When the animal learned that the only choice was between an environment that was too hot and one that was too cold, its decision to leave the cold environment may have been influenced by remembrance that the other environment would shortly become intolerably hot. Remaining in the cold courtyard would in no way be harmful, whereas an extended period in the hot environment could be lethal. Drowsiness and sleep sometimes appeared to depress the response to enter the hot box, especially when the brain stem was heated. If the body temperature fell below about 25°C or if it was below this level at the start, our lizards seldom entered the hot box unassisted. Cold-induced lethargy did not immobilize them, however, as they could easily be prodded to move at a body temperature of 15°C.

In all lizards except No. 8 (still alive 4 months after implantation), the placement of the thermodes was determined. The thermodes were straddling the optic chiasm and the preoptic region above it in lizards No. 6 and 21. In the others, the thermodes were 1.0 to 2.0 mm caudal to the optic chiasm; the effect of heating or cooling the brain stem was less than in lizards No. 6, 8, and 21. Thus there is a suggestion that the preoptic region is the thermally responsive region of the brain stem. In endotherms this same region is known to activate physiologic thermoregulatory responses when its temperature is displaced.

Bartholomew *et al.* (*5*), placing two lizards (*T. scincoides*) in a 40°C environment with a starting body temperature of 20°C, obtained heating curves; and in a 20°C environment, with a starting body temperature of 40°C, they obtained cooling curves. The rate of heating, at a body temperature of 30°C, was greater than the rate of cooling at the same temperature; the difference was attributed to the greater heat production during heating, so that the calculated conductance of the tissue and air, between the core temperature and environment, was the same for both heating and cooling. Their results probably mean that any circulatory adjustments that may be associated with body temperature were not shown to have thermoregulatory significance. We arrived at the same conclusion, since heating or cooling of the preoptic region of lizard No. 21 had no discernible effect upon either the heating or the cooling curves for this animal. Nor did we see any inflections in the normal heating or cooling curves (brain stem not heated or cooled) to suggest a change in blood flow from core to skin.

However, the heat capacity of animal tissue is great, so a method based upon heating or cooling curves is not sufficiently sensitive for detecting small thermoregulatory responses. We noticed that the vessels along the margin of the ventral scales are engorged with blood when the animal is hot (35°C), but we found that heating or cooling of the brain stem had no effect on the amount of blood in these vessels or on their rate of filling after they were emptied by gentle pressure.

Hyperventilation and gaping have been observed in heated lizards (*6*), and these we observed in *T. scincoides*; however, the associated loss of evaporative water had no discernible effect on the heating curves, nor did heating or cooling of the hypothalamus indirectly affect the heating curves by affecting the evaporative heat loss from the mouth. The only effect observed when the brain stem was heated while a heating curve was recorded was that the lizard struggled more vigorously and at a lower colonic temperature. Likewise, cooling of the brain while body temperatures were rising delayed the struggling until a higher colonic temperature was achieved.

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Ischemic Necrosis: Prevention by Stress

Abstract. *Complete interruption of the circulation, by means of a special clip, in a skin flap during 9 hours results in necrosis of the ischemic area. Prior treatment with various severe stressors (spinal-cord transection, prolonged restraint, quadriplegia due to transection of motor nerves, forced exercise, or cold baths), as well as systemic injection of epinephrine, norepinephrine, or chlorpromazine, offers virtually complete protection against this form of topical tissue injury.*

One hundred twenty female Sprague-Dawley rats with an average body weight of 100 g (range, 90 to 110 g) were separated into 12 equal groups and treated as indicated in Table 1.

Table 1. Prevention of necrosis of the skin by stress. In addition to the treatments listed, a skin flap was isolated from the circulation by a compressing clip as indicated in the text. All subcutaneous injections were administered on the abdomen. Times (minutes, hours, days) preceded by minus signs are the lengths of time before application of the treatment; plus signs, after treatment.

Treatment	Cutaneous necrosis (scale, + to +++)
None	+++
Spinal-cord transection	
Thermocautery between C7 and D1 at 0 hour	0
Restraint	
24 hours on a board, beginning at −15 hours	±
Quadriplegia	
Transection of motor nerves of all four extremities at −1 hour	±
Starvation	
Only water allowed from −48 hours to +9 hours	+
Forced exercise	
In drum, 30 cm in diameter, 12 rev/min, from −30 minutes to +6 hours and from +8 hours 30 minutes to +9 hours	+
Cold	
Kept at 9°C from −30 minutes to +9 hours	Trace
Epinephrine	
Subcutaneous injection of 0.8 mg at −30 minutes	Trace
Norepinephrine	
Subcutaneous injection of 1.5 mg at −30 minutes	0
Cortisol acetate	
Daily subcutaneous injection of 3 mg from −5th day to +1st day	+++
Cortisol sodium succinate	
Intravenous injection of 20 mg at −30 minutes	+++
Chlorpromazine	
Subcutaneous injection of 1.5 mg at −30 minutes	Trace

The clips were prepared from ordinary umbilical clamps (*1*) by covering the simple branch (the one not bearing a hook) with rubber tubing. After shaving the back of the animal with electric clippers, a skin fold was taken up between the fingers and compressed by the clip, which was left in position for 9 hours. The times of treatment are indicated in Table 1, the application of the clip being 0 hour. The techniques used for production of stress have been described in detail elsewhere (*2*). Intensity of necrosis was appraised, by semiquantitative inspection, in terms of a scale of + to +++ and was verified histologically (periodic acid-Schiff reaction and van Gieson technique) on the 4th day. Lesions in and immediately around the roughly circular line directly compressed by the clip were disregarded. Crust formation with subsequent rejection of the skin over all or part of the clipped area were taken as indicators of necrosis. Serial examinations on control rats, killed at intervals, showed that just after the removal of the clip the ischemic area was virtually normal except for intense degranulation of the mast cells. Edema with numerous hemorrhages in the microcirculation appeared approximately 15 minutes after the clip was removed, which suggests that the vascular system was particularly affected. This was followed, 6 hours later, by the formation of thrombi, consisting of aggregations of erythrocytes, and infiltration of serum and erythrocytes into the walls of larger arterioles and venules. Beginning at about this time the nuclei of all cells in the affected area underwent pycnosis, eventually disintegrating into amorphous basophilic bodies, while the collagen fibers became a homogeneous mass. Inflammatory infiltration and reactive hyperemia were noted only in the areas beneath the clips. Figure 1 shows the histologic appearance of both necrotic and essentially normal skin.

As shown by Table 1, all the severe stressors, as well as the high doses of catecholamines and chlorpromazine, offered considerable and, in some cases, total protection against the necrosis induced by prolonged interruption of the circulation. However, preliminary experiments had shown that smaller doses of catecholamines or chlorpromazine possess little, if any, prophylactic effect; hence, it remains to be seen whether these agents act merely as stressors or through their specific pharmacologic properties. Conceivably, during systemic stress, endogenous catecholamines might act as mediators of the protective action. It is dubious, however, whether efficacious amounts of these hormones could have been secreted, although selective release at nerve endings or activation by stress-induced conditioning factors may have augmented their potency. It is clear that even the enormous doses of glucocorticoids, administered either chronically as a pretreatment or suddenly just before application of the clip, failed to duplicate the protective action of stress.

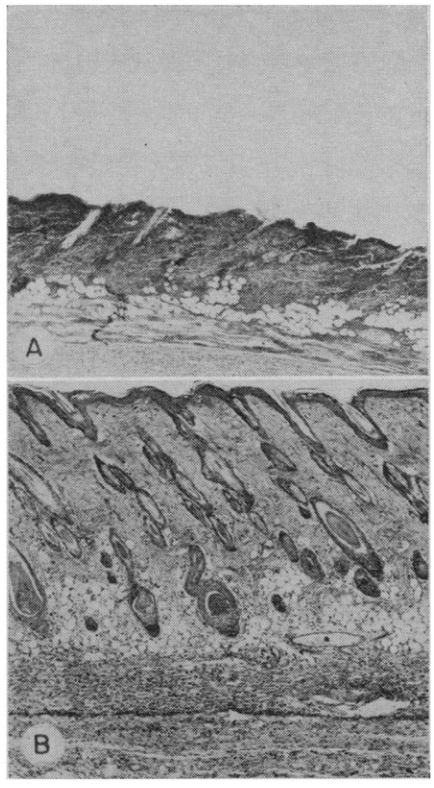

Fig. 1. (A) Histologic appearance of necrotic skin from control animal. (B) Essentially normal histologic structure of skin, except for mild inflammatory infiltration and degeneration of hair roots, in animal protected by chlorpromazine.

Chlorpromazine was tested because we had noted earlier that phenothiazines can protect the heart of the rat against infarctoid necroses elicited by chemical means (*3*, *4*). However, pretreatment with systemic stressors can also offer protection against this type of cardiac necrosis (*2*); hence, even here, the specificity of the pharmacologic action remains to be demonstrated.

Earlier work had shown that exposure to stress can protect the organism against a great variety of morbid lesions, including several forms of calciphylaxis, calcergy, inflammation (*3*), and thrombohemorrhagic phenomena (*5*). The observations reported here indicate that even the tissue damage induced by prolonged total interruption of the circulation can be prevented by systemic stress.

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Visual Discrimination of Temporal Order

Abstract. *Past research addressed to the minimum temporal separation necessary for the judgment of visual stimulus order has failed to control peripheral adaptation and masking effects. The present study employed pairs of brief stimuli with each member presented to a separate eye; that is, dichoptic presentations. Under these conditions, minimum separations for the correct discrimination of order were found to be far less than those obtained in experiments in which both stimuli were presented to the same eye or to both eyes.*

Several recent studies of perceived order (*1*) appear to have been inspired by the earlier research of Hirsh and Sherrick (*2*) in which vision, touch, and audition were compared with respect to the temporal separations necessary for the correct judgment of stimulus sequence. The compelling finding of Hirsh and Sherrick was the relative constancy of 20 msec among the three modalities and within vision irrespective of the retinal locus stimulated. Given the well-established differences among the senses in the discrimination of "one" versus "two" judgments (that is, judgments of fusion), Hirsh and Sherrick considered the modality independence obtained in the judgment of