978 $\pm$ 243	<0.001	2774 $\pm$ 130	<0.001	4049 $\pm$ 186			
W.D.	kcal/ml	1.0(11)		0.66(14)					
	Volume	3948 $\pm$ 239	<0.001	5519 $\pm$ 283					
	Calories	3948 $\pm$ 239	NS	3681 $\pm$ 189					

\*A homogeneous liquid formula diet obtained from an automatically monitored food dispensing device was the sole source of calories; no. of days in each experimental period is shown in parentheses; "p" denotes significance of difference between means, & NS not significant.

of 13 feeding periods, whether the formula was diluted or concentrated.

One of the experiments involving a nonobese subject is shown in greater detail in Figure 2A. In this subject (T.T.), calorie and volume intakes in response to alternate concentration and dilution of the machine-dispensed formula were measured for 51 days. Results during two typical experimental periods are shown in the figure in juxtaposition to those (Fig. 2B) obtained in a similar study of an obese patient.

#### Obese Adult Subjects

The food-intake responses of the obese adult subjects on the feeding machine are also summarized in Table 2. Although the subjects were instructed to obtain food from the dispensing apparatus whenever

hungry, they ingested only a small fraction of the calories needed to maintain their weight. Thus, all members of this group lost weight as long as they fed themselves by machine. There was no increase of volume intake in response to formula dilution and no decrease in volume intake after formula concentration. In two subjects (R.M. and M.G.), there were paradoxical drops in volume intake when the nutritive density of the formula was decreased.

Responses to alternate formula dilution and concentration in one obese subject (R.M.) are shown in greater detail in Figure 2B. This patient was studied for 53 days, and the results obtained during three of the five experimental periods are shown in the figure next to those (Fig. 2A) obtained in a lean young adult.

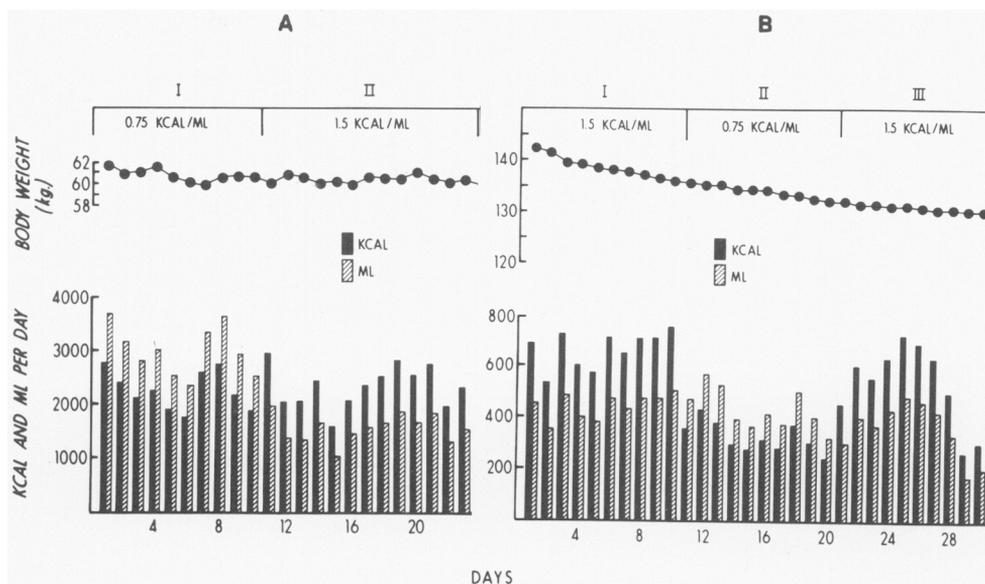


Figure 2. Responses of a Lean Adult Subject (A) and an Obese Adult Patient (B) to Concealed Variations in Nutritive Density. The lean subject (T.T.) spontaneously maintained a relatively constant energy intake by making appropriate adjustments in volume consumption. In contrast, the obese patient (R.M.) consumed far fewer calories than were needed to maintain body weight, and also failed to exhibit any adaptation whatever to the covert changes in caloric density.

### Obese Juvenile Subjects

The subjects with juvenile obesity appeared to adapt partially to the changes in caloric density. During the periods in which caloric density was 1.0 kcal per milliliter, energy intake was in excess of 3900 kcal per day (Table 2). When the formula was covertly diluted subject A.V. increased volume intake slightly, but not enough to maintain a caloric intake comparable to that achieved during intake of the more concentrated formula. In contrast, W.D. compensated for formula dilution with a striking increase in volume intake, thereby maintaining a near constant energy input.

These two obese juvenile subjects differed from the obese adult subjects in that they either maintained or gained weight while receiving the machine-dispensed formula.\*

### DISCUSSION

The data indicate that during periods of alternate caloric concentration and dilution lean young adult subjects spontaneously adjust the volume of formula diet ingested so as to maintain a near constant energy intake. This pattern of adjustment was exhibited

\*An attempt was made to study one additional obese adolescent subject under conditions of machine feeding. This 13-year-old boy (who weighed 131.5 kg) progressively diminished his caloric intake during the first (1.5 kcal per milliliter) seven-day period and refused to use the food-dispensing apparatus during the second (0.75 kcal per milliliter) 10-day period. Thus, it was not possible to ascertain the effect of varying nutritive density in this case.

by all the normal subjects over successive feeding periods totaling 121 days. The fact that the lean subjects showed only minor fluctuations in body weight during the consecutive periods of concealed caloric dilution and concentration is further evidence of their ability to regulate caloric intake at the physiologic level.

The results in lean young adults resemble those reported by Adolph<sup>4</sup> for normal rats. More than two decades ago, Adolph found that when the diet of rats was diluted by mixture with various proportions of nondigestible carbohydrates, the total bulk eaten increased promptly in direct proportion to the degree of dilution. From such results, he concluded that, within limits, rats eat for calories. The observations of Adolph have been confirmed and extended in the dog<sup>5</sup> as well as in the rat.<sup>5,9</sup>

In general, human body weight remains approximately constant for prolonged periods, with about  $\frac{2}{3}$  of day-to-day fluctuations within 0.5 per cent and  $\frac{1}{3}$  within 1.5 per cent of total body weight.<sup>10-12</sup> Despite such relative stability of body weight, there is little evidence for a fine temporal adjustment of the energy regulatory mechanism in man. For example, in studies reported by Durnin,<sup>13</sup> 59 of 69 subjects failed to show a significant correlation between the energy expended on any one day and the intake of calories on the same day. When the intake of calories was compared with the energy expenditure of the previous day, only four subjects exhibited a correlation between the two variables.

In contrast to lean young adults, the obese adults were unable to regulate caloric intake in the face of concealed changes in the nutritive density of the diet. Their weight loss during machine feeding confirms earlier results reported from this laboratory.<sup>8</sup> Observations by other workers have indicated that certain obese patients "deny hunger"<sup>14,15</sup> or fail to respond to "internal" (physiologic) cues that presumably signal hunger and satiety in the nonobese person.<sup>2</sup> Conceivably, the behavior of the obese adult patients under the conditions of the present study could be explained by postulating a lack of sensitivity of energy regulatory centers to internal "hunger" signals. In addition, it is likely that many obese subjects overeat for nonphysiologic reasons — for example, in an attempt to relieve anxiety or boredom, or out of hedonism. When, as in the present study, the eating situation is altered drastically and food stripped of its familiar trappings and reduced to mere calories and nutrients, the obese adult might be expected to respond to food like the normal rat previously made obese by force-feeding. When such animals are no longer force-fed their spontaneous food intake is greatly curtailed until they achieve normal body weight.<sup>16</sup>

The voracity exhibited by two obese juvenile patients is remarkable when compared to the meager intakes of their adult counterparts. Indeed, the food-intake behavior of these subjects is somewhat reminiscent of the bulimia of the hypothalamic hyperphagic rat during the "dynamic phase" that follows bilateral destruction of the ventromedial hypothalamic nuclei.<sup>17</sup> In addition, such animals increase their rate of weight gain still further when fed a calorically dense diet.<sup>18,19</sup> By the same token, the obese adults resemble in some respects hypothalamic rats in the "static phase" in which body weight reaches a plateau and the animal's food intake is reduced. In the static phase, the hypothalamic rat eats enough to maintain its increased weight but appears to become more sensitive to certain "external" stimuli (e.g., taste and consistence of food) that have little influence on the caloric intake of normal control rats studied under similar conditions.<sup>20,22</sup> Similarly, the obese adults in the present study readily consumed all the conventional food that was offered them in the hospital, but they greatly reduced food intake and lost weight rapidly when changed to the bland, "monotonous" diet dispensed on demand by the feeding machine.

By definition, all obese patients suffer from some sort of defect in energy-balance regulation; yet, in any given case, it is usually impossible to determine whether the accumulation of excess body fat has resulted from a physiologic aberration or whether the obesity is primarily "psychogenic." In the past, careful studies of obese patients have failed to disclose any metabolic abnormality sufficient to account for their corpulence.<sup>23,24</sup> Such abnormalities as have been reported<sup>25</sup> may have been secondary to

the obesity and therefore without etiologic importance.<sup>26,27</sup> On the other hand, a number of psychiatric observations have suggested that psychologic factors have an important etiologic role in the genesis of obesity.<sup>28,29</sup> More recently, it has been proposed that, in some cases, obesity may be determined early in life by formation within the body of an overabundance of adipose cells.<sup>30</sup> Yet, in such "constitutional" corpulence, one might expect to find a normal regulation of food intake within the framework of a body composition characterized by a relative excess of fat. The failure of the obese adults in the present study to adapt to concealed changes in the nutritive density of their diets suggests that a regulatory defect was present at the physiologic level. However, the data do not permit a judgment of whether the apparent derangement was primary or whether it resulted from the adiposity.

Obesity in man appears to be the manifestation of a variety of disorders affecting energy balance<sup>31</sup>; thus, it would be hazardous to form any etiologic generalizations about such a complex problem on the basis of results obtained in a small group of obese subjects, however carefully studied.

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## SPECIAL ARTICLE

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### TRENDS IN MEDICAL EDUCATION AND HEALTH SERVICES

#### Their Implications for a Career in Family Medicine

RICHARD M. MAGRAW, M.D.

**Abstract** The selection of careers from among available specialties partly depends on an assessment of trends in medicine. More obviously than other specialties those providing primary care (e.g., family practice) are "system-defined" — i.e., they are shaped and made real by the needs of the present system of care. Students now selecting careers in family medicine are acting on current assumptions about the medical-care system of the future, although opinion in academic medicine and among medical practitioners remains divided about

these issues.

This analysis of factors acting to shape the system of medical care indicates a slow, ponderous and steady movement toward emphasis on primary care, family medicine and family practice. That movement may be expected to accelerate during the next two or three years — a time that will be critical in determining whether the function of primary care and family medicine will be fully professionalized and built into the evolving American medical system.

**M**EDICAL students base their choice of a career among the more than 50 medical specialties, on a variety of personal considerations, but ordinarily have not fully taken into consideration the trends in or "needs" of the general system of care. Taking the "needs" of the system into account might be perceived as adding unnecessary complexity to the selection or as a limitation on personal prerogatives, but it is simply prudent. Most practitioners now in medicine have come to realize that independence in the present interdependent medical-care system is illusory and that it is incorrect to equate an avoidance of accommodation to that system with personal freedom. The maximizing of professional autonomy within the system is a more realistic style of work than insistence on a literal (and isolated) independence and self-sufficiency; participation in the system leaves greater time and energy for professional effectiveness and the pursuit of self-determined goals.

It is my thesis that many students considering a

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career in family medicine perceive that a career in tomorrow's medicine involves accommodation to a developing system, rather than simple entry into one of a variety of free-standing, independent and unconnected professional roles. If so, students' decisions must be weighted by their assessment of what will be needed in the evolving system in addition to their understanding of the established identities or roles of the several specialties today. In this regard it should be noted that although most people do not think of it in these terms, a professional role in primary care is "system-defined" — i.e., it is differentiated by the system of care itself. To say this with a different emphasis, a working network or system of services is required to reveal the role, to make it real and learnable. Moreover, it is within the framework of an actual and complete system of personal health services that family medicine or any role in primary care makes the most sense and seems most predictably stable.

Students' decisions to go into primary care or family medicine, then, are probably based on some set of assumptions or progression of logic as the following:

There is a pressing need for more primary