first few hours following ligation, and ulceration can often be detected within 4 to 5 hours.

In another experiment, 6 Shay rats were each given 0.2 g LS (Ca salt) in 1 ml water *per os* after ligation, and 6 controls were given 1 ml of water *per os*. The following day, although control stomachs were heavily ulcerated (an average of 12 ulcers per stomach was noted, many of them bloody), the stomachs of 4 of the treated animals were completely free of ulceration, one had 2, and one had 5 small ulcers (none bloody). The mechanism of this protection would appear to be different from that after injection of LS into the peritoneal cavity. The average volume of secretion in the stomachs of the treated animals was about the same as in the controls and the pH was more strongly acidic (compare Funk(4), but in this latter work it should be noted that while ox-bile protected against ulceration, it was also anti-secretory when given *per os* to the Shay rats).

Summary. Solutions of calcium lignin sulfonates injected immediately after ligation in the Shay rat (20 mg/100 g rat weight) afforded pronounced protection against ulceration as compared with controls. The same material given *per os* also protected Shay rats against ulceration, probably by a different mechanism.

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1. Brauns, F. E., *The Chemistry of Lignin,* Academic Press, New York, 1952.

2. Shay, H., Komarov, S. A., Fels, S. S., Meranze, D., Gruenstein, M., and Siplet, H., *Gastroenterology,* 1945, v5, 43; Shay, H., Sun, D. C. H., and Gruenstein, M., *ibid.,* 1954, v26, 906.

3. Loomis, T. A., and Beyer, R. E., *J. Pharmacol. Exp. Therap.,* 1953, v109, 21.

4. Funk, C., *Science,* 1952, v116, 638.

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Influence of Ascorbic Acid and Chlorpromazine on Body Temperature and Resistance of Mice to Drowning. (23290)

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Increased resistance to anoxia at low barometric pressure resulting from ascorbic acid has been recognized since the report of Gander(1) with Swiss ski troops. Comparable results have been reported with rabbits(2,3), and rats, mice and men(4,5). Because it is known that body temperature influences anoxic resistance to drowning a comparison of body temperature change following injections of ascorbic acid was made. Also injections of chlorpromazine, a hypothermic drug, were used.

Methods and materials. Adult mice of the RAP strain (75 males and 88 females) were divided into groups of 14 or 15. Controls were injected with distilled water of the same volume as that used with the experimentals. Ascorbic acid buffered to pH 7.3 with $NaHCO_3$ (10 mg in 0.5 ml of water) was injected intraperitoneally and after a lapse of 0, 30, 45, 60, 120 minutes the mice were drowned in water at 37.5°C. Drowning was accomplished by seizing the tip of the tail with a long hemostatic forceps and plunging the mouse under water. The last visible mandibular movement was taken as the criterion of death timed by an electric metronome and observed by at least 2 of the investigators simultaneously. Rectal temperatures were recorded by a L & N potentiometer using copper-constantan electrodes inserted to a marked depth each time. Chlorpromazine (Thorazine S.K.F.*), 25 mg/kg was injected i.p. for the second part of the experiment.

* Chlorpromazine (Thorazine) was kindly supplied by Dr. Edwin J. Fellows, Director of Biological Sciences, Smith, Kline & French Laboratories, Philadelphia, Pa.

TABLE I. Survival of Mice in Seconds of Drowning in Water of 37.5° after Receiving Ascorbic Acid (AA) or Chlorpromazine (CPZ) Intraperitoneally.

No. and sex	Body temp. Before inj.	Body temp. Before drowning	Survival (sec.) to drowning after lapse of 0 min.	30 min.	45 min.	60 min.	120 min.
15 controls (♀)	37.8 ± .3*	39.0 ± .2	46.6 ± 1.3				
15 AA (♀)	37.1 ± .2	33.6 ± .5		65.3 ± 2.9			
14 "	38.1 ± .2	34.4 ± .5			59.4 ± 2.7		
14 "	36.6 ± .2	35.4 ± .8					57.0 ± 2.4
15 controls (♂)			49.2 ± 1.4				
15 AA (♂)				58.3 ± 1.6			
15 "	—————†	——————			56.1 ± .9		
15 "						56.3 ± 1.2	
15 "							53.6 ± 1.9
15 CPZ (♀)	37.5 ± .1	32.2 ± .3		71.2 ± 2.9			
15 "	37.6 ± .2	27.8 ± .4					103.0 ± 3.2

* S.E. $= \sqrt{\frac{\text{S.D.}^2}{n(n-1)}}$.

† No body temperatures were measured with male mice, as this part of the exp. was done previously and is added here for completeness.

Results. Ascorbic acid lowered body temperature by about 4 degrees in 30 minutes which was maintained throughout the experiment (Table I). There was a gradual increase in temperature with the passage of time until normal temperature had been reached again. At 30 minutes after injection the female mice withstood drowning 40% longer than did the controls, while males survived 18% longer. Both males and females tended to approach survival time of the controls as the elapsed time grew longer. The changes following injection of chlorpromazine were more pronounced than with ascorbic acid. Two hours after injection the body temperature of the mice was only slightly higher than room temperature. The longest survival time occurred 120 minutes after chlorpromazine was injected, 103 seconds as compared to 37.8 seconds for the controls, an increase of 121%.

Discussion. Both ascorbic acid and chlorpromazine produce hypothermia which by itself prolongs anaerobic survival, as shown by morphine, ethyl alcohol and other chemical agents(6,7). Another possibility in prolonging anaerobic survival might be the increase of blood sugar which follows introduction of chlorpromazine(8). It further reduces metabolic rate concurrently with hypothermia which undoubtedly would prolong survival to anoxia(9). There still is the possibility that some other reaction than reduced temperature and metabolism may be involved.

Summary. Buffered ascorbic acid and chlorpromazine were injected intraperitoneally into mice and the effect on body temperature and anoxic resistance to drowning measured. Significant increases in survival time were noted with ascorbic acid and especially with chlorpromazine. Lowered body temperatures were noted with both compounds. When anoxic survival to drowning was measured, prolongation of life was increased to a maximum of 40% with ascorbic acid and 121% with chlorpromazine.

1. Gander, J., *Studien den Vitamin C-Stoffwechsel im Militär,* 1937, Als Manuskript.

2. Pfannenstiel, W., *Luftfartmed. Abhandl.,* 1938, v2, 234.

3. Dorhalt, G., *ibid.,* 1938, v2, 240.

4. Lucas, B. G., personal communication.

5. Peterson, J. M., *Nature,* 1941, v148, 84.

6. Madden, R. F., Stemler, F. W., and Hiestand, W. A., *Am. J. Physiol.,* 1955, v180, 121.

7. Dawson, J. F., and Hiestand, W. A., *Fed. Proc.,* 1955, v14, 36.

8. Norman, D., and Hiestand, W. A., *Anat. Rec.,* 1955, v122, 461.

9. Dundee, J. W., Scott, W. E., and Mesham, P. R., *Brit. Med. J.,* 1953, vII, 1244.

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