Hereditary Factors in Protein Nutrition

By PAUL F. FENTON, PH.D*

EVIDENCE is accumulating that an individual inherits a characteristic metabolic pattern just as he inherits the color of skin, hair, and eyes. In our studies with highly inbred strains of mice, we have taken as our basic premise that an animal's genic make-up determines its endocrine balance which in turn establishes its metabolic pattern. Very likely all of our strains of mice make use of the same metabolic pathways. However, the degree to which each pathway is utilized will differ to an extent determined by the endocrine balance. Observations of differences in carbohydrate and fat metabolism among our strains of mice already have been reported.[1,2,3] One of the greatest differences observed so far lies in the response to diets containing 50 per cent fat.[4] Confronted with diets of such high caloric density, three of our mouse strains, C57BL/Fn, C3H/Fn, and A/Fn, consume enough extra calories to become obese at three months of age. Only one strain, the I/Fn, remains lean under these conditions.

CALORIES AND LOW-PROTEIN DIETS

Our four strains differ somewhat in growth rates when fed normal diets. However, when the protein content of the diet is reduced to 10 per cent, marked differences in growth are observed.[5] These may be explained on the basis of differences in voluntary food intake or on the basis of differences in efficiency of protein utilization. Both possibilities have been investigated.

Using diets containing only 5 per cent protein, we measured the efficiency of protein utilization for growth over a period of 20 days following weaning.[6] Voluntary food intake was markedly greater for A and C3H animals than it was for the I and C57 strains. However, the efficiency of protein utilization for growth was significantly greater only in the C3H strain. To eliminate differences in food intake, A and C3H mice were fed the 5 per cent protein diet in the amounts voluntarily consumed by I and C57 animals (approximately 43g). Under these conditions, the A and C3H mice lost weight at a 20-day food intake adequate to support significant weight gains in the C57 and I strains. When the 43 g of the 5 per cent protein diet were fed to C3H and A mice together with unlimited amounts of a nitrogen-free supplement, growth was again possible. This suggests that the C3H and A strains have a higher caloric requirement but not necessarily a higher protein requirement. The experiments indicate that there are real differences in metabolic pattern aside from the inherited differences in voluntary food intake.

PAIR-FEEDING

As a further test of this contention, we fed a 30 per cent protein-50 per cent fat diet to both

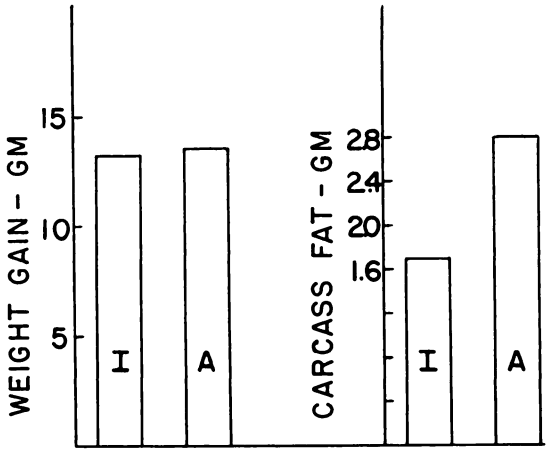

Fig. 1. Weight gain and fat deposition of two mouse strains under identical caloric intake.

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A and I strain mice. When fed *ad libitum*, this diet produces obesity in the A but not in the I strain. In the present experiment, however, mice of the two strains were carefully matched at weaning and then pair-fed for a period of 48 days. Average body weights of the two strains were virtually identical at the end of the feeding period. The I strain group, however, averaged 1.7 g of body fat while the A strain mice contained 2.8 g (Fig. 1). On the other hand, the nitrogen content of I strain mice was higher than that of the A group. Thus the A-strain mouse channels more of its available calories into fat depots and less into protein synthesis than does the I strain.

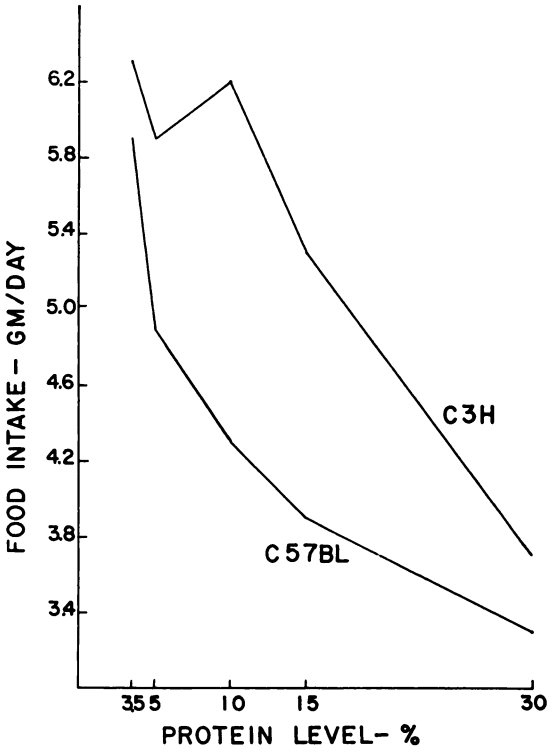

Fig. 2. Food intake at different dietary protein levels; 3.5 to 30 per cent.

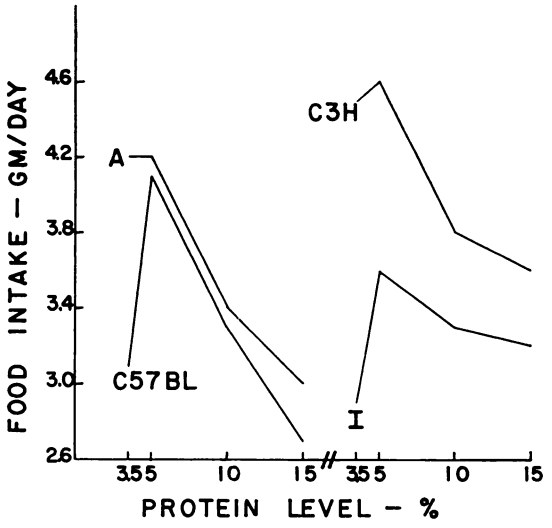

Fig. 3. Food intake at different dietary protein levels; 3.5 to 15 per cent.

PROTEIN LEVEL AND FOOD INTAKE

Experiments were also designed to look into the differences in food intake and, if possible, into the mechanisms underlying the differences. Brobeck and his associates[7] have suggested that food intake varies inversely with the protein level and thus with the specific dynamic action of the diet. A group of adult mice was fed a 30 per cent protein diet. Food intake was measured as soon as the body weight had stabilized. Thereafter the dietary protein level was dropped successively to 15, 10, 5, and 3.5 per cent. Food intake was greatest at the low protein levels and least with the 30 per cent protein diet (Fig. 2). In a second experiment the animals were stabilized on a 15 per cent protein diet. Later they received in succession the 10, 5, and 3.5 per cent protein diets. The mice were maintained at each protein level for considerable periods of time in contrast to the preceding experiment in which they were kept at each level for only one week. Again food intake increased as the protein level was lowered. However, when the 3.5 per cent level was reached, the food intake of C57 and I strain mice dropped sharply (Fig. 3). We suggest that this abrupt decrease in food intake is the result of a protein-deficiency state. If this is true, we have an indication that the C57 and I strain mice have a higher protein requirement than the A and C3H. This is supported by a nitrogen balance study[6] which showed the I strain to excrete more nitrogen than the A at several levels of nitrogen intake. In a further experiment the protein level of the diet was raised from 30 per cent to 50, 70, and finally 90 per cent. Food intake of I strain mice diminished with increasing protein level in accordance with Bro-

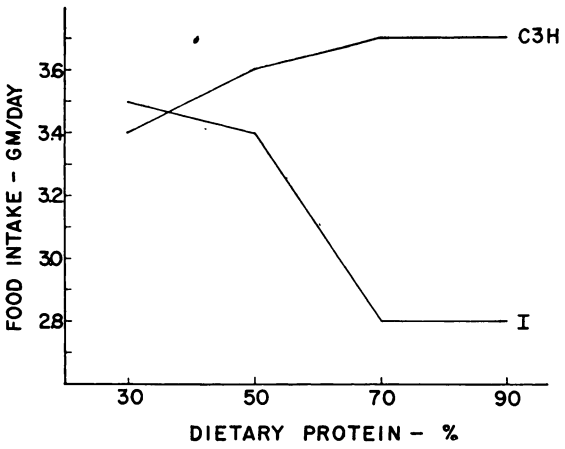

Fig. 4. Food intake at different dietary protein levels; 30 to 90 per cent.

beck's hypothesis. However, the C3H mice showed little change in food intake (Fig. 4). It must be remembered that the C3H mouse, as well as the A and to a certain degree the C57, exerts relatively poor control of its food intake.

GLUCOSE TOLERANCE

Glucose tolerance was determined in mice accustomed to different levels of dietary protein. Feeding a 90 per cent diet resulted in considerable elevation of the fasting blood sugar level. Otherwise the tolerance curve shows excellent utilization of glucose. The blood sugar levels observed in mice maintained on a 10 per cent protein diet were found to be generally lower than those of animals maintained on normal protein intakes. Glucose utilization, however, appeared not to be diminished. The data so far suggest that the effect of dietary protein level on food intake cannot be explained readily in terms of changes in glucose utilization.

GENETIC FACTORS

In our most recent experiments we have attempted to find out how metabolic patterns are inherited. Taking the A and the I strains which seemed to differ most drastically, we have started a series of crosses and backcrosses. Each line was tested by the following criteria: (1) rate of growth on a 10 per cent protein diet for 21 days after weaning, (2) endogenous N excretion, (3) weight gain on a 30 per cent protein-50 per cent fat diet, and (4) carcass composition after ten weeks on the high-fat diet. The results obtained so far indicate that each metabolic aspect studied is controlled by separate sets of multiple factors.

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