minimum 2 hours after nightfall. The difference in the percentage mortality between the highest and the lowest points of the curve is significant to more than 99.9 percent. The 14-hour period of falling sensitivity and the 10-hour duration of rise in the pattern in these light-dark 14 : 10 conditions could indicate some relationship of the internal organization of the organism to the duration of the light and dark phases—that is, to the photoperiod. Thus not only is the phase of the rhythmic pattern set by the alternating light-dark conditions, but the duration of different parts of the cycle may be regulated by the photoperiod. We attempted to examine this suggestion by testing mites from a colony maintained in a light-dark cycle of 12 : 12, but under such short-day lighting conditions at 25°C the appearance of diapausing forms prevented the continuation of the experiment.

Many of the standard methods of investigation of circadian organization cannot be utilized with the two-spotted spider mite. The method used here can provide information on the temporal organization of organisms which are too small to study with the normally used actograph techniques.

The findings of a marked sensitivity pattern to the acaricide should emphasize the importance of considering circadian organization in the evaluation and interpretation of toxicological experiments with insecticides and all biologically active chemicals.

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Gastric Erosions in the Rat: Effects of Immobilization at Different Points in the Activity Cycle

Abstract. *Predictable, cyclic patterns of activity were obtained from 30 male rats. Seventeen of these were subjected to physical immobilization just as they were approaching their period of peak activity and thirteen animals were restrained during the inactive phase of their cycle. Eight animals were found to have gastric erosions following the immobilization. All of these came from the group immobilized during the time they would have been in the active phase of their particular cycle.*

When rats are subjected to physical immobilization a certain proportion will develop gastric erosions in the body of the stomach. This is the lower, glandular portion of the stomach which contains acid-secreting cells. Previous research has demonstrated that animals found to have such erosions also have higher concentrations of pepsinogen in the plasma than animals without these lesions (*1*). Moreover, plasma pepsinogen concentrations, taken as a measure of gastric secretory potential, are predictive of erosion susceptibility (*2*). It was concluded (*2*) that a high pepsinogen concentration was neither necessary nor sufficient for the development of gastric erosions since all animals with high concentrations of pepsinogen did not develop erosions upon subsequent restraint, nor did a low pepsinogen concentration uniformly protect against such lesions. Apparently, then, different animals possessed of the same biological predisposition to gastric lesions responded differently to a constant stimulus situation. This is not unlike results which sometimes obtain in "stress" experiments with human subjects where it is hypothesized that an individual may not respond to what the experimenter defines as a "stress" because of the manner in which that person perceives or interprets the situation. The stimulus must be meaningful to the individual—and what may be meaningful is assumed to be a function of the individual's past history. There is no reason to assume that such an argument would not apply to animals lower than man, especially since there is a considerable amount of research in animals which indicates that past experiences influence responses to "stress," even though it is not always possible to predict the direction in which differentially stimulated animals will differ from controls. It was therefore of interest to determine whether differing perceptions of a particular nonspecific "stressful" stimulus on the part of animal subjects could be brought under experimental control.

One of the methods commonly used to induce gastric erosions in the rat is a period of physical immobilization accompanied by food and water deprivation. The greater the duration of immobilization, the greater is the percentage of animals that develop erosions (*2, 3*). Because of the nature of this stimulus, its opposite, "activity," suggested itself as a behavior which might predispose animals to lesions on a psychological or behavioral as well as a physiological level. It was hypothesized that an animal that was psychologically (and physiologically) prepared to be active would "perceive" stimulation in the form of bodily restraint as being more "stressful" than an animal that was psychologically (and physiologically) prepared to be inactive, and that, other things being equal (for example, the concentration of pepsinogen in the plasma), the former would be the more likely to develop gastric erosions.

Experimentally naive, male, Sprague-Dawley rats, each weighing approximately 400 g, were individually housed in cages adjoining activity wheels (Wahmann No. LC-34). Animals remained in these cages with free access to the wheels and with food and water always available for a period of 6 weeks. During the final 2 weeks the number of wheel revolutions was recorded by automatically photographing a bank of electrical counters at 3-hour intervals. To increase the variability in the time at which the peak activity periods would occur, the lights in the room housing these animals were kept on at all times.

A predictable pattern of high and low periods of activity was apparent in 30 of the 44 animals observed. Twenty-one of the 30 animals showed peak activity beginning somewhere between 6 p.m. and 3 a.m.; the maximum activity of the remaining animals occurred during the daylight hours. Some animals displayed a pattern in which the periods of maximal activity occurred within the same 3-hour period each day; other animals showed a cycle that was slightly greater than 24 hours in its periodicity. This latter type of rhythm is illustrated in the lower portion of Fig. 1. The upper graph is an example of a regular activity pattern.

The 30 animals were then subjected

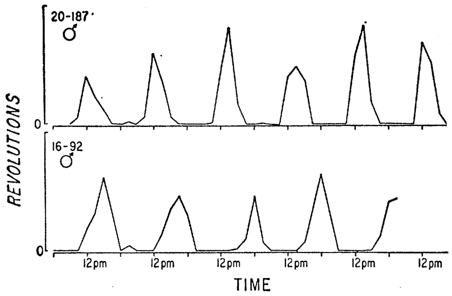

Fig. 1. Examples of rhythmic patterns of activity obtained from animals housed in activity wheels.

to 6 hours of immobilization in flexible wire mesh as previously described (*2*). On the basis of the activity pattern of the previous 5 or 6 days, 17 animals were immobilized at the beginning of the time they would have been entering their period of activity, and 13 animals were immobilized at the beginning of the time they would have been entering a trough in their particular cycle. After the period of immobilization, the animals were killed. The stomachs were removed, opened along the greater curvature, washed in saline, and the incidence of gastric erosions was recorded.

Eight animals were found to have gastric erosions. All of these came from the group immobilized during the active phase of their particular cycle. This difference in the incidence of erosions between the "peak" and "trough" animals is significant at less than the .01 level as determined by Fisher's exact probability test.

These data demonstrate conclusively the extent to which the prior state of an organism can influence its response to "stress." However, the experiment does not delineate the relative contribution of psychological as compared to physiological factors in determining this effect. For example, it was observed that of the 13 animals immobilized during a trough in their activity cycle, eight of these had some undigested food in their stomachs. In the group immobilized during their peak of activity there were two animals with food in their stomachs and neither of these developed gastric erosions. It is an impression gained from previous research with gastric erosions that the presence of food in the stomach offers some protection against the development of such lesions. Also, the research of Halberg and his associates (*4*) clearly demonstrates the existence of circadian rhythms in a variety of physiological processes, and the effects of such rhythms on responses to pathogenic stimulation. Some of these 24-hour rhythms undoubtedly parallel the activity rhythm, although their relevance to the development of immobilization-induced gastric erosions remains to be determined. In view of such data, however, it will be necessary to determine, for example, whether the plasma pepsinogen concentration, which is known to be related to the development of gastric erosions, exhibits cyclic variations which may be synchronized with the cyclic variations in activity, or, perhaps, if adrenal steroids, which do exhibit rhythmic variations, are related to the development of such lesions. Acknowledging the potential relevance of such variables, there is, nonetheless, some face validity to the behavioral hypothesis that the "perception" of restraint would be different for animals that are behaviorally prepared to be active or inactive.

In addition to the work of Halberg and his associates there have been other recent reports concerning the role of 24-hour rhythms in influencing sensitivity to stimuli such as x-irradiation (*5*) and drugs such as Nembutal (*6*). As in the experiment described here, such studies have not been concerned with periodicity in itself as much as with decreasing the commonly observed variability in response to the stimulus under study. The studies with drugs, for example, have been prompted by a recognition of certain physiological rhythms which might be expected to influence the rate at which the drug might be detoxified. Analagously, the present experiment was the result of a psychological orientation involving the behavioral relationship between overt activity and the suppression of overt activity which was the stimulus for a pathogenic process. Both approaches lead to the general conclusion that a consideration of the existing psychophysiological state of the organism is a meaningful factor in determining the organism's response to a superimposed stimulus.

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Homograft Sensitivity Induction by Group A Streptococci

Abstract. *Streptococcal cells can induce in the guinea pig a state of altered reactivity to skin homografts similar to that resulting from sensitization with homologous tissue.*

Recent reports have suggested the presence of an antigen or antigens in certain strains of group A hemolytic streptococci which exhibits or exhibit immunologic cross reactivity with human heart and skeletal muscle, as well as with rabbit tissues (*1*). This and other observations (*2*) lend support to the suggestion that similar antigenic structures may occur in groups as widely separated phylogenetically as bacterial and mammalian cells (*3*). This report is concerned with the induction of a state of altered reactivity to skin homografts in guinea pigs after treatment with suspensions of heat-killed group A, type 12 hemolytic streptococci.

Group A, type 12 hemolytic streptococci (*4*) were grown overnight at 37°C in Wannamaker's dialysate medium (*5*). They were collected and killed by heat, being placed in a 56°C water-bath for 45 minutes (*6*). The heat-killed bacterial cells were resuspended in Medium 199 (*7*), and a portion of the suspension was removed for dry-weight determinations. The remainder was emulsified in 10 ml of Freund's incomplete adjuvant (Difco). The emulsion (0.1 ml) was injected into each footpad of the animals. The test animals received dosages of the streptococcal cells ranging from 0.14 to 13.0 mg (dry weight). Four groups of control animals were included in the