experiments with dogs and with human subjects showed that its degree of penetration was low. Metrazol and hydrocyanic acid can be shown to produce their typical effects in dogs by sublingual administration, but the degree of penetrability is not striking and no effects were obtained in human subjects with relatively large doses. . . . The fat-water distribution coefficient of drugs is a dominant factor in determining their penetrability through the oral mucosa. . . . The majority of drugs . . . do not penetrate the oral mucosa in significant amounts, and it is unsound practice to rely on this technic with any drug whose effectiveness by this route has not been conclusively demonstrated." 50 references.

J. C. M. C.

GUNDERSEN, TRYGVE, AND LIEBMAN, S. D.: *Effect of Local Anesthetics on Regeneration of Corneal Epithelium.* Arch. Ophth. 31: 29–33 (Jan.) 1944.

"Clinically it has been observed from time to time that local anesthetics have an inhibitory influence on the regeneration of corneal epithelium. . . . Heretofore no attempt has been made to determine experimentally whether or not local anesthetics affect the regrowth of corneal epithelium. . . . Guinea pigs (4 for the study of each drug) were used as test animals. . . . The drugs used in these experiments were fresh preparations similar to those in daily use in the clinic of the Massachusetts Eye and Ear Infirmary. These drugs were solutions of 10 per cent cocaine hydrochloride, 4 per cent cocaine hydrochloride, 1 per cent butacaine sulfate, 4 per cent larocaine hydrochloride, 1 per cent phenacaine hydrochloride and 0.5 per cent tetracaine hydrochloride, all containing 0.5 per cent chlorobutanol. One per cent phenacaine hydrochloride and 0.5 per cent tetracaine hydrochloride in ointment form were instilled into the right eyes of the two other groups of guinea pigs. The left, or control, eyes of these animals were treated with ointment base containing no local anesthetic. The experiments for the 10 per cent cocaine hydrochloride and the 1 per cent phenacaine hydrochloride were carried out in duplicate series, and the eyes of the second series of animals were removed at varying intervals for histologic examination. Further studies were carried out to evaluate the influence of tonicity of the cocaine and the tetracaine solutions on the regeneration of corneal epithelium. . . . All of the local anesthetics tested had some delaying effect on the healing process of the corneal epithelium of the guinea pig. This effect is modified in degree by the concentration and the tonicity of the anesthetic agent. The pH is probably not a determining factor, since buffered solutions at a pH comparable to that of the anesthetics used showed relatively little inhibitory action. Of the various anesthetics tested, 1 per cent phenacaine hydrochloride and a hypertonic 0.5 per cent solution of tetracaine hydrochloride were the least toxic to the regenerating epithelium." 3 references.

J. C. M. C.

CHAPMAN, W. P.; ARROWOOD, JULIA G., AND BEECHER, H. K.: *The Analgetic Effects of Low Concentrations of Nitrous Oxide Compared in Man with Morphine Sulphate.* J. Clin. Investigation 22: 871–875 (Nov.) 1943.

"The purpose of this study is to report, on the basis of quantitative studies, that nitrous oxide in low concentration (consciousness not impaired, beyond a slight euphoria) has power to relieve pain comparable to that of morphine and yet does not have the undesirable side effects which limit the use of morphine. . . . Fifteen healthy

male subjects, varying in age from 18 to 34 years, were used in the heat radiation studies. All of these had been used in the morphine study of Chapman and Jones. The same subjects were used here in order to minimize the effects of individual variations, and 10 of these same subjects were used in the muscle ischemia observations. . . . Nitrous oxide in 20 per cent concentration in oxygen is as effective an analgetic agent as morphine in gr. ¼, or 15 mgm., dose, judged from the 2 types of pain considered here. Nitrous oxide at this concentration does not impair consciousness and is effective as long as it is not allowed to escape from the 'closed' respiratory system, whereas the morphine effect passes through a maximum and, since it is metabolized, the effect disappears. Unlike morphine, nitrous oxide in this concentration is not usually associated with undesirable side effects." 7 references.

J. C. M. C.

GREEN, H. D.; NICKERSON, N. D.; LEWIS, R. N., AND BROFMAN, B. L.: *Consecutive Changes in Cutaneous Blood Flow, Temperature, Metabolism and Hematocrit Readings during Prolonged Anesthesia with Morphine and Barbital.* Am. J. Physiol. 140: 177–189 (Nov. 1) 1943.

"In the course of studies under prolonged anesthesia of the peripheral circulatory reactions during hemorrhage and shock, decreased cutaneous blood flow, rise in rectal temperature and oxygen consumption and fluctuations of hematocrit readings were observed during the first six hours after induction of the anesthesia which complicated the interpretation of the changes in peripheral circulation and metabolism occurring in the development of the shock state. These observations necessitated a study of the serial changes following the anesthesia alone. . . . The effects of the various anesthetics were studied in 47 dogs. . . . The pre-anesthetic rectal temperature in our dogs ranged from 37.5 to 39.7 with an average of 38.5° C. Anesthesia with morphine alone caused an immediate and frequently maximal increase in cutaneous blood flow and a decline in rectal temperature to 34° to 37° C. These changes were often followed in 1 to 3 hrs. by a sharp reduction in cutaneous blood flow. The latter apparently was secondary to the temperature regulating reactions induced by the drop in rectal temperature. Sodium barbital, sodium pentobarbital, and chloralosane caused a similar initial increase in cutaneous blood flow and a drop of 0.5° to 1.5° in rectal temperature and a subsequent decrease of cutaneous blood flow; and in addition, induced an increase of oxygen consumption, often associated with shivering, and a rise of rectal temperature to 38.6° to 40.5° within 3 to 11 hrs. Anesthesia with morphine plus barbital accentuated the initial drop of rectal temperature.

"Hematocrit readings showed little change with morphine alone, but with either morphine and a barbiturate or one of the barbiturates alone the hematocrit reading dropped 5 to 10 cell volumes per cent within a few minutes after anesthesia and then slowly returned to and often above normal during the period of reduction of cutaneous blood flow and rise of rectal temperature. Changes in rectal temperature and cutaneous blood flow were minimized by maintaining the rectal temperature between 38° and 39° and were often abolished by elevating the rectal temperature to 39°–40° by warming the animal board. The heating had, however, no significant influence upon the initial decline and subsequent rise of the hematocrit reading in the dogs anesthetized with barbital. Both heart rate and mean arterial blood pressure were higher