

a slightly less than average number of apparently normal young through the usual gestational period. Of 7 rats given 1 μ g of estrone and 4 mg of progesterone daily, one died on day 22 following an attempt to deliver 6 large and 2 resorbing fetuses, and the other 6 when sacrificed on days 22 or 23 were found to have a total of 39 (3 to 9) living young and 16 (1 to 6) fetuses in various stages of resorption. Of the 10 rats given 1 μ g of estrone and 3 mg of progesterone, one died on day 21 without being able to deliver 9 term-size fetuses, 6 when sacrificed on days 21 or 22 were found to have a total of

36 (4 to 8) living young and 8 either recently dead or in various stages of resorption, and the remaining 3 when sacrificed on days 22 or 23 were found to have resorbing implants or no visible-implantation sites. It may be concluded, therefore, that 1 μ g of estrone and 4 mg of progesterone substituted for the ovaries and pituitary during the period of pregnancy between days 7 and 11, and for the ovaries alone from day 11 until term. The pituitary is only necessary during the first half of pregnancy in the rat, and then probably because of its gonadotrophic triad, FSH, ICSH and lactogenic hormone.

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Circulatory Effects from Cyclopropane Administered After Hemorrhage.*

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Clinical observations suggest that patients with recent extensive blood loss have an improvement of the circulation during cyclopropane anesthesia. With the onset of anesthesia, blood pressure and pulse pressure frequently increase and the pulse rate slows. These findings suggested laboratory observations under similar circumstances.

Method. Twenty-two experiments were performed on normal animals (18 dogs, 4 cats). No drugs other than cyclopropane, oxygen and a small amount of procaine were used. Arterial blood pressure determinations were made by cannulating a carotid or femoral artery after procaine infiltration. Hemorrhage was accomplished by direct rapid arterial bleeding until 25 to 30% of the estimated circulating blood volume had been withdrawn in an average of 5.7 minutes.

Cyclopropane was administered intermittently as a 30 to 50% mixture with oxygen, using the to and fro carbon dioxide absorption technic. Induction of anesthesia was

accomplished with a face mask, and maintained by using an endotracheal airway. Depth of anesthesia was determined by the character of the respirations and the activity of the eyelid and swallowing reflexes. When respirations became shallow or ceased in deep anesthesia, they were aided by rhythmic manual pressure on the rebreathing bag to eliminate the effects of hypoxia and hypercapnia. Observations were made in the 4 planes of surgical anesthesia. Cyclopropane administration was started at an average time of 29 minutes following the completion of bleeding and was maintained for an average period of 44 minutes.

In 13 dogs, venous blood samples were taken for hematocrit and plasma specific gravity determinations at 3 points in the experiment: (a) before bleeding (b) prior to the onset of anesthesia (c) at the completion of anesthesia. Hematocrit cell volume was measured in Sanforth-Magath tubes and plasma specific gravity was determined by the falling drop method of Barbour and Hamilton. Electrocardiograms were obtained

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at intervals throughout the period of experiment for 9 dogs.

One cat and 2 dogs were similarly prepared but received no cyclopropane. They were observed for 4 hours during which time no rapid fluctuations in blood pressure or pulse were noted after the initial effects of hemorrhage. Oxygen was administered by tracheotomy or endotracheal airway to 3 cats and 4 dogs after hemorrhage. Its use had no appreciable effect upon circulation.

Results. Mean arterial blood pressures averaged 120 mm Hg before, and 64 mm Hg after hemorrhage. Pulse pressures averaged 58 mm prior to, and 8 mm following blood loss. At the outset, the pulse rate in the dogs averaged 87 and increased to 174 after bleeding. In cats, the pulse rate rose from 210 to 303. All animals survived the experiment.

During surgical anesthesia with cyclopropane, the highest mean blood pressures averaged 104 mm Hg, the highest pulse pressures averaged 44 mm, and the pulse rate fell to an average of 71 in the dogs and 157 in the cats. It was noted that blood pressures were usually highest in the range between lower first and upper third planes of surgical anesthesia. The pulse pressure was often largest in the third or fourth plane and the pulse rate decreased progressively as anesthesia became deeper.

In the 13 dogs that had blood studies, the results were not uniform. Hematocrits after hemorrhage increased by an average of 3% in 6, decreased 2.4% in 5, and was unchanged in 2 dogs. After cyclopropane hematocrit values increased 3.6% in 6, decreased 2.5% in 6, and remained unchanged in 1 animal as compared with the values following hemorrhage. When compared with initial, pre-hemorrhage readings, there was an average increase of 4.25% in 8, a decrease of 5.25% in 4, and no change in 1 dog.

Plasma specific gravities after bleeding showed a decrease of 0.0013 (0.45 g protein) in 11 animals, an increase of 0.0013 (0.45 g protein) in 1, and no change in the other. After cyclopropane 6 animals showed a decrease of 0.0015 (0.51 g) and 7 an increase of 0.0007 (0.24 g) as compared with the

values following hemorrhage. When compared with initial control values, all 13 animals showed an average decrease in specific gravity of 0.0014 (0.48 g).

Nine animals in which electrocardiographic tracings were obtained showed various cardiac irregularities at some period during the experiment. Two showed an arrhythmia before cyclopropane administration. The irregularities noted were sinus arrhythmia, prolongation of conduction time, shifting pacemaker, premature ventricular contractions, auriculo-ventricular nodal rhythm, partial heart block, complete heart block, and multiple ventricular foci. Those of serious portent—partial and complete heart block, or multiple ventricular foci—were seen only in the deeper planes of anesthesia.

Discussion. These preliminary results tend to support the clinical observation that cyclopropane is a useful anesthetic agent in the presence of circulatory depression due to recent extensive blood loss. Its effect on blood pressure and pulse rate seem significant. The blood studies are brief and inconclusive, but the increase in plasma specific gravity after cyclopropane administration in 7 of 13 animals, when compared with the values following hemorrhage, is a deviation from the expected progressive decrease in specific gravities. All cardiac irregularities noted have been repeatedly observed since the first use of cyclopropane.¹ No animal of this group developed fatal arrhythmia. The electrocardiographic interpretations are suggestive of a vagal type of stimulation.

The mechanism of these effects from cyclopropane is not obvious. This drug exerts many parasympathomimetic effects,^{2,3} increases cardiac output,⁴ influences the various

¹ Meek, W. J., Hathaway, H. R., and Orth, O. S., *J. Pharm. and Exp. Therap.*, 1937, **61**, 240.

² Adriani, J., Martin, S. J., and Rovenstine, E. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1940, **45**, 785.

³ Adriani, J., and Rovenstine, E. A., *Am. J. Physiol.*, 1941, **133**, 192.

⁴ Robbins, B. H., and Baxter, J. H., Jr., *J. Pharm. and Exp. Therap.*, 1938, **62**, 179.

body fluid compartments, the spleen and other reservoirs of formed blood elements.⁵

⁵ Bonnycastle, D. D., *J. Pharm. and Exp. Therap.*, 1942, **75**, 18.

Conclusion. Preliminary observations seem to substantiate the clinical impression that cyclopropane is a useful anesthetic agent in the presence of circulatory depression due to rapid hemorrhage.

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Yolk Sac Complement Fixation Antigen for Use in Psittacosis-Lymphogranuloma Venereum Group of Diseases.

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The recognition in recent years of the frequency of human infections with several members of the psittacosis-lymphogranuloma venereum group of viruses¹⁻⁴ has led to an increased interest in procedures which aid in the laboratory diagnosis of these diseases. The demonstration of complement-fixing antibodies in the sera of patients convalescent from psittacosis and from lymphogranuloma^{7,8} has been used for establishing the etiology of these maladies. Considerable confusion has developed recently, however, regarding the interpretation of complement fixation reactions obtained in these diseases because of cross reactions displayed by the patients' sera with antigens prepared from tissues infected with the viruses of classical psittacosis and lymphogranuloma venereum and other members of this group of

agents.^{2,9-11} Although at present it is impossible to differentiate sharply between human psittacosis and lymphogranuloma by means of serological tests, it is possible, under appropriate conditions, to establish that a given acute illness was caused by a member of this group of viruses.³

The observations of several groups of workers suggest that the titers of sera from patients with psittacosis, closely related infections and with lymphogranuloma may differ somewhat when tested against homologous and heterologous antigens prepared from this group of viruses.^{2,9,10} Furthermore, pigeons recovered from ornithosis develop antibodies that fix complement with meningopneumonitis antigen but not with lymphogranuloma antigen.¹¹ The observations reported at this time extend those of others regarding the reactions of human convalescent sera with complement-fixing antigens of psittacosis and lymphogranuloma. In addition, a comparatively simple and safe method for preparing psittacosis antigen from highly infectious material is described.

Materials and Methods. Preparation of Psittacosis Antigen. Antigens containing

¹ Meyer, K. F., *Medicine*, 1942, **21**, 175.

² Eaton, M. D., and Corey, M., *PROC. SOC. EXP. BIOL. AND MED.*, 1942, **51**, 165.

³ Smadel, J. E., *J. Clin. Inv.*, 1943, **22**, 57.

⁴ Shaffer, M. F., Rake, G., Grace, A. W., McKee, C. M., and Jones, H. P., *Am. J. Syph.*, 1941, **25**, 699.

⁵ Bedson, S. P., *Lancet*, 1935, **2**, 1277.

⁶ Meyer, K. F., and Eddie, B., *J. Infect. Dis.*, 1939, **65**, 225.

⁷ Hecht, H., *Wien. Klin. Wschr.*, 1935, **48**, 1389.

⁸ McKee, C. M., Rake, G., and Shaffer, M. F., *PROC. SOC. EXP. BIOL. AND MED.*, 1940, **44**, 410.

⁹ Rake, G., Eaton, M. D., and Shaffer, M. F., *PROC. SOC. EXP. BIOL. AND MED.*, 1941, **48**, 528.

¹⁰ Eaton, M. D., Martin, W. P., and Beck, M. D., *J. Exp. Med.*, 1942, **75**, 21.

¹¹ Eddie, B., and Francis, T., Jr., *PROC. SOC. EXP. BIOL. AND MED.*, 1942, **50**, 291.