

observations reported by various clinicians^{3, 4, 5} and throw some light on the mechanism of analgesia produced by cobra venom as compared with that of morphine. The latest work⁶ on the physiology of pain seems to point to the hypothalamus as that part of the brain most intimately concerned with sensations of pain. Cobra venom produces analgesia through its direct effect on the hypothalamus or some lower synapse while the action of morphine is not restricted to that region but spreads over the cortical areas, thus depressing the animals' general behavior.

Summary. A comparative study of behavior of rats in the maze and the analgesia produced in them by morphine reveals that the two effects run parallel, *i. e.*, the greater the general depression, the greater the analgesia. In case of cobra venom, however, analgesia or heightening of the pain threshold is produced without any marked effect on general behavior of the animals.

10929

Sugar Alcohols. XIX. Relationship between Chemical Constitution and Speed of Hemolysis.

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In recent studies¹ concerned with the diuretic action of isomannide (1, 4, 3, 6 dianhydromannitol) it was observed that this compound hemolyzed red cells through osmotic pressure phenomena. This observation prompted the study of the hemolytic activity of a number of sugar alcohols and their anhydrides on the red cells of the dog. The hemolytic activity of certain of these compounds, namely, glycerin, ethylene glycol, erythrol and mannitol has been reported previously by Jacobs.²

The apparatus described by Jacobs³ was employed. The sugar

³ Macht, D. I., *Ann. Int. Med.*, 1938, **11**, 1824.

⁴ Macht, D. I., *M. Press*, 1939, **201**, 254.

⁵ Rutherford, R. N., *New England J. Med.*, 1939, **221**, 403.

⁶ Propper-Graghtchenkoff, N. I., *Acta Medica U.S.S.R.*, 1938, **1**, 110.

¹ Krantz, J. C., Jr., and Carr, C. J., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **39**, 577.

² Jacobs, M. H., *J. Cell. and Comp. Physiol.*, 1933-34, **4**, 161.

³ Jacobs, M. H., and Parpart, A. K., *Biol. Bull.*, 1931, **60**, 95.

alcohols and their anhydrides met the usual criteria of identity and purity as previously established by the authors. Solutions isosmotic with blood in recently boiled distilled water were prepared. The pH was determined by the glass electrode and the osmotic pressure was measured cryoscopically. Volumes of 20 cc of the solution were employed and 0.1 cc of freshly drawn defibrinated dog's blood supplied the red cells. The apparatus was standardized using water and saline solutions of various degrees of hypotonicity to establish the time hemolysis relationship. The time periods required for 90% hemolysis at 37°C are shown in Table I.

Using red cells from various species the rates of hemolysis caused by mannitol and isomannide have been compared. These data are shown in Table II.

TABLE I.
Rates of Hemolysis by Sugar Alcohols and Anhydrides.

Compound	pH	Freezing point—(°C)	Avg time for Hemolysis (90%) 3 exp.
Methyl Alcohol	7.20	.53	9 sec
Ethylene Glycol	7.18	.51	4 "
" Oxide	7.18	.55	5 "
Glycerin	7.05	.54	4 "
Epihydrin Alcohol	7.11	.54	10 "
Erythrol	7.00	.56	120 min
Erythritan	6.90	.58	12 sec
Isosorbide	7.18	.60	23 "
Penta Erythritol	7.20	.57	75 min
Arabitol	6.90	.56	75 "
Mannitol	7.09	.57	>240 "
Mannitan	7.18	.54	210 "
Isomannide	7.02	.59	8 sec
Styracitol	6.90	.59	120 min
Sorbitol	7.12	.57	150 "
Sorbitan	7.11	.58	135 "
Polygalitol	6.92	.60	120 "
Dulcitol	7.13	.54	>240 "
Inositol	6.90	.60	60 "
Pinitol	7.00	.55	70 "

TABLE II.
Rate of Hemolysis of Red Cells of Different Species by Isotonic, Neutral Solutions of Isomannide and Mannitol.

Species	Isomannide, Seconds	Mannitol, hours
Cat	6	>4
Rat	7	>4
Guinea Pig	7	>4
Human	9	>4
Dog	8	>4
Monkey	16	>4
Rabbit	11	>4
Ox	14	>4

All of the hemolytic phenomena in Table I have been shown to be osmotic in character and not erythrolytic, as in each case the hemolysis is prevented by isotonic salt solution. To avoid the influence of saline constituents upon the speed of hemolysis unbuffered solutions were employed, hence the variations in pH of the solutions of the compounds studied. Jacobs⁸ has stated that under certain conditions variations of 0.01 pH unit may produce a measurable effect upon the degree of hemolysis of red blood cells. In these experiments where effort was made to have the solute in isosmotic concentration, pH changes of much greater magnitude did not produce measurable changes in the speed of hemolysis. However, we may emphasize the necessity of considering the reported speeds of hemolysis as relative, dependent upon a great number of factors including individual variations among animals of the same species.

Summary. An inspection of the data shows that the sugar alcohols and their anhydrides up to 3 carbon atoms in the molecule rapidly hemolyze red cells. With erythritol containing 4 carbon atoms the hemolysis is slow, but that produced by its anhydride, erythritan, is rapid. The sugar alcohols containing 5 and 6 carbon atoms in the molecule and their monoanhydrides slowly hemolyze red cells. The double anhydrides, isomannide and isosorbide, cause rapid hemolysis. Mannitol hemolyzes the red cells of several species slowly; isomannide induces rapid hemolysis of the red cells of the same species.

10930

The Electroencephalogram of Schizophrenic Patients During Administration of Vitamin B₁.

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Recent studies¹ suggest that a deficient oxygen metabolism is present in schizophrenia. Increasing the rate of oxygen consumption in schizophrenics by means of thyroid² and dinitrophenol³ has resulted in some clinical improvement. Since vitamin B₁ is known to influence oxygen consumption of the brain,⁴ is seemed desirable to

¹ Hoskins, R. G., *Arch. Neurol. and Psychiat.*, 1937, **38**, 1261; Rheingold, J. C., *Psychsom. Med.*, 1939, **1**, 397.

² Hoskins, R. G., and Sleeper, F. H., *Am. J. Psychiat.*, 1930, **87**, 411.

³ Looney, J. M., and Hoskins, R. G., *Am. J. Psychiat.*, 1935, **91**, 1009.

⁴ O'Brien, J. R., and Peters, R. A., *J. Physiol.*, 1935, **85**, 454.