TABLE I.
Influence of Temperature and Ultraviolet on Experimental Polyarthritis of Rats.

	Controls* (70°F)		Exposure† (30 to 84°F)		Ultraviolet‡		Heat§ (102°F)
	Female	Male	Female	Male	Female	Male	Female
Composite arthrogram score	2.9	4.2	2.5	2.3	3.3	1.9	2.6
% showing gross joint involvement	95	100	80	65	75	60	88
% dead within 4 days	5	0	15	10	10	5	0
% total deaths	15	10	35	40	50	45	12
% dead or infected	100	100	95	70	100	90	88
% showing no symptoms	0	0	5	30	0	10	12

* Total No. of rats, 40.
† Exposure controls: 3 deaths were probably due to exposure, leaving 85% survived; total No. of uninoculated rats, 20; No. of inoculated rats exposed to cold, 60.
‡ Ultraviolet controls: No arthritis developed. One animal (male) died of undetermined cause; total uninoculated rats, 20; total inoculated and irradiated rats, 60.
§ Total, 8 rats.

scores than the inoculated controls kept at 70°F and not subjected to additional ultraviolet light. Only 75% of the females and 60% of males developed arthritis as compared with 95% and 100%, respectively, among the inoculated controls. The death rate was higher than that of the inoculated controls, being 50% for females and 45% for males as compared with 15% and 10%, respectively.

Conclusion. In the experimental polyarthritis of rats produced by the L_4 strain of pleuropneumonia-like organisms exposure to cold or increased ultraviolet light under the conditions used caused increased mortality but resulted in a smaller incidence and severity (females only) of arthritis; whereas, increased heat caused little deviation in mortality and arthritis involvement from the inoculated controls.

16820

Protein Intake and Leishmaniasis in the Hamster.*

ALBERT L. RITTERSON AND LESLIE A. STAUBER. (Introduced by J. B. Allison.)
From the Bureau of Biological Research and the Department of Zoology, Rutgers University, New Brunswick, N. J.

It has already been shown that the course of a parasitic disease may be altered by the level of protein intake of the host,[1-2] low levels of intake decreasing host resistance.

Leishmaniasis in the hamster was chosen for the present study because *Leishmania donovani,* the causative agent of kala-azar, a highly fatal human disease is an intracellular parasite living and reproducing in the vertebrate host within the cells of the so-called reticulo-endothelial or lymphoid-macrophage system.

Blockade of the R-E system,[3] *e.g.* with india ink, has been shown to result in a lowering of the resistance of the animal involved; but, to be effective, repeated injections of ink are necessary. The growth and reproduction of leishmania in the R-E cells is believed to constitute a functional blockade of this

* This work was supported in part by the Protein Metabolism Fund of the Bureau of Biological Research.

1 Seeler, A. O., and Ott, W. H., *J. Inf. Dis.*, 1945, **77**, 181.

2 Seeler, A. O., and Ott, W. H., *J. Nat. Malaria Soc.*, 1946, **5**, 123.

3 Jaffe, R. H., *Physiol. Rev.*, 1931, **11**, 277.

system with increasing numbers of parasites matching the compensatory hyperplasia of the R-E cells.

The problem under study was to learn the effect of such an endogenous blockade of the R-E cells on animals fed diets deficient in protein as well as on animals fed diets containing excess of protein.

Materials and methods. The Syrian hamster, *Cricetus auratus,* was chosen as the host because of its proven susceptibility to *L. donovani* and because the course of leishmaniasis in it is similar to that seen in man. Infection was obtained by the intraperitoneal inoculation of amounts of a saline suspension of hamster spleen, ground in a Ten Brock tissue grinder, suitable to produce severe infection in 60-100 days. The usual dose was equivalent to 20 mg of a heavily infected spleen. Aseptic precautions were observed in the transfer of the infection. The parasite used was of the Khartoum strain and obtained by us from Dr. A. P. Richardson of the Squibb Institute for Medical Research.

TABLE I.
Composition of the Hamster Diets Used.

Basic Protein (20%)	g
Casein	200
Primex or Crisco	250
Corn Oil	20
Cerelose	200
White Dextrin	257
Salt Mixture*	40
Cellu Flour	20
A, D, and E conc.†	1
Choline Chloride	2
Wilson's 1:20 liver powder‡	10
	1000

To each 1000 g add 0.372 g of vit. B mixture§ and 0.010 g vit. K.

Low Protein (10%)
Substitute in above:
100 g Casein
357 g Dextrin

High Protein (40%)
Substitute in above:
400 g Casein
57 g Dextrin

* Wesson, *Science,* 1932, **75**, 339.

† A, D, and E concentrate:

	g
Corn oil	41
A and D conc. (450,000 U. S. P. units of A) (90,000 U. S. P. units of D)	7
Alpha tocopherol	2
	50

‡ Armour's liver extract (23 ml) used in place of liver powder.

§ Vit. B mixture:

	mg
Thiamine hydrochloride	200
Riboflavin	400
Pyridoxine HCl	200
Niacin	1000
Calcium pantothenate	1100
Para-aminobenzoic acid	1000
Inositol	5400
	9300

The principal diet used was a modified mouse diet† (Table I). Although niacin is apparently not necessary in the diet of the hamster[4] it was included here since animals on protein deficient diets may not have the same requirements as animals on control diets. One or two weeks prior to inoculation all animals were placed on their test diets containing either high (40%), basic (20%) or low (10%) levels of protein. The protein used was casein. The high and basic protein diets allowed immature hamsters to gain weight at approximately a normal rate. All groups of hamsters ate the diet well.

Results. The results obtained may be summarized under the headings of survival, body weight changes, estimated number of parasites and organ weight changes.

Infected animals survived longer when maintained on the high and basic protein diets than on the low protein diet. The animals on the low protein diet (Fig. 1) were all dying when the experiment was terminated while those of the other 2 groups were in fairly good condition. Fig. 1 shows also that the fall in weight of the animals on the low protein diet to a value below their initial weight is a terminal phenomenon. High intake of protein, therefore, partially protects against the progressive emaciation characteristic of the disease.

Although this "protective" effect of the basic and high protein diets seems to be borne out by the relative numbers of parasites in the impression smears made from the

† Details of diet furnished in personal communication through courtesy of Dr. David Bosshardt, Sharp & Dohme Co.

4 Cooperman, J. M., Waisman, H. A., and Elvehjem, C. A., PROC. SOC. EXP. BIOL. AND MED., 1943, **52**, 250.

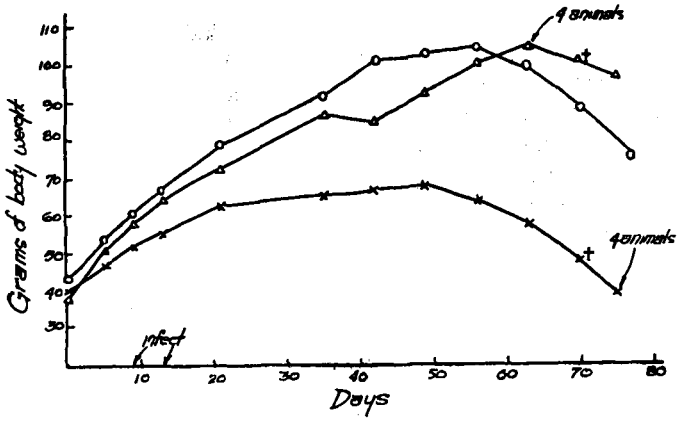

FIG. 1.

Weight curves of immature hamsters, infected with *Leishmania donovani*, fed experimental diets of different protein content: Δ High protein diet (40% casein); ○ Basic protein diet (20%); × Low protein diet (10%).

TABLE II.

Effect of Low, Basic and High Protein Diets on Organs and Organ-weight, Body-weight Ratios; and on the Parasite Counts of Growing Hamsters Infected with *Leishmania donovani*. All figures represent average values for the group. All animals were sacrificed between 75-77 days after being placed on the diets.

Conc. of protein in diet	No. of animals	Body wt (g)	Spleen wt (mg)	Spleen-wt body-wt ratio*	Liver wt (mg)	Liver-wt body-wt ratio*	Estimated No. of parasites
Low (10%)	5	38.1†	209.2†	5.3†	3248†	85.4†	++++
Basic (20%)	5	75.2	488.6	6.5	5143	68.3	++
High (40%)	5	96.2†	840.8†	8.7†	7097†	73.8†	+±

* Ratios expressed as milligrams of organ per gram of body weight.
† Averages represent only 4 animals of the group. One animal died before 75th day.

spleen at necropsy (Table II), when calculated on the basis of the estimated absolute numbers of parasites in the enlarged spleens the differences are much smaller. Indeed, the data seem to suggest that the reproductive rate of the leishmania may be nearly constant on all 3 diets.

The pathology observed was essentially that described by Meleney[5] all heavily-infected animals showing marked splenomegaly and hepatomegaly, both absolute and relative to body weight (Table II and Fig. 2). The liver-weight/body-weight ratio of the normal hamster is approximately 43 mg/g (range of ratio from 40-46 for animals 85-124 g body weight). The ratio in the infected animal usually does not increase quite 100% in value. The normal spleen-weight/body-weight ratio is about 1.4 mg/g for animals weighing from 85-124 g. In the infected

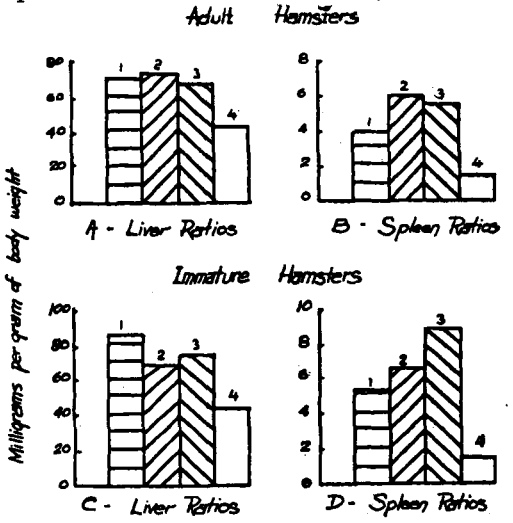

FIG. 2.

Organ weight, body weight ratios for adult and immature, infected and uninfected hamsters fed diets differing in protein content. 1, Low protein diet, infected; 2, Basic protein diet, infected; 3, High protein diet, infected; 4, Stock diet, uninfected.

[5] Meleney, H. E., *Am. J. Path.*, 1925, **1**, 147.

hamster this usually increases more than 300%. The spleen, therefore, is a better index of infection. Except possibly, for the relatively low ratios for the spleens of animals on low protein diets there are probably no significant differences in organ weight ratios under the dietary conditions studied.

Work is now in progress to determine the effect of kala-azar on the liver nitrogen in growing hamsters.

Summary. Protein intake influences the course of leishmaniasis in the hamster, deficient diets leading to earlier emaciation and death. Excess dietary protein seems to favor survival.

16821

Serum Cholinesterase in Some Pathological Conditions.*

M. G. LEVINE AND R. E. HOYT.†‡

From the Institute of Experimental Medicine, College of Medical Evangelists, Los Angeles, Calif.

Of the esterases in human blood, the one hydrolyzing acetylcholine into acetic acid and choline has received the most attention in recent years because of the supposed relationship of this enzyme to the physiology of nerve activity. Actually, recent work indicates that there are two enzymes involved. One, the so-called true or specific cholinesterase, is thought to be involved directly in the transmission of nerve impulses, whereas the non-specific or pseudocholinesterase has, as yet, no assigned function.

Since the activity of the latter enzyme is easily measured, and since it is present in a readily available material (serum) in hospital patients, it offers an opportunity to study variations in a basic enzyme system in a number of pathological conditions. Such variations in themselves may be of more importance when the nature and function of the enzyme itself is better understood, nevertheless these variations are a guide to alterations in the metabolism of the organ or organs producing, distributing and disposing of the enzyme.

We have confirmed the findings of those workers who have noted a great spread in the values for pseudocholinesterase in the serum of normal individuals. This may be seen in the summary of normal values in the tables which follow. This spread has confused many observers who have been unable to come to any conclusion as to variations from the normal of serum cholinesterase in numerous pathological conditions. However, such difficulties are obviated by using sufficiently large samples thus permitting statistical analysis.

Of the published information available, there is evidence to indicate a decrease in the value of the enzyme in liver damage[1–6] and in pernicious anemia in relapse.[7,8] We have observed the decrease in cases of liver damage

* Aided by a grant from the Cancer Research Grants Division, U. S. Public Health Service.

† With the technical assistance of Anita A. Suran, who was assisted in part by a fellowship from the California Tuberculosis and Health Association, Medical Research Committee.

‡ We are grateful to Dr. Emil Bogen, Olive View Sanatorium, for assistance in obtaining sera for our tuberculosis studies.

1 Antopol, W., Tuchman, T., and Schiffren, A., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 46.

2 Antopol, W., Schiffren, A., and Tuchman, L., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 363.

3 McArdle, B., *Quart. J. Med.*, 1940, **9**, 107.

4 Faber, M., *Acta Med. Scand.*, 1943, **114**, 72.

5 Kunkel, H. G., and Ward, S. M., *J. Exp. Med.*, 1947, **86**, 325.

6 Wescoe, W. C., Hunt, C. C., Riker, W. F., and Litt, I. C., *Am. J. Physiol.*, 1947, **149**, 549.

7 Sabine, J. C., *J. Clin. Invest.*, 1940, **19**, 833.

8 Meyer, L. M., Sawitsky, A., Ritz, N. D., and Fitch, H. M., *J. Lab. and Clin. Med.*, 1948, **33**, 189.