

variations in the amount run parallel with that of the liver. The fluorescence in adrenals is completely absent in the newborn infant. (2) It was found in the cells of the corpus luteum of the ovary, and the tubular and Leydig cells of the testes. (3) The normal kidney did not show the fluorescence, but it was found in 2 cases of nephritis. (4) It was found in small but varying amounts in the fat cells in different organs and in fat tissue. This was not in obvious relation with the amount in the liver.

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Effect of Variation of Blood Pressure on the Autonomic Nervous System.

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In our studies of the autonomic and somatic nervous system¹ we have frequently observed in the cat an inverse relation between blood pressure and pupillary diameter. The only reference in the literature to this phenomenon of which we are aware is a brief remark by Koch² that endosinusal pressure and pupillary diameter are indirectly related. Since his observations were not published in full, a brief report of our experiments seems appropriate. We have found regularly that in anesthetized cats (pentothal 40 mg/kg or chloralose 100 mg/kg) a rise of blood pressure produced by the injection of small amounts of adrenalin (5 to 20 γ /kg) is attended by a constriction of both the normal and of the acutely sympathectomized pupil. A similar effect may be brought about by raising the blood pressure by infusion of Ringer's solution (Table I). Occasionally it was observed that the increased parasympathetic tone as evidenced by the pupillary constriction in both sympathectomized and normal pupils was accompanied by a relaxation of the nictitating membrane. If on the other hand, blood pressure was lowered by amylnitrite, a dilation of the pupil occurred. This was observed to take place both after the removal of the adrenals and after the sectioning of the cervical sympathetic. From these observations we conclude that an increase

¹ Gellhorn, E., and Darrow, C. W., *Arch. Internat. Pharmacodyn.*, 1939, **62**, 114; Darrow, C. W., and Gellhorn, E., *Am. J. Physiol.*, 1939, **127**, 243.

² Koch, E., *Klin. Wochenschr.*, 1932, **11**, 225.

TABLE I.

Cat, 2.3 kg; 40 mg pentothal/kg intraperitoneally. Blood pressure recorded from the carotid artery. Bilateral adrenalectomy. 75 cc Ringer slowly infused into the femoral vein.

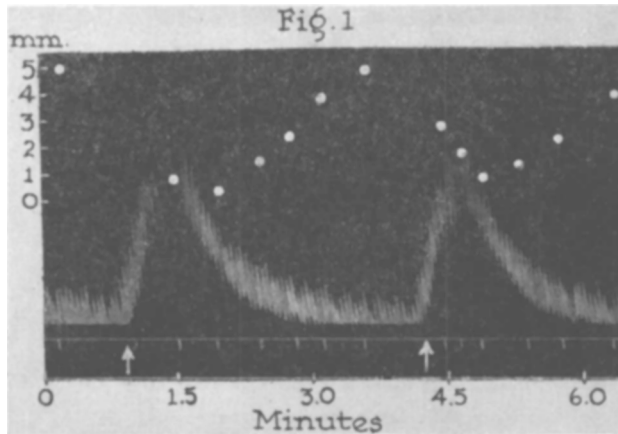
Blood pressure in mm Hg	Pupillary diameter in mm
110	5.0
120	4.0
130	0.8

in the blood pressure leads to a decrease in sympathetic and increase in parasympathetic tone, whereas a decrease in blood pressure has the opposite effect.

Although Koch's observations show that pressure variations in the carotid sinus produce similar changes of the pupil and nictitating membrane, as we have observed after administration of adrenalin and amylnitrite, it is interesting to point out that the carotid sinus and the depressor nerves are not indispensable for this reaction. After bilateral vagotomy and denervation of the carotid sinuses, the typical effects of adrenalin and amylnitrite are retained (Figs. 1 and 2). It is not unlikely that abdominal presso-receptors are involved.³

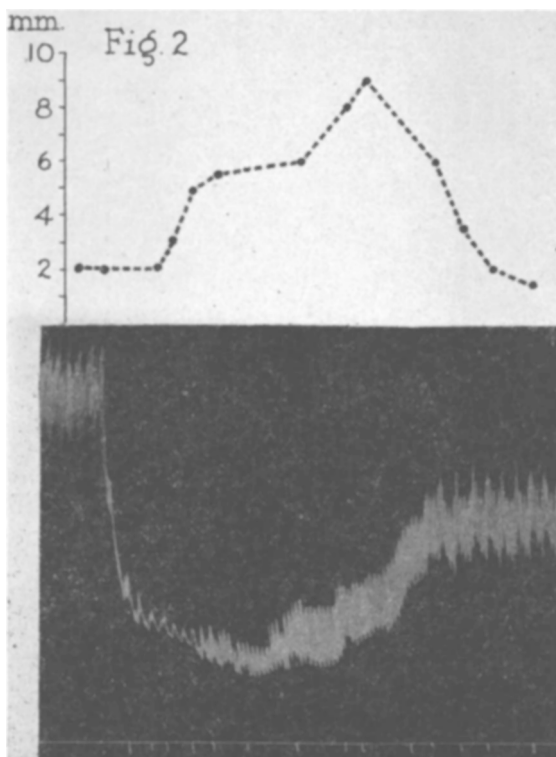
The great influence which the blood pressure exerts on the pupillary diameter is further illustrated by the following examples:

Pupillary dilatation following bleeding may be greatly delayed



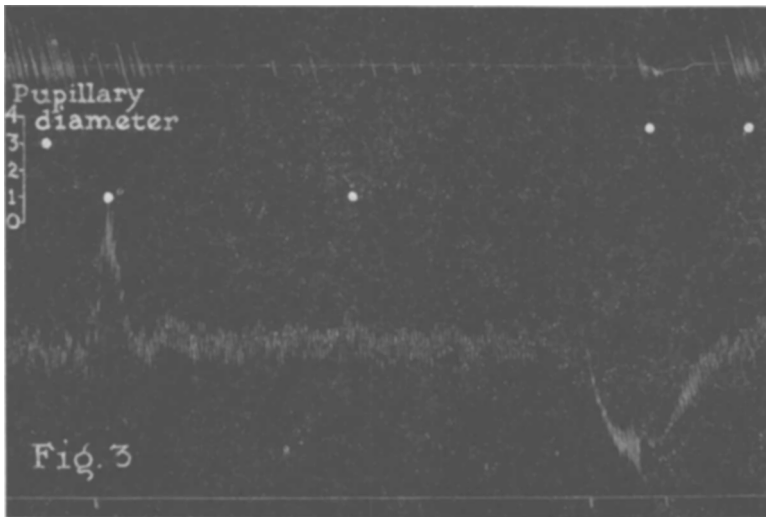
Cat, 2.4 kg. 100 mg chloralose subcutaneously. Bilateral vagotomy and denervation of the carotid sinuses. Upper curve: pupillary diameter in mm. Lower curve: blood pressure from the carotid artery. At the arrow, 0.0033 mg adrenalin was injected intravenously.

³ Heymans, C., Bouckaert, S., Farber, S., and Hsu, F., *Am. J. Physiol.*, 1936, **117**, 619.



Cat, 2.3 kg. Narcotized and operated as cat in Fig. 1. At the arrow, amyl-nitrite is inhaled.

when the blood pressure level during the bleeding is maintained by infusion of Ringer's solution, but occurs immediately once the pressure is permitted to fall. In earlier investigations, Gellhorn and Darrow showed that the injection of metrazol is typically accompanied by a marked fall in the blood pressure and a widening of the pupils due to parasympathetic inhibition and sympathetic excitation. It was further found that in animals deprived of their buffer nerves, metrazol caused not a fall but a rise of the blood pressure. It is interesting to note that in such conditions, the pupillary dilation was markedly diminished and that if the blood pressure rise was pronounced, it led finally to the actual constriction of the pupil. This seems to indicate that the tendency of metrazol to produce pupillary dilation is inhibited by the rise in blood pressure. Nor are the effects of variations in blood pressure restricted to the autonomic nervous system for they influence the somatic nervous system as well. Koch had already noted that a rise in intrasinusal pressure led to a general



Cat, 2.3 kg. Narcotized with chloralose 100 mg subcutaneously. Upper curve: convulsive movements recorded from the right hind leg. Middle curve: blood pressure from the carotid artery. Lower curve: first mark injection of 1 cc adrenalin 1:150,000. The second and third mark delimit the period of amylnitrite inhalation. Prior to the record, .2 cc 10% metrazol was injected intravenously.

quieting of the animal. We found likewise that adrenalin attended by a rise in blood pressure inhibits convulsions and that amylnitrite with a fall in pressure may increase them.⁴ Fig. 3 illustrated this relationship. In this experiment it was observed that the pupillary diameter was 3 mm before the injection of adrenalin. It decreased to 1 mm after adrenalin and this increase in parasympathetic tone was associated with an almost complete disappearance of metrazol convulsions. In the second part of Fig. 3 the cat inhaled amylnitrite. This caused a distinct increase in frequency and intensity of the convulsions and was accompanied by a dilation of the pupil from 1 to 3.5 mm.

Summary. 1. Increase in blood pressure induced by adrenalin or infusion of Ringer's solution leads to a decrease in pupillary diameter and to a relaxation of the nictitating membrane. A fall in the blood pressure induced by amylnitrite leads to a dilation of the normal and of the sympathectomized pupil. These observations indicate that a rise in blood pressure produces parasympathetic excitation and sympathetic inhibition, whereas a fall in blood pressure has the opposite results. 2. The effects produced by variations of blood pressure are

⁴ Gellhorn, E., Darrow, C. W., and Yesinick, L., *Arch. Neurol. and Psychiat.*, 1939, **42**, 826.

still present after bilateral vagotomy and denervation of the carotid sinuses. 3. The effects of variations of blood pressure are not restricted to the visceral nervous system but extend to the somatic nervous system, inasmuch as increase in blood pressure is associated with decreased somatic excitability and decrease in pressure is associated with increased somatic excitability.

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Production of "Prothrombin Deficiency" and Response to Vitamins A, D and K.

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This investigation was undertaken because it was found that rats receiving a diet containing 20% of mineral oil by weight developed a hemorrhagic tendency. On examining their "prothrombin time" it was found to be prolonged. It was thought that the large doses of mineral oil prevented the absorption of vitamin K as well as vitamin A and carotene.

Normal Prothrombin Time in Rats. Methods. The control diet consisted of Purina Dog Checkers and water *ad libitum*. The determination of the prothrombin time was made by a modification of Quick's¹ method. Two cc of blood obtained by cardiac puncture (22 gauge needle) under light anesthesia is drawn into 0.2 cc of 1.34% sodium oxalate solution. This is diluted to 4.0 cc with 0.9% NaCl solution and centrifuged. 0.1 cc of the diluted oxalated plasma is mixed with 0.1 cc of thromboplastin solution. 0.1 cc of 1.11% calcium chloride (anhydrous) solution is quickly added and the time for clot formation is recorded with a stop-watch. The thromboplastin solution was made by weighing, macerating and spreading fresh rat's brain on gauze so that 1 sq in. of gauze contains 0.5 g of fresh brain. This is dried and preserved at room temperature in a desiccator. When it is to be used, one of the squares is leached in 5 cc of saline solution (0.9%), and the solution incubated at 54°C for 10 min. The supernatant fluid is used. A fresh solution is made and checked for activity daily. The dried-brain-gauze preparation maintains its activity for several weeks. Chemically clean glassware was

¹ Quick, A. J., *J. Am. Med. Assn.*, 1938, **110**, 1658.