present. This difference became apparent only after the first week of food scheduling. The significant difference in the number of licks needed to consume one milliliter of water when food is present compared to the number of licks when food is absent clearly indicates that lick volume is not a constant. The difference in lick volume generated by the presence or absence of food can probably be related to differences in the frequency of licks under these two conditions. In the presence of food, the rat apparently licks at a rate that prevents the full amount of water from reaching the tongue. Thus, use of a lick count to determine volumes of ingested fluids by rats on different feeding schedules could be misleading. Also, examination of the volume-per-lick data derived from this experiment indicates that an animal's liquid intake can be modified by the presence of solid food.

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A note on the effects of chlorpromazine upon ulceration in the rat

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Four groups of rats were exposed to a highly ulcerogenic procedure. Three experimental groups were given programmed injections of three different concentrations of chlorpromazine and a control group received physiological saline. All drug concentrations significantly reduced ulceration relative to controls. The lowest concentration proved least effective in this regard, but no simple linear relationship was found between drug concentration and frequency of ulceration. A tentative hypothesis regarding an all-or-none protective function of the drug was suggested, and parameters for future research outlined.

There has been a substantial amount of research aimed at discovering and elaborating the parameters relevant to the production of stress-induced gastric ulcers in the rat (e.g., conflict, Sawrey & Weisz, 1956; conditioned fear, Mikhail, 1969; and operant control over aversive events, Weiss, 1968). However, there has been little systematic research concerning the effects of drugs on ulcer development, and, more particularly, there has been almost no work on the effects of chlorpromazine as an antiulcerogenic agent. There are suggestions in the literature that this drug, along with other central neurotropic substances, may effectively reduce stress-induced gastric ulceration and that it may be more effective in this regard than some other agents, i.e., morphine, atropine, and others (e.g., Zabrodin, 1965).

The present research represented an initial effort to examine some of the relationships between chlorpromazine and gastric ulceration in the rat in somewhat greater detail than has been reported previously. One specific purpose of this work was to study the effects of chlorpromazine in a highly ulcerogenic stress situation and to test varying concentrations of this drug in order to detect possible protective effects within this paradigm. The second specific goal was to attempt to discover a concentration level of the drug that effectively reduces or totally inhibits ulceration in a highly stressful setting. Thus, drug concentrations covering a wide range were selected and three values within this range were studied. It was predicted that these values would demonstrate a generally negatively related linear function between concentration level and the degree of gastric pathology.

DRUG

The drug utilized was chlorpromazine, 25 mg/cc (Smith, Kline, & French).

SUBJECTS

Ss were 109 male Long-Evans hooded rats, 100-115 days old and weighing between 345 and 370 g at time of testing. Ss were assigned randomly to one of four conditions in which the stock drug solution was diluted as indicated: 1/50th (N = 21); 1/20th (N = 20); 1/10th (N = 27); and saline control (N = 41).

APPARATUS

Twelve 11.5 x 11.5 x 12 in. Plexiglas boxes served as test cages. The grid floors of these cages were wired so that scrambled electric shock could be delivered simultaneously to all boxes via four Grason-Stadler E1064GS shock generators. All sides of the test cages were covered by black contact paper to provide visual isolation. Shock schedules were programmed via an LVE tape programmer, and stress-rest cycles were controlled by an LVE Multifunction Interval Timer.

PROCEDURE

The stress-rest schedule involved first food-depriving all animals for 48 h, placing them into the test cages, and exposing them to a 36-h stress-rest procedure. This consisted of alternating 2 h of shock (stress) with 2 h of no shock (rest). Thus, all Ss received a total of 18 h of stress and 18 h of rest on a 2-h alternating schedule. During each 2-h shock period Ss received 120 random presentations of a 2.0-mA, 2-sec footshock. This basic schedule was developed via preliminary research and was shown to be highly ulcerogenic (i.e., 89% of all pilot Ss ulcerated while no control Ss deprived for the total 84-h period showed gastric pathology). The first injection for

Table 1
Number and Percentage of Ss Ulcerating Per Group

Group	N	Number Ulcerating	Percent Ulcerating
1/50th	21	12	57
1/20th	20	3	15
1/10th	27	6	22
Saline	41	35	86

both drug- and saline-control Ss was administered at least 6 min prior to placing Ss in the test cages. All injections were 1 cc of the appropriate drug concentration or the same volume of physiological saline. Ss were reinjected with the appropriate dosage every 6 h following the first injection for a total of six injections over the 36-h stress-rest cycle. All injections were intraperitoneal. Since differences in S weights were not great, it was decided to administer equal volume of solutions and to keep drug concentrations constant within all groups.

Saline controls were always included in each set of 12 Ss so that throughout the entire experiment three to six controls were run concurrently with drug Ss.

Following each stress-rest session, Ss were sacrificed, their stomachs excised and opened along the greater curvature. Gastric mucosa were then examined by experienced raters and judged as to the presence or absence of ulcers and, when present, the number of ulcers was also recorded. Ulcers were defined as visible lesions associated with hemorrhage. Previous work utilizing three judges, two of whom were unaware of experimental conditions, had yielded interrater reliability coefficients of virtually 1.00 when judging presence or absence of lesions and almost equally high coefficients relative to ulcer counts ($r = .91$ and $r = .90$). Given this high level of reliability, only one of the judges was utilized in the present research.

RESULTS AND DISCUSSION

Ss in the drug treatment groups maintained an upright posture similar to that of saline controls. Also, these Ss reacted to shocks with jumping and squealing responses indiscriminable from the placebo-injected animals.

Table 1 shows the number and percentage of animals that ulcerated in each group.

It is clear from these data that chlorpromazine reduced the frequency of ulcer formation relative to the saline controls. Three statistical comparisons were performed. The significance of a difference between proportions was examined comparing each drug group with the control group, and corrections for continuity were made where appropriate (Guilford, 1956, p 221). All of these comparisons were significant (1/50th, $p < .02$; 1/20th, $p < .001$; 1/10th, $p < .001$).

While all three drug concentrations significantly reduced the rate of ulceration relative to controls, it is clear from the data that the 1/50th concentration is a far less effective dosage within the confines of the present procedure than either of the other two dosage levels. As is shown in Table 1, animals in the 1/50th condition ulcerated at a rate greater than 50%. Also, the data indicated that no simple linear relationship exists between the drug concentrations presently studied and reductions in gastric pathology.

Because drug concentrations were not adjusted for body weight, it is important to determine if body weight differences were systematically related to the presence or absence of lesions or to the number of lesions present. This is particularly important in the 1/50th group, where drug concentration was the weakest and where differences in body weight, at least in part, may have accounted for results. There were no systematic differences in body weight among the four groups. However, there was some within-groups variability relative to this dimension. Visual examination of the data revealed no systematic relationships between presence of ulcers and differences in Ss' weight within any of the groups. There was also no relationship between number of lesions observed and body weight.

The number of lesions present in the 35 ulcerated control Ss was highly variable, ranging from 1 to 15. The variability relative to number of ulcers observed in the 1/50th group was also substantial, ranging from 1 to 10. This, in conjunction with the fact that so few Ss in the 1/10th and 1/20th groups ulcerated, made parametric analysis of the data impossible. However, the general appearance of gastric tissue relative to an easily observable redness and inflammation is worth noting. The stomachs of all ulcerated drug-treated animals were indistinguishable from those of the ulcerated controls. That is, in addition to the presence of lesions, the stomach tissue was a characteristic bright red and clearly very irritated. This was also true of the six stomachs obtained from the nonulcerated controls. On the other hand, stomachs of nonulcerated drug-treated animals were characteristically normal in color and remarkably free of any signs of pathology. While evidence of this kind must be considered as only suggestive, it does at least raise the possibility that the development of lesions and general gastric pathology produced in the current procedure resembles something like an all-or-none process. That is, if the drug does somehow inhibit the pathologic changes related to ulceration, it does so in a complete sense. However, a failure of the drug to provide immunity from the development of gastric lesions appears to provide no more protection than is evident in saline-treated animals. Further systematic study of this proposition is needed.

While the present research has provided some additional data relevant to the effects of chlorpromazine on gastric ulceration, much remains to be done, even within the framework of the currently utilized research design. In this regard, a number of specific questions remain unanswered. For example, it is important to determine what, if any, interactive effects exist between drug concentration and the intensity of stress as determined by parameters such as duration of stress, intensity of shock, pattern of shock schedules, and differential stress-rest schedules. From the more physiological viewpoint, it is also necessary to determine the specific biochemical relationships that exist between drug action and the complex physiological and psychological components related to the mechanisms underlying ulceration. Future research should also focus upon questions relative to time-dose courses and specific titration levels of the drug as they affect the process. Perhaps this could be approached through more adequate control over titration via the use of techniques like microinjection. Finally, the question of the relationship of stress-rest cycles and drug intervention must be examined. For example, Polish, Brady, Mason, Thach, & Niemeck (1962) have suggested that lesion-producing biochemical activity occurs primarily during periods of rest rather than during periods of stress. Research aimed at determining how chlorpromazine acts upon this aspect of the ulcer-producing stress-rest procedure may clarify even more the process of ulcer formation as well as the particular role played by the drug in the elimination of stress-induced gastric pathology. Research along some of these lines is presently being formulated.

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