Pressor Effect of Increased Cerebrospinal Fluid Pressure and Vertebral Artery Occlusion With and Without Anesthesia

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When the blood supply of the brain is reduced, systemic arterial pressure rises. The response depends neither on the peripheral arterial baroreceptors nor on higher centers, but only on the presence of the medulla and the sympathetic outflow tracts.

For many years this pressor effect of medullary ischemia has been regarded as merely a pathological curiosity, and this appraisal is reflected in the following recent statement: "By itself the ischemia of the medulla oblongata is not a physiological regulator but a pathological factor disturbing the activities of the nerve cells of the vasomotor center, leading to the destruction of the nerve cells. The slight and brief rise in the general blood pressure seen in total anemia is an agonal premortal phenomenon of not only the vasomotor center but also of other nuclei of the medulla oblongata."

A large number of observations have been made since those of Cushing of the pressor effects of increased cerebrospinal fluid (CSF) pressure. As CSF pressure approaches systemic arterial pressure (SAP) the latter rises in such a way that a constant difference between the two pressures is maintained. There is strong evidence that this response is mediated by medullary ischemia rather than by non-specific reactions such as stretching of the dura. If so, the pressor response to medullary ischemia cannot correctly be described as either "slight," "agonal" or "premortal," because these responses are both large and sustained.

The pressor response initiated by the isolated perfused head, connected to its trunk only by the spinal cord, has recently been quantitatively studied. Systemic arterial pressure began to rise after mean cerebral perfusion pressure had been reduced below a value which was found to lie between 40 and 70 mm Hg in different experiments. SAP increased exponentially as perfusion pressure was lowered still further. These observations bring the pressor response to cerebral ischemia almost within the physiological range of SAP, because the SAP of young human adults falls during deep sleep to about 100/60, equivalent to a mean arterial pressure of 70-75 mm Hg. They also strongly suggest that the cerebral ischemic pressor response is likely to be operating in man when the SAP is low, as after blood loss.

Anesthesia reduces oxygen consumption of the brain, probably mainly by affecting the grey matter, which has the highest metabolic rate. It occurred to us that anesthesia, which has been used in almost all experiments, might make the brain more tolerant of small reductions in blood flow (additional to the reduction in flow which anesthesia itself produces), and thus raise the threshold at which the pressor response could be obtained. Decerebrate animals subjected to graded increases of CSF pressure maintain their mean systemic arterial pressure at levels 30 to 90 mm Hg higher than their CSF pressure, whereas intact anesthetized animals only maintain differences of 10 to 30 mm Hg. This suggests that the decerebrate animal is less tolerant of medullary ischemia than is the anesthetized one.

To find the threshold of response in unanesthetized animals, we have relied mainly on alterations of CSF pressure to bring about comparable alterations in the effective perfusion pressure of the brain, but have also studied the response to vertebral artery occlusion.
PRESSOR RESPONSE TO CEREBRAL ISCHEMIA

Methods

Twenty-six mongrel dogs, including 18 males, were used for the CSF pressure studies. Mean weight was 11.9 kg. Except for a few experiments in which anaesthesia was maintained throughout, the normal procedure was to implant, at a single operation, a catheter into the aorta through the central cut end of the left vertebral artery, and also a Feldberg cannula into a lateral ventricle of the brain. The end of the catheter was brought out through a stainless steel "collar stud" which was sutured to the skin at the back of the neck. These procedures were carried out with aseptic precautions, and full surgical anaesthesia, using 30 mg/kg pentobarbital sodium. Between two and five days later, when the animals had recovered from the operation, a harness with two attached Statham strain gauge manometers was strapped on in a position so that both gauges were positioned just above the shoulders. One gauge was connected to the aortic cannula, and the other was joined both to the cannula in the ventricle and to a long, thin polythene tube which led to a graduated reservoir at the side of the room or outside it. The harness was letchored by a stout cord to a spring anchored to the ceiling. The leads from the two manometers, together with the thin polythene tube, were loosely tied to the cord as far as the ceiling, and then led to the side of the room or outside it. The dog was thus free to walk about the room within the limits of the spring and cord. The reservoir was filled with fluid, as was the Statham manometer and the tubing connecting this to the Feldberg cannula. By shifting the reservoir up and down it was possible to bring about slow alterations in intracranial pressure, and to check easily what absolute pressure was being applied at the level of the medulla. Sterile cerebrospinal fluid removed from patients undergoing lumbar encephalography was used in 12 experiments; in the remainder, sterile 0.9% w/v sodium chloride solution was used. No difference was found between the responses to the injection of the two fluids. Since fluid was injected only very slowly, and in small quantities, no attempt was made to bring the fluid to body temperature.

In experiments performed without anaesthesia, the dogs were fed and given water initially and, in most cases, also given a tranquillising drug (1
Effects of altered CSF pressure on mean systemic arterial pressure in lightly anesthetized dogs. Presentation of data as in figure 1.

to 1.5 mg/kg prochlorperazine into muscle or into aorta, to encourage sleep. CSF pressure was not altered until the animal was sitting or lying quietly on the floor, with its eyes closed. In some experiments the dog was alone in the room and observed through a peephole; in others, the experimenter remained with the animal throughout.

For experiments under light anesthesia, 5-20 mg/kg pentobarbital sodium were injected into the aorta, and for full surgical anesthesia a dose of 30 mg/kg was used. Anesthesia was maintained as necessary by intramuscular injections. In some experiments, performed with deep anesthesia, a needle was passed into the cisterna magna through the skin of the back of the neck. When injections were made by this route it was found essential to bring the fluid up to body temperature in a heated bath, because otherwise the rapid injection of cool fluid lowered arterial pressure. No such effect was seen when small volumes of fluid were injected slowly into the lateral ventricle through the indwelling cannula.

When possible, respiratory movements were recorded by a string passed round the chest and attached at each end to a strain gauge by which changes in tension could be detected. Heart rate was measured in some cases by an integrating device triggered from the fast upswing of the arterial pressure contour, or from the electrocardiogram in dogs sufficiently anesthetized to allow placement of needle electrodes. All measurements were thus converted into electrical changes, which were recorded by a 4-channel Sanborn 150 oscillograph.

Three dogs with chronic renal hypertension were prepared by wrapping one kidney in Cellophane and removing the other two weeks later. In one further dog, a Goldblatt clamp was applied to the main renal artery and the other kidney removed.

In five dogs (mean weight 13.8 kg including four males) both carotid sinuses were cut out between ligatures, and a catheter passed down the stump of one common carotid artery into the aorta. Cuffs of thin rubber or Cellophane tubing were tied round each vertebral artery. These were connected to fine polythene tubing, by which they could be inflated. The tubing led out of the neck through the incision made for the stainless steel "collar stud." These dogs were studied two to seven days after operation, in much the same way as has already been described, except that the thin polythene tube, in this case connected to both cuffs, was led to a pressure bottle and manometer by which any desired pressure could be transmitted.

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PRESSOR RESPONSE TO CEREBRAL ISCHEMIA

Respiration (inspiration down) on expanded time scale
Expanded time scale (mins and secs)
Respiration amplitude (chest excursion)

Mean aortic pressure (mm Hg)

CSF pressure (mm Hg)

Heart rate (beat/min)

Pentobarbital i.m.

Time (mins)

FIGURE 3
Lightly anesthetized dog, with anesthesia sustained, and gradually deepened, by intramuscular injections of 5 mg/kg sodium pentobarbital every 30 minutes. From above down: five samples of respiratory movements (shown on an expanded time scale below) recorded from a strain gauge round the chest; the same record of respiration on a different time scale covering the whole 3-hour period of observation; mean aortic pressure, electrically integrated; CSF pressure, recorded from a manometer connected to a Feldberg cannula, the tip of which lay in a lateral ventricle (see text for a discussion of the significance of the falling CSF pressure curve); heart rate; timing of anesthetic injections (each of which produces a small deflection in the arterial pressure trace); time in minutes (whole record extending over about three hours).

to the cuffs. This pressure was also continuously monitored by a Statham strain gauge.

Results
EXPERIMENTS IN WHICH CSF PRESSURE WAS ALTERED
Thirty-two observations were made in 11 fully anesthetized dogs of the effects on systemic arterial pressure of raising and lowering pressure in a lateral ventricle. All measurements were made after at least five minutes equilibration at the altered CSF pressure level, and longer time was allowed if the SAP was still changing. Figure 1 summarizes the results. It is obvious that increased CSF pressure brings about only small increases of SAP until a level of CSF pressure is reached some 10-30 mm Hg below mean SAP. From this point on, SAP rises in parallel with CSF pressure.

Twenty-four observations were made in seven dogs lightly anesthetized with sodium pentobarbital. Lower CSF pressures were used because otherwise the dogs became restless. Figure 2 summarizes all the results, and shows that although the responses at higher initial levels of SAP were similar to those obtained with full surgical anesthesia, they are different at lower initial pressure levels, since there is now an appreciable systemic arterial pressor response to moderate increase of CSF pressure. Figure 3 shows a typical record.

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It was possible to complete 21 observations on six unanesthetized dogs. In early experiments, no difference in response was seen between animals before and after they had been given prochlorperazine. This drug was therefore routinely used in all later experiments, since it made the dogs quiet and easy to study. The animals were usually fed, and then watched until they had settled down on the floor with their eyes closed. Measurements of SAP were rejected unless the animals remained quiet and in the same position throughout. At least five minutes were allowed for equilibration at each pressure level, and longer if the levels were changing. Figure 4 summarizes the results. It was not possible to raise CSF pressure above about 40 mm Hg because higher levels woke and disturbed the dogs. With patience, however, it was possible to make enough observations at lower pressure ranges to characterize the normal response, which was qualitatively the same as that obtained at higher CSF pressure levels in anesthetized animals. Figures 5 and 6 show typical records, both extending over several hours. The systemic pressor response to a moderately increased CSF pressure is of gradual onset, taking one half to two minutes to begin, and sometimes several more minutes to develop fully. It tends to dwindle after several hours, during which dogs become more tolerant of raised CSF pressure, although the pressor response can still be restored by a further increase in CSF pressure. Figures 3, 5, and 6 suggest that the response, once initiated, outlasts the stimulus for about half an hour. This impression is misleading, and is created by an unavoidable artefact of CSF pressure recording. When a Feldberg cannula has been freshly inserted, it allows free movement of fluid in and out. The systemic arterial pressor responses to alterations of intracranial pressure are the same whether brought about from a lateral ventricle or from the cisterna magna. However, after a few days in situ, and particularly after CSF has been let in and out a few times, the cannula develops a thin, fibrous film across its tip. This allows fluid to enter freely, but prevents free exit. At the conclusion of the experiments shown in figures 3 and 5, a full anesthetic dose of pentobarbital was given, and intracisternal pressure was recorded while raising and lowering the pressure applied to the Feldberg cannula. Although intracisternal pressure rose in parallel with lateral ventricle pressure, when the applied pressure was removed, the intracranial pressure fell exponentially over a period of about half an hour. Thus there is every reason to suppose that the observed changes in systemic arterial pressure correspond fairly closely to the changes in intracranial pressure, whether the latter is rising or falling. Heart rate in all these experiments either increased slightly or did not change, unless CSF pressure was rapidly brought close to the mean SAP, in which case the well-known bradycardia was seen. Respiration was sometimes unaffected, but most commonly there was a small increase in depth and rate which reverted towards normal as the SAP rose. Large and rapid elevations of CSF pressure produced the familiar apnoea.

Four dogs with chronic renal hypertension were also studied in a similar way, with results which are summarized in figure 7. No remarkable difference in response was seen, and if anything such animals were less than

Circulation Research, Volume XII, February 1968
PRESSOR RESPONSE TO CEREBRAL ISCHEMIA

Unanesthetized dog given prochlorperazine (1.5 mg/kg) observed during five and one-half hours. From above down: CSF pressure (recorded as in figure 3; letter s indicates times at which the dog was standing up); aortic pressure; integrated mean aortic pressure; time in minutes.

Normally responsive to increased CSF pressure. This was especially notable in one dog whose mean arterial pressure, previously 170 mm Hg by femoral puncture, settled to about 100 mm Hg when resting quietly. The only exception was one animal with a very high arterial pressure and subconjunctival hemorrhages. This dog seemed very sensitive to the depth of anesthesia and showed variable responses at different times (fig. 7, panel B).

CONTROL EXPERIMENTS

Experiments were performed to test the present consensus of opinion that the pressor response to increased CSF pressure is the result of cerebral ischemia. Figure 8 shows one of three experiments in which bilateral vertebral artery occlusion, itself insufficient to raise arterial pressure, augmented the response to a standard increase of CSF pressure. In two further experiments it was observed that an infusion of angiotensin raised the threshold of response to a given increase of CSF pressure (fig. 9). Other experiments were performed to check the possibility that the systemic arterial pressor response might have been produced simply by mechanical obstruction of a large vascular bed by the increased intracranial pressure. After paralysis of the sympathetic nervous system by tetraethylammonium chloride (10 mg/kg) increase of CSF pressure to a level exceeding SAP did not produce a significant pressor response. Indeed, the SAP eventually fell with concurrent slowing of heart rate. Two dogs were subjected to spinal cord transection at level C_0 one and seven days prior to the experiment. Again there was no significant pressor response with light anesthesia.
Atropine (0.2 mg/kg) prevented the fall of blood pressure by preventing the slowing of heart rate. The lack of response after cord section was not due simply to the low level of blood pressure, because the response was still absent even when SAP was raised to normal levels by a continuous infusion of synthetic angiotensin II. In a conscious dog, whose cord had been sectioned at C2 24 hours previously, raised intraventricular pressure also did not appreciably raise the systemic arterial pressure.

In lightly anesthetized dogs after autonomic blockade with tetraethylammonium, and after spinal cord section, we observed a rise of SAP, accompanied by tachycardia, after the cerebral circulation had been restored by lowering CSF pressure. We provisionally interpret this response to mean that the totally ischemic brain produces a chemical substance which is swept into the blood stream when perfusion is restored. The effect tended to diminish and to disappear after one or two occlusions, and we did not further investigate it.

EXPERIMENTS IN WHICH VERTEBRAL ARTERIES WERE OCCLUDED

In five dogs we implanted inflatable vertebral artery cuffs, and cut out both carotid sinuses. These animals were studied two to seven days later, both in the conscious state, and when lightly and deeply anesthetized.

In two dogs no significant responses were seen: in these the vertebral arteries were narrowed and almost occluded by blood clots attached to the cuffs. Records were obtained from the remaining three dogs. No useful conclusions could be derived from experiments without anesthesia, because it was difficult to grade the degree of obstruction to the
arteries. Cerebral ischemia tended to occur suddenly, with the result that the dogs woke up and became excited, thereby rendering systemic arterial pressor responses meaningless. In one dog, inflating the cuffs produced reversible quadriplegia, together with an enormous rise in blood pressure. To avoid these difficulties, light anesthesia was used, with 10 mg/kg pentobarbital and 1 mg/kg prochlorperazine. Under these circumstances the height of the pressor response depended on the initial level of blood pressure, and was also influenced by the respiratory response.

Figure 10 is a typical record in which, at a mean systemic arterial pressure of about 80 mm Hg, small sustained increases in mean SAP were accompanied by small increases in the rate and depth of breathing. Figure 11 shows an animal in which the initial arterial pressure had been lowered by bleeding. The respiratory response was enormous, and dwarfed the small pressor effect. However, in figure 12, which is a comparable record from another animal whose pressure was lowered by controlled bleeding, the pressor response is dominant. The long sustained elevations of SAP towards the end of the record are accompanied at first by an increase in the rate and depth of breathing; but when the SAP is stabilized, the pattern of breathing is not appreciably different from that observed while the pressure was low and the cuffs deflated. Figure 12 shows not only that the pressor response to vertebral artery occlusion can be sustained without decrement for at least 30 minutes, and can be repeated over and over again, but also shows that the effect is not a mechanical one due to large artery obstruction. In this animal a cuff was put round the femoral artery, under local anesthesia, and inflations of this cuff are recorded at the signals “F.” No pressor response is seen.

In two animals the response to inflating the vertebral artery cuffs was observed before and after flooding the region of the cuffs with 1% procaine by means of auxiliary tubes attached to the cuffs. No difference in response was seen, and we therefore believe that the effects seen have been due to cerebral ischemia rather than to local stimulation of pain or stretch receptors.

Discussion

It seems likely that the pressor effects we have observed when increasing CSF pressure are due to a reduction of cerebral blood flow rather than to the stimulation of pain receptors by stretching of the dura or to mecha-
FIGURE 8
Summating effect on systemic arterial pressure of bilateral vertebral artery occlusion and increased CSF pressure. From above down: respiratory movements; heart rate; mean femoral artery pressure; CSF pressure (altered by means of an intracisternal needle); time in minutes. The vertebral arteries had been occluded for ten minutes before the start of the record: thereafter the periods of occlusion are shown by the solid bars on the time scale. CSF pressure was raised to the same mean value in every case: the mean SAP rose higher whenever the vertebral arteries were occluded at the same time. Carotid arteries and sinuses intact.

cal displacement of brain structures. This interpretation is supported by several observations.

1. The response to a threshold stimulus is lost if SAP is raised by an infusion of angiotensin (fig. 9) thus confirming previous observations of the effects of epinephrine infusion. Animals with chronic renal hypertension are probably less responsive than normal to increased CSF pressure (fig. 1), perhaps because of their high initial SAP. Cushing observed that an initially low SAP makes the brain more sensitive than usual to small increments of CSF pressure. These results suggest that the absolute level of applied CSF pressure is unimportant, and that the pressor response depends only on the difference between applied CSF pressure and mean SAP.

2. Vertebral artery occlusion, itself ineffective in raising blood pressure when the carotid arteries are intact, can augment the pressor response to increased CSF pressure (fig. 8). This suggests, but does not prove, that the effects of increased CSF pressure are mediated by cerebral ischemia.

3. The circulatory and respiratory changes obtained by increasing CSF pressure are similar to those obtained by occluding the vertebral arteries. The lack of any notable difference in response favors an identical effector mechanism.

4. Although we did not measure cerebral blood flow in these experiments, it is known from the work of others that increased CSF pressure reduces cerebral blood flow in proportion to the applied CSF pressure. The same relation has been found in patients whose cerebral tumors had brought about sustained increases of CSF pressure.

If we assume, therefore, that increased CSF pressure operates by reducing cerebral blood flow (more specifically, medullary blood flow) it appears that the pressor response to medullary ischemia may begin in unanesthetized animals within the range of SAP which normally obtains in sleep. The gradual rise in

FIGURE 9
The effect of an angiotensin infusion on the threshold of pressor response to increased CSF pressure. The solid bar on the time scale indicates the period during which pure synthetic angiotensin was infused at a constant rate sufficient to raise mean aortic pressure about 20 mm Hg. During the whole period of infusion, the CSF pressure had to be increased by about 20 mm Hg to produce a pressor response of comparable magnitude to that obtainable before the infusion began.
PRESSOR RESPONSE TO CEREBRAL ISCHEMIA

FIGURE 10

Response to bilateral vertebral artery occlusion in a lightly anesthetized dog whose carotid sinuses had previously been excised. From above downwards: respiratory movements; aortic pressure; integrated mean aortic pressure; vertebral cuff pressure (in the intervals between cuff compression a negative pressure was maintained at the cuffs to ensure that they remained collapsed); time in minutes.

the threshold of response which is seen in the course of prolonged experiments in unanesthetized dogs (e.g. figs. 5 and 6) is partly due to the progressive increase in systemic arterial pressure which always occurs. However, the effect cannot be wholly explained in

FIGURE 11

Record as in figure 10, taken from another experiment in which the respiratory response was dominant. In this animal the mean systemic arterial pressure was initially lowered by controlled bleeding (shown at 'B' at the bottom left corner).

this way. One possibility is that collateral anastomotic channels open up so that cerebral blood flow is restored. Reactive hyperemia of the brain can be demonstrated if CSF pressure is suddenly reduced after it has been increased for longer than a few minutes. When cerebral perfusion pressure is initially low, the pressor response to cerebral ischemia can be sustained without decrement as illustrated in figure 12 (last hour).

The results obtained by Kety et al. suggest that in patients with brain tumors, SAP is raised in strict proportion to the elevation in intracranial pressure and to the consequent
reduction in cerebral blood flow. It thus seems possible that a sustained increase of cerebrovascular resistance may eventually produce a sustained increase in SAP, perhaps because the effects of an increased collateral circulation are offset by the known tendency of the peripheral arterial baroreceptors to adapt to long-continued hypertension. A great deal of work has been done on hypertension produced in animals by intracisternal injection of kaolin, which is thought to act by increasing CSF pressure. However, the results have been inconclusive, because the CSF pressures have rarely been measured and because the degree of hypertension was slight. Unfortunately it is difficult to restrict permanently the cerebral blood supply of experimental animals, owing to the development of anastomotic channels.

Reference should be made to two series of observations made on unanesthetized human patients subjected to increased CSF pressure. Browder and Meyers state that SAP does not rise under these conditions. However, their results show some increase of blood pressure above resting level in all cases, even though the increases were small, as in some of our experiments. Their work is difficult to interpret because most of their patients had cranial defects which may have altered the effects of CSF pressure on medullary blood flow. Evans et al. also claim negative results, but most of their observations were made over too short a time to allow development of a pressor response. In neither of these series were observations made with the subjects asleep or in a fully relaxed state—conditions we have found necessary for consistent results in dogs.

We made a limited investigation of chronic renal hypertension in dogs with the idea that perhaps a renal humoral substance might constrict the small cerebral arteries and thus, under some circumstances, provide a big enough increase of cerebrovascular resistance to limit the lower level of blood pressure by a neurogenic mechanism. This might have provided a much needed link between the kidney and the brain. Preliminary tests showed that angiotensin causes essentially the same rise of blood pressure whether infused into the vertebral arteries or into the aorta (unpublished observations of Dickinson and McCubbin). This was not encouraging; and our later observations in chronic renal hypertension (fig. 7) also lend no support to this idea, and suggest that animals with chronic renal hypertension are, if anything, less than normally sensitive to a given fall in cerebral perfusion pressure. This may be simply because the initial pressure is high; the difference is not sufficiently marked to suggest useful clinical applications.

In normal animals, however, the possibility should now be considered that impending cerebral ischemia may set a lower limit to which blood pressure can fall during sleep. If so, some forms of high blood pressure in man might be initiated by a fixed, unrelaxable increase in cerebrovascular resistance, such as that already observed to be present in the larger arteries at necropsy in cases of 'essential' hypertension. We know that severe cerebral ischemia can occur in man, because he commonly suffers from spontaneous cerebral infarction, which animals, other than the giraffe, do not.

A theoretical objection to this concept is that respiratory stimulation has occasionally exceeded the pressor response (e.g. fig. 11) although more often it has been less and has sometimes been undetectable, (fig. 3), providing that CSF pressure has been raised slowly enough. Presumably similarly conflicting signals can be set up in the central respiratory control centers as can be set up in the vasomotor centers, because the local signal due to ischemia will be opposed by information from the peripheral chemoreceptors that ventilation is excessive. It is difficult to guess what the net response of these diverse influences might be over a long period of time. However, it appears that a pressor response without significant stimulation of respiration is the commonest pattern of reaction.

Our failure to find slowing of cardiac rate with moderate increase of CSF pressure confirms many previous reports. The well-known bradycardia only occurs consistently when brain stem ischemia is sudden and severe.
Cushing quoted the case of a patient with a slowly expanding intracranial lesion, whose blood pressure rose without change in pulse rate or respiration: "As in the experimental conditions, when the intracranial tension about the bulb is slowly and gradually brought to the neighborhood of the blood pressure the latter may rise to counteract its effects, without the production of the slow vagus pulse and deliberate respiration almost invariably seen in more rapid processes."

**Summary**

The intracranial pressures of conscious, lightly anesthetized and fully anesthetized dogs were altered by means of previously implanted intraventricular cannulas, while systemic arterial pressures were simultaneously measured. One vertebral artery was occluded in all these experiments by the catheter used to record aortic pressure. Increased intracranial pressure, which probably acts by reducing cerebral blood flow, caused a rise in systemic arterial pressure whose magnitude depended on the presence and depth of anesthesia. When anesthesia was not used, but when the animals were resting quietly, a significant pressor response occurred within the physiological range of CSF pressure. The response was typically of slow onset, developing over a period of one half to two minutes. It was reproducible, but tended to diminish gradually in the course of several hours if the experiment was continued, although it could be restored if CSF pressure was further increased.

The pulse rate tended to increase slightly,
or remain the same, providing CSF pressure was not increased too greatly or too rapidly. Respiratory effects were variable, but most commonly a slightly increased rate and depth of respiration occurred at first, with a return towards normal as the systemic arterial pressure rose.

Similar responses were seen during bilateral artery occlusion, by means of previously implanted inflatable cuffs, in dogs whose carotid sinuses had been excised. These effects were also slow in onset, and were accompanied by comparable respiratory changes. In anesthetized animals with intact carotid arteries, bilateral vertebral artery occlusion produced negligible pressor effects, but was found to augment the response to increased intracranial pressure.

Observations in four dogs with chronic experimental renal hypertension did not reveal notable differences, except that these animals may be less sensitive than normal to increases in intracranial pressure.

The results of these experiments are compatible with the hypothesis that basal systemic arterial pressure during sleep in some degree depends on the cerebrovascular resistance, although it will be important to determine the nature of the slow adaptation seen in these experiments. If this adaptation is brought about by compensatory cerebral vasodilation, this investigation is in accord with the concept of Dickinson and Thomson that some forms of chronic high blood pressure in man might be initiated by cerebral artery occlusion or narrowing of sufficient severity and extent to prevent adequate compensatory vasodilation.

References
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