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Received May 9, 1966. P.S.E.B.M., 1966, v123.

Sympathetic Control of the Dog's Nasal Blood Vessels.* (31538)

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The blood supply of the nose is important not only for the needs of the nasal tissues but also to warm and humidify the inspired air. The very rich vasculature with its large venous plexuses has been referred to as the erectile tissue of the nose(1a). Engorgement of the erectile tissue can hinder movement of air through the nose, for in places the air passages are narrow(1b). Vasoconstriction of the nasal blood vessels could reduce both the blood flow and blood content but not necessarily in the same proportion. The present work is the only one we are aware of, which shows quantitatively the marked constrictor effects of slow rates of nerve stimulation on the nasal blood content.

In his article on peripheral autonomic mechanisms Hillarp(2) reviewed the evidence which now has become very convincing that low frequencies of nerve impulses to the blood vessels are very effective in causing contriction or dilatation. Recent work, particularly that by Celander(3) and Folkow(4) indicate that almost maximal vasoconstriction or vasodilatation can be obtained at discharge rates of about or below 10 per second.

Method. Jackson's method of nasal plethysmography(5) was used on the anesthetized dog (35 mg/kg pentobarbital i.p). The nasal cavity is considered to be surrounded by unyielding bony walls and can be blocked off posteriorly and anteriorly. Any change in the volume of blood (blood content) of the nasal mucosa should result in the movement of air into or out of the nose. The nasal cavity is blocked off posteriorly by a rubber ball pushing the soft palate upward. The rubber ball is on a metal rod, and held in place by the Jackson head holder. The method was modified at the recording end in 2 respects. Electronic recording with a transducer and Physiograph was substituted for a tambour. Also between the nasal cannula, tightly secured in the anterior nares and the transducer was a 2500 cc air-containing reservoir immersed in a water bath at a constant temperature. There were also 2 side tubes leading to the reservoir. Both were closed during the recording. One was connected to a water manometer to check for leaks and the other for the purpose of calibrating aspirating known volumes of air with a syringe. The large reservoir was used to prevent changes in intranasal pressure greater than those occurring in normal, quiet respiration. The femoral arterial blood pressure was measured throughout all procedures. The sympathetic fibers in the cephalic end of the ansa subclavia, after section of the dorsal branch, were stimulated with square wave shocks for 30 seconds. Only the frequency was varied, so that frequencies of 4/min, 12/min, 2, 5, 10, 20 or 25 shocks per second were applied, while the other characteristics of the stimulating current were kept constant (3 volts and a shock duration of 15 msec). The observations were made on large or medium sized dogs.

Results. The cervical sympathetic nerve fibers of 10 dogs were stimulated for a total

* Supported by Grant H-3489 (USPHS) and Grant 571 from St. Louis Heart Assn.

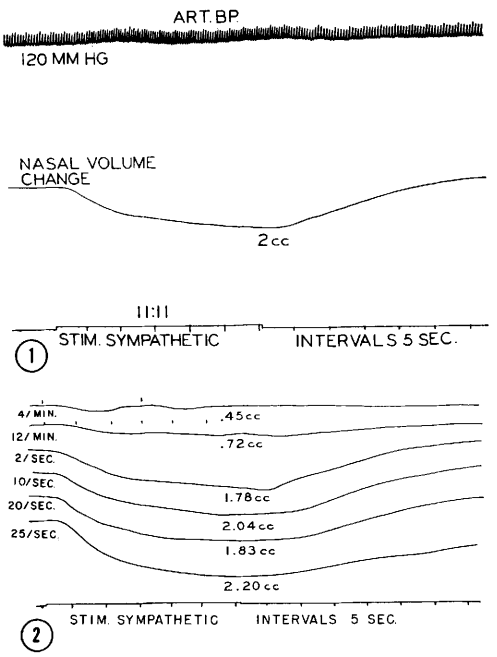

FIG. 1. Art. B.P.: femoral arterial blood pressure, nasal volume change in cc and time record at 5 sec interval, with sympathetic stimulation for 30 seconds. 11:11: identifies record by time of day when taken.

FIG. 2. Frequencies of stimulation of cervical sympathetic are shown on the left and respective decreases in nasal blood volume as indicated by a fall in pressure are shown on the abscissa. Time record and 30 sec period of stimulation are shown on bottom line.

of 249 times. Fig. 1 shows the nasal blood volume changes as indicated by a fall in pressure in the nose and recording system (downstroke) on stimulation of the cervical sympathetic for 30 seconds. In Fig. 2 the blood pressure records were deleted in order to show the reduction in nasal volume obtained on successive stimulations of the cervical sympathetic at frequencies of 4/min, 12/min, 2/sec, 10/sec, 20/sec and 25/sec, for a period of 30 seconds each. The 30 second period of stimulation was the guide for the placement of the records. All stimulations were unilateral. Fig. 3 shows the range in nasal volume changes for one standard deviation at various frequencies of stimulation. Fisher's t test was used to determine the significance of the differences between the means of the responses at the various frequencies. A P value of 0.05 or less was considered significant. The vasomotor responses obtained on stimulation of the sympathetic at 4/min were significantly less than the responses to all higher frequencies listed. This was also true for frequencies of 12/min.

The responses to a frequency of 2/sec exceeded those to a lower frequency but were significantly less than the responses to 10/sec and not significantly different from responses from frequencies of 5/sec, 20/sec and 50/sec. Fig. 2 shows a greater vasoconstrictor response to 25/sec than to 10/sec. The response to 25/sec is not significantly different from either the 2/sec or the 10/sec but lying much closer to the 10/sec response. Thus these experiments demonstrated progressive increases in the nasal vasoconstrictor responses with rise in frequency of stimulation of the cervical sympathetic fibers, with maximal responses being elicited by a frequency of 10/sec.

Miscellaneous observations. (a) A single volley can cause a measurable constriction. (b) Records were taken independently from each side of the nose, after blocking posteriorly with vaseline-gauze pack. In 101 trials constriction on the side contralateral to the sympathetic stimulation averaged about 6%

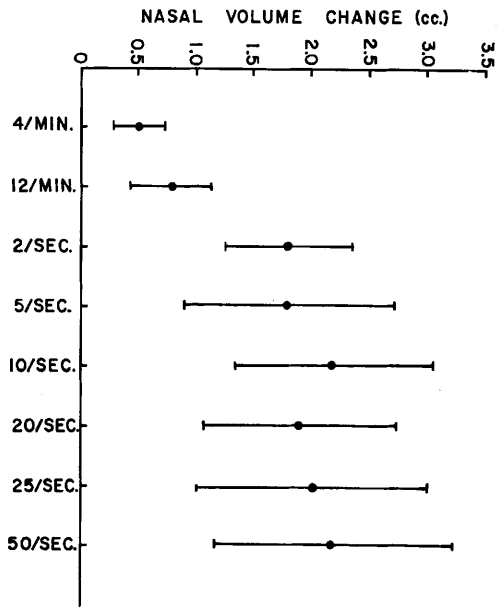

FIG. 3. Range of intranasal fluid (blood) volume changes for one standard deviation at various frequencies of sympathetic nerve stimulation.

as great as on the ipsilateral side. (c) The nasal mucosa was observed in one dog through 2 foraminae 1 to 2 cm in diameter. The foraminae were produced by a piece of wood lodged between the upper molars of the two sides of the mouth and were first seen when the wood and necrotic material were removed under pentobarbital. Stimulation of cervical sympathetic fibers caused marked pallor on the stimulated side. The pallor was observed visually and be means of color photography. The electrical stimulation was effective when applied to the cranial end of the cut right vagosympathetic or to the cranial end of the cut left cervical sympathetic fibers after separating them from the vagal fibers by Mizere's method(6). (d) The volume of the nasal cavities and upper nasopharynx, after blocking the nasopharynx according to Jackson's method was determined by measuring the volume of water required to fill it. Eight dogs ranging from 11.4 to 17.7 kg and averaging 14.7 kg had a nasal volume ranging from 8 to 60 cc, with an average of 21.8 cc. The determinations were made on dogs soon after death. The correlation of nasal volume with body weight was not close.

Discussion. Our experiments differ from those of Folkow(4) who measured the blood flow in other vascular areas than the nose, whereas we measured nasal blood volume changes for evidence of constriction. Our findings agree with his in indicating that a remarkably large range of vasoconstrictor response can be produced by a relatively low frequency of stimulation (10/sec or less).

The marked effectiveness of a low frequency of 2/sec suggests that nasal vascular tonus and reflex vasoconstriction might be mediated by a low frequency of sympathetic nerve impulses. There is reason to believe that vasoconstrictor tone elsewhere may be maintained by sympathetic frequencies of 1 to 2 impulses per second(2). Presumably the number of nerve fibers activated and their degree of synchronicity would also be important factors.

According to Mellander(7) the resistance vessels (precapillary) of the cat's leg showed almost the full-range of vasoconstrictor fiber control with 0 to 8-10 impulses per second, whereas the capacitance vessels (veins) generally gave maximum effects at 8/sec and nearly maximal constrictor responses were already obtained by stimulation frequencies around 4 impulses per second. Since the veins of the nasal mucosa are exceptionally large, the effectiveness of low frequency of constrictor impulses may apply with particular force to nasal blood volume changes.

Urdritz(8) made holes through the palate to pack and block the choanae and recorded with a Marey tambour. He considered the cervical sympathetic effects to be strictly unilateral. The dog's septum is very flexible and possibly his method gives better immobilization of the septum. On the other hand he may have overlooked a small (6%) change on the contralateral side. A contralateral effect might indicate (a) that some sympathetic fibers crossed the midline, (b) the sympathetic fibers of one side might innervate a blood vessel which supplies both sides of the nose, and (c) some vasoconstrictor agent released into the blood stream affecting both sides.

We consider the observed changes in pressure within the nasal cavity to be due primarily to vasoconstriction and decreased blood content. When the peripheral end of efferent sympathetic fibers were stimulated, the onset of constriction occurred too rapidly to be explained by a reflex, or humoral mechanism, the marked pallor of the nasal mucosa indicates decreased blood content, and the rapid recovery argues against tissue fluid changes. Care was taken to prevent air leakage or temperature changes. The cervical sympathetic also supplies the carotid sinus and hypothalamus which by reflex and/or humoral factors might modify the terminal portions of the constrictor response. From our experience with spinal cord transection and bilateral cervical sympathetic section, and from independent bilateral recordings(9), it seems likely that these factors are relatively unimportant.

Summary. While recording from a nasal plethysmograph, cervical sympathetic fibers to the nose were stimulated with a square wave current of varying frequencies. The other current characteristics were kept constant. Our results indicate that increasing the frequency of stimulation from 4/min to 10/

sec caused a change in nasal vasoconstrictor response of approximately the full range from minimal to maximal. A frequency of only 2/sec caused a moderately strong vasoconstriction, when many cervical sympathetic nerve fibers were stimulated simultaneously.

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Received May 16, 1966. P.S.E.B.M., 1966, v123.

A Comparative Study of Amniotic Fluid, Maternal Sera and Cord Sera by Disc Electrophoresis.* (31539)

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Existing information about amniotic fluid protein has been derived mainly from paper electrophoresis analysis(1,2,3,4,5,6). Since this procedure only separates serum fluids into the 5 major bands of albumin, α_1, α_2 β, and γ globulins, each of which is a mixture of proteins of different chemical structures and molecular weights, no quantitative information concerning the individual protein components has been obtained by the use of this technique. Studies on amniotic fluid done with immunoelectrophoresis have given qualitative information only(7,8). Derrington and Soothill(9) employed an immunodiffusion method for a quantitative study of amniotic fluid but they limited their investigation to 7 serum proteins.

The present paper reports the findings in a comparative study of individual proteins in amniotic fluid, maternal serum and cord serum when disc electrophoretic techniques combined with quantitative immunodiffusion were employed for the investigation. Acrylamide disc electrophoresis is a recently devised technique that provides routine separation of approximately 20 proteins from a serum sample as small as 3 microliters. Direct analysis of dilute liquids such as amniotic fluid is also possible since proteins in the fluid are automatically concentrated to high values in the stacking gel at the beginning of an experimental run prior to differentiation of proteins in the separating gel. The objectives in this study were 1) to quantitate as many individual amniotic fluid proteins as possible and to compare the proteins of the amniotic fluid to those of maternal and fetal serum; 2) to consider the origin of the amniotic proteins since, at present, investigators are divided among those who believe the amniotic fluid proteins arise from fetal serum, and those who feel their origin is maternal serum; and 3) to test the hypothesis that proteins of the amniotic fluid are derived from filtration through the semipermeable fetal membranes(9).

Materials and methods. Amniotic fluid, maternal serum and fetal serum from 12 normal pregnancies were examined. Amniotic fluid was obtained by needle aspiration at the beginning of labor. Maternal serum was drawn within 24 hours after delivery. Cord blood was employed as the source of fetal serum. For both disc electrophoresis and immunodiffusion studies, the amniotic fluids were concentrated 10× by dialysis against solid su-

* This work was supported in part by Grant CA-07826-02 from Nat. Cancer Inst., N.I.H., USPHS and Grant E-343A from Am. Cancer Soc.