

thiourea sulfate is also of interest and suggests that further investigation with this compound might be profitable. It is possible that the effect of S-methylisothiurea sulfate on growth is due to the phenomenon of metabolic antagonism.

Summary. A representative group of substances, previously reported to be lipotropically active, have been tested under standardized conditions. Under the present experimental conditions and in the amounts fed, S-ethylcysteine did not decrease the level of

the liver lipids, cystine betaine and S-methylcysteine exhibited a slight activity of questionable significance, inositol, dimethyl sulfide and S-methylisothiurea sulfate were of intermediate activity, and betaine and triethylcholine had approximately the activity of choline. Lipociac, at the 1% dietary level, was highly active lipotropically and stimulated growth to a greater degree than any of the other compounds tested. S-methylisothiurea sulfate depressed the growth rate.

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Effects of Temperature and Ultraviolet Light on Experimental Polyarthritis of Rats.*

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The experimental polyarthritis produced by the L-4 strain of pleuropneumonia-like microbes in rats is not strictly comparable to rheumatoid arthritis in man. However, because it responds to gold therapy similarly to rheumatoid arthritis, we consider it a method for studies of factors which might influence the arthritic processes and for making chemotherapeutic trials in animals.

In this study attempts were made to determine whether changes in environmental temperature or in ultraviolet irradiation would alter the course of the disease. This is of importance since, in man, it has commonly been supposed that changes in temperature and ultraviolet irradiation would alter the course of rheumatoid arthritis and the incidence of rheumatic fever. Therefore, we decided to evaluate the effects of these environmental changes with the object of increasing basic knowledge regarding the natural history

of the disease in the rat.

Exposure. Thirty male and 30 female albino rats weighing 100 g were placed in an outdoor shelter with open screen sides which protected them from wind, rain and sunshine but not from changes in temperature. The nocturnal temperature ranged from 30 to 45°F, mean 37°F; the diurnal temperature ranged from 46 to 84°F, mean 54°F, the overall range being 30 to 84°F, mean 45°F. The temperature records were made on an automatic thermograph. The average relative humidity was 86% at 5 A.M., 64% at noon, and 70% at 5 P.M.‡ The diet used was Purina Dog Checkers (compressed pellets containing protein 21%; fat 4%; fibre 6%; nitrogen-free extract 46%; and ash 9%). All animals were allowed free access to water. For one week prior to inoculation with pleuropneumonia-like organisms (P.L.O.§) the animals were subjected to exposure. They were then given intraperitoneally 2 cc of a

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‡ Official figures supplied by U. S. Weather Bureau, San Francisco.

§ Abbreviation used throughout to designate L₄ strain of pleuropneumonia-like organisms.

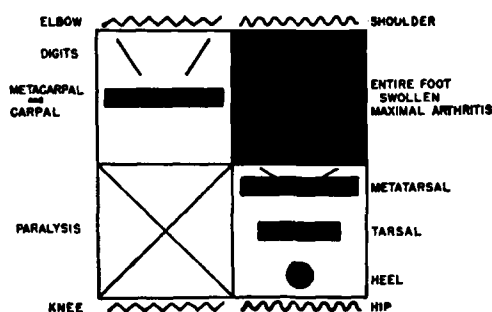


Fig. 1.

Athrogram for recording the extent of joint involvement in experimental polyarthritis of rats.

24-hour broth culture of P.L.O. The animals were examined for gross evidence of arthritis at the end of 4 days, daily for the next week, and then weekly for the following 6 months. The extent of arthritis was recorded on an athrogram (Fig. 1) which was a modification of Sabin's athrogram.¹ For scoring purposes numerical values were assigned corresponding to the extent of arthritic involvement. The score values ranged from 0 to 4 for each anterior extremity and from 0 to 5 for each posterior extremity; thus the athrogram score for any individual rat lay within a range of 0 to 18, 0 indicating no demonstrable arthritis and 18 indicating all 4 extremities were involved to a maximum degree. Single composite athrogram scores were calculated for each animal and group of animals to represent the maximal arthritic involvement during the 6-month period of observation. Ten animals of each sex were uninoculated and kept as controls. In addition to the 20 controls, 20 males and 20 females were inoculated and kept in the animal room as controls where the average daytime temperature was 70°F and the night temperature 58°F.

The rats exposed to cold responded by developing a heavy growth of fur; however, 3 of the uninoculated controls died presumably from the effects of exposure. In the inoculated group, 35% of the females and 40% of the males died, while only 80% and 65%, respectively, showed arthritis. There appeared to be no loss of body weight attributable to

the change in environment. The severity of arthritis according to the composite athrogram score was slightly less than that of the inoculated animals kept at 70°F and the uninoculated controls subjected to cold did not develop arthritis, but only 85% survived.

Heat. Eight female albino rats weighing 100 g were placed in a heated cabinet with an average temperature of 102°F for 24 hours with little variation. The animals were inoculated as described above with P.L.O. They had the same diet but were given thiamine hydrochloride in the drinking water, since rats kept at high temperatures rapidly develop thiamine deficiency. The animals kept at 70°F served as controls for this group.

Immediately after the animals were placed in the heated cupboard they ate less for 3 or 4 days and thereafter resumed normal food consumption. After 6 months of heating these animals had gained normally in body weight, and their tails became longer than those of the controls. Ten heated males died before the scheduled inoculation. Eight heated females, which were inoculated, showed composite athrogram scores slightly less than for the inoculated controls kept at 70°F. Only 88% of these females developed arthritis as compared with 95% for the controls. The total mortality of these females was only 12% as compared with 15% for the inoculated controls, 35% for those subjected to exposure, and 50% for the females subjected to ultraviolet light.

Ultraviolet Irradiation. Thirty male and 30 female albino rats were exposed for 6 months to constant ultraviolet irradiation supplied by a Westinghouse Type S-1 ultraviolet lamp at a distance of 5 feet. The average temperature remained constant at 82°F. Ten animals of each sex were used as uninoculated controls.

A few of the irradiated rats developed a mild conjunctivitis, but there was no increase in body weight or food consumption. Among the uninoculated controls subjected to ultraviolet light one animal died of undetermined cause and none developed arthritis. Among the inoculated animals the females had higher and the males lower composite athrogram

¹ Sabin, A. B., and Warren, J., *J. Bact.*, 1940, 40, 823.

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 arthrograph 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 polyar-

thritis of rats produced by the L₄ 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.

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Protein Intake and Leishmaniasis in the Hamster.*

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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

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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.