

High Resistance of Rhesus Monkeys to 90 Plus Per Cent Oxygen.

MARTIN FRIEDRICH AND DAVID M. GRAYZEL. (Introduced by A. E. Sobel.)

From the Departments of Medicine and of Pathology, Jewish Hospital of Brooklyn.

The use of very high oxygen concentrations for clinical purposes has for many years been restricted by the inability of the lower mammals to live safely in continuous oxygen concentrations exceeding 70%. Barach¹ has shown that rabbits can live in 60% concentrations even as long as 3 months. He² considers 70% the safe top level for them. Oxygen mixtures between 80 and 100% produce irritant inflammatory lesions in the lungs of rabbits, dogs, cats, mice, rats, birds and other small laboratory animals, when used continuously for 2 to 5 days.^{3a, 3b} The animals employed in these experiments had high metabolic rates and rapid respiratory rates. Rabbits have a respiratory rate of about 100 to 150 per minute. It is interesting to note that turtles and frogs,^{3b} with extremely slow respiratory rates, are able to live safely in oxygen concentrations of 90+% for months, when the temperature is maintained at 70° F. However, when the temperature of the oxygen is raised to 99.5° F, they develop pulmonary edema. The Rhesus monkey⁴ with a normal rate of 24 to 40 gives us an animal with a respiratory mechanism anatomically and physiologically more closely resembling the human. With one exception, in which one monkey was employed, no workers have used Rhesus monkeys in their experiments. In our work 14 rabbits were used as controls, 2 at a time being exposed to the same atmospheres as the monkeys.

Experiments. Four Rhesus Monkeys and 2 rabbits were placed in a Barach-Thurston

oxygen tent containing soda-lime, with a specially sealed canopy, and the concentration was raised to 90-95% and maintained at this level continuously for 20 days. Every 4 days 2 rabbits died and were replaced by 2 new controls. On the fourth day the monkeys developed slight anorexia. On the fifth day one of them coughed and developed dyspnea. On the sixth day all 4 monkeys appeared bright again and regained their appetites. On the eleventh day 3 monkeys were active and eating well. On the sixteenth day the first monkey died. On the eighteenth day another died. After 20 days the concentration was gradually reduced and 2 monkeys, apparently healthy, were removed. Roentgenograms of the chest were checked. One was entirely negative and the other showed 2 small areas of infiltration.

Eight Rhesus Monkeys (6 new ones and 2 survivors of the previous experiment) and 4 rabbit controls (two at a time every 4 days as in the previous experiment) were placed in 90-95% oxygen atmosphere. One monkey coughed on the third day, all appeared well and active on the fourth day. On the fifth day they developed anorexia, were apathetic, and a few of them had labored breathing. On the sixth day one died; on the seventh another died and 4 were active and normal. Two more died on the eighth day and 2 on the tenth day. Two were removed in good health and remained well. These 2 monkeys were survivors from the first experiment. During this experiment the tent temperature frequently dropped to 60°. In both experiments oxygen and carbon dioxide analyses were performed 5-15 times daily. Humidity per cent and tent temperature were simultaneously observed.

Autopsy Findings. The significant findings at autopsy were confined to the lungs. The other organs were normal and showed only passive congestion.

¹ Barach, A. L., *Am. Rev. Tuberc.*, 1926, **13**, 293.

² Barach, A. L., *N. Y. State Med. J.*, 1937, **37**, 1095.

^{3a} Karsner, H. T., *J. Exp. Med.*, 1916, **23**, 19;
^{3b} Binger, C. A. L., Faulkner, J. M., and Moore, R. L. J., *J. Exp. Med.*, 1927, **45**, 849.

⁴ Hartman, C. G., and Strauss, Wm. L., *The Anatomy of the Rhesus Monkey*, Williams & Wilkins, Baltimore, 1933.

In the rabbits the process in the lungs was diffuse and involved all the lobes. The surfaces were purple red except at the margins where the tissue was pink and crepitant. The lobular markings were distinct. The bronchi and bronchioles contained a pink frothy fluid and the cut surfaces were wet. Scattered throughout were numerous granular raised areas. Microscopically the lung preparations showed extensive congestion and edema with numerous foci of pneumonia.

In the monkeys the process was patchy and far less extensive. The greater portion of the lungs were pink and air-containing. The cut surfaces, however, were moist and the bronchioles contained some pink frothy fluid. Some granular areas were also noted, particularly in the lower lobes. Microscopically the lungs showed congestion with some edema and a few small foci of pneumonia. There were also some small areas of emphysema.

Summary and Conclusions. Ten normal Rhesus Monkeys continuously exposed to 90+ % oxygen appeared to maintain good

health for a 5-day period. Then the reaction was variable. Anorexia first appeared, then apathy, drowsiness, cough and dyspnea. Survival periods ranged from 6 to 18 days in 8 monkeys. Two were alive at the end of 20 days and remained in good health. Pairs of rabbits used as controls died after 4 days and were replaced by new controls who again died after 4 days. Autopsies were performed and showed a slight amount of congestion and exudate in the lungs resembling a mild pneumonia in the monkeys, while the rabbits showed extensive pneumonia. The marked difference in reaction of the two sets of monkeys suggests that there may be a difference of resistance to 90+ % oxygen in different strains, or that lowering the tent temperature to 60° may have played a role in diminishing their resistance. The reaction of the Rhesus Monkeys suggests the possibility that it may be safe for human beings to be exposed continuously, if necessary, to a 90-95% oxygen concentration for periods up to 5 days.

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Studies on the Action of Penicillin. III. Bactericidal Action of Penicillin on *Meningococcus in vitro*.

C. PHILLIP MILLER AND ALICE ZIMMERMAN FOSTER.

From the Department of Medicine and the A. B. Kuppenheimer Research Foundation, The University of Chicago.

The meningococcus is highly susceptible to penicillin although it is gram-negative. In this respect as in its reaction to certain germicides, it resembles the gram-positive bacteria.¹ A preceding communication² reports a study of the action of penicillin on meningococcus *in vivo*.

Methods. Suspensions of meningococci grown for 6 hours on agar slants were made up in gelatin-Locke's solution or broth to contain approximately 10^8 microorganisms per

ml. After the addition of other ingredients the tubes were slanted on a rack and incubated in that position to expose the maximum surface to the air. Samples were withdrawn at frequent intervals and 10-fold dilutions made in gelatin-Locke's solution. Loopfuls were cultured from appropriate dilutions by careful streaking onto the surface of blood agar plates. Each bacterial count was based on 3 platings. Repeated checks on the accuracy of this method showed it to be adequate for the purposes at hand and better for meningococci than the ordinary methods involving the use of poured plates. Plate cultures were examined after 24 hours' incubation in

¹ Miller, C. P., *Proc. Soc. Exp. Biol. and Med.*, 1942, **49**, 197.

² Miller, C. P., and Foster, A. Z., *Proc. Soc. Exp. Biol. and Med.*, in press.