

peutic efficacy on the basis of *in vitro* results of sulfonamide action have been commented upon elsewhere.⁴ The activity of a drug *in vitro* does not necessarily parallel its activity in experimental animals or in human subjects. *In vitro* tests may be useful as preliminary guides to *in vivo* studies, but cannot substitute for them.

Summary. When small inocula are planted in a semi-synthetic medium, sulfadiazine and sulfathiazole are bactericidal in concentrations as low as 1 or 2 mg % on *E. coli*, *Shigella paradysenteriae* (Flexner) and *S. choleraesuis (suipestifer)*; and in 5 mg % on *S. enteritides*, *S. schottmülleri* and *S. typhimurium (aertrycke)*. In the latter concentration they are bacteriostatic for *S. paratyphi* and in 10 mg % they are bactericidal for *Klebsiella pneumoniae*, type A.

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Radiosensitivity of Skin of New-Born Rats. III. Sensitivity at Different Temperatures.*

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(Introduced by J. H. Bodine.)

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In a previous paper¹ it has been reported that temperatures of 0-5°C during roentgen irradiation (1,300 r) decreased the amount of injury produced in the skin of new-born rats. In a second series of experiments² this increased resistance of animals irradiated at 0-5°C was studied quantitatively for dosages ranging from 300 to 3000 roentgens. The purpose of this investigation was to determine whether the resistance would change quantitatively with increasing temperature.

The animals were of the same strain used in the previous studies.[†] The temperature was controlled during the irradiation by placing the animals in a double walled box, constructed of transparent sheet plastic, containing water at the desired temperature. The

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¹ Evans, T. C., *J. Roentgenol. and Rad. Ther.*, in press.

² Evans, T. C., Robbie, W. A., Goodrich, J. P., and Slaughter, J. C., *Proc. Soc. Exp. Biol. and Med.*, 1941, **46**, 662.

[†] These animals were kindly supplied by Dr. Emil Witschi from his rat colony.

temperature of the skin before and after the irradiation was determined by means of a thermocouple. Experiments indicated that the rectal temperature changed very rapidly to that of the skin at low and at high temperatures, but at room temperature the interior of the body was slightly warmer than the skin.

The radiation used was unfiltered except for 1 mm of cardboard and 2 sheets of 0.5 mm plastic. The radiation was delivered at 130 K.V. peak and 5 ma. The half-value layer was ca. 1.5 mm aluminum. The intensity in the box at 26°C was 137 roentgens per minute. The target distance was 30 cm.

The exposed skin was a 6 x 9 mm area to one side of the mid-ventral region of the abdomen. Both ventral and dorsal skins were examined microscopically 2 weeks later, and the extent of injury determined in units as described in a previous report.²

Fig. 1 shows some typical results of irradiation at different temperatures. These animals were litter mates and each was given the same dosage. No epilation is visible in the animals treated at 0° and 6°C. The rat irradiated at 17°C shows slight epilation and the one at 37°C shows complete epilation. Twenty-five new-born rats have been irradiated in this investigation, and the results are summarized in Fig. 2. The width of each block indicates the variation in temperature from the beginning to the end of the irradiation and the height of each block is twice the standard error of the mean of the determinations as made several times by each investi-

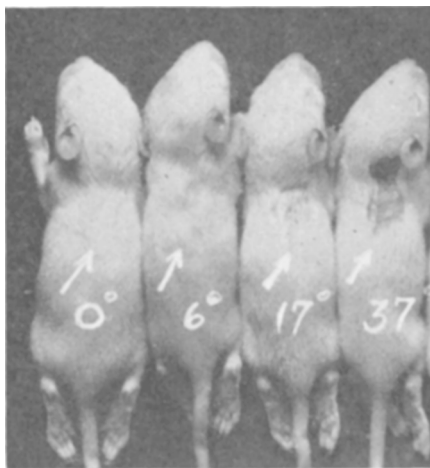


FIG. 1.
Littermates 14 days after irradiation with a dosage of 2010 roentgens.

gator. The highest temperature employed was 40°C which was as high as the animal could tolerate for the 15-minute period. Although much individual variation is evident, the data clearly show that the sensitivity increases as the temperature is raised. It is interesting to note that the variation produced at the different temperatures covers a range of injury which is equivalent to that produced by 0 to 2500 roentgens.

The quantitative relationship between the effect and the temperature indicates the possible importance of one or more metabolic processes in determining the amount of injury produced by the radiation. Although the heart rate, breathing, etc. of such new-born

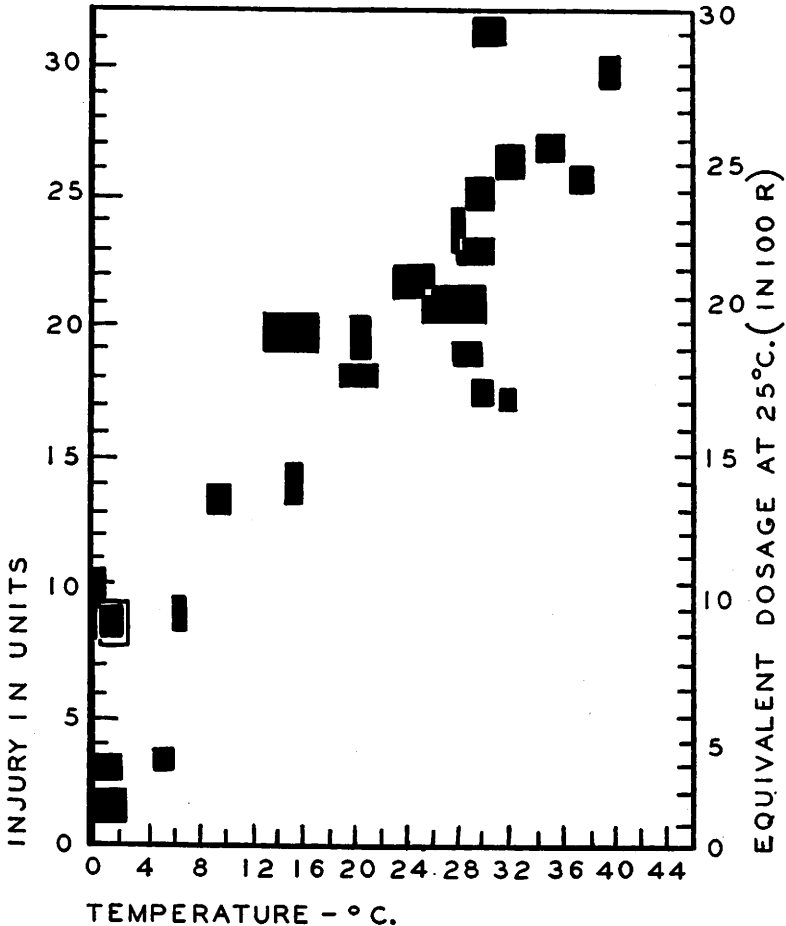


FIG. 2.

A graph showing the amount of injury produced at different temperatures.

animals are generally regarded as dependent on temperature, it seemed worthwhile to test the relationship on these animals.

With the assistance of Professor T. L. Jahn, electrocardiograms were made at different temperatures. The first experiment was begun at 26.5°C and the heart was beating 225 times a minute at this temperature. The temperature was then lowered to 16.5° and the heart beat rate immediately dropped to about 125 per minute. After the animal had been at 10° for 10 minutes the rate was about 30 per minute. The rate after 30 minutes at 10° was only 18 per minute. The temperature was then reduced to 1-2°C and the rate dropped to 2 per minute. The temperature was raised to 26.5° and after an hour the rate had increased to 250 per minute. The rate at 35° was 350 and at 40° the maximum of 400 beats per minute was obtained. A temperature of 45° proved to be too warm, as the rate dropped from 375 to 100 in 15 minutes, and after 5 more minutes the rat was dead.

In another experiment, a new-born rat was placed on ice and the heart-beat rate was found to reach the minimum within 10 minutes. This corresponds roughly to the rate of cooling of the skin. After it had been held to the minimal rate for 20 minutes the animal was placed again at room temperature. Within 5 minutes the rate had increased from zero to 22 per minute. After 53 minutes at room temperature the rate had increased to 165 beats per minute.

The rate of breathing and the rate of oxygen consumption were also found to be increased by raising, and decreased by lowering the temperature.

Since the circulation and respiration were found to respond to temperature in much the same way as the radiosensitivity it is quite possible that the temperature exerts its influence on radiosensitivity through its control of metabolic processes such as these.