A similar distribution of radioactive gold in the α and β globulin fractions was obtained in a specimen of fluid aspirated from the pleural cavity of a patient 6 days after the intrapleural injection of 56 mc of Au^{198}.

The method of filter paper electrophoresis has established that radioactive colloidal gold is bound to the α and β globulin fractions of plasma proteins. Even more important, this previously introduced method is a simple tool for studying the distribution of radioactivity in blood and its proteins.

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The Multiple Etiology of Obesity: Production of Two Types of Obesity in Littermate Mice[1]

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A number of types of experimental obesity have been studied in this and other laboratories (*1*): hypothalamic obesity in the rat, yellow obesity (dominant) in the mouse, the hereditary (Mendelian recessive) obese-hyperglycemic syndrome,[2] thalamic obesity in the monkey, hereditary (Mendelian recessive) obesity in the Shetland sheep dog, immobilization obesity in the rat, and goldthioglucose obesity in the mouse. Unfortunately, these obesities have usually been produced in different animal species or at least in different strains, and their metabolic similarities and differences have rarely been studied simultaneously. We wish to report here, first a comparison between two types of obesity in different strains of mice, and next the establishment of these two types in littermate animals with direct comparison of metabolic characteristics.

The hereditary obese hyperglycemic syndrome is characterized in particular by extreme overweight (limit weights of 50–115 g as compared to 25–30 g) and by a form of hyperglycemia sensitive to diet and to growth hormone and extremely resistant to large doses of insulin (*2*). Recent evidence (*3*) indicates that these animals are characterized by oversecretion of a hormone secreted by the alpha cells of the islets of Langerhans, of which growth hormone is the tropic hormone.

Goldthioglucose obesity (*4*) is produced by injection of the LD_{50} dose of goldthioglucose. About 30% of the animals that survive injection become obese, the limiting weight is in the 50–95 g range. No metabolic study has been conducted in these animals.

The blood glucose levels, effect of insulin, and effect of growth hormone were determined in 3 groups of Swiss mice: goldthioglucose-treated obese animals (range 40–54 g), goldthioglucose-treated nonobese animals (range 20–24 g), and untreated controls (range 20–28 g). These animals had been injected 8 mo previously with 15 mg of goldthioglucose.[3] The same procedure was conducted simultaneously in 3 groups of animals of the genetically obese stock, obese (80–115 and 40–55 g), and nonobese (18–27 g) mice representing age and weight controls, and described in Table 1, and 1 group of nonobese littermates of young hereditarily obese animals, made obese (40–56 g) by goldthioglucose injection. This last group represented the obese survivors of 5 equal groups of 20 animals injected with 15, 25, 35, 40, and 50 g of goldthioglucose. None of the animals injected with 15 or 25 mg had developed obesity; all animals injected with 50 mg died. Eight of the 20 animals injected with 35 mg and 9 of the 20 animals injected with 40 mg died. Three animals injected with 35 mg and 9 animals

TABLE 1. Effect of growth hormone on blood glucose in goldthioglucose obesity and in the hereditary obese hyperglycemic syndrome.

Animals			Blood glucose (mg %)	
Type	Number	Weight (g)	Untreated	After growth hormone
Goldthioglucose treated, obese Swiss	12	45.3 ± 4	118 ± 9	110 ± 14
Goldthioglucose treated, nonobese Swiss	12	22.8 ± 0.7	107 ± 11	105 ± 6
Untreated Swiss	12	24.0 ± 2	105 ± 7	97 ± 6
Hereditary obese-hyperglycemic, 3½ mo old (weight controls)	8	45.2 ± 3	160 ± 20	303 ± 4
Hereditary obese-hyperglycemic 9 mo old (age controls)	8	92.0 ± 11	298 ± 41	485 ± 82
Nonobese *ob ob* littermates	12	23.8 ± 4	115 ± 7	116 ± 16
Nonobese *ob ob* littermates made obese by goldthioglucose	8	45.2 ± 5	124 ± 15	106 ± 12

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[2] The term hyperglycemia, which represents a condition either found naturally in the obese animals or immediately elicited by small doses of growth hormone to which the nonobese animals are insensitive (*5*) is much to be prefered to the term "diabetes" previously used. If by diabetes is meant the insulin-free condition, the obese animals are not diabetic.

[3] Supplied by Schering Corp., Bloomfield, N. J. These animals were given by G. Brecher, National Institute of Arthritis and Metabolic Diseases, Bethesda, Md.

injected with 40 mg developed, in 2–3 mo, weights exceeding 40 g.

Blood glucose levels before and after growth hormone treatment are given in Table 1. The dosage used was 2 mg/day for 3 consecutive days before the determination. It is readily seen that goldthioglucose obese animals do not show hyperglycemia as do the hereditarily obese hyperglycemic animals. The fact that this difference does not simply reflect strain idiosyncracies is demonstrated by the fact that the littermates of *ob ob* mice[4] made obese by goldthioglucose show blood glucose levels in the normal range. Similarly, goldthioglucose obese animals, whether Swiss or littermates of *ob ob* mice, do not exhibit any increase in blood glucose when treated with growth hormone, as do mice with the hereditary obese-hyperglycemic syndrome. In the latter, the response is so quantifiable that it has been made the basis of a method of determination (*5*).

Finally, it was found that subcutaneous injection of one unit of insulin was enough to cause hypoglycemic convulsions in all groups of Swiss mice (including the goldthioglucose obese animals), in nonobese littermates of *ob ob* mice, and in littermates of *ob ob* mice made obese by goldthioglucose treatment. By contrast, as reported previously (*2*), the blood glucose of animals with the obese hyperglycemic syndrome is totally unaffected by one unit of insulin, hardly affected by 20 units of insulin, and the animals can survive injection of even larger doses.

The profound metabolic difference between the two types of obesity is all the more striking in that the siblings, whether genetically obese or chemically obese, are completely identical in external appearance. Although fat deposition in all cases is dependent on positive caloric balance, these findings illustrate the fact that the existence of such a positive balance is not per se an explanation of obesity. It is simply a restatement of the first law of thermodynamics. In all cases, the real problem is to find the primary causes of this relative hyperphagia. Obesity appears to be a common end-result of syndromes of profoundly diversified etiologies (*1*).

[4] By *ob ob* mice is meant the animals in which the hereditary syndrome is present.

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Experiences with Transplantation of the Lung

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Relatively few studies pertinent to the transplantation of lung tissue have been made. Several workers have described (*1–3*) various types of autogenous and homologous lung transplants and have demonstrated the technical feasibility of such procedures.

Our initial experiences (*4*) were concerned with transplantation of the entire left lung from one dog to another. The left lung was removed from a donor animal by transecting the left auricle, the left main pulmonary artery, and the left bronchus. Left pneumonectomy was then done in the recipient animal. The donor lung was grafted to the recipient animal by anastomosing the left auricle, the left main pulmonary artery, and the main stem bronchus. Following these anastomoses, the grafted lung expanded, blood flowed throughout it, and to all gross inspection it appeared normal.

In a control group of 10 such homologous lung grafts the animals survived from 1 to 12 days with death usually resulting from pneumonia. Microscopic examination of the transplanted lung tissue at autopsy suggested that the changes were due to tissue incompatibility. In another group of 3 dogs wherein the donor and recipient animals were littermates, the survival period ranged from 13 to 30 days, significantly longer than the control group. In an attempt to alter the systemic antigen-antibody response, other groups of 3 dogs each were given benadryl (150 to 200 mg daily), cortisone (35 to 45 mg daily), or total body radiation (400 r) during their immediate postoperative course. Those animals receiving benadryl or total body radiation showed no appreciable difference in survival from the control dogs. Those to which cortisone was administered survived longer, from 12 to 18 days.

Subsequently we became interested in the role of the spleen and its possible effect in the viability of lung transplants. That splenectomy may reduce an animal's ability to produce antibodies has previously been demonstrated (*5*). In a group of 5 dogs splenectomy was done concomitantly with homologous left lung transplant. In another group of 6 dogs (the re-

[1] Markle Scholar in Medical Sciences.

TABLE 1. Survival in homologous lung transplants.

Group	Number of dogs	Days of survival
Control	10	1, 2, 2, 3, 3, 4, 7, 11, 11, 12
Donor and recipient littermates	3	13, 20, 30
Benadryl	3	5, 6, 6
Cortisone	3	4, 12, 14
Radiation	3	4, 7, 8
Splenectomy at time of transplant	5	2, 4, 7, 7, 8
Splenectomy preceding transplant	6	2, 5, 5, 7, 8, 9