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Etiology Of Spontaneous Subarachnoid Hemorrhage

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ETIOLOGY OF SPONTANEOUS SUBARACHNOID HEMORRHAGE*

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The term "subarachnoid hemorrhage" is misleading whether or not the adjective "spontaneous" is added to it and owes its popularity to the presence of blood in routine examinations of C.S.F.; but this fact provides no indication as to the source, and does not exclude bleeding in other areas or into other spaces. Spontaneous means nontraumitic and cannot be equivalent of "idiopathic" or "causeless".

The meningeal hemorrhages constitute a complication of other types of lesions. They are simply an event of the pathological picture, generally if not always the last. Similarly to the other forms of intracranial hemorrhage they result from a variety of conditions. The bleeding comes from arteries, veins, capillaries, or sinuses. The vessel walls can be damaged by trauma or diseases. Under the latter are included heterogenous conditions ranging from gross vascular lesions to minimal and obscure processes.

The separation of the subarachnoid hemorrhage from the other intracranial forms of hemorrhage is more artificial than real. The division into ventricular, cerebral, and meningeal (subarachnoid and subdural) types is commonly accepted; yet, any of these frequently occur in association. A "pure" subarachnoid hemorrhage is a relative rarity. The presence of blood in the cerebrospinal fluid constitutes no proof of its meningeal origin but only an indication of how it has leaked. Often subdural hemorrhage bursts through the torn fragile arachnoid, or subarachnoid bleeding resulting from cerebrifugal spread of the hemorrhage, and at times, the subarachnoid hemorrhage is confined to its own system. It is to this group that we intend to refer more specifically here.

Subarachnoid hemorrhage has a wide etiology. Because some cases are obscure, the well established causes of the majority should not be underestimated. For obvious reasons it will be very difficult to distinguish hemorrhagic leptomeningitis from lepto-meningeal hemorrhage as well as the pial and subpial varieties.

If all cases of presence of blood in the subarachnoid space are considred, Courville has shown that more than half are due to external trauma, whereas many others occur during the neonatal period or as a result of extension to the ventricular system of a parenchymatous cerebral hemorrhage. Exclusion of such cases will leave a group in which the picture of "spontaneous subarachnoid hemorrhage" will be recognized.

Spontaneous subarachnoid hemorrhage has been used to designate the clinical condition in which the patient is seized with a sudden, unexpected and usually un-explained attack of severe pain in the head. This picture has been known since the middle of the 19th century when Wilks (1859) gave a brief account of the post-mortem examination of four cases, and Gintrac (1869) who in his book "Maladies de l'appareil nerveux" includes a chapter upon meningeal hemorrhages including thirty-four cases

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of spontaneous subarachnoid hemorrhage, thirty-two previously presented and two of his own. Bramwell (1886) appears to have been one of the first to associate this condition with a ruptured intracranial aneurysm and described what he termed meningeal hemorrhage following rupture of an aneurysm at the carotid termination. It was not until much later that it became generally recognized that spontaneous subarchnoid hemorrhage was of aneurysmal origin. This was due to the work of Symonds (1923-1924) and his detailed description of spontaneous subarachnoid hemorrhage which awakened interest in this important problem. Since then the literature on intracranial aneurysm has assumed enormous proportions and intracranial aneurysms have migrated from the post-mortem room where they were often a chance finding to the bedside.

Anatomical considerations: The arachnoid membrane according to Froin may be considered as consisting of two layers: parietal and visceral. The parietal layer consists of a sheet of endothelial cells lining the internal surface of the dura mater. The visceral layer consists of a thin, transparent sheet of connective tissue covered with endothelial cells which, upon its external surface, is separate from, but lies closely applied to, the parietal layer. Internal to this layer is the pia mater, which is attached to, and therefore follows exactly, the surface of the brain and spinal cord. The potential cavity existing between the parietal and visceral layer of the arachnoid is commonly known as the subdural space. The space which lies between the arachnoid and the pia mater is the subarachnoid space. This latter is normally occupied by the C.S.F. Although it is a true space in the sense that all parts of it are in direct communication with one another, it is to some extent broken up by innumerable trabeculae passing between the arachnoid and pia mater.

The arachnoid is closely applied over the cerebral surface and convolutions but it bridges the sulci. In the base the arachnoid is loosely applied to the brain with large spaces — cisternae — of fluid in free communication with the spaces around the cerebral vessels and with the subarachnoid spaces of the spinal cord.

Into the subarachnoid space blood may enter from different sources:

a. The parietal layer may be ruptured by blood into the subdural space.
b. Hemorrhage from the brain may rupture through the pia mater into the subarachnoid space.
c. Cerebral hemorrhage may rupture into a ventricle and thus gain access to the subarachnoid space (cerebro-meningeal hemorrhage of Froin).
d. Hemorrhage may come from a vessel rupturing in the subarachnoid space.

The hemorrhage into the cistern can extend freely into the spinal subarachnoid space. Over the surface of the brain the narrow sulci often prevent a rapid extension of the blood into the cisterns and in this way may permit local accumulations of blood to expand until the hemorrhage ruptures into the cerebrum (Froin's meningo-cerebral hemorrhage). In cases of basal hemorrhage the extravasation may spread widely over the cerebral sulci and into the spinal subarachnoid space from basal cisterns.

Incidence:

The incidence of spontaneous subarachnoid hemorrhage varies according to the different authors. This variation is explicable on the basis of the material studied.

Table I

Incidence of Subarachoid Hemorrhage

Authors	Total Cases	No. Deaths of S.S.H.
Martland (1939)	2500 sudd. death	54 (2%)
Moritz and Zamcheck (1946)	1200 " "	60 (5%)
Helpern and Rabson (1950)	2030 " "	95 (4.7%)
Adams and Cohen (1947)	329 C.V.A.	19 (5.8%)
Russell-Brain (1954)	200 C.V.A.	30 (15%)
Russell D. S. (1956)	461 autopsies (intracr. hem.)	96 (20.8%)

Ohler and Hurwitz (1932) reported that in the Boston City Hospital in an eighteen month period there were three hundred and fifty-three cases of cerebral vascular accidents and twenty-four cases (6.7%) of subarachnoid hemorrhage.

Adams and Cohen (1947) in a study of incidence of proved vascular diseases of the brain in three hundred and twenty-nine autopsied cases found that arteriosclerosis and encephalomalacia (thrombosis or infarction) was responsible in 41% and meningeal hemorrhage (ruptured aneurysm) occurred in about 5.8%.

Russell-Brain (1954) mentioned that the number of deaths from vascular lesion of N.S. in England and Wales according to the Registrar General's figures in 1942 was 56.048 and in 1952 it was 69.388 or approximately 14% of the total deaths. In two hundred cases of cerebrovascular disease, one hundred from hospital wards and one hundred private patients, Russell-Brain found that hypertension was present in approximately 50% of the cases. Subarachnoid hemorrhage occurred in thirty of the patients (15%).

Kristiansen (1956) in a clinical and radiological evaluation of spontaneuos subarachnoid hemorrhage at the general hospital of Oslo (population 400,000 inhabitants) during the five year period (1950-1954) reported that there had occurred one hundred and thirty cases of spontaneous subarachnoid hemorrhage, and its incidence in relation to the general population of Oslo is calculated in three cases per 50,000 of living persons.

Martland (1939) analyzed a group of two thousand five hundred cases of sudden death and of these fifty-four (2%) were due to subarachnoid hemorrhage.

In a survey of 40,000 autopsy protocols in the Armed Forces Institute of Pathology (1942-1946) Moritz and Zamcheck found one thousand two hundred cases of sudden death in apparently healthy soldiers. Three hundred and fifty of these were due to heart disease, one hundred and ten to meningococcemia, one hundred and forty to obscure causes, and ninty-one (7%) to intracranial hemorrhage. Sixty of this latter group were subarachnoid hemorrhages from proved or presumed congenital aneurysms.

A statistical survey made by Helpern and Rabson (1950) in the office of Chief Medical Examiner, New York City, found that subarachnoid hemorrhage caused 4.7% of two thousand thirty cases of sudden death (nontraumatic). This represented 25.7% of the three hundred and seventy fatalities from diseases of the N.S.

These figures are influenced by the type of hospital from which they are reported; if they were gathered in a general hospital, more cases of cerebral hemorrhage most likely would be reported, while in a specialized neurosurgical service, a greater proportion of cases of subarachnoid hemorrhage would be admitted. In the anatomical series one would expect a greater number of cases of intracerebral hemorrhage, as the prognosis of this condition is more serious than subarachnoid hemorrhage alone.

It seems reasonable to conclude that subarachnoid hemorrhage acounts for about 8% of the cerebral vascular disease (Walton) and it is less common than intracerebral hemorrhage of hypertensive or arteriosclerotic origin. It is also an important cause of sudden death.

Series of cases of spontaneous subarachnoid hemorrhage resulting from ruptured intracranial aneurysms are compiled in Table II. From the analysis of the data collected from general and specialized services, one can conclude that ruptured intracranial aneurysms are responsible for subarachnoid bleeding in about 34% to 60% of the cases. This finding seems to be in contradiction with the most general assumption that ruptured aneurysms are responsible for about 90% of this syndrome.

Table II

Incidence of Intracranial Aneurysms in S.S.H.

(Clinical-Path. Series)

Authors	No. Cases S.S.H.	Suspected or Proved Aneurysms
Timberlake and Kubik (1952)	422	280 (60.6%)
Hamby (1952)	130	44 (34.6%)
Walton (1953)	312	65 (20.8%)
Walsh (1956)	461	249 (54%)
Kristiansen (1956)	130	58 (43%)
Bebin and Currier (1956)	713	243 (34%)

Etiology:

However, aneurysmal or angiomal rupture are considered the commonest cause of spontaneous subarachnoid hemorrhage. From time to time this condition has been described as occurring in many other pathological conditions. In such cases recognition of the etiological lesion is important from the standpoint of therapy.

Subarachnoid Hemorrhage

Among the specific causes of spontaneous subarachnoid hemorrhage are included numerous conditions which are summarized in the following table.

Table III
ETIOLOGY OF SPONTANEOUS SUBARACHNOID HEMORRHAGE

A. INTRACRANIAL
1. Aneurysms
2. Angiomas and other vascular malformations
3. Arterial rupture without aneurysm
4. Neoplasms
5. Blood dyscrasias
6. Dural and venous thrombosis
7. Inflammatory conditions of the brain and meninges
8. Miscellaneous disorders

B. INTRASPINAL
1. Angiomas and other vascular malformations
2. Aneurysms
3. Neoplasms
4. Blood dyscrasias
5. Polyarteritis nodosa
6. Generalized toxi-infective conditions

When one considers all the lesions that can produce bleeding in the subarachnoid space, a very diverse cause can be obtained. Courville listed the causes of one hundred and forty-nine cases found in one thousand five hundred autopsies. In this group were included thirty-five cases of injuries and diseases of the new born. Sands made the study of one hundred and twenty cases of subarachnoid hemorrhage in which 7.5% he attributed to trauma; 25% to arteriosclerosis; 13.6% to infectious diseases; 20% to intracranial aneurysm; and 22% to miscellaneous causes which included brain tumors, blood dyscrasias or were secondary to intracerebral hemorrhage.

MISCELLANEOUS CAUSES OF SUBARACHOID HEMORRHAGE

Focal vascular necrosis
Polyarteritis nodosa
Anaphylactoid purpura
Hemorrhagic nephritis
Acute rheumatism
Sunstroke
Alcoholism
Insulin therapy
Metrazol administration

Gull already noted that the apparent rarity of intracranial aneurysm as a cause of hemorrhage was probably due to the fact that they were not looked for specifically, and he stated that in "young persons dead of apoplexy if a large effusion of blood is

found specially over the surface of the brain in the meshes of the pia mater, the presence of an aneurysm is probable." The faliure to find an aneurysm during the routine post-mortem examination does not exclude that probability as it has been pointed out by Schmidt (1931). He believed that the great majority of, and perhaps all, fatal spontaneous subarachnoid hemorrhages were due to aneurysms. Richardson and Hyland also emphasized the care necessary at necropsy to exclude an aneurysm as the cause of an otherwise unexplained hemorrhage. Hamby in a study of the records of one hundred and thirty patients with spontaneous subarachnoid hemorrhage excluding as cause of bleeding tumors, intracerebral hemorrhage, trauma, and blood dyscrasias found that out of forty-seven cases, the cause of bleeding was a ruptured aneurysm in 44 (93%).

It is evident that subarachnoid bleeding can occur in a variety of diseases. The analysis of series of cases leads to the conclusion that the spontaneous subarachnoid hemorrhage ordinarily is from a ruptured aneurysm of one of the arteries in or near the circle of Willis.

Since the advent of angiography it has been possible to subdivide cases of subarachnoid hemorrhage into three main groups: a. cases in which an aneurysm can be displayed; b. cases harbouring an angioma or other vascular malformations and, c. cases in which no causal lesion can be demonstrated excluding all cases of spontaneous subarachnoid hemorrhage due to general disease processes.

Intracranial aneurysms:

Krayenbuhl gives Morgani (1761) credit for the first description of two aneurysms of the posterior cerebral arteries and according to Fearnsides, Biumi (1765) of Milan was the first to describe an aneurysm found at autopsy. Although aneurysms arising from the cerebral arteries have been recognized for a century or more, it is only during recent years that their clinical manifestations have become fully documented and their life history appreciated.

The papers on Beadles (1907) and Fearnsides (1916) were largely of pathological interest. Symonds in 1924 gave a detailed description of the clinical picture of spontaneous subarachnoid hemorrhage which he related causally to a rupture with a cranial aneurysm, and since the introduction of the angiography by Egaz-Moniz (1927), the interest in intracranial aneurysms has developed enormously. Proof of this fact rests in the excellent monographs and books on this subject, thus the book of Hamby on intracranial aneurysm dealing with symptomotology, signs, treatment, and prognosis according to the exact anatomical position of the aneurysm on the intracranial vascular tree.

Incidence:

Even though numerous statistical analyses have been published on this subject, it is very difficult to assess the incidence of intracranial aneurysms. The difficulties arise from the fact that until recent years this lesion was only or almost only described in post-mortem material.

In 1890 Pitt reported that in nine thousand autopsies at Guy's Hospital between 1869-1888, nineteen cases (0.25%) of embolism and aneurysm occurred. Turnbull,

Table IV

Incidence of Intracranial Aneurysms
(Autopsy Series)

Authors	No. Autopsies	No. Aneurysms
Pitt (1890)	9000	19 (0.2%)
Turnbull (1918)	6,751 (compl.) 4,547 (head)	42 (0.92%)
Mitchell and Angrist (1943)	3080	42 (1.1%)
Courville (1945)	30,000 (50% head)	96 (0.58%)

pathologist of the London Hospital, reported that in 1913 six thousand seven hundred and fifty-one autopsies with 4,547 examinations of the head in which 1.36% of aneurysms of the aorta were found and forty-two (0.92%) of intracranial aneurysms were identified.

Mitchell and Angrist in 3,080 routine autopsies found forty-two (1.1%) aneurysms in thirty-six patients. Courville in a series of 30,000 autopsies in 55% of which the head was examined, found ninety-six (0.58%) intracranial aneurysms.

Richardson and Hyland found forty (0.87%) intracranial aneurysms in 4,618 autopsies.

From the consideration of this data it is difficult to situate the incidence of intracranial aneurysm in the general population. A percentage of 0.5-1% is considered by Hamby as the most reasonable.

Sex and Age:

In general it is accepted that more intracranial aneurysms occur in women than in men. The statistical data seems to prove this assertion. McDonald and Korb found five hundred and seventy-four women and five hundred and nineteen men; Richardson and Hyland twenty-two women and eighteen men; Hamby fifty women and forty-one men; Falconer fifty-six women and forty men.

Concerning the age of presentation of this condition, Dandy made a generalization that is in agreement with most reported series. Few cases are found under the age of twenty; thereafter, the decades contain about an equal number until the age of seventy after which they decline.

Dandy's youngest patient was eight years old and his oldest eighty-one. Dial and Maurer reported the case of a two year old child and numerous other cases have been reported in childhood. In the McDonald-Korb series (1125 intracranial aneurysm) the youngest patient was one and a half years old and the oldest eigthy-seven. They gave the age distribution of five hundred and forty-five intracranial aneurysms: under twenty years 11%, between twenty-one years of age and forty 35%, and over forty 54%. One may assume that about half of the cases of intracranial aneurysms occur after the age of forty years.

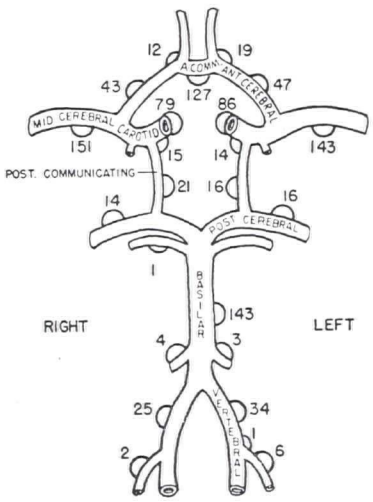
Location of Aneurysm:

The literature in this respect is very extensive and numerous careful compilations have already been made and analyzed from several points of view. The following table and diagram summarizes the incidence of aneurysmal formations in the various cerebral arteries.

Table V

Location of Aneurysms

Authors	Total	Carotid tree	Vert-Bas. tree
McDonald and Korb (1939)	888	735 (83%)	153 (17%)
Riggs and Rupp (1943)	172	155 (90%)	17 (10%)
Hamby (1952)	93	79 (84%)	14 (16%)
Falconer (1954)	110	105 (95%)	5 (5%)
McKissock and Walsh (1956)	249	213 (85%)	15 (6%)



Distribution and location of 1125 intracranial aneurysms collected by McDonald and Korb.

From the statistical information some general conclusions of practical clinical interest can be made. Almost all the intracranial aneurysms are situated at an angle branching off a major artery. Three principle sites are preferential ones: a. the junction of the internal carotid artery and its posterior communicating branch; b. the junction of anterior communicating artery with either anterior cerebral arteries, and c. the first point of branching of the middle cerebral artery with the fissure of Sylvius.

As these sites are all in the carotid arterial tree or in the anterior half of the circle of Willis (83%), they are more likely to be demonstrated by arteriography and more accessible to surgical treatment.

Multiple aneurysms:

They occurred according to Dandy in approximately 15% of his cases. He reported one hundred and thirty-three in one hundred and eight patients. Riggs and Rupp found 28% of multiple aneurysms in one thousand four hundred and thirty-seven autopsies. One of their cases had as many as five aneurysms. Hamby found ninety-four aneurysms in eighty-six patients; eight of these (9.3%) had multiple aneurysms.

Types of aneurysms:

Various types of intracranial aneurysms have been described, the etiology of which may be evident or extremely obscure and elusive. Different classifications have been suggested. Walsh and King provided the following descriptive working classification.

Table VI

INTRACRANIAL ANEURYSMS

I. ARTERIOVENOUS ANEURYSMS
   a) Carotid cavernous: Chiefly fistulas between internal carotid artery and cavernous sinus.
   b) Cirsoid, including the cerebral arteriovenous fistulas and malformations.

II. ARTERIAL ANEURYSMS
   a) SACCULAR
      1. Miliary — the result of atheromatous changes.
      2. Mycotic — through deposition of septic emboli in arterial walls.
      3. Post-traumatic.
      4. Atheromatous of Circle of Willis.
      5. Congenital — "berry" aneurysms of Circle of Willis and other cerebral arteries.
   b) FUSIFORM — chiefly of internal carotid, vertebral and basilar arteries.

Of these different types of intracranial aneurysms we will consider briefly only the three most common types: congenital, atherosclerotic, and mycotic.

Congenital aneurysms: They constitute the majority of intracranial aneurysms. The significance of developmental defects and arteriosclerosis in aneurysmal formations in the elderly subject with hypertension and atherosclerosis is difficult to evaluate. Bremer's and Padget's theory of their development from persistent remnants of the embryonic vascular network seems very attractive. It may well be that almost all intracranial aneurysms, excluding the mycotic or infective group, have a developmental basis in the form of defects in the media at arterial junctions, but secondary factors of hypertension, arteriosclerosis or focal degeneration of the arterial wall play an important part both in the evolution of the aneurysm and its subsequent rupture. From the greatest incidence of rupture in the fourth and fifth decade and prevalence of demonstrable degenerative changes in the wall of the sac one can conclude that these factors are of great significance, but the basic pathology of 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. The medial defect is of developmental origin, but the gap in the elastic membrane is due to degenerative changes. The precise combination of these lesions varies from case to case and Carmichael (1950) states that no valid distinction can be made between the so-called congenital and arteriosclerotic aneurysms.

Arteriosclerotic aneurysms of the "pure" type are relatively uncommon. Severe atherosclerosis may give origin to fusiform aneurysmal dilatations of arteries of the circle of Willis and particularly of the basilar and internal carotid arteries. Richardson and Hyland (1941) found two arteriosclerotic aneurysms both fusiform and involving the basilar artery in their series of fifty-three cases. Dandy found twenty-two of his type and regarded the saccular or "berry" aneurysms as congenital and the fusiform aneurysm of the larger arteries as arteriosclerotic in origin.

Mycotic aneurysms: These aneurysms are due to impaction in a cerebral vessel of infective emboli with subsequent softening of the vessel wall. The complication occurs during the course of a septicemia usually accompanying bacterial endocarditis though these aneurysms may result from other forms of chronic septicemic conditions. They are small saccular aneurysms showing marked inflammatory changes in their wall. They tend to occur in the distribution of the middle cerebral artery. They may be found at a distance from the circle of Willis and in the substance of the brain. Mitchell and Angrist found in their series that eleven of forty-two aneurysms were mycotic. Seven were produced by subacute bacterial endocarditis. The usual clinical manifestation of mycotic intracranial aneurysm is a sudden cerebro-vascular accident such as subarachnoid hemorrhage, sudden hemiplegia, etc., occurring in a well established diagnosis of infective disease.

Other types: Syphilitic intracranial aneurysms are rare. Fearnsides (1916) found no evidence of syphilis in any of his fifty-one autopsy cases and Turnbull (1918) did not see any example of a syphilitic aneurysm in over six thousand necropsies. Richardson and Hyland stated that lues causes 90% of aneurysms elsewhere in the body but plays little role in the formation of cerebral aneurysms. Syphilitic infection produces obliterative arteritis and thrombosis of smaller muscular and elastic arteries such as the cerebral arteries which explains the rarity of cerebral aneurysms of syphilitic origin. There are, however, a few cases of this type of the basilar artery on record.

Aneurysmal dilatation of the smaller vessels may occur in polyarteritis nodosa and the cerebral vessels are occasionally affected. The necrosis of the vessel wall especially the media with inflammatory changes in the adventitia resulting in narrowing of the lumen and thrombosis with subsequent infarction and aneurysmal formation may cause subarachnoid bleeding.

Angiomas and other vascular malformations:

Recently the knowledge of the clinical and pathological features of intracranial angiomas has increased considerably. It is now realized that far from being rare, as were thought, these developmental vascular anomalies are a frequent cause of subarachnoid hemorrhage, cerebral hemorrhage and symptomatic epilepsy.

Subarachnoid Hemorrhage

The term angioma suggests that these lesions are tumors. It is actually almost universally accepted that these are not true neoplasms. These lesions are considered as the second most common cause of subarachnoid hemorrhage accounting for a possible 5-10% of cases according to Falconer (1954). He found twelve instances in one hunrded and forty-eight patients suffering from spontaneous subarachnoid hemorrhage. Walsh (1956) indicated an incidence of fifty-three cases (11%) in four hundred and sixty-one of subarachnoid hemorrhage. Recently Paterson and McKissock (1956) surveyed the symptomotology and treatment of one hundred and ten cases of intracranial angiomas. Of these, sixty-three (57%) of their patients were males and forty-seven (43%) were females. In the majority of instances the diagnosis was confirmed by angiography and in some at the operation. In ninety-two patients an angioma was found in one or the other hemisphere. In one case the angiography suggested bilateral angiomas.

The most common site is in the middle part of the hemisphere (sylvian point) sixty-one cases; then follow in frequency the posterior group (parieto-occipital region) twenty cases, and anterior group (frontal or fronto-parietal region) eleven cases. In the central region (thalamus, basal ganglia, and midbrain) there were nine cases. Others were found in corpus callosum, three; posterior fossa, three; intraventricular, two; and orbital, one.

Dorothy Russell (1954) classified these lesions as hamartomas considering the following groups:

1. Telangiectasies: These are of essentially capillary structures and are most often found in the pons. Spontaneous subarachnoid hemorrhage is rarely recorded.
2. Cavernous hemangioma: They favor a subcortical site in rolandic area or basal ganglia.
3. Arteriovenous hamartomas: They are a common source of spontaneous hemorrhage (subarachnoid and intracerebral).

In the Paterson and McKissock series spontaneous subarachnoid hemorrhage was the commonest sign and was encountered in forty-six patients or 42% of the total (one hundred and ten patients). In forty-two instances a subarachnoid hemorrhage occurred with or without signs indicative of an association intracerebral hemorrhage. In four cases the evidence favored the occurrence of intracerebral hemorrhage. Other common symptoms are epilepsy, twenty-nine patients (26%), periodic migrainous headache, sixteen patients (15%), and progressive hemiparesis, eight patients (7%). These lesions manifest themselves in early life or in adulthood. The average age of onset of symptoms is twenty-four years as nearly 70% of patients had their first symptoms before they were thirty, the majority in their second or third decades (Paterson and McKissock). The youngest patient was an infant of one year having seizures and the oldest a man of fifty-seven when he noticed that his first symptom was the onset of numbness of the left fingers.

The classical type of these lesions is a mass of arteries and veins in the meninges which burrows into the subjacent brain and may eventually rupture into the lateral ventricle or produce a hematoma in the cerebral substance. Small lesions of this kind

are found at: 1. *cerebral convexity,* sometimes concealed in the depths of a sulcus, perhaps involving the subjacent cortex or subcortical white matter. Microscopically they are made up of enlarged tortuous and malformed arteries and veins. Eleven of the twenty of the cases described by D. Russell were of this type. 2. *central* predominantly of venous type are found in the white matter region of the choroid plexus of the lateral ventricle, the veins of corpus striatus and the small veins of Galen. Five cases of Russell belong to this group. 3. *cerebellar,* they occupied the central white matter and could measure a few millimeters in diameter. This group included six cases out of twenty of Russell's series.

In the Sturge-Weber-Dimitri syndrome in which an angioma of the brain and meninges is associated with a facial angioma (nevus flammeus), bleeding may occur originating a subarachnoid hemorrhage. Walton (1953) reported a case of multiple hereditary hemorrhagic telangiectasia as a cause of spontaneous subarachnoid hemorrhage.

Arterial rupture without aneurysmal formation:

In the literature there is an occasional reference to cases in which subarachnoid hemorrhage resulted from a rupture of an atherosclerotic artery at the base of the brain (Walton).

In the series reported by Taylor and Whitfield (1936), one patient died from subarachnoid hemorrhage resulting from rupture of apparently healthy vessels at the bifurcation of the internal carotid artery. A similar case of such an uncommon event was described by Bagley (1928).

Intracranial neoplasms:

Spontaneous subarachnoid hemorrhage in brain tumors is a very rare eventuality. In the one hundred and twenty-four cases of subarachnoid hemorrhage reviewed by Symonds, only two could be attributed to intracranial tumor or cyst. Globus and Sapirstein in a study of ninety-four cases of brain tumors found some evidence of subarachnoid bleeding in twenty-one patients. In the majority of these cases the C.S.F. showed xanthochromia only in a small number (six cases of metastatic carcinoma). It was frankly bloody.

Profuse subarachnoid hemorrhage occurs rarely as the first symptom of a cerebral glioma and meningiomas; however, there are a few examples of such an event (Burges, Echols and Rehfeldt, Walton).

Evident bleeding into the subarachnoid space occurs relatively often in cases of metastatic carcinoma to the brain, particularly in bronchogenic metastatic carcinomas.

Primary or secondary malignant intracranial melanomas are liable to produce sudden subarachnoid hemorrhage that may cause confusion with aneurysmal rupture. The C.S.F. in these cases was grossly bloody in the majority of cases and xanthochromic in several. According to Vigneras sixteen of the thirty-five cases of metastatic melanoma of the brain showed bloody or xanthochromic C.S. In one melanin was demonstrated in the C.S.F. and also melanuria. In the Schnitker and Ayer series there was evidence of subarachnoid hemorrhage in twenty-six (46%) of fifty-six cases of intracranial melanomas.

Subarachnoid Hemorrhage

Northfield and Russell mentioned that death due to subarachnoid hemorrhage occurred in two cases of osteochondroma of the base of the skull observed by them. We had the occasion to perform an autopsy on a case of subarachnoid hemorrhage due to chordoma of the basis of the sphenoid.

List and associates suggested that rapidly growing pituitary adenomas may outstrip their blood supply, thus producing infarction. When this occurs the neoplasm becomes a rapidly swelling hemorrhagic mass which may produce bleeding into the subarachnoid space.

Blood dyscrasias:

Many blood diseases may be complicated by spontaneous subarachnoid bleeding. These include: hemophilia (Gintrac, Timberlake and Kubik), pernicious anemia (McMullen), aplastic anemia, leukemia and agranulocytosis (Strauss). It should be mentioned here that subarachnoid hemorrhage occurring during liver disease is accompanied by severe jaundice and probably subarachnoid bleeding may occur during anti-coagulant therapy.

Dural and venous thrombosis:

Attention to the occurrence of meningeal hemorrhage in cases of thrombosis of the superior sagittal sinus was directed by Gintrac, Hayem, Froin, Klein and Lereder; they described a similar case in which subarachnoid hemorrhage resulted from thrombosis of the right lateral sinus and internal jugular vein. In only one of the eleven cases of venous thrombosis during pregnancy, described by Kendal, did the C.S.F. show presence of blood. Walton described a case of subarachnoid hemorrhage in an infant five months old due to thrombosis of the sagittal sinus resulting from acute otitis media.

Inflammatory conditions of the brain and meninges:

The early accounts by Gintrac, Hayem, and Froin emphasized the association of subarachnoid hemorrhage with acute bacterial infections, infective fevers, anthrax, meningitis, and meningoencephalitis. Sands referred to cases in which tonsillitis, meningococcal septicemia, and brain abscess respectively were complicated by the occurrence of subarachnoid hemorrhage. It has been suggested that in cases of this nature a large vessel or numerous small vessels are eroded by the fulminating inflammatory process (Walton).

Biber reported subarachnoid hemorrhage occurring in cases of tuberculous meningitis in which the underlying pathological process is an arteritis with dilatations in the meningeal vessels. However, recent reports of large series of cases of tuberculous meningitis failed to support the assertion. The thrombosis and the resulting infarction following the vascular occlusions are more common and hemorrhage the exception.

Syphilis, contrary to general accepted assertions in early literature, is rarely a cause of subarachnoid hemorrhage.

Arteritis produced by aspergillosis of the brain has produced a typical subarachnoid hemorrhage in a case (McKee). Similar episodes have been recorded in relapsing fever (Demar and Walmsley). This raises the possibility that the mechanism of bleeding was due to generalized vascular changes rather than to the primary infection.

It is well known that subarachnoid hemorrhage may occur during the course of subacuate bacterial endocarditis. In this condition usually the hemorrhagic episode results from rupture of a mycotic aneurysm. However, in some rare cases of this disease subarachnoid hemorrhage is the initial manifestation before other symptoms of the disease have been recognized (Stein, Starrs). However, in certain cases in which patients died of cerebral vascular accidents in the course of subacute bacterial endocarditis, no aneurysmal dilation of the arteries can be demonstrated. Frequently the hemorrhage is primarily intracerebral with spread to the subarachnoid space. Martland has suggested that it is produced through the general toxic effect upon the vessel wall.

Miscellaneous causes of subarachnoid hemorrhage:

This constitutes a group of hetereogenous conditions resulting in subarachnoid bleeding.

Focal vascular necrosis resulting in subarachnoid hemorrhage and occurring in elderly hypertensive patients within a few days of uncomplicated abdominal operation was reported by Kernohan and Woltman in four cases. All were fatal and at necropsy the bleeding was found arising from rupture of a vertebral artery in two cases and a posterior inferior cerebellar artery in two. The microscopic examination of the arteries revealed that the rupture was due to a focal aseptic necrosis of the vessel's walls. That, according to the authors, had occurred as a result of thrombosis of the vasa vasorum.

Polyarteritis nodosa:

This disease occasionally involves the blood vessels of the brain with subarachnoid hemorrhage complicating its course (Wechsler, Foster and Malamund, Summers).

Bleeding into the subarachnoid space has also been described *anaphylactoid purpura* (Miller), in patients with hemorrhagic nephritis (Sands), and in patients with acute rheumatism. Walton suggested that it is possible that a general allergic vascular response was accountable for the subarachnoid hemorrhage in these conditions.

Other miscellaneous agents apparently concerned in the etiology of individual cases of subarachnoid hemorrhage include *sunstroke* (Bouquet, Doufor cited by Symonds); *scurvy* and *alcoholism* (Strauss and Tarachow). The same authors noted the presence of tuberculous diabetes and Hodgkin's disease in certain cases of subarachnoid hemorrhage. They suggested an etiologic relationship but it seems that association was only fortuitous. Finally, subarachnoid hemorrhage has also been reported in insulin therapy and Metrazol administration (Freed and Wofford, Pedersen).

Spontaneous spinal subarachnoid hemorrhage:

The spontaneous spinal subarachnoid hemorrhage is very rare and less widely recognized. The distinction of this condition from the intracranial spontaneous subarachnoid hemorrhage is not always easy and it is likely that patients with spontaneous spinal subarachnoid hemorrhage are sometimes thought to be suffering from the much commoner intracranial type of bleeding. A survey of the published reports shows that isolated cases of this form of spinal hemorrhage have been described usually in reviews of the spinal vascular abnormalities.

Subarachnoid Hemorrhage

The first observation of subarachnoid hemorrhage confined to the spinal theca was that of Duverney (1868) who described a case of a magistrate who died suddenly of a particular form of apoplexy. The autopsy of this case disclosed a normal appearance of the brain and its membranes, but a large hemorrhage filled the spinal subarachnoid space.

Vigneras, in his monograph upon this subject, remarked that when such hemorrhages occurred spontaneously, they could be attributed to syphilis, alcoholism, or hemophilia, but in many cases it was impossible to ascertain the cause. Other cases resulted from trauma or were secondary to neoplasms of the cord and meninges.

The clinical symptomotology of spinal subarachnoid hemorrhage falls conveniently into three groups (Hensen and Croft):

1. The results of the entry of blood into the spinal subarachnoid space: sudden and agonizing pain in the back "coup de poignard" of Michon; bilateral sciatica; strongly positive Kernig's sign.
2. Symptoms and signs of intracranial extension of the hemorrhage. These follow very rapidly when the hemorrhage is in the cervical region.
3. Symptoms and signs due to involvement of the spinal cord and nerve roots. These may result from the accompanying hematomyelia or the cord may be compressed by blood, blood clot or both.

Etiology:

1. *Spinal angiomas:* They are undoubtedly the commonest cause of spinal subarachnoid hemorrhage. Examples of this type have been published by Balk (1900), Wybur-Masson (1943), Walton (1953), and Hensen and Croft (1956). In the Hensen and Croft series of seven cases, the post-mortem examinations of three of their cases disclosed that two had vascular hamartomas (spinal angiomas). Nevertheless, hematorrachis is not always a common symptom of spinal angiomas. Sargurt (1925), Globus and Doshay (1929), Epstein, Beller, and Cohen (1949), and Brion, Netsky, and Zimmerman (1952) have published series of four, four, six and nine cases of spinal vascular anomalies respectively, all without subarachnoid hemorrhage. On the other hand, Trupp and Sachs (1948) had three examples of hemorrhage among their seven patients. Hematomyelia and hematorrachis may occur together Wyburn-Masson (1943), but they are frequently divorced. Hemorrhage from angiomas may be precipitated by trauma (Brion et assoc.).
2. *Aneurysms* are very rare in the spinal vasculature. One of the patients in Hensen and Croft's series died of an aneurysm of the posterior spinal artery.
3. *Neoplasms:* Krayenbuhl (1947), Roger, Paillas, and Duplay (1949), and Fincher (1951) have drawn attention to the occurrence of subarachnoid hemorrhage with intradural neoplasms. Ependymomas in the lumbar sac are the commonest spinal neoplasm to bleed. Spinal hemangioblastomas, though rare, may be a cause of subarachnoid hemorrhage because of their connection with the pia.
4. *Polyarteritis nodosa:* Hensen and Croft reported a case of spinal subarachnoid hemorrhage presenting periarteritis nodosa and found two other additional cases in the records of Bernhard Baron Institute of Pathology of London.

5. *Blood dyscrasias:* They are a rare casue of massive spinal subarachnoid bleeding. Yuhl (1925) reported a patient who suffered from spontaneous, subdural, and subarachnoid spinal hemorrhage while under treatment with Dicoumerol.
6. *Generalized toxi-infective conditions:* The occurrence of spinal hemorrhage in the course of typhoid fever has been mentioned. Syphilis, and alcoholism are of little importance in the etiology of this syndrome.

Summary:

Spontaneous subarachnoid hemorrhage usually results from rupture of an intracranial aneurysm, or less frequently a cerebral angioma (hamartoma). It can also occasionally result from a variety of pathological conditions. These in the intracranial variety of subarachnoid hemorrhage include: neoplasms, blood dyscrasias, venous thrombosis, inflammatory conditions, focal vascular necrosis, vascular allergy, and even insulin and Metrazol therapy.

Spinal subarachnoid hemorrhage is usually the result of vascular malformations of the spinal cord and meninges; occasionally it results from intraspinal neoplasm, and, more rarely from miscellaneous etiologic conditions.

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