single oral dose. Continuous oral treatment using 100 mg(9) or 50 to 100 mg(10) every 4 or 6 hours usually relieves symptoms of ulcer.

Summary. (1) A new chemical compound has been found which has high oral and parenteral parasympathetic blocking activity. This compound, N,N dimethyl 4-piperidylidene 1,1 diphenylmethane methyl sulfate (Prantal), is unique in its specificity of action within the parasympathetic system, *i.e.*, it primarily inhibits gastric motility and gastric secretion. The intravenous sympathetic ganglion blocking dose is 50 to 100 times that required for intravenous parasympathetic blockade. (2) In dogs, roentgenologic observations of the movement of barium sulfate from the stomach indicate that orally administered Prantal delays gastric emptying time more effectively, and is longer acting than methantheline bromide. Additional dog experiments showed the ability of Prantal to reduce the volume and titratable total acid of gastric secretions. (3) After oral medication in dogs, Prantal produced no mydriasis at doses which inhibit gastric motility for several hours, whereas methantheline bromide caused mydriasis which persisted for one to 3 hours. In rabbit tests by topical application to the eye, mydriasis occurred with a 0.1% concentration of methantheline bromide, whereas 1.0% of Prantal was not mydriatic; mydriasis occurred at the 2.0% concentration of Prantal. By intravenous injection in rabbits methantheline bromide caused mydriasis at 1.0 and 2.0 mg/kg doses; no mydriasis occurred at 2.0, 4.0 or 8.0 mg/kg doses of Prantal.

10. Other private communications to the Clinical Research Division, Schering Corp.

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Regulation of Breathing in Man at Altitude.* (19146)

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Peracute hypoxia occurs in an aviator at high altitude if he loses his oxygen supply or if he suffers sudden decompression. The time that he will retain consciousness depends upon several factors, some of which have been reported(1). It has been shown that the addition of carbon dioxide to the inspired air increases the consciousness time of man at altitude(2). This investigation has been extended for the purpose of studying the relative influence of hypoxic and carbon dioxide stimuli upon pulmonary ventilation in the peracute hypoxic state. A simulated altitude of 25,000 feet was selected for the reason that in previous tests it was found that this altitude was somewhat marginal in its effect upon consciousness, the loss of which occurs only after several minutes. This allows sufficient time to record pulmonary ventilation for a few minutes and permits any respiratory change to reach an approximate steady state. Thus the pattern of the rapid hypoxia response can be more clearly observed.

Procedure. Ten experimental subjects were used in this investigation. They were medical students, physically fit and in good health. All had previous experience in the low pressure chamber during exposures to simulated high altitude. From 4 to 6 separate tests were made on each subject. Pulmonary ventilation was determined from photokymographic records as previously described(1). Thus a continuous record of pulmonary ventilation was obtained. Standard Air Force A-13 oxygen masks were used. These were fitted to prevent leakage and a leakage test was

* Work done under contract with the Aero Medical Laboratory, Air Research and Development Command, U.S.A.F.

1. Hall, F. G., *J. Applied Physiol.*, 1949, v1, 490.

2. Hall, F. G., PROC. SOC. EXP. BIOL. AND MED., 1949, v70, 487.

made during each experiment. No leakage greater than 1% was observed. Each subject was instructed and trained in manipulation of the useful consciousness tester as previously described(1). A continuous record of each subject's response was obtained for the full duration of each test.

Each subject was brought to a simulated altitude of 25,000 feet (282 mm Hg.) while breathing 100% oxygen. After allowing 2 minutes for adjustment to this altitude the subject was switched from oxygen to one of 3 gas mixtures. He was kept on the gas mixture for 5 minutes and then returned to 100% oxygen. Three gas mixtures were used: A, 20.9% O_2, 0.04% CO_2, 79% N_2; B, 88% O_2, 11.6% CO_2, 0.4% N_2; C, 20.9% O_2, 11.6% CO_2, 67.5% N_2. Gas analyses were made on each gas mixture during each individual test by the standard Haldane procedure. Tests were made to ascertain if the sequence of using the various gas mixtures was important. The mixture of 88% O_2 and 11.6% CO_2 was used in the first and last test. Results showed that the sequence was not important.

Results. The results of 40 simulated flights with 10 subjects are summarized in Fig. 1. In each test the pulmonary ventilation was

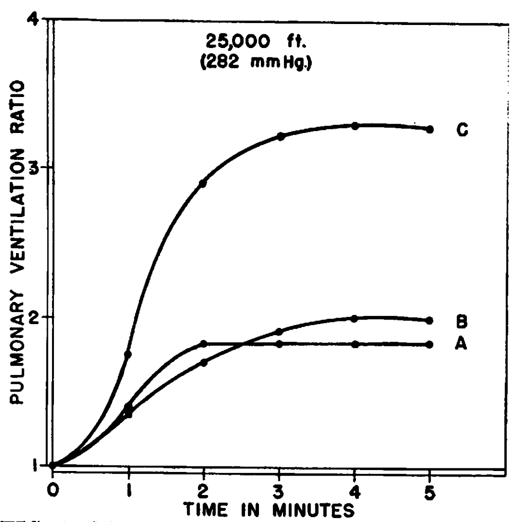

FIG. 1. Mean pulmonary ventilation ratios of 10 subjects breathing various gas mixtures at a simulated altitude of 25000 feet (282 mm Hg). The composition of inspired air in curve A, O_2 20.9%, CO_2 .04%, N_2 79%; curve B, O_2 88%, CO_2 11.6%, N_2 .4%; curve C, O_2 20.9%, CO_2 11.6%, N_2 67.5%.

measured for the period during which the subject was breathing 100% oxygen and then for the subsequent period in which he was breathing a particular gas mixture. The determinations were made for one minute intervals and the pulmonary ventilation ratios were calculated by defining the ventilation during breathing of 100% oxygen as unity. Because of variations in pulmonary ventilation among individuals it was considered more desirable to use ventilation ratios and have each subject his own control. The results shown are the mean values obtained for ten subjects.

It will be observed from inspection of Fig. 1, that at a simulated altitude of 25,000 feet the hypoxic "drive" of a subject breathing ambient air causes an increase in pulmonary ventilation approximately equal to that when he is breathing a relative high concentration of oxygen along with 11.6% CO_2. When, however, the oxygen concentration equal to that of the ambient air is breathed with 11.6% CO_2 a much higher pulmonary ventilation occurs.

Responses to hypoxic and carbon dioxide stimuli were fairly rapid as can be seen in curve A and B respectively. In both cases a steady level of pulmonary ventilation was maintained after 2 minutes.

It can be questioned whether or not the difference in the nature curve A and B is significant. Perhaps a plausible explanation is that due to the low oxygen reserve of the transport system the hypoxic stimulus operates quickly while the CO_2 stimulus acts more slowly because of the buffering effect of the alkaline reserve.

It should also be mentioned that in 4 of the 10 subjects breathing ambient air consciousness was lost a few seconds before the end of the 5 minute period. This did not occur when carbon dioxide was added to the inspired air. This is further confirmation of previous findings(2) at higher altitudes.

Discussion. Otis *et al.*(3) have pointed out that hypoxia and hypocapnia are additive in their effects upon performance. Gray(4) has theorized that pulmonary ventilation is determined by the algebraic sum of separate

3. Otis, *et al. Am. J. Physiol.*, 1946, v146, 207.

4. Gray, J. S., *Science*, 1946, v103, 739.

factors. The report by Dill and Zamcheck (5) give quantitative experimental evidence of the effects of adding carbon dioxide to inspired air deficient in oxygen at sea level. These authors concluded that the addition of carbon dioxide to inspired renders a low partial pressure more tolerable by increasing arterial saturation. The results presented herewith are in agreement with these authors. They also show the rapidity of the response to hypoxia and hypercapnia, and something about the interaction of these two factors. These results would seem to indicate that the potency of the hypoxic stimulus is not fully manifested when man breathes ambient air at altitude. In Fig. 1, curve A shows the ventilatory response to breathing ambient air which involves both hypoxic and hypocapnic stimuli. Curve B, shows the ventilatory response to hypercapnia at the same altitude but with adequate oxygen for full saturation of blood. Curve C, shows the additive effect of hypoxia and hypercapnia. It would seem that the difference in the ventilatory response shown in curves B and C must be due to the hypoxic stimulus since the concentration of carbon dioxide in inspired air is the same. Of course the p CO_2 of alveolar air will be slightly lower in C due to the increase in ventilation and the p O_2 will be slightly higher. Thus these two interacting factors appear additive in their effects.

5. Dill, D. B., and Zamcheck, N., *Am. J. Physiol.*, 1940, v129, 47.

Summary. When man breathes ambient air at high altitudes an hypoxic stimulus causes a rapid increase in pulmonary ventilation. The full effect of this hypoxic stimulus is counteracted, however, by concomitant hypocapnia. With the addition of carbon dioxide to inspired air a more effective response to the hypoxic stimulus is manifested. It is concluded that hypoxia and hypercapnia are separate stimulating factors and additive in their effects and that regulation of respiration at altitude depends upon the manner of their interaction.

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Effect of Electroconvulsive Shock on Body Temperature of the Rat. (19147)

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Rosvold(1,2) suggested that elevation in body temperature may have contributed to the disruptive effect of electroconvulsive shock on nest building behavior in rats. The present study was designed to demonstrate the effect of electrically induced convulsions on the temperature of the rat.

Subjects and method. Twenty male hooded rats 150-180 days of age were divided evenly into a control and an experimental group. They were placed 2 to a cage size 8" x 9" x 11" in which fox chow and water were available at all times, and were housed in a room in which the temperature was maintained between 70-80°F. A convulsion was induced in the experimental animals at 9 a.m. daily during the shock periods by administering a 50 milliampere current for 0.2 second through clip electrodes attached to the ears. The electrodes were fastened to the ears of the control animals, but no current was delivered. By inserting a thermometer eight and one-half centimeters into the rectum of the restrained rat for 2 minutes, temperatures were taken on 2 different animals from each group at 9 a.m., 12 n., 3 p.m., 6 p.m., and 9 p.m. The temperature of any particular animal was taken at a different time on successive days, no animal being examined at the same time in a 5-day period. The following schedule was followed:

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1. Rosvold, H. E., *J. comp. and physiol. Psychol.*, 1949, v42, 118.

2. Rosvold, H. E., *J. comp. and physiol. Psychol.*, 1949, v42, 207.