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THE EFFECT OF RAISED INTRACRANIAL PRESSURE ON THE CEREBRAL BLOOD FLOW

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ONE of the most important conclusions derived from recent work on brain metabolism is the constancy of the cerebral blood supply. This has been clearly shown by Lennox (1936) and Lennox and Leonhardt (1931) in a large group of subjects. Gibbs, Gibbs, and Lennox (1935) have also found that sleep has little effect upon the blood supply of the brain, while Gibbs, Lennox, and Gibbs (1934) have shown that epileptic attacks do not result from a change in the total blood flow. Mental work, however, caused a small increase in the cerebral blood flow, due probably to a dilatation of the cerebral vessels (Lennox and Leonhardt, 1931). The evidence so far seems to indicate that, within limits, a constant rather than a rich supply of oxygen is necessary for the normal functioning of the brain.

The object of the present series of experiments was to ascertain whether increased intracranial pressure, as produced by intracranial tumour, has any effect on this constant cerebral blood flow. It appeared that raised intracranial pressure might possibly exert an effect on the large venous channels, thus causing a partial obstruction to the venous outflow and thereby slowing the cerebral circulation. A series of experiments was first performed on a group of un-anæsthetized human subjects, the results of which indicated that in some cases intracranial tumour did have such a slowing effect. The investigations were then carried further, using cats with artificially produced tumours, in an endeavour to confirm the results obtained in man with neoplastic tumours.

Methods

The cerebral blood flow has been ascertained by measuring the difference in the oxygen and carbon dioxide contents of the blood entering and leaving the brain, the

two samples of blood being taken practically simultaneously. In man the arterial blood was obtained by puncture of the brachial artery and the venous blood by puncture of the jugular bulb. In the cat the arterial blood was obtained from a cannula in the femoral artery and the venous blood from the superior longitudinal sinus, the needle being introduced into this sinus near the anterior part of the brain and passed posteriorly to the torcula, whence the sample was withdrawn. The venous blood obtained in these ways from man and cat should, therefore, be a good representation of the blood coming from the brain as a whole.

The principle of this method of measuring the cerebral blood flow depends upon the amount of oxygen taken up and the amount of carbon dioxide given off as the blood passes through the brain tissue. These amounts will depend upon two factors, first, the rate of metabolism of the brain tissue and, secondly, the volume of blood passing through the brain in a given time. If it is assumed that the rate of the metabolism of the brain remains constant with the patient or animal lying quietly at rest, the arterio-venous differences of oxygen and of carbon dioxide will vary inversely with the volume of blood flowing through the brain in unit time.

All human subjects were unanæsthetized and had been lying at rest in bed for some time before the blood samples were taken. Punctures of the brachial artery and of the jugular bulb were made with the patient lying on his back in a horizontal position. Five c.c. of blood were withdrawn from each puncture and put under paraffin oil without contact with air, coagulation and glycolysis being prevented by 0.2 per cent. potassium oxalate and 0.1 per cent. sodium fluoride respectively. The blood was put on ice and analyses were begun almost immediately. As soon as the blood samples were obtained, the intracranial pressure was measured by ventricular tap or lumbar puncture with the patient still lying in the horizontal position.

All cats were anaesthetized with chloralose (75–80 mgm. per kilogram body weight intravenously), and they were left for $1\frac{1}{2}$ hours after the administration of the anaesthetic before the blood samples were taken. This interval was allowed for the effects of the small amount of ethyl chloride and ether, used before chloralose injection, to wear off. It was found that after this time the arterio-venous oxygen difference remained constant for about 2 hours, but that after 2 hours this difference gradually increased. Thus in all experiments blood samples were taken $1\frac{1}{2}$ –2 hours after the chloralose was administered. In this way, constant figures were obtained in normal cats, as will be seen later. The cats were always in the same position, lying horizontally on a table with the head slightly raised and held firmly in a clamp. A narrow longitudinal hole was made in the skull with a dental drill just posterior to the bregma, so that a needle could be passed along the superior longitudinal sinus to the torcula. Blood samples obtained from the sinus and from the femoral artery were dealt with in the same manner as in the case of human subjects described above. The blood pressure was recorded on a drum from a cannula in the femoral artery.

The human subjects with raised intracranial pressure were all suffering from intracranial tumour. In the experiments with cats a group of controls was treated in the way described, while in another group an artificial tumour was introduced into the cranial cavity from 3 to 6 weeks before the blood samples were taken. For the introduction of these artificial tumours, the cat was anaesthetized with nembutal (35 mgm. per kilogram body weight intraperitoneally), a small hole about $\frac{1}{8}$ in. in diameter was made in the skull with a dental drill, and a mass of cotton wool soaked in paraffin wax of a melting point of 50° C. was carefully introduced extradurally with curved forceps. At post mortem it was found that a rounded tumour was in this way produced, causing a marked dent in the brain substance at the site of the tumour. The size of the tumour introduced was always about 0.7 to 1.0 c.c. in volume, the sudden introduction of larger masses than this causing the death of the animal. The tumours were inserted in two positions in two groups of animals, (a) in the frontal region just beneath the coronal suture and (b) in the cerebellar region beneath the level of the tentorium cerebelli. The two groups of cats were then allowed to recover and

live for three to six weeks, when they were anaesthetized with chloralose and blood samples were removed as already described. No symptoms were observed with the group of cats with frontal "tumours," and in only two of the cats with cerebellar "tumours" were any symptoms noticed. These two cats showed marked ataxia the day after the operation, and this persisted, although it became somewhat less marked. All cats were very well and in excellent condition when the blood samples were taken.

The percentage saturation of the hæmoglobin with oxygen, the oxygen capacity and carbon dioxide content of the blood were determined with the Haldane blood gas apparatus completely immersed in a water bath.

RESULTS

The Effects of Intracranial Tumour on the Cerebral Blood Flow

A. Experiments on Man.—Fig. 1 shows the arterio-venous oxygen differences and the percentage saturation of hæmoglobin in the arterial and jugular blood in 23 cases of intracranial tumour in man. The arterio-venous carbon dioxide differences are practically identical with the oxygen differences, so they are not plotted in the figure. The first column shows the results of the 23 cases as a whole. The mean arterio-venous oxygen difference is 7.6 c.c. per 100 c.c., while the arterio-venous carbon dioxide difference is 7.8 c.c. per 100 c.c. The percentage saturation of the hæmoglobin is 95 in the arterial blood and 54 in the jugular blood. In this series of experiments a group of normal subjects to act as controls has not been investigated. Lennox and Lennox and Leonhardt, however, have investigated a very large series of more or less normal cases, and they find that the arterio-venous oxygen difference is approximately 6.2 c.c. per 100 c.c., while the percentage saturation of the jugular blood is 62. As they find that these values are fairly constant, their figures can be taken for comparison as being average normal values. The average results obtained in 23 cases of intracranial tumour, therefore, show a higher arterio-venous oxygen difference and a lower percentage saturation of the jugular blood than normal. Should the average rate of metabolism of the brain tissue be the same in both groups of cases, then it can be concluded that the cerebral blood flow must be slower in the group of cases with intracranial tumour.

The second and third columns in Fig. 1 show the original group of 23 cases divided into two groups, first, nine cases in which the tumour was situated in the frontal or parietal cortex and, secondly, 13 cases in which the tumour was either in the cerebellum, mid-brain, or in the region of the basal ganglia (four cerebellar tumours, two acoustic tumours, five basal ganglia tumours, and two tumours in the temporal lobe invading the basal ganglia). The situation of the tumour in all cases was confirmed either at operation or post mortem. In the first group of cases the average arterio-venous oxygen difference is 5.8 c.c. per 100 c.c., carbon dioxide difference 6.0 c.c. per 100 c.c., and the percentage saturation of the jugular blood 62. In the second group the arterio-venous oxygen difference is 8.3 c.c. per 100 c.c., carbon dioxide difference 8.5 c.c. per 100 c.c., and the percentage saturation of the jugular blood 51. There is thus a definite difference between these two groups of cases, those with tumours mainly in the frontal or parietal cortex giving results similar to normal, whereas those with tumours in the posterior fossa or in the basal ganglia appear to have

a cerebral circulation that is slower than normal. The intracranial pressure of the first group averaged 280 mm. cerebrospinal fluid, the highest value being 430 mm., while the second group averaged 320 mm. cerebrospinal fluid, the highest value being 520 mm. These pressures were taken with the patient lying in the horizontal position, and are therefore to be regarded as above normal.

One case has not been included in the second and third columns of Fig. 1. This was a case with a meningioma in the region of the occipital cortex. The intracranial pressure was 280 mm. cerebrospinal fluid, the percentage saturation of the arterial blood was 96 and of the jugular blood only 17, giving an arterio-venous oxygen difference of 15.2 c.c. per 100 c.c. and a respiratory quotient of 0.95. The arterio-venous blood sugar difference of 20 mgm. per 100 c.c., corresponded to the arterio-venous oxygen difference of 15.2 c.c., assuming that carbohydrate only was being utilized. In spite of this great difference between the arterial and venous blood the patient felt and appeared to be quite well. A

Fig. 1.—The arterio-venous oxygen differences and the percentage saturation of the hæmoglobin of the arterial and jugular blood in a series of 23 cases of intracranial tumour. In the right half of the figure, the upper determinations are for arterial blood and the lower for jugular blood.

- The group as a whole.
- Cases with tumour in the frontal and parietal regions.
- Cases with tumour in the posterior fossa and basal ganglia.

Fig. 2.—The arterio-venous oxygen differences and the percentage saturation of the hæmoglobin of the arterial and jugular blood in cats.

- Group of normal cats.
- Group of cats with frontal "tumour."
- Group of cats with cerebellar "tumour."

month after the complete removal of the tumour, the hæmoglobin of the jugular blood was 60 per cent. saturated, and the arterio-venous oxygen difference was only 5.5 c.c. per 100 c.c. As the results of this case are so greatly outside the limits observed in the other 22 cases, they have not been included when the group was differentiated, but it appears that the tumour must have exerted some influence on the cerebral blood flow.¹

B. Experiments on Cats.—Although the two groups of cases above are not very large, it appears that it is the position of the tumour rather than the increased intracranial pressure *per se* which might affect the cerebral blood flow. Because of these results, experiments were performed on cats with the intro-

¹ The detailed results of these experiments in man are shown in Table 1. The letters V and L indicate whether the C.S.F. pressure was ventricular or lumbar.

TABLE 1

	C.S.F. PRESSURE, M.M. C.S.F.	OXYGEN IN BLOOD						CO ₂ CONTENT OF BLOOD, VOL. PER CENT.			RESPIRA- TORY QUOTIENT
		ARTERIAL		JUGULAR		A-V DIFFERENCE	ARTERIAL	JUGULAR	A-V DIFFERENCE		
		PER CENT. SATURATION	CONTENT	PER CENT. SATURATION	CONTENT						
Cases with pos- terior fossa or basal ganglia tu- mours.	V 180	95	15.2	43	6.9	8.3	51.6	60.9	9.3	1.12	
	L 420	95	19.8	50	10.4	9.4	54.8	62.0	7.2	0.77	
	V 290	99	16.9	44	7.5	9.4	41.5	51.2	9.7	1.03	
	V 270	98	17.1	60	10.6	6.5	48.6	54.5	5.9	0.91	
	V 215	96	16.6	54	9.4	7.2	59.0	66.7	7.7	1.07	
	—	94	18.7	49	9.6	9.1	48.6	57.3	8.7	0.96	
	V 520	96	19.5	54	11.0	8.5	51.3	59.8	8.6	1.01	
	L 230	97	22.3	48	11.0	11.3	35.8	50.3	14.5	1.27	
	L 400	95	19.6	61	12.6	7.0	48.4	55.1	6.7	0.96	
	V 350	95	18.0	55	10.4	7.6	51.7	61.1	9.4	1.24	
	—	95	16.0	40	6.7	9.3	50.0	59.0	9.0	0.97	
	V 300	94	15.0	50	7.9	7.1	62.1	69.5	7.4	1.04	
	V 320	95	14.6	50	7.7	6.9	50.6	57.5	6.9	1.00	
320	96	17.6	51	9.3	8.3	50.3	58.8	8.5	1.03		
Cases with tumours in the frontal or parietal regions.	V 310	95	15.8	66	10.5	5.3	54.7	60.0	5.3	1.00	
	V 430	98	18.8	61	11.7	7.1	52.6	59.6	7.0	0.99	
	V 230	95	19.7	56	11.6	8.1	52.1	60.2	8.1	1.00	
	L 280	92	18.1	59	11.5	6.6	47.5	54.2	6.7	1.01	
	V 220	96	17.5	77	14.0	3.5	60.7	63.7	3.0	0.86	
	L 170	91	17.1	63	11.5	5.6	43.0	48.4	5.4	0.97	
	V 320	97	14.4	55	8.1	6.3	44.7	53.3	8.6	1.37	
	L 300	96	15.1	61	9.5	5.6	53.7	59.6	5.9	1.05	
	L 280	89	13.8	61	9.5	4.3	40.6	44.6	4.0	0.93	
	280	94	16.7	62	10.9	5.8	50.0	56.0	6.0	1.03	

duction of artificial tumours in the frontal and cerebellar regions, as already described in detail. The results of these experiments are shown in Fig. 2. A group of 22 normal cats shows that the average arterio-venous oxygen and carbon dioxide differences are 5.3 c.c. per 100 c.c., while the percentage saturation of the arterial blood is 95 and of the sinus blood 60. The individual figures as shown in Fig. 2 are very constant, with only small variations. The average percentage saturation of the sinus blood, 60, is practically identical with that of normal unanæsthetized human subjects, 62, but the arterio-venous oxygen difference is lower, because the hæmoglobin content of cat's blood is lower than that of human blood, the oxygen capacity in a group of 50 cats being only 14.2 c.c. per 100 c.c.

The arterio-venous oxygen differences of a group of nine cats with frontal "tumour" practically all fall within the limits of the normal group with an average of 4.8 c.c. per 100 c.c., while the arterio-venous oxygen differences of a group of 15 cats with cerebellar "tumours" nearly all fall above the limits of the normal group, with an average of 6.7 c.c. per 100 c.c. The percentage saturations of the arterial and sinus blood in the group of frontal "tumours" are 92 and 57, that is, the same difference as in the normal group. The corresponding figures in the group of cerebellar "tumours" are 94 and 49, the difference in percentage saturation being thus 11 greater than in the normal group. If the average rate of metabolism of the brain tissue is the same in these groups of cats, the blood flow must be slower in the group with cerebellar "tumour" than in the group with frontal "tumour" of the same size or in the normal group.

The blood pressure in all groups of cats was very constant. The average mean arterial blood pressure of the normal group was 124 mm. Hg, frontal "tumour" group 125 mm. Hg, and the cerebellar group 127 mm. Hg, individual variations being between 105 and 140 mm. Hg. The changes observed in the arterio-venous oxygen and carbon dioxide differences in the different groups of cats could therefore not be accounted for by changes in the mean arterial blood pressure.

The effects of the "tumours" in cats on the size of the ventricles can be seen in Fig. 3. In practically all cases the cats with cerebellar "tumours" showed a definite degree of hydrocephalus, whereas those with frontal "tumours" showed no change from normal. Of the 23 human cases described above, the ventricles have been studied by ventriculography in 17 cases, nine from the group with cerebellar or basal ganglia tumours and eight from the group with frontal or parietal tumours. The ventricles in the latter group have a total capacity that is approximately normal, whereas those in the former group are on the whole much increased in size.

The Coefficient of Oxygen Utilization.—Another indication of the differences described is seen in the coefficient of oxygen utilization, that is, the ratio of the oxygen taken up by the tissue to the oxygen available in the arterial blood. Table 2 shows that in the group of human cases with tumours in the frontal or parietal regions, the coefficient of oxygen utilization is 35 per cent., which corresponds closely with the figure of 35.6 per cent. obtained in a group of

normal subjects by Williams and Lennox (1939), and that in the other group of tumours the coefficient of oxygen utilization is 47 per cent. Similarly, in the groups of cats the normal figure of 38 per cent. corresponds with that of 38 per cent. for the frontal "tumour" group, whereas in the group with cerebellar "tumours" the coefficient of oxygen utilization is much higher, 48 per cent. In both groups of human cases and in the three groups of cats the oxygen capacity of the blood is approximately the same (Table 2), although the slightly lower oxygen capacity and percentage saturation of the arterial blood of the group of frontal "tumours" in cats will give the same coefficient of oxygen utilization as normal in spite of the fact that the arterio-venous oxygen difference is lower. On the whole, however, these figures should give a fair indication of the cerebral blood flow. The amount of blood flowing through the brain in any given time will therefore be approximately 30 per cent. less in the case of cerebellar or basal ganglia than in the case of tumours in the frontal or parietal regions or in normals. This change is about the same in the human cases as in the experiments with cats.

Fig. 3.—Two sections from each of three cats' brains in approximately comparable positions in each, showing the size of the ventricles. (a) Normal brain. (b) Brain from cat with frontal "tumour." (c) Brain from cat with cerebellar "tumour."

TABLE 2

	OXYGEN CAPACITY	OXYGEN IN ARTERIAL BLOOD	OXYGEN IN VENOUS BLOOD	COEFFICIENT OF OXYGEN UTILIZATION
Human subjects: Frontal and parietal tumour group ..	17.4	16.7	10.9	35
Cerebellar and basal ganglia group	18.0	17.6	9.3	47
Cats: Control group	14.6	14.1	8.8	38
Frontal "tumour" group ..	13.5	12.7	7.9	38
Cerebellar "tumour" group ..	14.7	14.1	7.4	48

The Effect of Removal of the Intracranial Tumour in Man.—In five cases the arterio-venous oxygen differences have been measured before operation and from 1 to 3 months after the removal of the intracranial tumour (three total and two subtotal removals), all patients being very well and completely recovered from the operation. The results are shown in Table 3. Although this group is very small, the results indicate that in two cases in which the arterio-venous oxygen difference was normal before operation, no change was observed after operation, whereas in three cases where the arterio-venous oxygen difference was high before operation, a definite fall was observed after operation ; so that the post-operative figures all fall within the range of normality with a mean of 6.3 c.c. per 100 c.c. It seems, therefore, that in those cases with a high oxygen difference, the presence of the intracranial tumour is probably the cause. A larger group of cases is necessary before this can be established with certainty by this method.

TABLE 3.—ARTERIO-VENOUS OXYGEN DIFFERENCE, C.C. PER 100 C.C.

BEFORE OPERATION	AFTER REMOVAL OF TUMOUR
9.4	7.5
8.1	6.3
15.2	5.5
5.3	5.5
6.6	6.5

The Effect of Sudden Rise in Intracranial Pressure in Man.—So far it is the long-standing effects of increased intracranial pressure that have been considered. The effects of a sudden rise in the intracranial pressure have also been investigated. This has been done in six patients who have previously had a cerebellar decompression by removal of a large part of the occipital bone and opening of the dura and in five patients with a subtemporal decompression (three cases) or a small bone defect after removal of a supratentorial tumour (two cases). By pressure on the decompression the intracranial pressure, as measured by a needle in the lateral ventricle, could be raised from normal to 600 or 700 mm. cerebrospinal fluid without causing any inconvenience to the patient. Before pressure was applied, samples of blood were obtained from the jugular bulb and brachial artery in the usual way. While pressure was being applied to the decompression the needle, closed by a stillette, was left in the jugular bulb. After the intracranial pressure had been maintained at about 600 mm. cerebrospinal fluid for approximately 5 minutes, a further sample of jugular blood was

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withdrawn. The results are shown in Table 4. In the six cases with cerebellar decompressions, the pressure in each case was raised from approximately normal to 500–700 mm. cerebrospinal fluid and maintained on an average for 5 minutes. In the first three cases there is a marked fall in the percentage saturation of the jugular blood, and a rise in the arterio-venous oxygen difference. The percentage saturation of the jugular blood in these three cases was very low, namely, 26, 22, and 25, yet no signs nor symptoms of this low oxygen saturation were observed. Two cases showed no appreciable difference, while the sixth showed a definite rise in the percentage saturation of the jugular blood and a fall in the arterio-venous oxygen difference. The blood pressure in this last case rose sharply from 140/100 to 160/115 when pressure was applied and fell sharply to the original level when the pressure was released. A third blood sample taken from the jugular bulb 2 minutes after the pressure had been released showed that the percentage saturation and arterio-venous oxygen difference had regained their original levels. The sudden rise in blood pressure, therefore, would account for the sudden increase in the blood flow when the pressure was raised.

TABLE 4

CASE NUMBER	BEFORE PRESSURE APPLIED			DURING PRESSURE ON DECOMPRESSION		
	PER CENT. SATURATION OF JUGULAR BLOOD	A-V O ₂ DIFFERENCE	BLOOD PRESSURE	PER CENT. SATURATION OF JUGULAR BLOOD	A-V O ₂ DIFFERENCE	BLOOD PRESSURE
CEREBELLAR DECOMPRESSIONS						
N. L. 3915	60	6.5	—	26	11.6	—
E. B. 4015	55	5.9	—	22	10.2	—
A. Y. 4436	50	7.1	130/80	25	11.0	135/90
G. C. 2040	43	8.3	—	42	8.6	—
W. M. 3921	45	8.5	122/78	48	8.0	126/78
M. M. 3121	58	5.4	142/100	73	3.1	160/114
	52	7.0	—	40	8.8	—
SUBTEMPORAL DECOMPRESSIONS AND PARIETAL BONY DEFECTS						
E. S. 2579	58	4.7	—	53	5.4	—
C. G. 3968	63	5.4	—	64	5.2	—
N. L. 4363	50	6.9	112/68	51	6.8	118/74
M. B. 4486	40	9.3	120/80	45	8.2	130/92
M. W. 4441	62	4.3	143/74	62	4.3	166/77
	55	6.1	—	55	6.0	—

The five cases with subtemporal decompressions or with bony defect in the parietal region showed on the whole no change in the cerebral blood flow when pressure was applied to the decompression. The intracranial pressure was not measured in all these cases, but in those cases with subtemporal decompression, where it was measured, the pressure could be raised to 600 mm. cerebrospinal fluid by pressing on the decompression. Thus, though the rise in all cases may not have been as great as in those cases with a cerebellar decompression, because the bony defect was smaller, the intracranial pressure was undoubtedly raised considerably.

Although this series of observations is not large, it appears that when the intracranial pressure is raised by exerting pressure in the temporal or parietal regions, the blood flow is not appreciably affected. Pressure exerted posteriorly at the base of the skull, on the other hand, may in some cases, but not in all, produce a very marked slowing of the cerebral circulation. Three of the cases in this group are interesting in that the percentage saturation of the jugular blood was reduced to 26, 22, and 25 without any inconvenience whatever to the patient. No signs of acute oxygen lack were present and the patients felt quite well. Lennox, Gibbs, and Gibbs (1935) have shown that when the percentage saturation of the jugular blood is suddenly reduced below about 25, unconsciousness takes place. This was certainly not the case with the three patients mentioned above. In another case, described earlier, the percentage saturation of the jugular blood was only 17, and yet the patient was very well and showed no signs of lack of oxygen. It is probable that in this case the percentage saturation was gradually reduced over a long time, but in the three cases described above the change was produced rapidly.

The results of these experiments, on the whole, agree reasonably well with the experiments in cases of long-standing increased intracranial pressure as a result of intracranial tumour. In both series of experiments pressure exerted at the base of the brain posteriorly will in general cause a slowing of the blood flow, whereas pressure exerted in the frontal or parietal regions has little effect.

Discussion

The measurement of the actual volume of blood passing through the brain per minute has met with many difficulties, and an accurate method has not yet been devised. Wolff (1936), Quastel (1939), and Chute and Smyth (1939) review the results so far, and note the great discrepancy between the values for the oxygen uptake per 100 gm. of brain tissue per hour when this is measured *in vivo* and *in vitro*. The values obtained *in vivo* range from 450 to 840 c.c., and *in vitro* from 80 to 300 c.c. If a figure of 600 c.c. oxygen per 100 gm. per hour is applied to the experiments on human subjects described above, assuming a brain of normal size, the cerebral blood flow would be 2.34 litres per minute in the group with tumours in the frontal and parietal regions and 1.65 litres per minute in the group with posterior fossa or basal ganglia tumours. As the total cardiac output in man at rest is only 4–6 litres per minute, it seems unlikely that such a high proportion should pass through the brain. Chute and Smyth find that in the perfused cat's brain the average oxygen consumption is only 200–300 c.c. per 100 gm. per hour, figures which agree more closely with the *in vitro* experiments. If a figure of 250 c.c. be applied to the human brain in the present series of experiments, the cerebral circulation would be 980 c.c. per minute in the first group and 683 c.c. per minute in the second group. Similarly, the rate of cerebral blood flow in the cat (assuming an average brain of 30 gm.) would be 24 c.c. per minute in the normal group, 26 c.c. per minute in the group with frontal "tumours," and 19 c.c. per minute in the group with

cerebellar "tumours." These estimates, which are based on the oxygen consumption found in different circumstances (perfused head), may not be applicable to my experiments, but provided the oxygen consumption of the brain per 100 gm. per hour is the same in each group of cases considered, a general idea of the approximate changes in the cerebral blood flow in the different groups of intracranial tumour can be obtained.

Williams and Lennox (1939) have investigated a group of 13 cases suffering from raised intracranial pressure resulting from trauma, tumour, or infection. They find an average arterio-venous oxygen difference of only 6.6 c.c. and a carbon dioxide difference of 6.8 c.c. per 100 c.c., and conclude that raised intracranial pressure has practically no effect on the cerebral blood flow. In my series the figures for the whole group were definitely higher (Fig. 1), and it appears that in certain locations intracranial tumour does have a slowing effect on the blood stream.

It has been suggested that the position of the tumour rather than the actual intracranial pressure, within limits, may account for the changes described. A tumour in the posterior fossa or in the basal ganglia seems more likely to exert a greater effect on the large venous channels which converge at the base of the brain than a tumour in the frontal or parietal cortex. Cairns (1939) has shown that the intracranial pressure is not uniformly distributed throughout the brain in intracranial tumour. The local pressure effects of such a tumour may be much greater than the effects produced in the more remote parts of the cranial cavity. It therefore seems probable that a tumour in the cerebellum, midbrain, or basal ganglia will produce a much greater pressure effect on the large venous channels converging at the base of the brain than will a tumour confined to the frontal or parietal cortex.

It must be remembered that the method of ascertaining the cerebral blood flow which was used in the above series of experiments will give an indication of the total cerebral blood flow only, and not of local changes which may occur in different parts of the brain. It seems quite probable that a tumour in the frontal or parietal cortex will produce local changes in the cerebral circulation, but these changes will not be evident in the arterio-venous oxygen difference of the blood entering and leaving the brain as a whole. Similar changes will no doubt occur locally with tumours of the cerebellum or basal ganglia, but because of the proximity of the large venous channels converging at the jugular foramen, a slowing of the total circulation will be produced, as the results of the series of experiments show.¹

The rise of venous pressure necessary to bring about the changes described is probably not very great. Bedford (1937) has measured the venous pressure at the torcula in dogs, anaesthetized with ether, after the introduction of artificial subtentorial tumours, and finds no change from normal. This is rather surprising in view of observations at operation with local or general anaesthesia. Cairns (1939) has described how in cases of cerebellar tumours at operation,

¹ Williams and Lennox have shown that in cases with angiomas and vascular tumours the jugular blood has a very high oxygen content. In my series of experiments, however, there is no case of intracranial angioma.

the venous pressure is often greatly increased and bleeding from the veins may be severe. This bleeding may be diminished by lowering the intracranial pressure in these cases, which suggests that the large veins have been partially obstructed. Rise in arterial pressure does not occur until the intracranial pressure approaches the arterial pressure (Cushing, 1901), a figure which is not, or only rarely, observed in cases of intracranial tumour. It is probable that the venous pressure is partly raised by dilatation of the arterioles and capillaries as a result of the rise of carbon dioxide tension caused by the slowing of the blood stream. This would tend to increase the blood flow, but, as the results of my experiments show, this compensatory mechanism cannot totally overcome the obstruction to the large venous channels, and a general slowing of the cerebral circulation results. Thus the raised venous pressure is probably brought about primarily by obstruction to the venous outflow and secondarily by dilatation of the small vessels caused by a rise in the carbon dioxide tension. Further evidence of raised venous pressure is shown in some cases of long-standing increased intracranial pressure by the dilatation of the emissary veins which can be seen in radiographs in the region of the external occipital protuberance. These emissary veins are in direct communication with the large venous sinuses, so it appears that the pressure in these sinuses is raised. Because of the obstruction to the venous outflow at the base of the brain, more blood will therefore escape through these emissary veins.

Summary

The arterio-venous oxygen and carbon dioxide differences of the arterial blood and of the venous blood coming from the brain have been investigated in a group of unanæsthetized human subjects suffering from intracranial tumour, and in cats in which artificial tumours had been inserted extradurally in the frontal and cerebellar regions about 3-6 weeks previously.

The arterio-venous blood gas differences indicated that an intracranial tumour produced a slowing of the cerebral circulation in some cases. An attempt to differentiate the group on the basis of the position of the tumour has been made. With moderate increase in intracranial pressure, tumours in the frontal or parietal regions have little effect on the total cerebral circulation, whereas tumours in the cerebellum or basal ganglia have a slowing effect. This applies to the experiments with cats as well as with man.

The difference observed in the two cases is explained by the local pressure effects of the tumour, a tumour at the base of the brain having a greater influence on the large venous channels as they converge towards the base of the skull than a tumour in the frontal or parietal cortex.

In a small group of cases, removal of the tumour in man has reduced the arterio-venous oxygen difference to normal where this was previously high.

A sudden large rise of intracranial pressure in man by mechanical pressure on a bony defect over the cerebellum, produced for decompression, showed a marked slowing of the cerebral circulation in some cases, whereas a similar rise of pressure caused by mechanical pressure in the fronto-temporal or parietal regions showed no change.

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