

# FATTY, A NEW MUTATION IN THE RAT

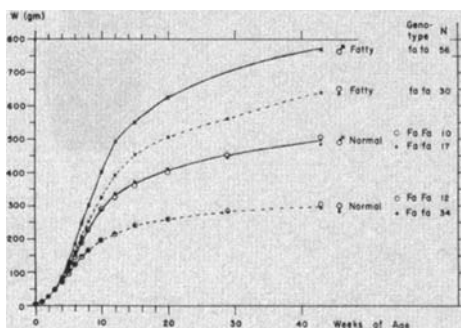
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THE mutation designated "fatty" appeared spontaneously at this laboratory in the 13M rat stock<sup>10</sup>. Two obese young were found in one litter and regularly, with approximately 25 percent incidence, in three more litters from the same parents. The condition appears to be due to a single recessive gene. The symbol *fa* has been chosen for the fat allele and *Fa* for the normal.

The obese condition is first noted by weight and appearance as early as three weeks of age and is very apparent by five weeks. Figure 10 shows the obvious difference in shape between adult fatties and normals. Figure 9 not only depicts the difference in the course of growth but also indicates that in body growth the heterozygotes do not differ from the normal homozygotes. Food intake observations show that fatties overeat, like other obese animals.

While the male fatties have sex organs of generally normal appearance and have occasionally been fertile, the females show a small, underdeveloped uterus and are uniformly sterile. Therefore, phenotypically normal heterozygotes of both sexes must usually be depended upon for continuing the stock.

Second to the obese appearance, the most striking sign of fatty is lactescence (milky appearance) of the blood serum. This sets in shortly after weaning, is universally found, and soon becomes very intense. Total fatty acids of the serum reach ten times the level in non-obese rats, and cholesterol and phosphatides are raised by about a factor of four. Blood lipid levels remain very high even after an 18-hour fast. On the other hand, blood sugar does not rise above the normal range in fed or fasted fatties.



MEAN WEIGHT CURVES

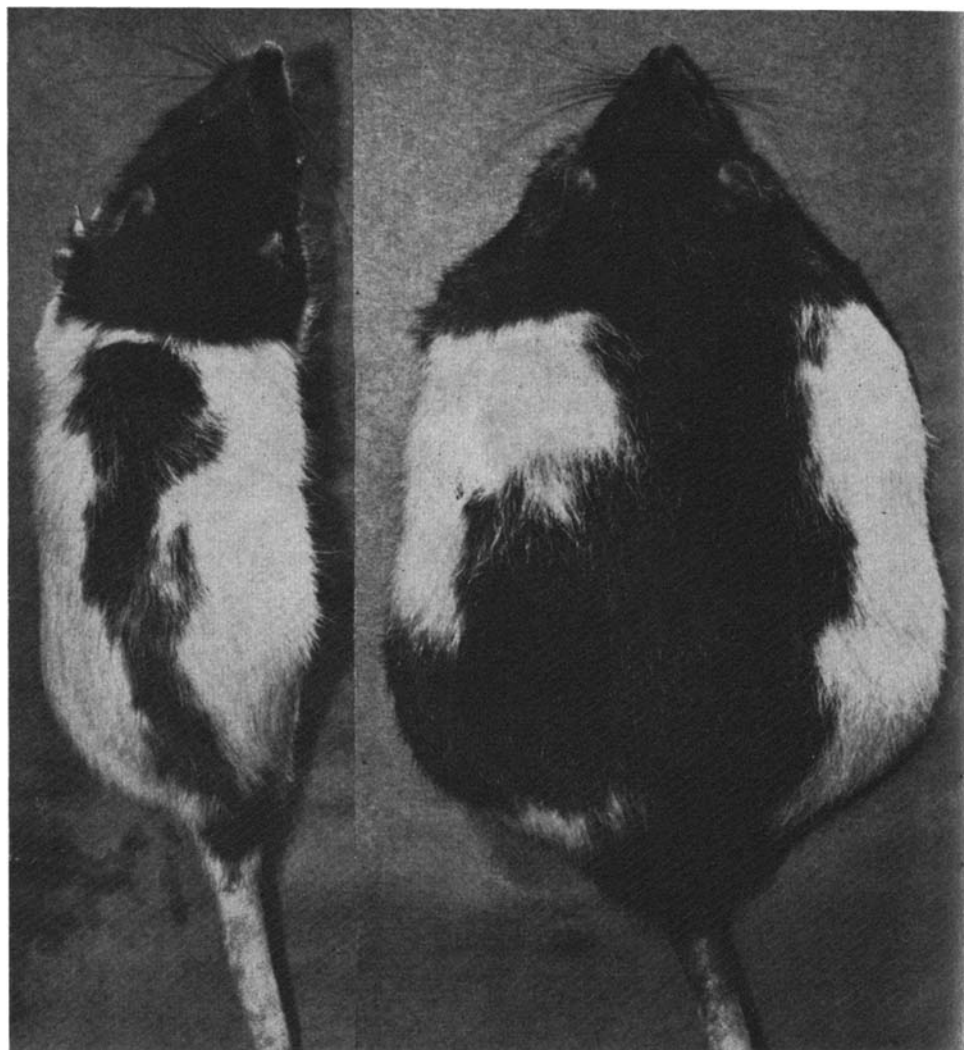
Figure 9

Mean weight curves of fatties and normal controls are illustrated graphically. The heterozygous and normal homozygous animals grow similarly.

As fatties approach a year of age, a serious kidney lesion develops, like that described by Brobeck<sup>4</sup> in the obese rat produced by surgical injury to the hypothalamus.

Table I records the results of various breeding experiments, all supporting the hypothesis that the fatty condition is produced by a single recessive gene. The expected yield of fatties was found for two mating types: one-half of the animals produced in the mating type of line 1 and one-fourth of those produced in the mating type of line 3 were fatties. The genetic constitution of the phenotypically normal offspring produced by each mating type was explored: for lines 1 and 2 the offspring should be, and were, all heterozygotes; for line 3, two-thirds of them should be heterozygotes and of the 24 tested, 14 proved to be so; for line 4, one-half should be heterozygotes and of the 27 tested, 14 proved to be so.

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### **BROTHER AND FATTY**

**Figure 10**

A normal rat is shown with his fatty brother. They are 10 months of age and weigh 447 and 1035 grams, respectively.

Various other fat laboratory animals are known. There are several strains of obese mice, including the hyperglycemic (*obob*)<sup>7</sup>, the adipose (*adad*)<sup>8</sup>, and heterozygotes of yellow (*A<sup>y</sup>a*)<sup>6</sup>. These three genes are all different. There are also obese mice of the CSH silver strain<sup>9</sup>, and an obese New Zealand strain<sup>2</sup>, which differ physiologically or metabolically from the obese hyperglycemic.

Rats can become obese when certain hypothalamic lesions are surgically produced<sup>4</sup>. In such rats Brobeck has found a marked hyperphagia but only moderate rises in serum fatty acids and cholesterol, which do not exceed a factor of two. Thus it appears that this experimental obesity is due to inactivation of the hypothalamic "satiety center," and, in contrast to the fatties, there is no outstanding abnormality in lipid metabolism. A corresponding condition can be caused in mice either by surgically produced hypothalamic lesions or by the injection of goldthioglucose<sup>5</sup>. Here, also, there is no marked hyperlipemia, and food restriction prevents excessive fat accumulation. Extreme obesity can be produced in rats by feeding certain high-fat diets<sup>3</sup>. This is called nutritional obesity and again the deciding factor is simply excessive food intake. The rat fatties, and the hyperglycemic obese mice<sup>1</sup>, have a more basic

metabolic disturbance than simply an increased appetite. When restricted to a normal food intake, they are still obviously fat in appearance. Therefore, in these two cases, it is indicated that there is an abnormality in intermediary fat metabolism.

As a subject of investigation, obesity is currently of interest in a number of respects. Every occurrence in experimental animals of a condition of interest in human medicine offers new useful channels of investigation. It may be noted in this connection that in spite of a blood cholesterol level four times that ordinarily encountered in rats, the aortas at a year of age have so far shown no signs of atheromatous plaques.

#### Summary

An obese rat mutation, *fa* (called fatty), is described. Breeding experiments show that it is due to a single recessive gene. The obesity is apparently of metabolic origin, being associated with obviously deranged lipid metabolism leading to very high blood lipid levels.

#### Literature Cited

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TABLE I. Breeding experiments\*

| Matings                                | Offspring |      | Breeding tests of phenotypically normal offspring |      |        |                               |        |
|--|-----------|------|---|------|--------|-------------------------------|--------|
|  | Litters   | Rats | Fatties ( <i>fafa</i> )                           |      | Tested | Heterozygotes ( <i>Fafa</i> ) |        |
|  |           |      | Obs.  | Est. |        | Obs.                          | Est.   |
| $\frac{fafa \times Fafa}{3 \quad 5}$   | 6         | 36   | 19  | (18) | 8      | 8                             | (8)    |
| $\frac{fafa \times FaFa}{1 \quad 2}$   | 2         | 16   | 0   | (0)  | 12     | 12                            | (12)   |
| $\frac{Fafa \times Fafa}{54}$          | 49        | 381  | 94  | (95) | 24     | 14                            | (16)   |
| $\frac{Fafa \times FaFa}{17 \quad 25}$ | 26        | 182  | 0   | (0)  | 27     | 14                            | (13.5) |

\* Table entries represent numbers of rats or litters; estimated numbers are in parentheses. Genotype assignment: *fafa*, fatty; *Fafa*, phenotypically normal capable of producing fatty young; *FaFa*, phenotypically normal incapable of producing fatty young.

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### Tooth Decay Inherited?

Some persons may be born with inherited resistance to tooth decay, a Michigan State University research team reported recently to the International Association for Dental Research.

Dr. Sam Rosen, now at Ohio State University, reported on a series of experiments conducted to determine the role of heredity in the development of dental caries. Other participants were Dr. Gerald T. Coleman, Dr. Anand C. Sawant, Dr. Harrison R. Hunt and Dr. Carl A. Hoppert.

The researchers used two strains of rats, one inbred to be susceptible to caries, and one resistant to development of caries. They

cross-bred the strains and studied the offspring.

Usually, Dr. Rosen said, the offspring resembled the caries-resistant parent slightly more than the caries-susceptible parent, indicating a tendency for the gene controlling resistance to be dominant.

There was no difference, they found, whether the mother was caries-resistant or caries-susceptible. This suggests that the progeny's hereditary constitution, determined at conception, was responsible for the degree of caries susceptibility, and that both parents contribute to it.



### Correction—Inheritance of Taillessness in Manx Cats

An error appeared in the recent paper by Neil B. Todd, "The Inheritance of Taillessness in Manx Cats" (*Jour. Hered.* 52:228-232. 1961). On page 229, the first sentence in the fourth paragraph of column one should read

"Data on the reciprocal cross of a tailed female to a Manx male are scant" rather than ". . . of a tailed male to a Manx female . . ."

—The editors regret the error.