Raised intracranial pressure and cerebral blood flow

2. Supratentorial and infratentorial mass lesions in primates

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SUMMARY Changes in cerebral blood flow with increasing intracranial pressure were studied in anaesthetized baboons during expansion of a subdural balloon in one of two different sites. With an infratentorial balloon, cerebral blood flow bore no clear relation to intracranial pressure, but was linearly related to cerebral perfusion pressure. Apart from an initial change in some animals, cerebrovascular resistance remained constant with increasing intracranial pressure, and autoregulation appeared to be lost from the outset. With a supratentorial balloon, cerebral blood flow remained constant as intracranial pressure was increased to levels around 60 mmHg, corresponding to a cerebral perfusion pressure range of approximately 100 to 40 mmHg. Cerebrovascular resistance fell progressively, and autoregulation appeared to be effective during this phase. At higher intracranial pressure levels (lower cerebral perfusion pressure levels), autoregulation was lost and cerebral blood flow became directly dependent on cerebral perfusion pressure. The importance of the cause of the increase in intracranial pressure on the response of the cerebral circulation and the relevance of these findings to the clinical situation are discussed.

In a previous study the effect of raised intracranial pressure on cerebral blood flow was examined during infusion of fluid into the cisterna magna of anaesthetized baboons (Johnston, Rowan, Harper, and Jennett, 1972a). Three sequential phases were observed; an initial phase in which cerebral blood flow remained relatively constant (intracranial pressure 0–50 mmHg), a phase of hyperaemia (intracranial pressure 50–85 mmHg), and finally a phase in which cerebral blood flow fell progressively with further increase of intracranial pressure (intracranial pressure > 85 mmHg). These observations differ from previous reports and add to the already considerable variation in both clinical and experimental findings on the effects of raised intracranial pressure on cerebral blood flow (Kety, Shenkin, and Schmidt, 1948; Greenfield and Tindall, 1965; Langfitt, Kassell, and Weinstein, 1965; Zwetnow, 1970; Lowell and Bloor, 1971). The clinician, measuring intracranial pressure or even cerebral perfusion pressure, lacks, therefore, a secure basis from

which to draw quantitative conclusions about cerebral blood flow in states of intracranial hypertension.

The response of the cerebral circulation to raised intracranial pressure will depend, in general terms, on changes in perfusion pressure and vascular resistance. Such changes will themselves be influenced by factors such as the cause and time course of the increase in intracranial pressure. It is therefore unrealistic to attempt to define a single type of quantitative relationship between either intracranial pressure or cerebral perfusion pressure and cerebral blood flow. Attention should be directed to the different patterns of response of the cerebral circulation which may be evoked by different forms of intracranial hypertension.

The aim of the present study has been to examine changes in cerebral blood flow occurring during increased intracranial pressure due to a focal mass in either the supratentorial or the infratentorial subdural space. The effect of the site of the lesion on the response of the

cerebral circulation has been interpreted in terms of changes in cerebral perfusion pressure, cerebrovascular resistance and autoregulatory function.

METHODS

Baboons weighing between 9.5 and 12.5 kg were used. Anaesthesia was induced with phencyclidine hydrochloride (10 mg) and thiopentone sodium (60 mg), and maintained with phencyclidine hydrochloride, suxamethonium chloride, and nitrous oxide/oxygen mixture. Controlled ventilation was continued throughout using a Starling pump delivering a tidal volume between 150 and 250 ml., adjusted to maintain an arterial $p\text{CO}_2$ of approximately 40 mmHg. A continuous slow intravenous infusion of 0.9% saline was given during each experiment. The following parameters were measured.

INTRACRANIAL PRESSURE This was measured continuously from a polyethylene cannula inserted into the right lateral ventricle via a twist drill hole 1 cm lateral to the bregma. In the majority of animals cerebrospinal fluid pressure was also recorded from either the cisterna magna or the lumbar subarachnoid space via a polyethylene cannula inserted under direct vision. Pressures were measured using strain gauge transducers (Bell and Howell), calibrated against a mercury column and recorded on standard two-channel paper chart recorders (Devices).

CEREBRAL BLOOD FLOW Two methods were used: (1) a series of ^{133}Xe clearance curves were obtained at approximately 30 minute intervals. A slug injection of 0.5 mCi ^{133}Xe , dissolved in 0.45 to 0.55 ml. saline at constant temperature, was given via a polyethylene cannula in the proximal stump of the right lingual artery (the external carotid artery having been ligated). The rate of clearance of gamma activity was measured using a collimated 1 in. sodium iodide crystal detector placed over the right parietal region. Cerebral blood flow was calculated from the initial slope and by the height over area technique using the 10 minute correction. (2) An electromagnetic flow probe (Nycotron) was placed on the exposed right common carotid artery after ligation of the external carotid artery.

OTHER PARAMETERS Systemic arterial pressure was measured using a polyethylene catheter placed in the abdominal aorta via the left femoral artery. Superior sagittal sinus and jugular venous pressures were monitored in some experiments from indwelling catheters. Both these and the arterial pressure were

measured using the same type of recording system as that used for the intracranial pressure. Arterial $p\text{CO}_2$, $p\text{O}_2$, and pH values were estimated immediately before each injection of ^{133}Xe . End tidal CO_2 was continuously monitored using an infra-red analyser (Capnograph). Arterial packed cell volume (PCV) and haemoglobin levels were estimated at intervals throughout each experiment.

INCREASE OF INTRACRANIAL PRESSURE Intracranial pressure was raised by adding small quantities of fluid to a latex balloon at approximately 30 minute intervals, each addition of fluid being adjusted to raise the intracranial pressure by 10 to 20 mmHg. All experiments were continued until the cerebral blood flow became too low to record accurately.

Two series of experiments were carried out according to the site of the subdural balloon:

1. *Infratentorial series* (five animals) The balloon was placed over the lateral aspect of the right cerebellar hemisphere through a laterally placed suboccipital burr hole.

2. *Supratentorial series* (five animals) The balloon was placed over the parietal region of the left cerebellar hemisphere via a parietal convexity burr hole.

In all experiments the cranial defects were sealed with dental cement after balloon placement. At the end of each experiment the position of the balloon was checked by post-mortem examination to establish that it had not impinged directly on any major blood vessels or caused intracranial haemorrhage.

RESULTS

The levels of intracranial pressure reached before there was a marked reduction of cerebral blood flow differed according to the site of the balloon. In those animals with an infratentorial balloon blood flow fell at an earlier stage of increasing intracranial pressure (38–77 mmHg) than those with a supratentorial balloon (42–131 mmHg). In addition, the volume of fluid added to the balloon to reach these levels of intracranial pressure was less in the infratentorial group (approximately 5 ml.) than in the supratentorial group (14–22 ml.). Both groups of animals showed a marked transient blood pressure response with each addition of fluid to the balloon. The relation of this hypertensive response to the level of intracranial pressure and

FIG. 1. Relationship between intracranial pressure (ICP) and cerebral blood flow (CBF): Data from all five experiments in each group. (a) Infratentorial balloon. (b) Supratentorial balloon.

the presence of intracranial pressure gradients have been described in detail elsewhere (Johnston, Rowan, Harper, and Jennett, 1972b).

Control levels of cerebral blood flow, intracranial pressure, blood pressure, and other parameters were similar in the two groups. The relationship between the observed changes in cerebral blood flow and intracranial pressure, cerebral perfusion pressure and cerebrovascular resistance, together with observations on autoregulatory function will be considered separately for the two groups of animals.

INFRATENTORIAL BALLOON *Intracranial pressure and cerebral blood flow* No clear relationship between intracranial pressure and cerebral blood flow emerged in this group of animals. The variability of the overall relationship between these two parameters is exemplified in Fig. 1a, which plots cerebral blood flow ($^{133}\text{Xenon}$ clearance) against intracranial pressure for all cerebral blood flow measurements in this group. It can be seen that both high and low cerebral blood flow values occurred, in different animals, at relatively low levels of intracranial pressure,

FIG. 2. Relationship between cerebral perfusion pressure (CPP) and cerebral blood flow (CBF): Data from all five experiments in each group. (a) Infratentorial balloon. (b) Supratentorial balloon.

FIG. 3. Corresponding changes in cerebral perfusion pressure (CCP) and internal carotid artery blood flow (arbitrary units) with the transient blood pressure response at time of balloon inflating (infratentorial balloon).

FIG. 4. Changes in cerebrovascular resistance (CVR), with increasing intracranial pressure (ICP). (a) Infratentorial balloon. (b) Supratentorial balloon.

and the level of intracranial pressure at which a significant and sustained reduction of blood flow occurred was also quite variable. Thus, reduction of blood flow to values of less than 30 ml./100 g/min was associated with a wide range of intracranial pressure levels from 7 to 74 mmHg. A further feature in this group was the relatively low level of intracranial pressure at which cerebral blood flow had fallen to negligible levels or had ceased altogether. The actual intracranial pressure levels at which this occurred were 38, 45, 47, 37, and 77 mmHg respectively in the five experiments.

Cerebral perfusion pressure and cerebral blood flow The relationship between cerebral perfusion pressure and cerebral blood flow was quite uniform, in contrast with that between intracranial pressure and cerebral blood flow described above. A linear relationship was found between these two variables when all cerebral blood flow values were plotted against the corresponding cerebral perfusion pressure values for the five experiments in this group (Fig. 2a). The close correlation between cerebral perfusion pressure and cerebral blood flow was particularly apparent during the marked transient increases in blood pressure which occurred with each injection and could be associated with relatively little change in intracranial pressure. During these changes, cerebral blood flow increased and the flow changes, as measured by the common carotid artery flow probe, exactly paralleled the changes in blood pressure and cerebral perfusion pressure (Fig. 3). The substantial alterations in blood pressure, both hypertension and hypotension, which were prominent in this group of animals, together with the close correlation between cerebral blood flow and cerebral perfusion pressure, help to explain the considerable variability in the relationship between intracranial pressure and cerebral blood flow.

Cerebrovascular resistance Values of cerebrovascular resistance in this group tended to remain relatively constant over an approximate intracranial pressure range of 10 to 60 mmHg. In two of the five animals there was an initial increase in cerebrovascular resistance with the first increase in intracranial pressure, this being

followed by a sharp reduction in resistance to a relatively constant level during the remaining increase in intracranial pressure. A further two animals showed only an initial sharp fall in cerebrovascular resistance before reaching a relatively constant level, while the remaining animal maintained a relatively constant cerebrovascular resistance before a final fall. These changes are shown in Fig. 4a. The overall pattern was, therefore, one of quite pronounced initial changes in cerebrovascular resistance, followed by maintenance of a relatively constant level as intracranial pressure was increased through the range from 10 to 60 mmHg.

Autoregulation If the relationship between cerebral perfusion pressure and cerebral blood flow be accepted as an indication of autoregulatory function, it would seem that autoregulation was lost from the time of the first addition of fluid to the infratentorial balloon in all five animals in this group. The relationship between cerebral perfusion pressure and cerebral blood flow was approximately linear for each animal, as with the composite curve from all five experiments (Fig. 2a). Evidence for the loss of autoregulation is also to be found in the close correspondence between the transient increases in blood pressure, cerebral perfusion pressure and cerebral blood flow which occurred with each addition of fluid to the balloon (Fig. 3). Substantial changes in supratentorial intracranial pressure during the blood pressure increases in the later stages of each experiment presumably reflect a passive increase in cerebral blood volume associated with the change in cerebral perfusion pressure. Apart from the site of the balloon, the preparation and anaesthetic were identical in the two groups of animals in the present study and also in the previously reported study (Johnston *et al.*, 1972). In the other groups autoregulation was intact, at least until the later stages of cerebral compression, so it seems unlikely that loss of autoregulation can be attributed to factors other than the site of the balloon.

Summary There was no clear relationship between intracranial pressure and cerebral blood flow with expansion of an infratentorial balloon in this group of animals; a marked reduction of

FIG. 5. Changes in intracranial pressure (ICP), blood pressure (BP), and internal carotid artery blood flow with addition of 0.5 ml. saline to supratentorial balloon at arrow. (Carotid artery flow in arbitrary units approximating to ml./100 g/min.)

cerebral blood flow occurred over a wide range of intracranial pressure. In contrast, cerebral perfusion pressure and cerebral blood flow were closely related. This applied both to the transient changes in blood pressure and cerebral perfusion pressure, which occurred with each addition of fluid to the balloon (Fig. 3), and to the whole period of increased intracranial pressure (Fig. 2a). After quite marked initial changes cerebrovascular resistance tended to remain relatively constant with further increase of intracranial pressure after the initial balloon expansion. These findings suggest that auto-regulation was lost from the time of the first expansion of the balloon.

SUPRATENTORIAL BALLOON Intracranial pressure and cerebral blood flow A relatively uniform relationship between intracranial pressure and cerebral blood flow was seen during expansion of the supratentorial balloon, in contrast to the findings with the infratentorial balloon (Fig. 1b). In all five animals cerebral blood flow was maintained during the initial phase of intracranial hypertension. Beyond a certain level of intracranial pressure, however, cerebral blood flow began to fall with further increase of intracranial pressure. The range of intracranial pressure at which a greater than 10% reduction of cerebral blood flow from the mean control levels had occurred was, however, wide (41–131 mmHg). The range was much narrower (41–61 mmHg),

if the one animal which showed exceptional preservation of cerebral blood flow to a high level of intracranial pressure is excluded. This single exception nevertheless illustrates the considerable variation which can occur, even in this group. The levels of intracranial pressure at which cerebral blood flow had fallen to negligible levels, or had ceased altogether, were higher than those seen in the infratentorial group; 55, 131, 75, 79, and 32 mmHg respectively in the five experiments. The last value of 32 mmHg occurred in an animal in which the mean arterial pressure dropped sharply to around 40 mmHg at the time of the major reduction in cerebral blood flow.

Cerebral perfusion pressure and cerebral blood flow The relationship between cerebral perfusion pressure and cerebral blood flow was also relatively uniform in this group, the flows never falling more than 10% below control levels over a cerebral perfusion pressure range of 32 to 108 mmHg (Fig. 2b). The levels of cerebral perfusion pressure at which cerebral blood flow fell below 30 ml./100 g/minute were 32, 36, 45, 54, and 64 mmHg in each of the five experiments. In addition, during the transient changes in cerebral perfusion pressure caused by the transient hypertensive episodes at the time of each balloon inflation, cerebral blood flow (as measured by the common carotid flow probe) remained constant in most instances—apart

FIG. 6. Comparison of mean cerebral blood flow (CBF) values for 20 mmHg ranges of cerebral pressure (CPP) with infratentorial balloon (left) and supratentorial balloon (right).

from a 30 second fall before autoregulation became effective (Fig. 5). During the later period of each experiment, when cerebral blood flow had started to fall significantly, transient blood pressure and cerebral perfusion pressure changes were, however, reflected in corresponding changes in cerebral blood flow.

Cerebrovascular resistance Changes in cerebrovascular resistance in this group of animals were also in contrast to those seen in the previous group (Fig. 4b). Cerebrovascular resistance tended to fall progressively as intracranial pressure increased through an approximate range from 10–60 mmHg. This fall was associated with a relatively constant level of cerebral blood flow. Beyond this range of intracranial pressure in three animals cerebrovascular resistance remained constant or rose slightly while in the remaining two animals cerebrovascular resistance continued to fall. The overall pattern in this group was, therefore, one of a progressive fall in cerebrovascular resistance with increasing intracranial pressure, with the resultant preservation of a relatively constant level of cerebral blood flow.

Autoregulation With expansion of a supratentorial balloon autoregulation remained effective as intracranial pressure was increased up to a level of approximately 60 mmHg (Fig. 1b). This corresponded to a range of cerebral perfusion pressure of approximately 40–100 mmHg (Fig. 2b). Effective autoregulation was seen during the marked transient changes in intracranial pressure and blood pressure which occurred at the time of each balloon inflation (Fig. 5). As the cerebral perfusion pressure fell below 40 mmHg autoregulation appeared to be lost and cerebral blood flow then became linearly dependent on cerebral perfusion pressure. This loss of autoregulation did not occur as a sudden transition but seemed to take place progressively over a relatively narrow range of decreasing cerebral perfusion pressure, around the levels indicated above.

Summary A relatively uniform relationship between cerebral blood flow and intracranial pressure was seen with expansion of a supratentorial balloon, blood flow being maintained around control levels over a range of intracranial pressure up to approximately 60 mmHg.

Similarly cerebral blood flow remained quite constant over a wide range of cerebral perfusion pressure down to approximately 40 mmHg (Fig. 6). During this phase of intracranial hypertension transient changes in blood pressure and cerebral perfusion pressure which occurred with each addition of fluid to the balloon were associated with only very transient changes in cerebral blood flow (Fig. 5). The maintenance of a constant level of cerebral blood flow as intracranial pressure was increased was associated with a progressive fall in cerebrovascular resistance. These findings suggest that autoregulation remained effective within the ranges of intracranial pressure and cerebral perfusion pressure indicated. Beyond these levels autoregulation was progressively lost and blood flow became directly dependent on cerebral perfusion pressure.

DISCUSSION

The present results, together with those of the previous study (Johnston *et al.*, 1972) show that changes in cerebral blood flow which occur with raised intracranial pressure depend on the way in which intracranial pressure is increased. With infusion of fluid into the subarachnoid space three phases were seen. Up to intracranial pressure levels of approximately 50 mmHg, cerebral blood flow remained constant. At intracranial pressure levels between 50 and 85 mmHg, a period of hyperaemia occurred with considerable increase in cerebral blood flow. With further increase of intracranial pressure a progressive fall in cerebral blood flow took place and flow appeared to be directly dependent on cerebral perfusion pressure. In the present study, with expansion of an infratentorial subdural balloon, cerebral blood flow bore no clear relationship to intracranial pressure. Both high and low cerebral blood flow values were recorded through a wide range of intracranial pressure. Cerebral blood flow in animals with an infratentorial balloon did, however, correlate closely with cerebral perfusion pressure throughout, the relationship between these two parameters being almost linear. Raising intracranial pressure by expansion of a supratentorial subdural balloon produced a third type of response: cerebral blood flow being maintained at a relatively constant level through a wide range of both intracranial

pressure (0–60 mmHg) and cerebral perfusion pressure (100–40 mmHg). Beyond these levels blood flow became progressively more directly dependent on cerebral perfusion pressure. The differing relationships between cerebral blood flow and cerebral perfusion pressure with the two balloon sites are contrasted in Fig. 6. These observations, using different methods of raising intracranial pressure under the same basic experimental conditions and over the same periods of time, help to explain the variability which is such a feature of previous experimental and clinical studies of the inter-relationship between intracranial pressure and cerebral blood flow (Kety *et al.*, 1948; Greenfield and Tindall, 1965; Huber, Meyer, Handa, and Ishikawa, 1965; Langfitt *et al.*, 1965; Zwetnow, 1970; Lowell and Bloor, 1971).

It seems, therefore, that the mechanisms which control cerebral blood flow behave differently according to the cause of the increase in intracranial pressure. The two major factors controlling cerebral blood flow are the *cerebral perfusion pressure*, defined as the difference between the mean systemic arterial pressure and the mean intracranial pressure (Zwetnow, 1968) and the *cerebrovascular resistance*, defined as the ratio of cerebral perfusion pressure to cerebral blood flow. Both factors may be influenced by a wide variety of further factors. Quite apart from this the definitions themselves depend on certain assumptions, some of which may be open to question. It is probable that it is in the differing effects which different methods of raising intracranial pressure have on these factors that the explanation of the variability in previous observations is to be found.

The level of cerebral perfusion pressure at a particular level of intracranial pressure depends on the level of systemic arterial pressure. The time course and magnitude of the response differed according to the method used to increase intracranial pressure so that at a given level of intracranial pressure cerebral perfusion pressure differed in each type of intracranial hypertension. Further, the definition of cerebral perfusion pressure depends on two assumptions; firstly, that the mean arterial pressure represents the effective cerebral arterial inflow pressure, and, secondly, that intracranial pressure represents the effective venous outflow pressure. It is

probable that neither of these assumptions is completely justified. The magnitude of the arterial pressure drop between extra- and intracranial vessels may vary, in states of raised intracranial pressure, both with changes in arterial pressure and with changes in intracranial pressure (Kanzow and Dieckhoff, 1969). The approximation of the intracranial pressure to the effective venous outflow pressure may also differ according to the level of intracranial pressure. A close correlation is known to exist between intracranial pressure and cortical subarachnoid vein pressure over the lower ranges of intracranial pressure (Shulman, 1965; Shulman and Verdier, 1967). This relationship has not yet been explored, however, for the higher ranges of intracranial pressure, although such an investigation is being carried out in this laboratory. In addition, marked morphological changes have been observed in the major dural venous sinuses in extreme intracranial hypertension (Wright, 1938; Kinal, 1964; Shapiro, Langfitt, and Weinstein, 1966; Osterholm, 1970). Such changes may have an important bearing on venous outflow pressure. Finally, doubt has been raised as to whether intracranial pressure itself remains uniform, even within the same intracranial compartment, in states of raised intracranial pressure (Weinstein, Langfitt, Bruno, Zaren, and Jackson, 1968; Brock, Beck, Markakis, and Dietz, 1972).

Calculated values for cerebrovascular resistance have also shown a different pattern of change according to the method used to increase intracranial pressure. Expansion of an infratentorial subdural balloon led to a sharp initial change followed by a relatively constant level of cerebrovascular resistance, whereas a supratentorial subdural balloon gave rise to a progressive fall in cerebrovascular resistance (Figs 4a and b). In the previous study, using infusion of fluid into the cisterna magna, cerebrovascular resistance fell during the initial increase of intracranial pressure, then remained constant during the hyperaemic phase.

The patterns of change in vascular resistance reflect the relative influence of the factors which control resistance and capacitance in the cerebral vessels in different forms of intracranial hypertension. A localized supratentorial mass may, by causing brain shift, lead to distortion and

mechanical obstruction of the superficial cortical veins. An infratentorial mass may, by local stimulation of the brain-stem, have marked influence on sympathetic activity and therefore influence cerebral blood flow by altering the diameter of both the extraparenchymal intracranial vessels and the large vessels in the neck (Harper, Deshmukh, Rowan, and Jennett, 1972). Raised intracranial pressure due to infusion of fluid into the subarachnoid space may be associated with changes in the local vessel environment, thus altering the response of these vessels to local metabolic stimuli.

The changes in vascular resistance which have been considered above and which act to preserve blood flow in the face of a changing cerebral perfusion pressure are subsumed under the term autoregulation. In a previous study it was shown that autoregulation was effective in maintaining a relatively constant blood flow over an intracranial pressure range of approximately 0–50 mmHg (Johnston *et al.*, 1972). At higher levels of intracranial pressure, autoregulation still seemed to be effective, during the period of hyperaemia, although the blood flow appeared to be reset at a higher level for a given value of cerebral perfusion pressure. After the period of hyperaemia autoregulation was lost and blood flow became directly dependent on cerebral perfusion pressure. In the present study, with the supratentorial balloon, autoregulation remained intact down to cerebral perfusion pressure values around 40 mmHg before being lost. With the infratentorial balloon, however, autoregulation appeared to be lost from the time of the first balloon expansion.

Three distinct patterns of response were therefore seen but, while these patterns were consistent within each group, there is, as yet, no clear evidence as to the cause of these differences of autoregulatory function. The findings, may, however, be of some value in elucidating the nature of autoregulation in the cerebral circulation. Previously, attempts have been made to discover a single central mechanism which is responsible for autoregulation. While this may be possible if the term is used in the narrow sense, referring to the mechanism by which the diameter of the cerebral resistance vessels (arterioles) is controlled (Green, Rapela, and Conrad, 1964), it seems much less possible if autoregulation is con-

sidered in the wider sense as the overall preservation of blood flow in the face of possible compromising factors. The present results are, in fact, in harmony with the view that a number of complex inter-related compensatory mechanisms exist to preserve blood flow in situations in which the blood supply to the brain may be jeopardized by increased intracranial pressure. It seems likely that the form which the overall compensatory response takes will depend, among other factors, on the cause and time course of the increase in intracranial pressure.

It is apparent from these considerations that attempts to define a comprehensive quantitative relationship between either intracranial pressure or cerebral perfusion pressure and cerebral blood flow will be unsuccessful. Further, while the different methods used to increase intracranial pressure in these studies may be said to stimulate different clinically occurring lesions, there is no certainty that the patterns of response described are directly applicable to the clinical situation. The clinician remains on very uncertain ground when trying to gauge cerebral blood flow from measurements of intracranial pressure. In conclusion it should be emphasized, therefore, that, while raised intracranial pressure may lead to a reduction in cerebral blood flow, there is no justification at present for attempting to draw quantitative conclusions about cerebral blood flow from clinical measurements of either intracranial pressure or cerebral perfusion pressure. Before this is possible, much more remains to be learned about the mechanism of autoregulation, the factors which may affect autoregulation, and the assumptions underlying the concepts of cerebral perfusion pressure and cerebrovascular resistance.

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