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DISCUSSION: THE PATHOLOGY OF SPONTANEOUS INTRACRANIAL HÆMORRHAGE

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Spontaneous Intracranial Hæmorrhage

The qualification "Spontaneous" in the title of this discussion eliminates all varieties in which trauma plays a part. To narrow the field still further I propose to exclude the neo-natal period. In addition I shall omit the numerous and varied conditions in which the brain is the site of multiple small hæmorrhages, and confine myself to significant large hæmorrhages. In assessing what is significantly large it is of course necessary to relate size to the site: a relatively small focus may be of fatal consequence in the brain-stem, but one of similar size in the cerebrum may be compatible with survival.

In the following analysis[1] of intracranial hæmorrhages, occurring in the necropsy records of the London Hospital in the period 1912-1952, an arbitrary limit of 1·5 cm. was fixed for the lower limit of hæmorrhages in the brain-stem, and 3 cm. for the cerebrum and cerebellum. In examples that approximated closely to these dimensions the clinical notes were helpful in assessing their significance and hence their inclusion or exclusion.

Table I gives the total number of cases and the main categories in their analysis. The *hypertensive group* constitutes about 50% of the total. The majority here (155, or 67%) were diagnosed as benign hypertension; the rest (77, or 33%) as either malignant (M.H.T.) or nephritic hypertension. These figures are only approximate since the diagnosis for the earlier decades often rests upon the macroscopic appearances of the kidneys and the age of the patient. Many in the benign group were elderly subjects with gross vascular degeneration and only slight or moderate degrees of cardiac hypertrophy. *Congenital defects in the media* of the main cerebral arteries led to the formation and subsequent rupture of a berry aneurysm in 92, and rupture without aneurysm in 4, totalling 96.

TABLE I

I.	Hypertensive	232
II.	Congenital medial defects in cerebral arteries (92 cases with aneurysm)	96
III.	Blood diseases	36
IV.	Mycotic aneurysm	28
V.	Vascular hamartoma	21
VI.	Arteritis (no aneurysm)	13
VII.	Neoplasms	9
VIII.	Arterial degeneration (No cardiovascular hypertrophy)	7
IX.	Various	3
X.	Cause not found	16
	Total	461

In the group of *blood-diseases* acute leukæmia was responsible for major hæmorrhage in 15 cases, thrombopenia in 13, aplastic anæmia in 3, other anæmias in 3, erythrocythæmia in 1 and hæmophilia in 1.

Neoplasms, which include both primary and secondary growths, form a surprisingly small group in view both of their considerable number in our necropsy material and current conceptions concerning their liability to give rise to spontaneous hæmorrhages of significant size.

Arteritis in Table I signifies purulent inflammation and rupture without aneurysm-formation. This was due to pyæmia in 10 examples. In 3 it complicated purulent leptomeningitis. It is of interest that polyarteritis nodosa finds no place in this series. Our sole example as a cause of hæmorrhage involved the spinal cord.

[1]I am greatly indebted to my Assistants, Dr. C. W. M. Adams and Dr. D. Ireland-Jones for their help in this.

The study of intracranial hæmorrhage from the point of view of its anatomical situation leads to the separation of groups involving (1) the subdural space, (2) the leptomeninges and (3) brain substance. In many instances, however, the hæmorrhage is not confined to one level.

(1) *Subdural hæmorrhage.*—Accepting the view that the subdural hæmatomas of middle-aged and elderly subjects are the result of trauma, in the absence of other causes demonstrated at necropsy, there are only 23 non-traumatic cases in our series where the subdural space formed the main site. Blood-diseases accounted for 11 of these; congenital aneurysms for 7; mycotic aneurysms for 2 and neoplasms for 3.

(2) *Subarachnoid hæmorrhage.*—The principal cause is rupture of a berry aneurysm. Mycotic aneurysms, blood diseases and persistent hypertension may also be responsible for primary subarachnoid hæmorrhage, and some of those for which a cause was not found fall also into this group.

Histopathology of congenital aneurysms.—Though it is generally accepted that their formation is based upon a congenital defect in the media of the main cerebral arteries it has been widely contended that the secondary factors of hypertension and focal degeneration of the arterial wall play an important part both in the evolution of the aneurysm and in its subsequent rupture. Our figures confirm the growing recognition that this is a catastrophe of middle-age rather than of the early decades. The greatest incidence of rupture is in the fifth and sixth decades; there are no proved examples with rupture in the present series below the third decade. Cardiac hypertrophy was recorded in 12 of the 96 examples. From these considerations, and from the prevalence of demonstrable degenerative changes in the wall of the sac it is difficult to escape the conclusion that these secondary factors are of paramount importance. But the argument that the basic pathology is a congenital defect in the media is supported by the demonstration of associated defects of a similar character without degeneration, and at sites remote from branching, in the splanchnic arteries.

(3) *Brain. Hypertensive hæmorrhage.*—Table II shows the principal sites affected. The classical site in the basal ganglia, with rupture into the adjacent ventricle, accounts for most of the total of 232, and the numbers assigned to the benign and nephritic groups (including malignant hypertension) are roughly proportionate to the totals in these. In the cerebral white matter and cerebellum there is a preponderance in favour of benign hypertension, but this is definitely reversed in the brain-stem where malignant hypertension and nephritis collectively preponderate.

TABLE II.—HYPERTENSIVE: SITES

1.	Basal ganglia (Benign: 104)	151
2.	Cerebral white matter (Benign: 17)	21
3.	Pons and mid-brain (Benign: 14)	32
4.	Cerebellum (Benign: 15)	18
5.	Subcortical: Cerebrum (Benign: 1)	4
6.	Meninges (Benign: 4)	6

The explanation for this rests upon the vascular pathology responsible for the hæmorrhage. In benign hypertension the perforating cerebral arteries show a replacement of the muscle of the medial coat by fibrous tissue. Atheroma in the intima may lead to thrombosis rather than rupture but, in the absence of gross atheroma, rupture is apt to occur. This of course is deduced from the appearance of arteries seen in the neighbourhood of a hæmorrhage; the chances of observing the vessel or vessels that are actually responsible for the catastrophe are remote. The pathology of such vessels has been the subject of controversy since the time (1868) that Charcot and Bouchard ascribed apoplexy to miliary (more accurately sub-miliary) aneurysms. When it was later demonstrated that these so-called aneurysms were in reality either subadventitial hæmorrhages, or extravascular clots, the view gained currency that these formations were the result of hæmorrhage and not a predisposing cause. Actually sub-miliary aneurysms can occasionally be demonstrated upon the perforating arteries, as reported by Green (1930) who found one in each of two cases in the careful examination of 10 hypertensive subjects. The vessels concerned, as illustrated in his colour-plate, are in obvious degeneration; leakage of blood is demonstrated by pigment in the adjacent tissues.

In malignant hypertension the characteristic form of arterial and, especially, arteriolar degeneration is a fibrinoid necrosis ("necrotising arteritis") (Fig. 1). A fluffy zone of exudate with similar staining properties often extends beyond the adventitia. Though this change may be widely dispersed in the vessels of the cerebral cortex and subjacent white matter, and associated then with the punctiform or larger hæmorrhages and œdema that go with "hypertensive encephalopathy", the pons is affected with remarkable frequency even when little is demonstrable elsewhere in the brain. It is therefore suggested that this is the reason for the predominance of pontine hæmorrhage in the malignant and nephritic forms of persistent hypertension.

Furthermore it may reasonably be argued that this individual form of degeneration is based upon *vascular spasm.* In support of this it is only necessary to quote two sets of experiments by Byrom: (1) The production of necrotising arteritis in rats by the injection of repeated doses of vasopressin (1937); (2) the direct observation of arterial spasm in the cerebral arteries of the living animal, in association with malignant hypertension, as quoted by Clifford Wilson (1953) in his Oliver-Sharpey lectures.

In 7 of our cases cerebral hæmorrhage was caused by arterial degeneration of the benign hypertensive type in the absence of persistent hypertension and cardiovascular hypertrophy. These were all in the sixth decade and later. Two will be illustrated. (1) P.M. 39/36, a male aged 55. The hæmorrhage formed a large mass, measuring 6 cm. from before back, beneath the hind end of the island of Reil and extending back into the occipital lobe (Fig. 2). The onset of referable neurological disturbance had been sudden, at 2 months before death, and the character of the clot, which was brown and pultaceous, agreed with this history. Dissection of the regional vessels revealed no alternative cause for the condition. Microscopically the border of the hæmorrhage gives evidence of chronic inflammatory reaction, moderate gliosis and free iron in macrophages. Death was precipitated by arteriography, using thorotrast. (2) P.M. 339/51, a male aged 79 (Fig. 3). Right hemiplegia occurred suddenly two days after prostatectomy. Though he subsequently improved slightly his speech was affected and he died in hospital 5 months later from pulmonary embolism. This hæmorrhage (5 cm. in its greatest dimension) has undergone surprisingly little change in spite of its duration and, although there is some increase of collagenous tissue at the periphery, it has certainly not reached the stage of encapsulation.

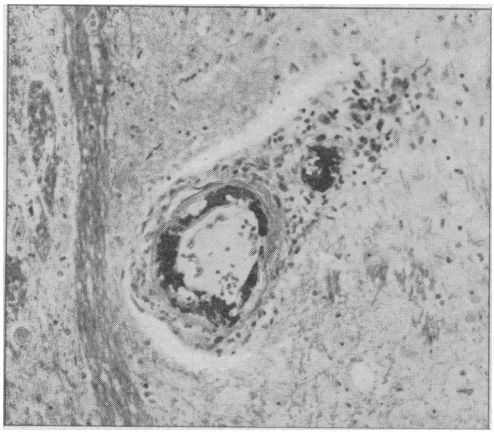

FIG. 1.—Perforating artery of pons showing early stage of fibrinoid change (black) in malignant hypertension Phosphotungstic-acid hæmatoxylin. × 114.

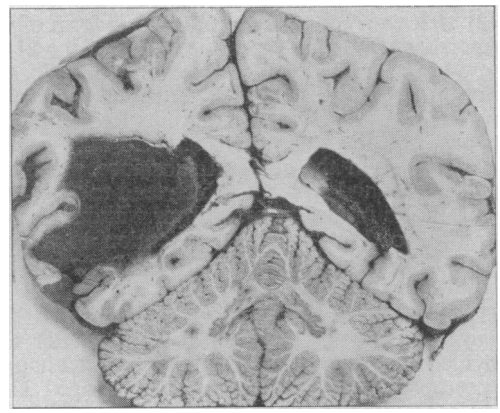

FIG. 2.—Coronal section of brain (P.M. 39.1936). The hæmorrhage reaches the ventricular wall but has not ruptured it.

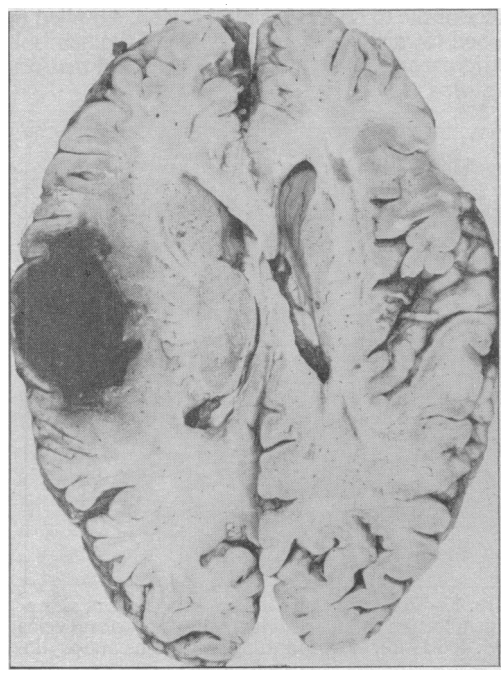

FIG. 3.—Horizontal section of brain (P.M. 339.1951).

Vascular hamartomas.—Any of the recognized types of vascular hamartoma can give rise to spontaneous hæmorrhage.

(1) *Telangiectases.*—These, of essentially capillary structure, are most often found in the pons. They are usually a chance necropsy finding, unsuspected clinically. Spontaneous hæmorrhage has rarely been recorded as a complication, and none occurs in our series.

(2) *Cavernous hæmangioma.*—These favour a subcortical site in the Rolandic area, the basal ganglia and less commonly other parts of the brain. In occasional examples they are multiple. Blood can certainly ooze from them producing pigmentation of the neighbouring tissues, but major hæmorrhages are very rare. In the present series there is one example of multiple cavernous hamartoma (P.M. 441/47, a male aged 56) where the symptoms of a third-nerve palsy and slight extravasation of blood into the C.S.F. suggested the diagnosis of a leaking berry aneurysm on the circle of Willis, and craniotomy was performed on the strength of this. The brain in this case revealed a large number of widely scattered cavernous foci (42 in all) of different sizes. The largest occupied the corpus callosum and foramen of Luschka respectively and were probably responsible for the hæmorrhage. A unique feature was the presence, in the left third nerve, of a small cavernous lesion which was responsible for the palsy.

(3) *Arterio-venous hamartoma.*—This form of vascular anomaly is a notable source of spontaneous hæmorrhage, and is responsible for 20 of the 21 cases of the series classified as vascular hamartoma. These lesions manifest themselves in early life, the majority (7) being found during the 2nd decade followed by the 1st (4 cases), 3rd and 4th decades (3 each). The classical type is the formidable tortuous mass of arteries and veins in the meninges of the middle cerebral area of supply, which burrows into the subjacent brain and may eventually rupture into the lateral ventricle, or produce a hæmatoma in the cerebral substance. These, however, produce symptoms—convulsive attacks, audible bruit and so forth, which lead to their detection. Though sometimes observed in childhood, the examples in our series, with or without hæmorrhage, have been in young or middle-aged adults.

I wish to draw particular attention to a group of small lesions of this kind which, without premonition, may give rise to sudden large and fatal hæmorrhage. They are found in our experience at the following sites :—

(1) *Cerebral convexity*, sometimes concealed in the depths of a sulcus and perhaps involving the adjacent cortex and subcortical white matter more extensively than the meninges. Illustration is provided by a case in which the hamartoma happened to be readily visible on inspection of the brain at necropsy. This was from a woman, aged 32, who was pregnant at 32 weeks. She had suffered from excessive vomiting. Sudden onset of headache, with giddiness, vomiting and collapse led on to deep coma and spasticity of all limbs. Blood was found in the C.S.F. on lumbar puncture. A left sub-temporal decompression revealed a small subdural hæmatoma. She died 4 days after the onset. At necropsy a massive hæmorrhage extended in the white matter of the left cerebrum from the temporal horn to the occipital pole. This was related to a small tangle of vessels in the meninges over the ventral aspect of the temporo-occipital region, supplied by a branch of the posterior cerebral artery; the veins drained towards the lateral border of the hemisphere.

Microscopically, enlarged tortuous and malformed arteries and veins penetrate the brain substance (Fig. 4).

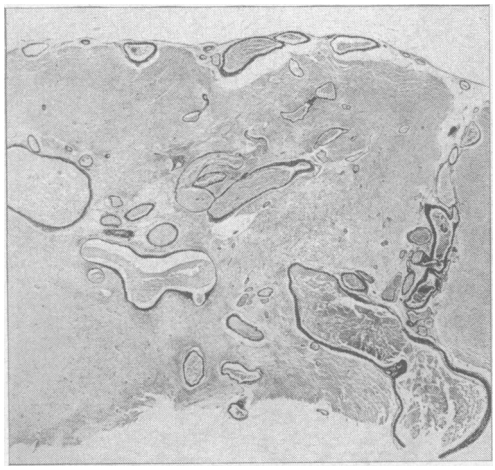

FIG. 4.—Cortex of temporo-occipital region, showing penetration by enlarged tortuous arteries and veins (P.M. 408.1948). Phosphotungstic-acid hæmatoxylin. × 5·5.

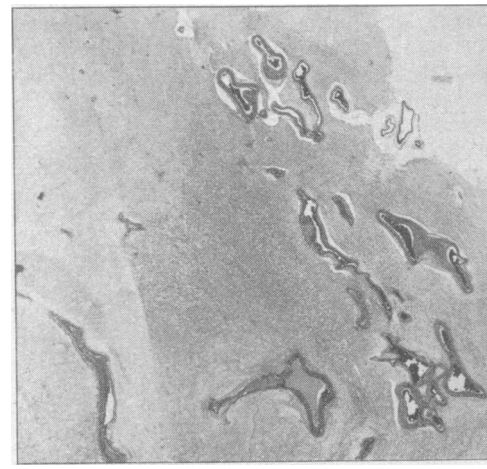

FIG. 5.—Arteriovenous hamartoma near head of caudate nucleus in boy aged 11 (P.M. 295.1938). Masson's trichrome. × 5·6.

Though this example is from an adult, it has been our experience that what might be termed the cryptic type of case seems most often to occur in children. In fact 11 of my 20 arteriovenous hamartomas are from subjects ranging from 16 years downwards. The onset is always catastrophic: the

"bolt from the blue", without warning, and death within 24 to 48 hours as a rule. In 4 of these 11 cases the lesion has lain in the middle cerebral area of supply.

(2) In 5 the hamartoma has been central, predominantly venous, and affecting part or the whole of the pathway leading from the choroid plexus of a lateral ventricle, the vein of the corpus striatum and lesser vein of Galen. This lesion may be obvious from its magnitude on dissection of the brain; on the other hand, it may be so small that it can be missed. In illustration of this I would quote the case of a boy aged 11 (P.M.295/38) who collapsed at school in the manner already described. A massive recent hæmorrhage occupied the white matter from the frontal region to the coronal level of the splenium of the corpus callosum. A tributary of the vein of the corpus striatum, crossing the head of the caudate nucleus was enlarged but no abnormal artery could be seen. On section a small group of vessels with thickened walls lay between the abnormal vein and the border of the hæmorrhage, the area measuring 0·7 × 0·5 cm. Microscopically this was confirmed (Fig. 5). Stains for elastic fibres demonstrated that arteries as well as veins contributed to the hamartoma. This introduces the question as to whether pure venous malformations do in fact exist. They have been described in the literature by many authorities. Though some of our examples are predominantly venous, an arterial element has been constantly found on microscopic examination. This does not imply the presence of arteries which might be interpreted simply as incidental, but that these arteries are abnormal both in size and structure.

(3) The third site of importance is the *cerebellum*, accounting for 2 of our 11 cases. Again the lesion may be remarkably inconspicuous. I have encountered several unruptured, and thus clinically silent, examples of this kind as chance necropsy findings. They have occupied the central white matter of a lateral lobe, measuring only a few millimetres in diameter.

It is thus understandable that, in some cases, the lesion responsible for a large spontaneous hæmorrhage may itself be destroyed in the event. It is more than likely that some of our cases in the category "cause not found" are of this kind, and in particular those of the early decades. In life the venturesome neurosurgeon nowadays may successfully evacuate the hæmorrhage, as described in recent articles by Miss Beck (1953) and by Werner (1954). Miss Beck will deal further with this subject.

The pathologist, on the other hand, is best advised also to evacuate the clot, and thereafter to fix the brain before attempting to discover these small lesions. The multiplicity of petechiæ in the softened tissue about the main hæmorrhage makes this in any event a difficult task, but a hand-lens will help in the detection of tortuous vessels with thickened walls.

Frequent as the cryptic hamartomas appear to be in relation to fatal hæmorrhage, there is little about them in the literature. A good account is however given by Margolis *et al.* (1951) who reviewed the subject and reported a series of 4 cases.

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Mr. M. A. Falconer (Director, Guy's-Maudsley Neurosurgical Unit, London):

Surgical Pathology of Spontaneous Intracranial Hæmorrhage Due to Aneurysms and Arteriovenous Malformations

Until recently our knowledge of this subject was based largely upon autopsy findings. However, the increasing use of cerebral arteriography and the advances of neurosurgery have enabled us not only to demonstrate during life most cerebral aneurysms and arteriovenous malformations, but also to treat them successfully. Consequently we are becoming aware of aspects of their pathology that are not readily apparent in autopsy material alone.

Case-material.—This study is based upon 148 consecutive patients with spontaneous "subarachnoid" hæmorrhage, investigated under my care during the eight years up to January 1954. The diagnosis of subarachnoid hæmorrhage requires qualification for often there is intracerebral, intraventricular, and even subdural bleeding as well. Two characteristic features are, firstly, a sudden or rapid onset of headache with or without impaired consciousness, but with perhaps a stiff neck and kernigism, and secondly, the presence of blood in the cerebrospinal fluid. Often neurological signs, such as a third cranial nerve palsy, hemiparesis, aphasia, or hemianopia, are also present, indicating focal

cerebral damage. However, cases with gross hemiplegia and coma, typically seen in middle-aged and elderly people with evidence of widespread arterial disease, were not included in my series, for in them a massive intracerebral hæmorrhage secondary to generalized vascular degenerative disease was presumed to be present. Furthermore, most cases of this type are quickly fatal.

The presence of blood in the C.S.F. was confirmed in most of my patients, but in a few in whom lumbar puncture was not performed during the acute stages, it was presumed from the clinical picture. The first 69 patients were investigated in New Zealand (Falconer, 1951), and the remainder in the Guy's-Maudsley Neurosurgical Unit (Falconer, 1952). All except Case I were investigated by carotid arteriography, generally performed bilaterally, while vertebral arteriograms were obtained in 10 of the 31 patients in whom carotid studies were normal. The following findings were made:

Intracranial aneurysms in	100 patients.
Arteriovenous malformations in	12 „
Intracerebral hæmatomas without obvious cause in	7 „
Cerebral tumours in	3 „
No cause ascertained in	26* „
	148 patients

* 6 of these patients have since died, and at autopsy 4 were found to have saccular aneurysms (basilar artery 2, internal carotid artery 1, middle cerebral artery 1).

Hæmorrhage Due to Aneurysms

These findings support the prevailing view that leaking intracranial aneurysms are the commonest cause of spontaneous subarachnoid hæmorrhage, accounting for possibly three-quarters of all cases (Richardson and Hyland, 1941; Magee, 1943; Hamby, 1948). These lesions are still often erroneously termed ruptured "congenital" aneurysms, with the implication that they generally cause symptoms by sudden rupture in young persons. However, they are really acquired lesions occurring at a site of congenital weakness, and they do not usually cause symptoms until later life and then by seepage rather than by frank rupture. They are also multiple in more than 10% of cases. Histological evidence indicates that they arise from the interaction of two factors: (1) focal degenerative changes in the intima and elastica of the arterial wall, and (2) a congenital deficiency of the muscular layer, such as occurs typically at the angle of branching of an artery (Carmichael, 1950).

Forty-four of my patients with aneurysms were males and 56 females, a curious preponderance of females which has been noted by others and which is unexplained (U.K. Registrar-General's statistics; Ask-Upmark and Ingvar, 1950; Dinning and Falconer, 1953). In Table I the age-distribution of

PERCENTAGE AGE INCIDENCE

AGE –	10-19	20-29	30-39	40-49	50-59	60-69	70+
100 PATIENTS WITH DEMONSTRATED ANEURYSMS *present series*	5	15	17	28	22	11	2
118 HOSPITAL CASES OF SPONTANEOUS SUBARACHNOID HAEMORRHAGE *Richardson & Hyland's series*	3	13	18	25	21	16	3
250 CASES OF SUDDEN DEATH FROM RUPTURED ANEURYSM. *Keith Simpson's series*	2	3	8	14	23	28	22

Table I

these patients has been compared with that of a well-known unoperated series of hospital cases (Richardson and Hyland, 1941) and of a series of forensic cases in which bleeding aneurysms had caused sudden and unexpected natural death (Keith Simpson's series—Dinning and Falconer, 1953).

The age-distributions in the first two groups are identical, reaching their peak incidence during the fifth and sixth decades of life. In the forensic series, however, the peak incidence is delayed a decade or more later, indicating that death from aneurysms as opposed to morbidity usually occurs later in life, and in the same age-range as death from rupture of an arterio-sclerotic artery.

A total of 110 aneurysms were demonstrated in my 100 patients, multiple aneurysms being disclosed in 9. The distribution of all these aneurysms is depicted in Fig. 1, and conforms to established autopsy

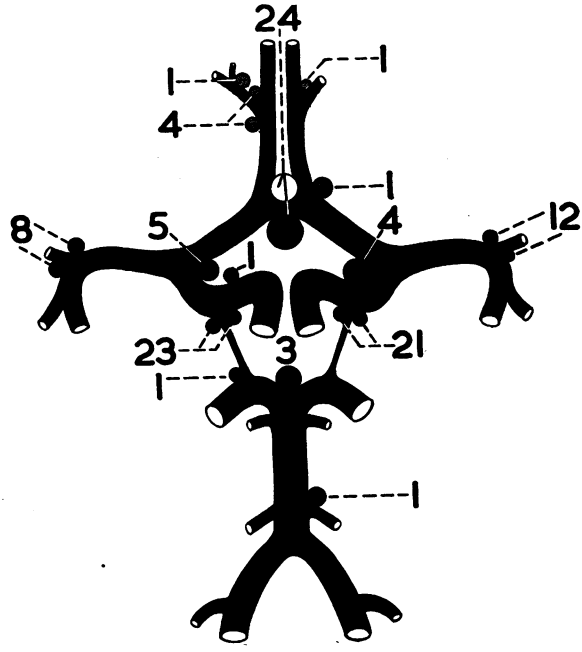

FIG 1.—Sites of aneurysms demonstrated angiographically in 100 patients.

patterns (Richardson and Hyland, 1941; Hamby, 1948). With 2 exceptions all the aneurysms were situated at an angle of branching of a major cerebral artery. The three principal sites were (*a*) the junction of the internal carotid artery and its posterior communicating branch, 44 examples, (*b*) the junction of the anterior communicating artery with either anterior cerebral artery, 24 examples, and (*c*) the first point of branching of the middle cerebral artery within the fissure of Sylvius, 20 examples. As these sites are all on the carotid arterial tree, carotid arteriography will demonstrate most aneurysms, whereas vertebral arteriography is required in only a few cases. Examples of arteriograms of aneurysms in various sites are shown in Figs. 2, 3, 4 and 5. Almost all the aneurysms encountered were between 0·2 and 1·5 cm. diameter, and in only 3 instances was the diameter 2 cm. or more. If necessary, most aneurysms can be readily exposed at operation without sacrificing any brain substance.

Intracranial aneurysms are associated with anomalies of the circle of Willis in, perhaps, as much as one-third of cases (personal observations). Thus in 8 of my 23 cases of aneurysm of the anterior communicating artery both anterior cerebral arteries distal to the communicating artery could be filled only from one carotid artery, indicating a deficiency in the circle (Fig. 3).

From histological evidence bleeding would usually appear to result from a dissecting process affecting the wall of the aneurysm, leading to seepage of blood, rather than from a frank rupture of the sac (Hyland and Barnett, 1954). Our operative findings support this view, for if an aneurysm is exposed at operation following a recent hæmorrhage, one often sees a red spot on its fundus suggesting an intramural hæmorrhage. A sudden burst occurring spontaneously would quickly be fatal, and may well account for a massive extravasation of blood throughout the subarachnoid spaces.

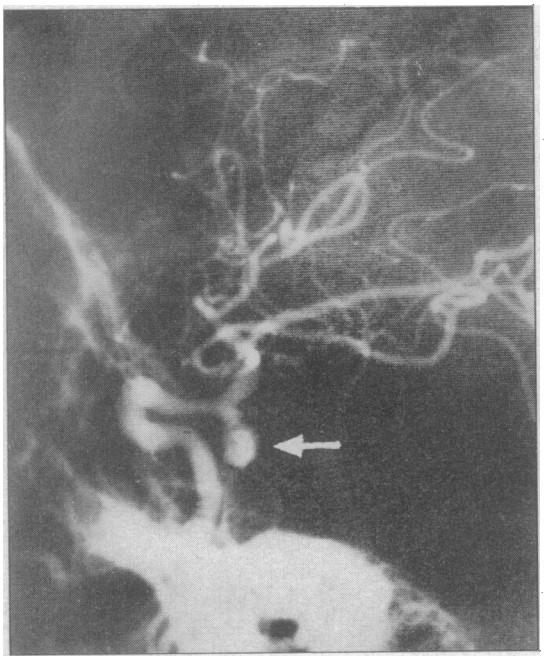

FIG. 2.—Aneurysm at junction of internal carotid and posterior communicating arteries (carotid arteriogram—lateral projection).

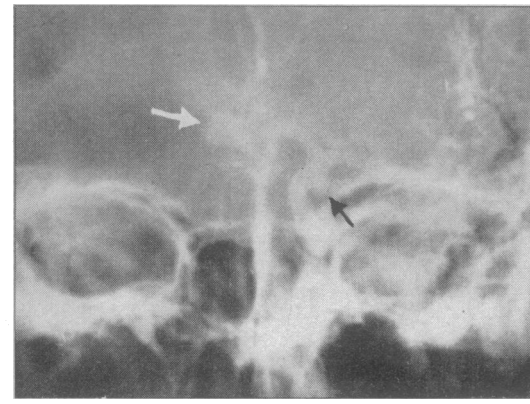

FIG. 3.—Two aneurysms, one (white arrow), arising from anterior communicating artery and the other (black arrow) at junction of internal carotid and posterior communicating arteries. Both were approached successfully at operation.

Such a massive extravasation is never seen at operation. Sizable but focal intracerebral and subdural hæmatomas may be encountered at operation, but as regards the subarachnoid space at the most one meets with only a little patchy clot. By and large therefore it is more correct to describe these

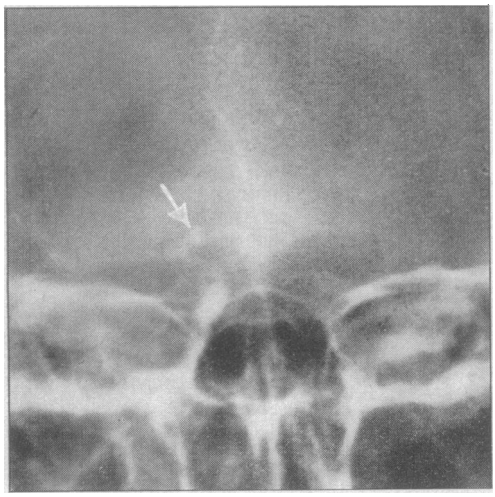

FIG. 4.—Tiny aneurysm arising from carotid bifurcation (carotid arteriogram—A.P. projection). Note also moderate degree of spasm of anterior and middle cerebral arteries.

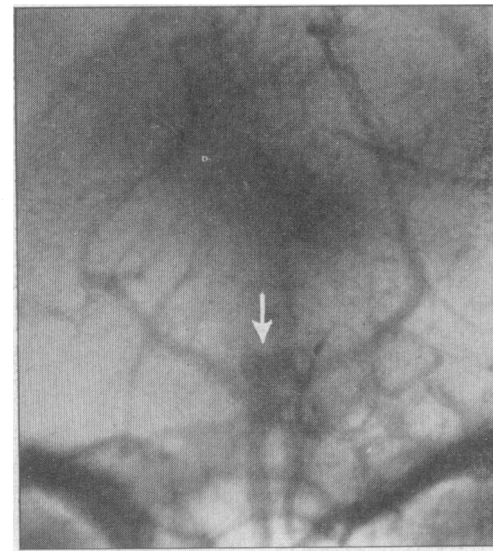

FIG. 5.—Aneurysm at bifurcation of basilar artery (vertebral arteriogram—A.P. projection).

aneurysms as "leaking" than as "ruptured", especially as the actual amount of blood which enters the cerebrospinal fluid, even in a marked case of subarachnoid hæmorrhage, may be as little as 3 c.c.

(Lindsay, 1950). Again symptoms of subarachnoid hæmorrhage seldom appear during strenuous exertion (Magee, 1943; Ask-Upmark and Ingvar, 1950; and personal observations). Possibly the dissecting process also accounts for this observation, for it may be that, although exertion may initiate the process, a period of time is required before the process is completed to the point of leakage. Arterial hypertension is not a significant factor, for its incidence is not appreciably raised in this condition.

Aneurysmal bleeding may occur not only into the subarachnoid space, but also into the cerebral substance and occasionally even into the subdural space. While many aneurysms of the circle of Willis lie within the basal cisterns, and so bleed primarily into the subarachnoid space, aneurysms on the distal arteries as well as those projecting upwards from the anterior communicating artery or from the carotid bifurcation tend to be surrounded by brain substance, and consequently bleed into the frontal or temporal lobes, and only secondarily burst into a ventricle or into the subarachnoid space (Fig. 6 A, B). At autopsy the causal aneurysm in such cases may be obscured, and unless the pathologist deliberately dissects the distal cerebral arteries he may not even suspect its presence.

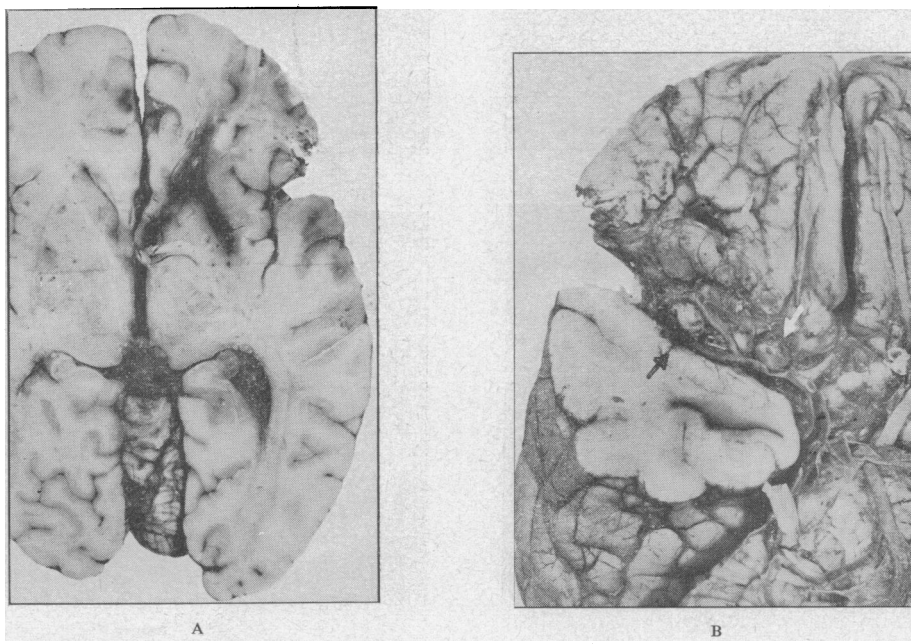

FIG. 6.—(A) Intraventricular hæmorrhage resulting from (B) aneurysm at carotid bifurcation (white arrow). Note absence of subarachnoid clot, and also second aneurysm (black arrow) on middle cerebral artery.

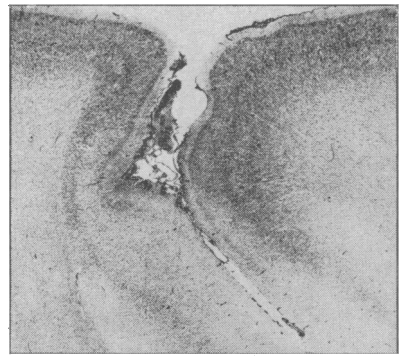

FIG. 7.—Section of frontal cortex showing focal necrosis of the cortex in the depth of a sulcus. Nissl. × 5·2.

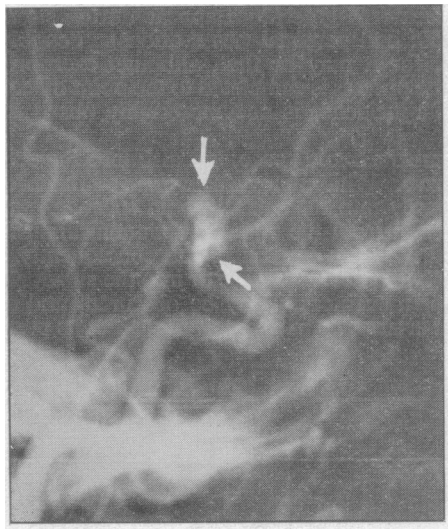

FIG. 8 A

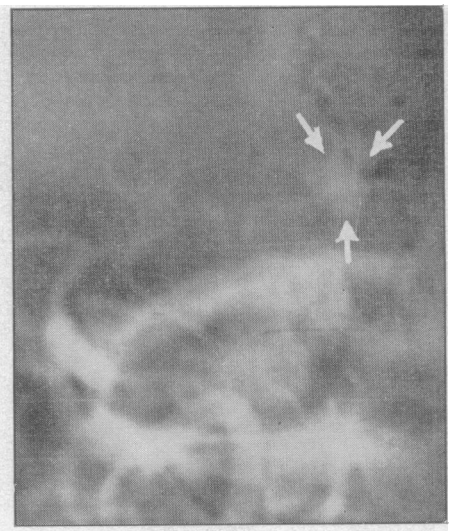

FIG. 8 B

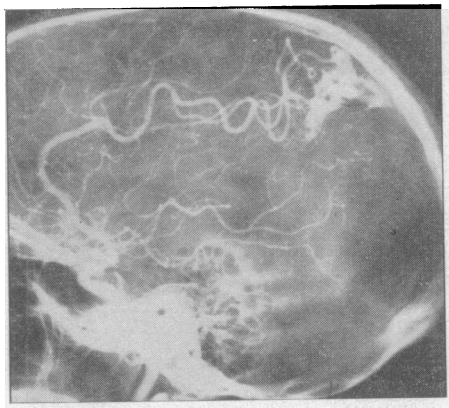

FIG. 9 A

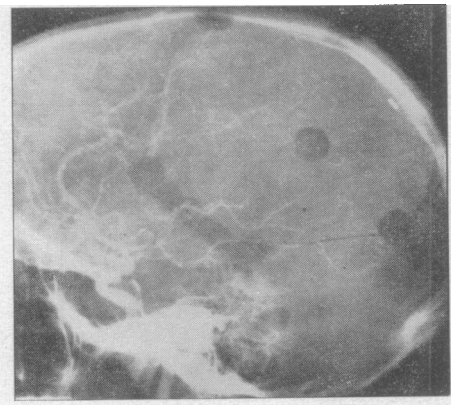

FIG. 9 B

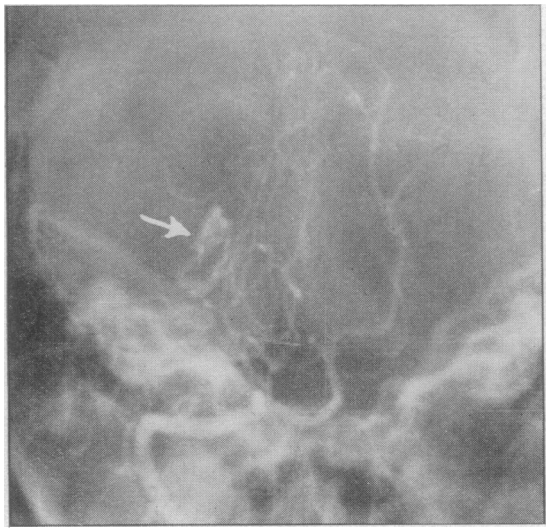

FIG. 10

FIG. 8. — Aneurysm of middle cerebral artery associated with gross vasospasm (carotid arteriograms—(A) lateral and (B) A.P. projections). Notice marked narrowing of terminal portion of internal carotid artery and of anterior cerebral artery, while middle cerebral artery is so grossly attenuated as to be almost invisible.

FIG. 9. — (A) Arteriovenous malformation at termination of anterior cerebral artery. Note large calibre of artery, and also two large veins draining posteriorly from lesion. (B) Following excision of lesion the calibre of the anterior cerebral artery has resumed its proper proportions, while the draining veins are no longer filled.

FIG. 10.—Arteriovenous malformation of right superior cerebellar artery (vertebral arteriogram —A.P. projection). This was successfully operated on by proximal clipping of the feeding artery.

Occasionally an aneurysm may bleed into the subdural space either by direct contact or by rupture of an intracerebral hæmatoma on the surface of the brain (Logue, 1951; Clarke and Walton, 1953); there were two examples in my series, both successfully treated. Arteriography often gives a clue to the presence of these intracerebral and subdural hæmatomas.

There is yet another mechanism by which leaking aneurysms can produce symptoms; this involves the associated vasospasm. As Graeme Robertson (1949) has pointed out, focal necrosis can occur in subarachnoid hæmorrhage at sites remote from the aneurysmal lesion, and without an obvious reason like intracerebral hæmorrhage or arterial thrombosis. A good example of this was found in a case of leaking aneurysm of the left anterior cerebral artery in which death took place, without any arteriographic or operative intervention, 6 days after the onset of symptoms. At autopsy (Dr. A. L. Woolf) the bleeding was entirely subarachnoid, and there was no thrombosis or obvious obstruction of any cerebral artery. Yet a patch of cortical necrosis was found in the territory of the left middle cerebral artery (Fig. 7). To explain such a finding Robertson postulated cerebral vasospasm. Arteriographic evidence of the existence of such spasm is often forthcoming if the investigation is undertaken during the stage of acute symptoms. An instance is furnished by Fig. 8 A, B, where arteriography performed within two days of the onset of symptoms showed gross constriction of the middle cerebral artery supplying the aneurysm, as well as marked but lesser constriction of the terminal portion of the internal carotid artery and of the anterior cerebral artery. Ecker and Riemenschneider (1951) and Norlén and Olivecrona (1953), like myself, have seen such spasm of the cerebral arteries fairly often with recent intracranial hæmorrhage, but not in the quiescent stages, nor in cerebral tumour material. Neurophysiologists hold that the only local stimulus which will send an artery into contraction is a traumatic one. Perhaps the dissecting process in the wall of the aneurysm is such a stimulus, for it seems likely that this spasm acts as a local protective reflex which limits and halts the seepage of blood. It may also account for the high rate of fatalities and hemiplegia that complicate carotid ligation performed in the presence of recent hæmorrhage (Schorstein, 1940). Further, it may explain why attempts at carotid arteriography within a few days of bleeding are liable to be followed by a transient hemiparesis. Hence I now, whenever possible, defer cerebral arteriography for a week to 10 days after the last hæmorrhage, an interval which is short of the period—2 to 4 weeks after the initial attack—when the risks of recurrent bleeding are at their highest.

Hitherto the prognosis of bleeding aneurysms has been deadly, and statistics from various sources confirm the dictum of Ask-Upmark and Ingvar (1950) that out of 5 patients with subarachnoid hæmorrhage treated conservatively, three will die sooner or later from its effects, one will be left crippled, and only one will make a good recovery. The future lies in timely surgical intervention, and the various points considered here are all pertinent. Considerations of operative technique are outside this paper, but it may be permissible to say that 96 of my 100 patients were submitted to carotid or vertebral ligation and/or to an intracranial attack on the aneurysm, with 13 deaths (mortality rate 13%) and with 13 instances of marked residual disability. However, since adopting, in December 1951, the policy of delaying arteriography and operation whenever possible for a week or more after the last hæmorrhage, as well as of using arterial hypotensive anæsthetic techniques, the last 32 of these patients have been operated upon with only 1 death (3% mortality), 2 instances of residual hemiplegia (6% disability), and 2 instances of marked mental slowing similar to that seen after leucotomy—27 cases (84%) made a good recovery. The surgery of leaking intracranial aneurysms is thus passing into the stage of consolidation.

Hæmorrhage Due to Arteriovenous Malformations

These lesions are the second common cause of subarachnoid hæmorrhage, accounting for possibly 5% to 10% of cases. More malformations manifest themselves by epilepsy than by hæmorrhage, but when they do bleed the clinical picture is often indistinguishable from that of subarachnoid hæmorrhage due to leaking aneurysm; any differences are qualitative rather than absolute. The association with epilepsy, the occurrence of bleeding in childhood, or a history of attacks of bleeding extending over many years, is more suggestive of malformation than of aneurysm. No very large series of cases has yet been reported. Of my 12 cases, 11 were in females and only 1 in a male, while their ages ranged from 3 years to 44 years. Mackenzie (1953), however, in his 12 cases observed an equal sex incidence with an age range of between 15 and 45 years.

Professor Russell has dealt with the pathological considerations of these lesions. They are really arteriovenous fistulæ, and can usually be readily shown by arteriography (Figs. 9 A, B and 10). A striking feature is that the main feeding artery or arteries is of larger bore than the neighbouring cortical arteries, and shunts arterial blood directly into large dilated veins, so that the malformation is fed with blood at the expense of the rest of the brain. This is clearly confirmed when angiographic studies are repeated after excision of one of these lesions (Fig. 9).

Thanks to the pioneering work of Olivecrona and Riives (1948), of Norlén (1949), of McKissock (1950) and of Jaegar (1950) the surgical treatment of these lesions has now become standardized (Falconer, 1952). The procedure of election is excision of the malformation, and this is generally practicable with lesions affecting the convexity of the hemispheres. Where it is not practicable, as

in deep-seated lesions, the feeding artery can be clipped and any associated intracerebral clot evacuated (e.g. Fig. 10). All my 12 cases were benefited by operation, and all survived.

I wish to thank my colleagues, Dr. A. C. Begg and Dr. R. D. Hoare, for the arteriographic studies, Miss S. Treadgold for Fig. 1, and Mr. C. E. Engel for most of the photographic reproductions.

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Miss Diana J. K. Beck (Department of Neurosurgery, The Middlesex Hospital, London):

Operable Intracranial Hæmorrhage

In the past three and a half years I have operated on 11 consecutive cases of intracerebral hæmorrhage. I shall give an account of the pathology of this condition in the living, and shall make no more reference to surgery than is necessary to emphasize that timely and appropriate surgical intervention saves lives and certainly diminishes residual disability.

The ages of these patients ranged from 35 to 62 years; 8 were women and 3 men. It is of interest that all but one of these hæmorrhages lay within the territory of the middle cerebral artery.[1] 7 were left-sided, 3 temporal, 2 lower parietal, 1 mid-Rolandic and 1 inferior frontal. Of the 4 situated in the right hemisphere, 3 were frontal and 1 occipital.

All of these patients presented as acute cerebrovascular catastrophes; 2 had been aware of abnormal phenomena such as transitory speech disturbance, weakness or paræsthesiæ in a limb in the preceding weeks or months, so that the possibility of hæmorrhage into a neoplasm had to be considered. Headache had been experienced by all. The conscious state varied from drowsiness to coma. In 3 Cheyne-Stokes' respiration was present. In all but 1, the occipito-temporal, there was hemiplegia of varying degree, often profound and sometimes complete. Complete hemiplegia and complete hemianæsthesia were present in 1 case. Sensory disorders were demonstrable in the lower parietal lesions, and in these and in those in the temporal and occipito-temporal regions, there was hemianopia as judged by the confrontation test. 8 of the patients had been aphasic before lapsing into unconsciousness.

All of these patients were seriously ill, 9 desperately so; it seemed almost unwarranted to intervene in those with Cheyne-Stokes' respiration.

[1] Since reading this paper, one patient, the subject of long-standing hypertension, has died of a massive right cerebellar hæmorrhage nearly three years after a large left temporal hæmatoma was removed.

8 had a high blood-pressure when first seen, ranging from 270/170 to 180/120. 3 of the 11 still have, and all of these were known to be hypertensive before operation.

Lumbar puncture was performed in 9; the fluid was blood-stained in 5, usually deeply so; in 2 ventricular puncture was necessary as part of the operative procedure; in these the fluid was xanthochromic and in each the protein content was raised, 70 mg.% and 140 mg.%. In 1 patient from whom an excessive amount of clear cerebrospinal fluid had been removed, the lumbar puncture resulted in tentorial herniation; in this instance the protein was 55 mg.%, there were two red blood corpuscles per cmm. and an unexplained pleocytosis of 78 lymphocytes per cmm.

In every case a clinical diagnosis was made of the presence and situation of an intracerebral hæmorrhage, confirmed by angiography in 10 cases. In some the angiograms were of poor quality, not because of technical imperfections but, I think, because of ischæmia associated with a rapidly expanding lesion or because of compression, thrombosis or spasm of vessels. In 1 case in which angiography suggested a subdural and an intracerebral clot, ventriculography demonstrated a communication between the ventricle and the clot-containing cavity.

The operative procedure consisted in each case in turning an appropriate osteoplastic flap to expose the cortex. The hæmatoma was completely removed in 9 through a transcortical incision and in the other 2 by tapping through the cortex; in these 2 the collection was fluid and the saline used for gentle irrigation of the cavity returned clear. Solid clot was removed by a combination of natural extrusion, suction and the use of pituitary rongeurs.

Operative Findings.—Six of these hæmorrhages were subcortical and 5 were deep, i.e., the surface of the clot was 3 cm. or more from the cortical surface.

In some, ventricular tapping or the use of 50% sucrose intravenously was necessary for safe opening of the dura.

The appearances varied according as the hæmorrhage was subcortical or deep. In the subcortical group, the exposed brain was highly congested, tense and without pulsation. Thrombosed veins were seen in some with linear hæmorrhages alongside. Localized bulging of a violet or plum colour was seen; sometimes there was yellow staining of the brain and in one instance the cortex was glazed and greenish in colour. The first sign of rupture of the clot through the arachnoid was observed in one case as a bead of coagulated blood. Although in the deep clots there was often congestion of superficial small vessels, it was noted that there was invariably widening and pallor of the gyri overlying the summit of the clot, and these also felt soft to the gently palpating finger. In one case a significant subdural clot had doubtless arisen from rupture of an intracerebral clot still in situ, for there was a ragged tear in the cortex. In three cases there were fragments of degenerate brain amongst the solid clot, but in all nine cases in which a transcortical incision was made, the remaining cavity was smooth and white-walled: it looked as though lined by ivory. The size of the cavity varied from $5 \times 4 \times 3$ cm. to $7 \times 6 \times 5$ cm.; in two of the largest there were in addition to solid clot 60 c.c. of dark fluid blood, and in a third 10 c.c. The contents of two cavities were entirely fluid. There was an active bleeding point seen in the depths of the cavity in 3 cases; only one of these was a hypertensive subject.

Results.—All these patients came under my care from three and a half years to four months ago. All have survived: the result is very good in one, good in eight, (all of these have returned to their normal occupations), fairly good in one and fair in one. I have not been able to relate in detail the dramatic stories of these patients, some of which have been recorded already (Beck, 1953). Although only three of these patients have remained hypertensive since operation, I have no doubt that the others harbour defects in the walls of their cerebral vessels and I should like to suggest that some at least have small angiomatous malformations not demonstrated by angiography.

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Dr. W. H. McMenemey (Department of Pathology, Maida Vale Hospital, London):

The Significance of Subarachnoid Bleeding

As a rule it is not difficult to distinguish true subarachnoid bleeding from normal fluid contaminated with blood shed by the diagnostic needle, especially if the fluid is collected in two, or preferably three, containers. In accidental puncture of a vein there will be decreasing amounts of blood in the three tubes as the needle is washed through by the cerebrospinal fluid. This is the most reliable method of

distinction. There are two less certain ways of telling: (1) the presence of xanthochromia in the centrifugalized supernatant fluid, which is usual in subarachnoid hæmorrhage; (2) the presence of a clot, which may occur with traumatic puncture of a vein.

If, however, lumbar puncture is resorted to within a few hours of the commencement of a subarachnoid hæmorrhage hæmolysis may not have developed; on the other hand xanthochromia may be seen in accidental hæmorrhage under three conditions: firstly, if the contamination is heavy and the erythrocyte count exceeds 150,000—200,000: the faintest trace of colour may then be noticed by reason of the liquid component of the contaminating blood, provided it is of average pigmentation; secondly, if for any reason—and amongst them we would list a precariously distended aneurysmal sac which has been responsible for recurrent incidents—the protein content before contamination has exceeded 150 mg. % and so has just appreciably tinged the fluid before the admixture of fresh blood; and thirdly, if perchance the receiving vessel has been contaminated by some markedly hæmolytic substance such as a detergent. But in addition to these three causes of xanthochromia one must keep in mind the possibility that one may be dealing with the fluid from an oozing aneurysm or a resolving hæmorrhage with the superimposed complication of a "bloody tap". Only a careful analysis of the contents of the three separate tubes will serve to recognize this mixture.

The presence of a clot in one or two of the tubes is strong evidence in favour of accidental bleeding, but it may only be expected if the erythrocyte count exceeds 200,000 (Badoux, 1951). It is seldom noted in true subarachnoid hæmorrhage unless the bleeding is torrential, and this is rare and always quickly fatal.

It seems to be the experience of most observers that blood will begin to hæmolyse in the subarachnoid space within twelve to twenty-four hours. Some authors, including French and Blake (1950) and Richardson and Hyland (1941), believe that on occasions hæmolysis may be delayed up to three or even four days; while others, including Merritt and Fremont-Smith (1937), are of the opinion that it may begin to show at four hours. Exactly how long erythrocytes may remain unhæmolysed in the lumbar sac is less easy to determine because it is not always possible to say when the aneurysm responsible for the initial bleed ceased to ooze; nor, in fact, can one exclude the possibility of a minor recurrence of bleeding or of a small independent bleeding due to congestion. The careful studies of Froin, made just fifty years ago, indicate that the process of hæmolysis of the erythrocytes is well advanced and often complete by the ninth day, and this I imagine is in accord with most people's experience. Richardson and Hyland (1941) found that, on average, erythrocytes had disappeared by the ninth day but in one case they were present on the nineteenth day. To some extent there would appear to be a quantitative factor involved, because the bigger the hæmorrhage the longer it takes to disappear.

The reason why erythrocytes lyse more quickly than one would expect, having regard to their known survival time in the bloodstream, is not clear. Swollen and ghost forms of erythrocytes are seen within a few hours of the beginning of the hæmorrhage, but only a minority of the cells is affected in this way. However, the hydrogen-ion concentration of cerebrospinal fluid rises rapidly once it has been withdrawn (Lange and Harris, 1944), so this fact must be taken into account when the erythrocytes are being studied in the laboratory. The milieu of the cerebrospinal fluid seems to be favourable for the process of hæmolysis and for this reason may present opportunities for its study. Blood in the subarachnoid space acts as a foreign body, hence hæmolysis, and later removal of the altered blood pigments by histiocytes, is to be expected. Histiocytes may be active sometimes before hæmolysis is apparent: even the neutrophils seem capable on occasion of engulfing the erythrocytes (Froin, 1904). For the unexpected contingency of a subarachnoid hæmorrhage one does not need to postulate the elaboration of a hæmolysin, although its employment by the organism as a means of coping with a large hæmorrhage is not an impossibility. Once the delicately adjusted erythrocytes leave the security of their normal environment of the plasma and are cut off from their normal source of oxygen, their inherent instability is increased: swelling and stromatolysis take place, the normal process of wear and tear being accelerated. The physico-chemical basis of hæmolysis is a complicated one and in subarachnoid hæmorrhage may have to do with the permeability of the erythrocyte's membrane to inorganic anions and cations, or perhaps with an impairment of its natural ability to expel sodium.

Hæmolysis is usually maximal about the fifth day. Because the hæmolytic process and the catabolism of the liberated hæmoglobin are going on continuously, spectrometry and bilirubin estimations are of little value, although interesting results were reported by Symonds (1923). Bilirubin appears early in the process of hæmolysis, sometimes within twenty-four hours of the onset of the hæmorrhage.

The length of time the products of hæmolysis persist in the subarachnoid space depends upon the amount of bleeding which has taken place, the presence of any hæmatoma (particularly in the ventricles), the briskness of the histiocytic response and the efficacy of the circulation of the fluid. It depends, too, upon the diluting effect of any therapeutic lumbar punctures. If the hæmorrhage is small

discoloration will have vanished within about sixteen days, but more often it lasts for twenty-eight days or more. The average in the series of cases reported by Richardson and Hyland (1941) was twenty days, the longest being thirty-nine days. If the bleeding has been of any size a raised protein may persist in the lumbar sac for longer than this.

For the surgeon who is visualizing the aneurysm prior to his attack, the duration of the bleeding is of some importance. Lindsay (1950) has implied that bleeding is often slight and more in the nature of an ooze. Certainly the descriptions given by recovered patients of a "sudden snap in the head" and of "a feeling of cold water rushing down the neck" are hardly consistent with an ooze, but perhaps these abnormal sensations are exaggerated in the sensorium. A consideration of the erythrocyte count, the leucocyte count, the differential count and the protein content may repay study. If the leucocytes and erythrocytes are in normal blood proportions one may assume that the hæmorrhage is active, or at any rate very recent. On about the third to fifth day the neutrophil count will fall and the lymphocyte count will rise. The lymphocytosis is absolute as well as relative and is a reactive phenomenon, which may persist for up to four weeks (Richardson and Hyland, 1941). Essick (1920) found lymphocytes and macrophages, derived from the mesothelial cells of the arachnoid, in the fluid as early as the second twenty-four hours, while Hammes (1944) found histological evidence of a commencing reaction within two hours of the bleeding. The lymphocytic response is, however, a variable factor and this variability may depend, in part, upon the degree of distension of the subarachnoid space. The neutrophils disappear because they are absorbed in the clots and because they are engaged in phagocytosis. The leucocyte count may exceed the calculated figure of one cell for every 500 erythrocytes if, as is often the case, there is an associated blood leucocytosis, and also if there has been any degree of hæmolysis.

Jackson (1949) found experimentally that the agent in blood which caused the greatest meningeal response was the hæm component: she believed it was probably bilirubin, as Bagley (1929) suggested. Hæmolysed erythrocytes, which contain free hæmoglobin, caused a greater cellular response than fresh whole blood but considerably less than degenerated blood or oxyhæmoglobin. Occasionally one may get an unexpected leucocytosis in the cerebrospinal fluid which may raise the suspicion of a meningitis.

Of greater value than the white-cell count is the protein content of the fluid. Alajouanine, Thurel and Durupt (1946) pointed out that the proteins might diffuse into the circulating fluid while the cellular elements of the blood were trapped in a clot in the depth of a sulcus. If, therefore, the amount of protein found is greater than the amount expected by reason of the lumbar erythrocyte count, one may deduce either that the protein was raised before the incident or that a hæmatoma is also present. It is generally accepted that an erythrocyte count of 1,000 per c.mm. will account for 1 mg. of protein per 100 ml. Swamy and Subramaniam (1951) give rather higher values, i.e. 10,000 R.B.C. accounting for 15 mg. If, therefore, the protein content is 140 mg. and the erythrocyte count is 100,000 one can deduce that the cerebrospinal protein was in normal amount before the bleeding and also that there is no appreciable hæmatoma. But if the protein is 140 mg. and the erythrocyte count is 15,000 one would assume that the protein was raised before the bleeding or that there is a sizeable hæmatoma present. Of course, these observations are of value only if the fluid is obtained within a few hours of the bleeding. If the withdrawal of fluid is delayed until the fourth or fifth day considerable hæmolysis may have occurred and the protein content will then be disproportionately high. After the first puncture, however, there is introduced the complicating factor of the dilution of the protein in the lumbar pool.

Because, in general, a higher proportion of blood is to be expected in the lumbar sac than in the ventricles, attempts at calculating the amount of bleeding which has taken place are apt to be fallacious. Especially is this so if a clot has formed in a sulcus or in a horn of a ventricle. If the erythrocytes are evenly dispersed and there is no hold-up a bleeding of 3 ml. should—as Lindsay (1950) has shown—give a count of 100,000 per cmm. Indeed, on purely theoretical grounds he has estimated the volume, duration and velocity of the bleeding and also the radius of the rupture in the wall of the aneurysm. Perhaps his most valuable deduction is that the withdrawal of fluid by lumbar puncture in a bleeding patient is not fraught with that danger which is sometimes attributed to it. If, over a period of one minute, sufficient fluid is removed to lower the pressure by 100 mm. it carries the same risk as a rise of 7·3 mm. in the systolic pressure spread over the same period of time. Much more dangerous than the withdrawal of fluid, therefore, are the acts of coughing, straining, or struggling, or the pain of administering a local anæsthetic.

A clear and colourless fluid does not exclude a diagnosis of spontaneous subarachnoid hæmorrhage. Martin (1931) referred to a case where the cerebrospinal fluid was free from blood on the fifth day, while a case reported by Cookson (1933) produced a clear fluid but, on counting, there were 500 erythrocytes, which is about the limit of visibility.

The finding of blood-stained fluid is less constantly met with in true intracerebral hæmorrhage (about 70% of cases), while it is distinctly rare in cerebral thrombosis.

Finally, one must recall the fact that a spontaneous subarachnoid hæmorrhage does not always betoken disease in the brain; the cause may be low down in the cord itself, sometimes without obvious localizing symptoms. Most often the cause is a vascular anomaly of the cord, but recently Fincher (1951) has collected cases of hæmorrhage in association with intradural tumours of the lumbar sac.

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