Dynamics of the Circulation in Acute Hypertension Produced by Stimulation of the Cerebral Cortex

By HERBERT G. LANGFORD, M.D., JOHN L. PATTERSON, JR., M.D. AND RENO R. PORTER, M.D.

Electric stimulation of motor areas of the cerebral cortex of the dog is followed by a prompt rise in systemic blood pressure, without significant changes in heart rate or cardiac output. Small increases occurred in lesser circuit pressures.

Stimulation of areas of the cerebral cortex of dog, cat, monkey, and man is followed by a prompt rise in arterial blood pressure. No data are available to indicate whether this is due to increase in peripheral resistance or increase in cardiac output, nor is there any information as to whether comparable changes are produced in the lesser circulation. There are, however, a number of analogous situations which bear upon this. In man anxiety usually causes an increase in cardiac output, as measured by ballistocardiography, with decrease in peripheral resistance, but at times may cause elevation of blood pressure with increase in peripheral resistance. In the dog, acute hypertension produced by section of the buffer nerves is associated with maintenance of cardiac output and an increase in peripheral resistance. Acute hypertension produced by the intracisternal injection of fibrin is accompanied by a marked increase in pulmonary venous pressure and, at times, pulmonary edema.

In the present experiments, observations were made of blood flow and blood pressure phenomena in the greater and lesser circuits, both before and during the hypertension produced by electric stimulation of the cerebral cortex.

From the Departments of Medicine and Neurological Science, Medical College of Virginia, Richmond, Va.

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Methods

Thirty-nine mongrel dogs were studied as follows: Preliminary craniotomy under pentobarbital anesthesia with removal of bone over the motor area of both cerebral cortices usually was done on the animal the day prior to the experiment. Occasionally craniotomy was done immediately prior to the experiment using light ether anesthesia. On the day of the experiment tracheotomy was performed after copious local infiltration with promine hydrochloride HCl 1 per cent. Decamethonium 2 mg was given intravenously as required to block muscle movement. Artificial respiration was maintained by intermittent positive pressure into a tracheal cannula. A double lumen catheter was wedged under fluoroscopic control into a branch of the pulmonary artery to provide pulmonary arterial and pulmonary "capillary" (wedge) pressures. Another catheter was placed in the right atrium. An arterial sound was inserted via the left common carotid artery with its tip in or near the aorta. Pressures were measured with three Statham strain gages and one Sanborn electromanometer, and recording was done with a 4-channel Sanborn Poly-Viso. The transducers were placed at a level approximately midway between sternum and spine. It was not possible to obtain all measurements on every animal.

Cardiac output was determined by the Remington pressure pulse contour method and the indicator-dilution method of Stewart as modified by Hamilton. Injection of the dye T-1524 was made into the right atrial catheter and blood sampling at 1 sec. intervals was done from the carotid arterial sound or more frequently from a femoral artery. Mean aortic and pulmonary arterial pressures were calculated as 1/2 pulse pressure plus diastolic pressure. Planimetric measurement of mean pressures was made from twenty paired (peak and trough of respiratory oscillation) pulmonary arterial pressure pulse contours. The correct mean factor thus determined was 0.355, which agreed well with the conventional ¼. Surface area of the dogs was calculated by the formula of Cowgill and Drabkin.

The motor cortex of the brain was stimulated with platinum bipolar electrodes with an irregular size.
wave current of 3-4.5 volts from an inductorium. Two time sequences of stimulation were used: a single 10 sec. stimulation in early experiments and the other, used for most of the experiments, alternating with 10 sec. stimulations of the left and right cortex for 90-180 sec.

Results

The response to alternating cortical stimulation of the aortic, right atrial, pulmonary arterial and pulmonary "capillary" (wedge) pressures are shown in figure 1, taken from an experiment which was typical save for slightly greater rise in wedge pressure than was usual. In most experiments, the rise in aortic pressure began promptly, usually within 3 sec., and the pressure reached a peak or plateau in an average of 34 sec. There were slight increases in mean right atrial and pulmonary arterial pressures, associated with changes in contour and widening of the amplitude of oscillation, as well as a small rise in pulmonary wedge pressure in most cases.

Tabulation of our data* revealed that in the alternating stimulation series the average increase in mean aortic pressure was 83 mm. Hg. Mean systolic pressure rose 98 mm. Hg and mean diastolic 69 mm. Hg. The calculated mean pulmonary arterial pressure rose 5.5 mm. Hg, while the systolic pressure rose 11.1 mm. Hg and the diastolic 2.2 mm. Hg. These changes obviously were associated with a widened amplitude of oscillation. In numerous experiments there was no increase in diastolic pressure in the pulmonary artery, but a moderate increase in systolic pressure and in calculated mean pressure. This occurred despite constancy of rate and cardiac output.

Mean pulmonary wedge pressure in the entire group rose 2.6 mg. Hg and right atrial pressure 2.0 mm. Hg, both increases being statistically significant. Careful screening of the wedge pressure contours recorded at 50 mm./sec. paper speed yielded 15 animals with contours showing appreciable pressure oscillation with the cardiac cycle as well as the respiratory cycle, yet with definitely "venous type" contours. These observations we consider to represent reliable wedge pressure data.

* Tabular summary of these data will be supplied by the authors on request.

In these 15 animals there were mean rises with cortical stimulation of 2.5 mm. Hg in wedge and 75 mm. Hg in mean aortic pressure, which represented a 1 mm. Hg rise in wedge pressure for each 30 mm. Hg rise in aortic pressure.

In 5 animals subjected to alternating stimulation, all of the functions measured were obtained on each animal. The mean pulmonary arterial pressure was determined by planimetry in each animal of this group. The blood pressure, blood flow and heart rate responses to cortical stimulation are very similar to those in the larger group of animals.* This was also true of responses in the animals given a single period of cortical stimulation (table 1), the major differences being smaller changes in all of the pressures measured.
Heart rate showed either no change or a small increase with cortical stimulation. The mean increase was less than 3 per cent.

There was only slight discrepancy between the behavior of the mean cardiac index as determined by the indicator-dilution method, in which there was a 1.8 per cent increase at the peak of the aortic pressure rise, and as determined from the aortic pressure pulse contours, in which there was a 7 per cent, 

\[ (p > .05) \] fall in cardiac index. The actual values for the cardiac index given by the contour method for the control and peak pressure periods were respectively 32 per cent and 38 per cent lower than the values given by the dye method. It should be noted that these comparative figures are not from identical groups of animals. Cardiac output measurements by both of the methods used were obtained in 6 animals in which the pressure pulse contours met the criteria of validity. In one of these, because of the very early recirculation of the dye, the Dow formula \(^{10}\) was used in the calculation. The cardiac index by the indicator-dilution (dye) method in this group showed a 20.5 per cent mean rise, whereas the same function as determined by the contour method showed a 4.3 per cent fall. Neither of these changes from the control values reached the 5 per cent level of statistical significance.

Pressure contours which met the criteria of validity were recorded in 7 animals during the period of rapid pressure rise following the onset of cortical stimulation. These data demonstrated a striking stability of the mean cardiac index throughout the period of pressure rise from control to peak level. Because of an increase in mean heart rate of 23 beats/min., which occurred during the first two-thirds of the pressure rise, the mean stroke index in the group showed a gradual fall during the same period amounting to 22 per cent. A considerable part of the heart rate change was due to 1 animal, which had an increase in rate of 75 beats/min. As the pressure neared the peak of its rise both the mean stroke index and heart rate became stable.

Figure 2 shows peak pulmonary capillary pressure plotted against peak aortic pressure. The equations of the lines of regression are:

\[ x = 0.055 y - 2.5, \]
\[ y = 10.9x + 112.2, \]

and the coefficient of correlation 0.77 \((p < .001)\). The correlation between increase in aortic pressure and increase in pulmonary wedge pressure was also significant but somewhat less close \((r = 0.67, p < .01)\). Significant correlation was not demonstrated between aortic pressure and right atrial pressure or between pulmonary arterial and right atrial pressure at the peak of the aortic pressure rise.

No pulmonary edema was disclosed in any of the animals by gross sectioning of the lungs immediately after the experiments.

**Discussion**

As the cardiac output changed very little, the increase in blood pressure was of necessity primarily due to increased peripheral resistance. As the heart rate also did not change, and the vascular resistance alterations were relatively minor in the lesser circuit, the gross hemodynamic changes invite comparison with those observed in essential hypertension. The analogy is close but at present must be considered as superficial, as we are comparing an acute hypertension in a paralyzed dog with a chronic hypertension in man. However, the main hemodynamic difference between this preparation and essential hypertension, the slight increase in pulmonary capillary pressure, may be because this is an acute hypertension and left ventricular hypertrophy has not occurred.

The recent demonstration \(^{4}\) that the acute elevation of blood pressure in the dog with
section of the buffer nerves is due primarily to increased peripheral resistance is compatible with the possibility that in our preparation the same sympathetic fibers are activated as are controlled by the feed-back from the carotid sinus and aortic arch. However, at least some of the fibers controlling blood pressure are found in the pyramidal tract at the medullary pyramid, where the tract consists solely of axons of cortical origin and spinal termination. Two studies which suggest that other modes of autonomic activation may produce different patterns of response are those of Levy and colleagues, and Hamilton and colleagues. These workers demonstrated a marked rise in peripheral resistance immediately after buffer nerve section, with little change or a slight fall in cardiac output but with an abrupt rise in heart rate. The absence of change in heart rate in our preparation may be explained by competition between sympathetic and vagal outflow to the heart. In the dog with acute hypertension secondary to buffer nerve section only the sympathetic outflow would be operative.

The lower values for cardiac index given by the pulse contour method as compared with the indicator-dilution method were probably due, at least in part, to the high arterial pressure levels in these animals. Such a discrepancy has previously been noted at high diastolic pressures, although the ultimate explanation is not clear.

As cardiac output was maintained against an increased resistance with little or no change in rate, an analysis of how this occurred involves exploration of how Starling's law may be applied to the intact animal. The measurements required for direct evaluation are not available. However, if we assume that increased wedge pressure reflected increased left atrial pressure, which in turn followed increased end-diastolic pressure, it seems fair to postulate that some increase in length of left ventricular fibers was necessary to maintain cardiac output in the face of increased resistance. However, this change was probably minimized by the direct effect upon the cardiac muscle of sympathetic stimulation.

Sarnoff and Berglund found that the rise in aortic pressure consequent to the intracisternal injection of fibrin was accompanied by tachycardia, a rise in pulmonary venous pressure and a rise in vena caval pressure. Their mean and maximal aortic pressure rises were slightly larger than ours. However, many of their experiments showed a marked rise in pulmonary venous and vena caval pressure, with a moderate rise in peripheral resistance. A comparable increase in peripheral resistance in our preparation resulted in only small rises in pulmonary wedge and right atrial pressure. If these workers were activating to the same degree the same autonomic outflow as was activated in our preparation, the assumption might be advanced that due to the extensive surgery and the chloralose-urethane anesthesia, the ventricles in their preparation were less contractile and therefore actually were failing. An alternative and intriguing explanation is that their type of stimulation may activate autonomic nerves to the systemic veins to a relatively greater degree than occurred in the experiments reported here, with resulting venoconstriction and shift of blood to the lesser circuit.

Of great interest were the larger rises in the pulmonary arterial than in pulmonary wedge mean pressures, with resulting increase in the pulmonary arterial-pulmonary wedge pressure gradient. The validation of the 1/3 rule for determining mean pressure in our preparation has been considered. In some experiments this was due to increase in both systolic and diastolic pressure; therefore, we are forced to suggest that as cardiac output or rate did not change, this represented pulmonary arterial vasoconstriction.

**SUMMARY**

Electric stimulation of the motor cortex of the dog's brain produced an acute systemic hypertension due to marked vasoconstriction, without change in cardiac output. Small increases occurred in right atrial, pulmonary atrial and pulmonary wedge pressures. Heart rate usually remained constant. A significant correlation was found between mean aortic and pulmonary wedge pressures at the peak of the hypertension. This finding
HYPERTENSION WITH CEREBRAL CORTICAL STIMULATION can be explained on the basis of the operation of Starling's law in the intact animal preparation used in this study.

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SUMMARIO IN INTERLINGUA

Le stimulation electric del cortice motori de cerebros canin produceva acute hypertension systemic in consequentia de marcate grados de vasoconstriction non accompagnate de alterationes del rendimento cardiac.

Parve augmentos occurreva in le pression dextero-atrial, pulmo-no-atrial, e pulmo-cuneate. Le frequentia cardiac remaneva generalmente constante.

Al culmine del hypertension un correlation significative esseva notate inter le valores medie del pression aortic e del pression pulmo-no-cuneate. Iste constatation pote esser explicate super le base del lege de Starling que es applicable al animales intacte usate como preparatos in le presente studio.

REFERENCES


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