still in a positive rather than a negative growth phase at this time, and the amount of enzyme released by disintegrating parasites should be relatively small.

The lack of change in serum aldolase indicates that *T. lewisi* has little or no effect on rat skeletal muscle which is a primary source of the enzyme(6). In view of the low levels of aldolase in *T. lewisi* cells, it is not surprising that this enzyme was not elevated in the serum during the period of population decline.

In view of these data it seems that *T. lewisi* has more stressful effects on its host than previously suspected. The fact that some enzymes appear to be released from rat tissues during the parasitemia suggests that *T. lewisi,* either by chemical or mechanical means, may alter the cellular membrane. This effect, however, is only temporary since the serum enzyme levels return to normal when the parasitemia disappears. Although some pathogenic trypanosomes produce elevated serum enzymes in their hosts(8,9), the mechanism responsible is probably different from that of *T. lewisi* since pathogens produce very definite tissue lesions(8). Further studies elucidating the mechanisms underlying the alterations described here should prove valuable in advancing our basic knowledge of the host-parasite relationship.

Summary. Glutamic-oxalacetic transaminase (GOT), and glutamic-pyruvate transaminase (GPT), but not aldolase, were elevated in the serum of rats infected with *Trypanosoma lewisi.* Increased serum transaminase activity is believed to come from the host's tissues, which presumably are damaged by the parasite, as well as from the disintegrating parasite cells. All 3 enzymes were also present in lysed parasite cells. Here, transaminase activity was high, but aldolase was present in only minimal amounts. GPT was 9-fold more concentrated than GOT.

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Strain Differences in Susceptibility of the Rat to Dietary Cirrhosis.* (30833)

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In the course of experiments with dietary cirrhosis in rats certain strains appeared to be more susceptible to the development of the disease than others. However, there have been few reports in which a study of strain differences has been recorded. Engel(1) and Copeland(2) indicated that genetic factors may be involved in the susceptibility of rats to renal injury produced by acute choline deficiency. These authors compared 2 strains which differed in their minimal requirement for choline. These differences persisted on inbreeding for several generations and seemed to have no relation to rate of growth. Although their studies do not deal with cirrhosis they are pertinent since dietary cirrhosis can

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TABLE I. Composition of Diet.

Vitamin-free casein*	4.0
L-cystine	.5
Wesson oil	10.0
Salt mixture†	3.0
Vitamin mixture‡	1.0
Cornstarch	81.5
	100

The cirrhosis producing diet is patterned after that devised by Daft, Sebrell, and Lillie(5).

* Nutritional Biochemicals.

† Hubbell, R. B., Mendel, L. B., and Wakeman, A. J., J. Nutr. 14:273, 1937.

‡ Vitaminized cornstarch, of which 1 g supplied the following in milligrams: thiamine HCl, 1.25; riboflavin, 0.625; calcium pantothenate, 0.625; pyridoxine HCl, 0.25; nicotinic acid, 12.5; p-aminobenzoic acid, 10.0; folic acid, 0.25; menadione U.S.P., 0.1. A weekly supplement containing vit A 2500 units, vit D 360 units and alphatocopherol 2.4 mg was fed each rat.

be produced by more protracted deficiency of choline.

Gillespie and Lucas(3) observed differences in the susceptibility to cirrhosis of Wistar rats derived from 2 sources. Both groups of animals were fed the same choline-deficient diet. One group failed completely to develop the disease, whereas the other developed moderate to severe cirrhosis. The animals developing cirrhosis required 13 g food for each gram of weight gained, whereas the rats not developing cirrhosis required 8.5 g food per gram weight gained. The authors suggested that rats with poorer utilization of food had a greater requirement for choline, which in turn rendered them susceptible to cirrhosis.

Patek and deFritsch(4) presented evidence for genetic factors in the resistance of the rat to dietary cirrhosis on the basis of inbreeding experiments with Sprague-Dawley rats. There appeared to be no difference between resistant and susceptible animals with respect to intake of food or rate of growth.

In the present experiment comparison was made of 4 different strains of rats in their susceptibility to dietary cirrhosis. Sharp differences in strain susceptibility occurred which did not appear to be related to intake of food or rate of growth. It is suggested that genetic or host factors were largely responsible for these differences.

Methods. Two successive studies were carried out, each involving a period of 5 months. In the first experiment 3 strains of rats comprising 62 animals were compared. In the second study 4 strains comprising 83 animals were similarly compared. Both studies began in late October in consecutive years. Only male animals were employed.

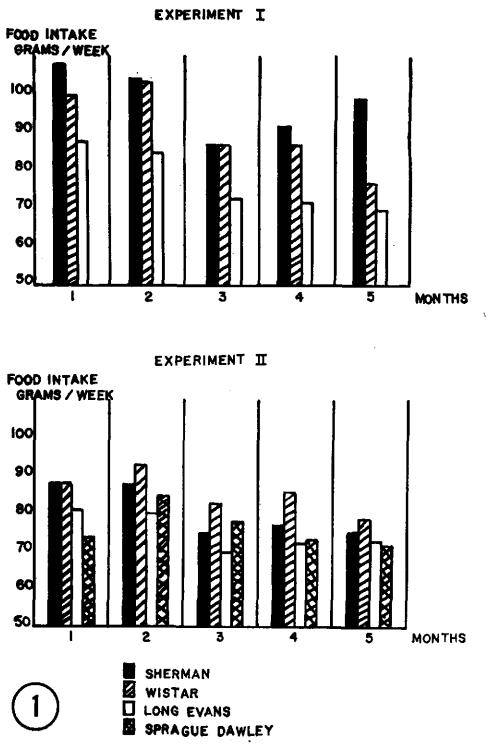
The rats were approximately 5 weeks old and weighed 60 to 80 g. They were housed in individual, suspended cages with wire meshed floors in an air conditioned room. A nutritious chow diet† was fed the animals for 1 to 3 weeks until they weighed about 130 g. They were then fed a standard cirrhosis-producing diet (Table I) which was based on that described by Daft, Sebrell, and Lillie(5). All rats were fed *ad libitum*. The feeding cups had narrow necks which allowed minimal spillage. Food intake was recorded weekly and body weights were recorded on alternate weeks.

At 5 months the animals were killed by exsanguination with the use of light ether

TABLE II. Incidence and Degree of Fibrosis in Different Strains.

No. at onset of exp	No. surviving 5 mo	Fibrosis 0	1+	2+	3+	4+	% cirrhosis (3+ 4+)
		Experiment 1					
21 Wistar	20	1	0	1	0	18	90
21 Sherman	20	5	3	3	2	7	45
20 Long-Evans	15	9	1	2	1	2	20
		Experiment 2					
21 Wistar	21	5	2	2	8	4	57
21 Sherman	17	3	3	5	4	2	35
20 Long-Evans	16	16	0	0	0	0	0
21 Sprague-Dawley	17	5	0	3	7	1	47

† Ralston Purina Laboratory Chow.



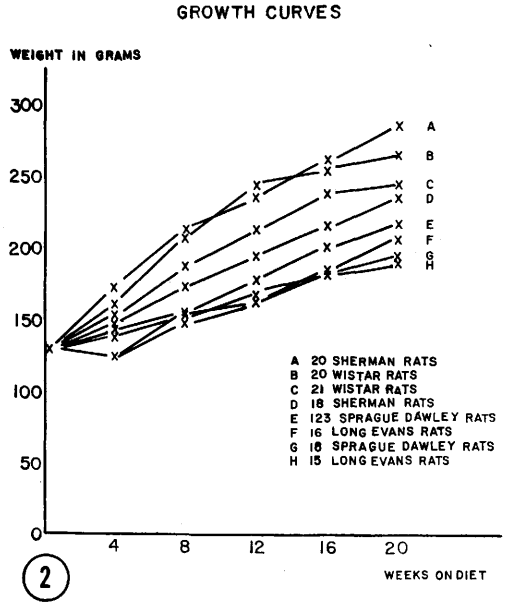


FIG. 1. Average weekly intakes of food.
FIG. 2. Growth curves.

anesthesia. Sections of liver, spleen, heart, lung, and kidney were removed for histopathologic examination. Specimens of tissue were fixed in Zenker's solution and in 10% formalin. The tissue sections were embedded in paraffin by the usual methods, cut at 5 mm, and stained with hematoxylin and eosin and Masson's trichrome stain.

Results. Histopathology: The degrees of fibrosis present in the livers at necropsy are recorded in Table II. Specimens showing 3+ or 4+ fibrosis were considered to be cirrhotic.‡ The incidence of cirrhosis was greatest in the Wistars, somewhat less in the Sherman strain, and considerably less in the Long-Evans strain in each experiment. The frequency of cirrhosis differed in the two series. The basis for this is not clear unless it is related to a greater food intake in the first experiment, or some other environmental factor. The Sprague-Dawley rats in Experiment 2 had an incidence close to that of the Sherman.

The combined incidence for cirrhosis (3+ and 4+ fibrosis) in the 2 experiments was as follows:

Wistar 73%; Sherman 40%; Long-Evans 7.5%; and Sprague-Dawley 47% in Exp. 2.

Food intake. Average weekly intakes of food, shown in Fig. 1, were higher for all groups in the first experiment than in corresponding groups of the second experiment. The basis for this variation is not evident. In general there was a decline in intake as the experiments progressed, and as the animals developed cirrhosis. The Wistar and Sherman strains had the greatest food intake. There was no significant difference between these two. The Long-Evans strain consistently ate less than the Wistar and Sherman in each experiment. The Sprague-Dawley rats, included in the second experiment only, had a food intake close to that of the Long-Evans strain.

‡ Degree of fibrosis was estimated as described previously(6). In brief, an increase of periportal fibrosis alone was 1+; an extension of periportal fibrosis into adjacent parenchyma was 2+; bands of connective tissue extending between portal areas was 3+; completely encircled bands or nodules of connective tissue were 4+. Those with 3+ and 4+ fibrosis also showed degenerative cellular changes and inflammatory cellular reactions.

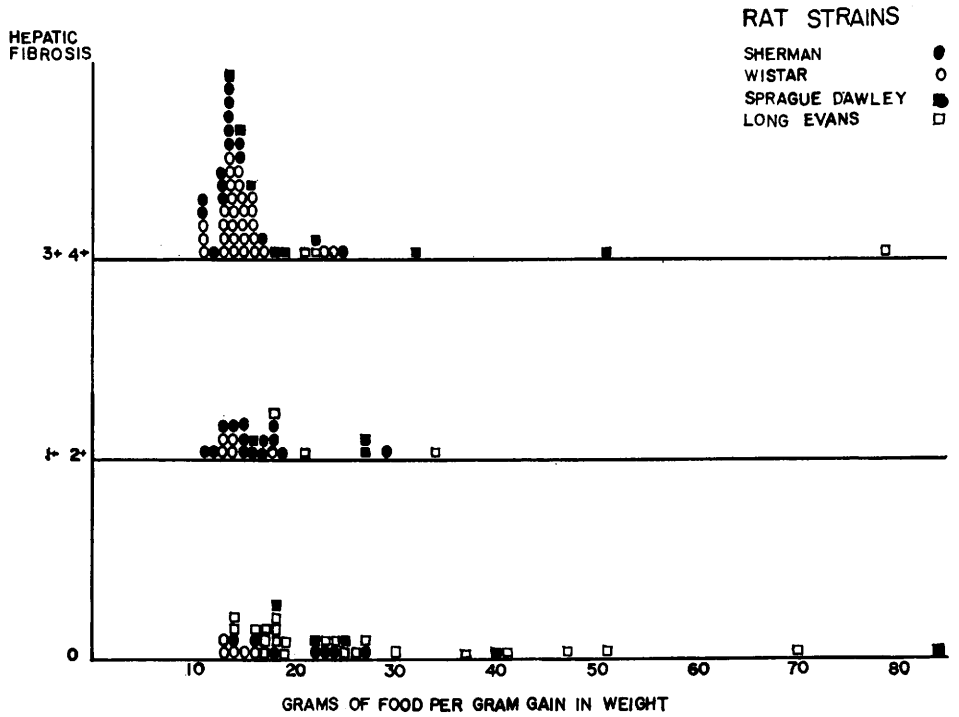


FIG. 3. Incidence and degree of fibrosis with relation to grams of food eaten per gram gain in weight.

Growth. Growth rates (Fig. 2) were higher in the Sherman and Wistar strains than in the Long-Evans and Sprague-Dawley rats. Inasmuch as Sprague-Dawley rats were not employed in the first experiment, a series of 123 rats of the strain fed the same diet in a previous experiment was included in the figure for comparison (*cf.* group E). Their growth curve was similar to that of the Sprague-Dawley rats in the present study (group G).

Relation of fibrosis to food utilization. Fig. 3 shows the incidence and degree of fibrosis at varying levels of food utilization. In this context utilization refers to the grams of food eaten per gram of weight gained during the 5 months of observation. It is evident that the Wistar and Sherman rats ate less food per gram of weight gained than did the Long-Evans or Sprague-Dawley rats. That is, the Wistar and Sherman strains had more efficient utilization of food with respect to growth. These differences did not appear to be related to the development of cirrhosis. For example, within each group the ratios were approximately the same for animals that developed cirrhosis as for those that failed to develop the disease.

In brief, although there are differences in the ratios of food intake to weight gain among the several strains of rats tested, this ratio does not seem to be correlated with the susceptibility to cirrhosis.

Discussion. The experiments revealed differences in strain susceptibility to dietary cirrhosis in the rat. The Long-Evans strain, which developed the least cirrhosis, also had the lowest food intake and growth rate. Although food intake and growth rate can influence the development of cirrhosis, they do not appear to account for the changes observed.

Gillespie and Lucas, on comparing 2 groups of Wistar rats, suggested that differences in susceptibility to dietary cirrhosis were probably due to differences in available choline. This was based upon the observation that the group of rats developing cirrhosis required more food per gram of weight gain than the group which was resistant to the disease.

Although this is an attractive hypothesis it is not substantiated by the present study, since there was no correlation between this ratio and the development of cirrhosis. Nevertheless, it is possible that animals developing cirrhosis have a relative inability to absorb or utilize choline, which defect might not be reflected in the ratio of food intake to weight gain.

Although differences in incidence of cirrhosis occurring in Experiments 1 and 2 suggest the influence of environmental factors, nonetheless the relative frequency of cirrhosis in the various strains remained constant. In each series the incidence of cirrhosis was greatest in the Wistars, less in the Sherman, and considerably less in the Long-Evans.

The present experiments suggest that conditions other than food intake or growth rate played a determining role in the varied susceptibility of different strains of rats to cirrhosis. Presumably these conditions are constitutional in nature. The mechanism responsible for these changes is not evident.

Conclusion. The present study reveals differences in strain susceptibility to dietary cirrhosis in the rat. Although environmental factors, such as food intake and growth rate may influence susceptibility to cirrhosis, they do not fully account for the changes observed. It is inferred that inherited traits in some unknown fashion exert an important effect on the susceptibility of the rat to dietary cirrhosis.

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In vitro Incubation of Rat and Rabbit Thyroid with L-Tyrosine-C^{14}, Sodium Iodide-I^{131}, and L-Mono- and Diiodotyrosine-C^{14}-I^{131}.* (30834)

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Reports of the fate of tyrosine-C^{14} added to the media bathing surviving thyroid tissue have been possibly conflicting. Dobyns found that some C^{14} was incorporated into iodothyronine but not iodotyrosine in rabbit thyroid slices(1), but Dillard *et al* recently found that none was converted into thyronine or its analogs by beef thyroid slices or rabbit thyroid homogenate(2). The present communication provides further data bearing on this problem and extends the observations to the fate of labelled iodide, tyrosine, and iodotyrosine in surviving rat and rabbit tissues. The results of these experiments provide further insight into the mechanisms of thyroxine biosynthesis and show that species differences exist in the conversion of the labelled substrates under these conditions.

Methods. The rabbits were adult New Zealand albinos; the rats were adults of the Long-Evans or Sprague-Dawley strains (Table I). Purina Rabbit Chow and Staley's Rockland Rat Diet were fed respectively. Food and tap water were given *ad lib*. The animals were killed by ether, blow on the head, or .22 caliber gunshot through the spine and heart. The thyroids were quickly dissected out and kept on cooled glass. Excess surrounding tissue was quickly trimmed away. In some experiments the glands were minced with a razor or scissors into fragments about 1.0 mm thick, weighed and placed in incubation medium. Homogenization prior to in-

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