Technical Papers

Sterility Induced in Growing Rats on a Tryptophane-deficient Diet

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While conducting experiments to determine the rate of recovery[1] of growing rats after being fed various deficiency diets, the author discovered somewhat different results in the case of the tryptophane-deficient animals. When they reached maturity, all the rats who had lacked this essential amino acid in their diet were found to be sterile. Since only one brief reference to such an occurrence could be found, and this with regard to male rats only, a further study was instituted, and its results are reported herein.

Throughout the entire project, albino rat pairs ranging in age from 28 to 48 days were used for experimental subjects, and in each case a pair of litter mates was used for controls. The experimental animals were fed a deficient diet[2] similar to that of Albanese and Buschke (*1*) for periods ranging from 3 to 18 days and then returned to the colony diet[3] which was fed the controls throughout the investigation.

In all cases the original matings were observed until the animals were at least 100 days old, by which time all but one of the control pairs had produced a litter. Since there had been no evidence of any sexual interest between the experimental pairs during this period, they were separated and mated to controls which had been proven fertile. The 38 deficient control crosses were observed for 90 days, and since there was no evidence of coitus, all but 10 of the matings were sacrificed and their gonads and pituitary removed for histological observation. The remaining animals were observed for an additional 60 days, and when they too were shown to be sterile, they were sacrificed as were the others.

The observations reported here show rather conclusively that growing rats, when fed a diet lacking tryptophane, even for as short a period as 3 days, manifest sterility, and that both sexes are affected similarly. This, furthermore, lends support to the belief that this amino acid has numerous specific actions in addition to aiding in the synthesis of body proteins. Further observations should show whether this specific action is on the gonads directly or through some other organ indirectly.

[1] Rate of recovery as used here refers to the time necessary for a deficient animal, after being returned to a normal diet, to equal the relative length and weight of its litter mates reared entirely on the normal or control diet.

[2] The exact composition of the diet was as follows: potato starch, 40 grams; bacto-gelatine, 30 grams; sucrose, 10 grams; olive oil, 10 grams; castor oil, 5 grams; and basic salt mixture, 5 grams. The salt mixture was composed of: NaCl, 1.73 grams; $MgSO_4$, 5.45 grams; K_2HPO_4, 9.54 grams; $CaH_4(PO_4)_2 \cdot H_2O$, 5.40 grams; Na biphosphate, 3.47 grams; Fe citrate, 1.18 grams; Ca lactate, 13.00 grams.

[3] The colony, or control, diet consisted of Friskie's Dog Food supplemented twice weekly with lettuce leaves.

Reference

1. ALBANESE, A. A., and BUSCHKE, W. *Science*, 1942, **95**, 585.

The Effect of Environmental Temperature on Mouse Susceptibility to Poliomyelitis Virus

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Environmental temperatures have been shown experimentally to play a significant role in modifying resistance to infectious disease of bacterial origin (*1*); hence, an investigation was made to determine whether environmental temperature affects the course of a virus disease, such as poliomyelitis. The virus was obtained from Dr. John F. Toomey, Western Reserve University, Cleveland, Ohio.

For the test, three groups of mice were acclimated to temperatures of 13° C., 22° C., and 32° C. Although referred to as a group, the mice held at 13° C. were kept in small cages, six to a cage, to prevent too much huddling. Three-week-old mice of relatively uniform weight (13–15 grams) were employed, and each group was held at its respective temperature for three weeks. Thus, the mice were six weeks old when finally tested for susceptibility to the virus.

After becoming acclimated to a given temperature, all the mice adapted to that temperature were subdivided into six groups. Three of the subgroups received intracerebral injections of 0.05 ml. of a 3-per cent infected brain-cord suspension. The remaining subgroups served as controls. One infected and one control group were kept at each of the three experimental temperatures, regardless of the temperature to which they had been originally adapted.

The mice acclimated to 13° C. and held at that temperature after inoculation never showed symptoms of paralysis in less than 11 days, with 13 days being required to establish 50-per cent mortality. In contrast to this, mice adapted to 22° C. and held at that temperature after injection showed 50-per cent mortality

at the end of seven days, and mice acclimated to and held at 32° C. began showing symptoms and dying as early as the fifth day. The mice originally acclimated to 13° C. and kept at 22° and 32° C. after injection showed greater susceptibility than those allowed to remain at 13° C. Conversely, mice originally adapted to 22° and 32° C. exhibited a greater resistance to infection, as indicated by a prolonged incubation period, when kept at 13° C. than when held at the temperatures to which they had first been acclimated (Table 1). Brain-cord material recovered by sacrificing some

TABLE 1

THE EFFECT OF ENVIRONMENTAL TEMPERATURE ON SUSCEPTIBILITY OF WHITE MICE TO POLIOMYELITIS VIRUS

Temperature to which mice were acclimated for 3 weeks prior to inoculation	Temperature at which mice were kept after inoculation with virus, numbers injected, and days elapsed before appearance of symptoms and mortality in 50 per cent of each group*					
	13° C.		22° C.		32° C.	
	No. mice	Incubation	No. mice	Incubation	No. mice	Incubation
13° C.	48	13 days	48	9 days	12	7 days
22° C.	48	9 days	48	7 days	12	6 days
32° C.	12	9 days	12	6 days	12	5 days

* All experimental groups were controlled with noninfected mice that received the same environmental treatment.

of the infected mice and treated with a known poliomyelitis virus neutralizing serum lost its infectivity.

Since the experiment was repeated several times, mice from the same source were not always available. This, however, did not appear to alter the course of infection. Other factors, such as weight, feed, and dosage of virus were kept relatively constant. Hence, environmental temperature must be considered as the major factor contributing to the variation in incubation periods.

In view of the fact that metabolic rates tend to increase upon exposure to cold and decrease at higher temperatures, the data collected in this investigation could be interpreted as indicating the rapid growth of the virus, and the resulting symptoms of disease to be dependent upon a disturbance of the normal metabolic rate of the host. If the data under discussion could be applied to the human, one might assume that among occupants of temperate zones the shift from cool temperatures of the spring to the heat of summer creates an added susceptibility, not only through much greater opportunity for exposure to virus, but also through a decrease in the metabolic rate of the host, a condition possibly favoring rapid growth and spread of virus through the tissues of the host. Likewise, increases in the metabolic rate brought about with the onset of cooler temperatures of the autumn might interfere sufficiently with virus growth to lengthen the incubation period and permit certain infected individuals to develop resistance before exhibiting definite symptoms of poliomyelitis. It might even account for sporadic cases of the disease occurring in winter as a result of late summer infection and a prolonged incubation period. In advancing this concept, one would have to assume the need for a relatively gradual environmental temperature change, since work done on monkeys (*2*) has shown that the shock induced by sudden exposure to extreme cold after infection actually increases susceptibility, as well as the severity of the disease.

If one were to accept the thesis that a decrease in the metabolic rate creates an optimal condition for the growth of the virus and thereby increases host susceptibility, it would be difficult to explain why poliomyelitis is not more prevalent in the tropics and also why adults with their lower metabolic rates are not more highly susceptible than children. While it is true that poliomyelitis occurs in tropical regions, it seems seldom to assume the epidemic proportions so common in temperate zones during summer months. With regard to the susceptibility of children, it must be borne in mind that poliomyelitis is most prevalent in the five to nine age-group. These are not only the years when exposure may be relatively easy, but also constitute the period when the metabolic rate is declining rapidly after reaching a peak at approximately age five. Thus, the possibility of a "critical" or optimal metabolic rate of the tissues for virus growth being more readily obtainable between the ages of five and ten cannot be ignored. Even though any change in metabolic rate of the tissues as a result of external temperature variations may be very slight, possibly only that slight disturbance of normal metabolism is required to promote increased susceptibility or resistance. In other words, seasonal temperature fluctuations and the resultant metabolic disturbances, particularly toward a decrease in the metabolic rate, might be considered as being more conducive to susceptibility than prolonged exposures to relatively high, yet stable, temperatures.

References

1. MILLS, C. A., and SCHMIDT, L. H. *Amer. J. trop. Med.*, 1942, **22**, 655.
2. MILZER, ALBERT, LEWIN, PHILIP, and LEVINSON, SIDNEY. *J. Bact.*, 1943, **45**, 78.

Scanning Science—

The so-called Liebig's condenser was not devised by Liebig, but by a student of medicine at Göttingen, Christian Ehrenfried Weigel. Liebig never claimed to be the inventor of his condenser, but describes it in his *Handbuch* (1843) as "der Göttlin'sche Kuhlapparat," while Göttling in his *Almanach* (1794) rightly ascribes its invention to Weigel, who was then professor of botany and chemistry at Greifswald.

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