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# Relapse in obesity treatment: biology or behavior?[1,2]

*James O Hill and Holly R Wyatt*

Despite substantial efforts directed toward obesity treatment, our long-term success rate remains poor (1, 2). Although many obese individuals can lose weight, most cannot maintain the weight loss for periods longer than a few months to a year (1, 2). A major point of controversy among obesity experts is whether the high degree of recidivism after weight loss is due to biological or behavioral factors. Some investigators conclude that weight regain is inevitable as a result of strong biological pressures to return the subject to an obese body weight (3). Others believe that the inability to maintain substantial lifestyle changes over time is the main culprit in weight regain (4). The results of the meta-analysis published by Astrup et al (5) are directly relevant to this debate. These authors suggest that a low resting metabolic rate (RMR) may contribute to weight regain in some formerly obese subjects.

Astrup et al (5) identified published studies in which RMR was measured in formerly obese and control subjects. They then performed a traditional meta-analysis of 12 studies that met predetermined criteria. Additionally, they obtained individual subject data from 124 formerly obese and 121 control subjects from 15 studies and analyzed the difference in RMR between groups. The traditional meta-analysis performed on the 12 studies concluded that RMR was lower, by ≈5%, in the formerly obese subjects than in the control subjects. One caveat is that the analysis used RMR divided by fat-free mass. This was necessary to perform the analysis, but this method of expressing RMR is problematic (6, 7). The analysis performed on the individual subjects was, in our opinion, more useful. The difference in RMR between the 124 formerly obese and 121 control subjects was marginal ($P = 0.09$) when RMR was appropriately adjusted for fat-free mass and body fat mass. Furthermore, Astrup et al suggested that the 3–5% lower RMR in the formerly obese group was entirely accounted for by 15% of the formerly obese subjects who had a low RMR, defined as >1 SD below the mean. This was in comparison with 3% of control subjects with a low RMR.

These results provide something for investigators on both sides of the biological-behavioral debate. Those with a bias toward metabolic factors can point to the significantly lower RMR in the formerly obese subjects in the meta-analysis and the larger proportion of formerly obese subjects with a low RMR. Those with a behavioral bias can point out that most (85%) of the formerly obese subjects did not have a low RMR.

The study of formerly obese subjects is not simple because such a subject group is almost certainly heterogeneous. Astrup et al do a nice job of pointing out the limitations in the published studies. For example, it was not always clear how long the subjects were weight stable, the sample sizes were often small, and many studies relied on skinfold thicknesses or bioelectrical impedence to measure body composition. Additionally, the effects of weight loss on RMR may depend on the amount of weight loss, the duration of weight loss, and the method of weight loss. We must be careful in making firm conclusions about a population of subjects on the basis of so few formerly obese subjects studied to date. For example, we found that RMR was not lower in a group of 40 formerly obese subjects in the National Weight Control Registry than in 46 control subjects (8).

If we assume that the 124 subjects studied to date are representative of the population of formerly obese subjects, what can we conclude? First, there is little evidence of a low RMR in most formerly obese subjects. A visual inspection of Figure 1 in the report by Astrup et al shows that the distribution of adjusted RMRs was similar in the 2 populations. The authors chose a cutoff of 1 SD from the mean and showed that there were more formerly obese than control subjects >1 SD below the mean, but a similar proportion of formerly obese and control subjects 1 SD above the mean. They suggest that a low RMR may be present in a subset of formerly obese subjects (15% by this definition). Although it remains possible that with larger numbers of subjects RMR would be found to be slightly lower in the other 85% of formerly obese subjects, any difference is likely to be small. Second, there is little reason to believe that variations in RMR are predictive of weight gain. Data from several prospective studies in never-obese adults and children suggest that a low RMR is not a good predictor of weight gain (9, 10). Certainly, 3% of the control subjects were maintaining a normal body weight despite a low RMR and 8% of the formerly obese subjects actually had a high RMR. This raises the question of why they were obese in the first place if RMR is a key determinant of the development of obesity.

We have spent a great deal of time looking unsuccessfully for defects in energy expenditure to explain the development of obesity and the difficulty in maintaining weight loss. Although there is more to learn in this area, we must devote more time to under-

[1] From the Center for Human Nutrition, University of Colorado Health Sciences Center, Denver.

[2] Address reprint requests JO Hill, Center for Human Nutrition, Box C225, University of Colorado Health Sciences Center, Denver, CO 80262. E-mail: James.Hill@uchsc.edu.



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standing the role of behavioral factors in weight gain and weight maintenance. We believe that for most obese subjects, weight regain is due more to an "environmental relapse," in which it is impossible to maintain appropriate diet and physical activity patterns within an environment that promotes energy intake and discourages physical activity, than to a "metabolic relapse," in which the individual is driven back to an obese state by biological factors. We must provide a clear message to obese patients and their treatment providers. We believe this message should be that although maintaining a weight loss is not easy, it should not be seen as a futile attempt to overcome a predestined biological drive to reattain an obese state.

Astrup et al (5) have done a great service to the field by bringing together this body of data. The techniques used were solid and the results are extremely useful. If we could change one thing in the paper, however, we would rewrite the last sentence of the abstract to state that a low RMR, either genetic or acquired, is not a likely cause of relapse in most formerly obese subjects.

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