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Subarachnoid Hemorrhages and Intracranial Aneurysms

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INDEX

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I. SUBARACHNOID HEMORRHAGES AND INTRACRANIAL ANEURYSMS

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Approximately 40% of all patients with primary subarachnoid hemorrhages die during the initial attack and 40% of the survivors expire due to the disease sometime within the following five years. Approximately 2% of all sudden deaths are ascribed to subarachnoid hemorrhage (Martland[21]). During the past few years, progressive improvements in diagnostic and therapeutic procedures for subarachnoid hemorrhage have been instituted. These should greatly reduce not only the mortality but also the morbidity of subarachnoid hemorrhages. This report concerns the experience gained at the University of Minnesota in treatment of 69 patients with subarachnoid hemorrhages and 18 additional patients with intracranial vascular abnormalities but who did not have a subarachnoid hemorrhage.

The existence of subarachnoid hemorrhage as a clinical entity has been well established for over a century. In 1859 Wilks[41] gave a brief account of the autopsy findings in four cases and in his "Diseases of the Nervous System" (1883) he has a note on both symptoms and pathology of subarachnoid hemorrhage. Gull[16] in 1859 reported on 62 cases of aneurysms of the intracranial vessels and correlated them with symptoms of subarachnoid hemorrhage. He stated that although one may clinically suspect the existence of an aneurysm, there are no symptoms upon which to base more than a probable diagnosis. Gintrac[13] in his textbook on "Maladies de l' appariel Nerveux" (1869) included thirty-four cases of subarachnoid hemorrhage and commented on the etiology, pathology, and symptoms. In 1904 Froin's thesis "Les hemorragies sousarachnoidiennes"[12] with his careful studies of cerebrospinal fluid both immediately after hemorrhage and during the process of hemolysis was an unrivaled contribution to our knowledge of these conditions. He divided subarachnoid hemorrhages into three types: (1) cerebromeningeal (primary intracerebral hemorrhage with rupture into the subarachnoid space), (2) primary subarachnoid hemorrhage, and (3) meningocerebral (primary subarachnoid hemorrhage extending into adjacent cerebral tissue). This division has been of utmost clinical importance in explaining the sequence of symptomatology. Subsequently, there have been numerous reports in the literature stressing symptomatology (Ingvar[17], Symonds[36], Strauss et al[34], Merritt[22], Sands[31]), pathology (Fearnsides[10], Forbus[11], Richardson and Hyland[27], Sahs and Keil[30]), and treatment (Wolf et al[45], Strauss and Tarachow 35, Schorstein[33], and Dandy[7]).

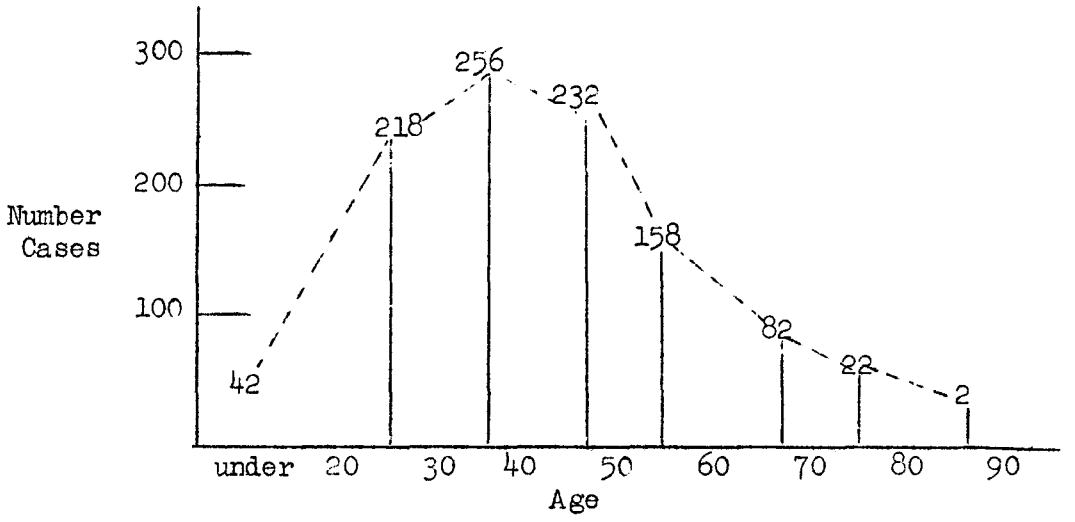
Incidence

Age - Subarachnoid hemorrhage may occur irrespective of the age of the patient. Noran[24] has reported the case of a 28 day old child who died from a subarachnoid hemorrhage and Richardson and Hyland[27] reported death in two patients over 80 years of age to be from this cause, but in general, subarachnoid hemorrhage is a disease of relatively young people. Fearnsides[10] reported an age range from 19 to 53 years with an average age incidence of 38 years. Wilson[44] reported a range from 14 to 67 years with an average of 44.3 years. Sahs'[30] cases were almost identical in age with those of Wilson. Strauss[34] found an age range from 17 to 68 years with an average of 31.3 years. The incidence for 1,012 cases collected from the literature is given in Graph 1.

Sex - Subarachnoid hemorrhage occurs with approximately equal frequency in the sexes. Of 408 cases collected from the literature, 221 (54%) were males and 187 (46%) were females.

Etiology

Subarachnoid hemorrhage may occur secondary to an intracerebral hemorrhage (cerebro-meningeal hemorrhage of Froin) in which case the bleeding point may be rarely from an aneurysm, but more likely a primary rupture of the vessel without evidence of aneurysm is the cause.



Graph 1

Age Incidence of Subarachnoid Hemorrhage

Primary subarachnoid hemorrhage may occur from numerous causes. Foremost among these is rupture of an aneurysm. Infrequent causes are rupture of an angioma, rupture of an otherwise normal vessel due to trauma, blood dyscrasia (purpura, pernicious anemia, leukemia) or toxemia and rupture of an arteriosclerotic vessel. After a thorough review of the literature, Schmidt[32] concluded that subarachnoid hemorrhage in the great majority of cases was caused by a ruptured aneurysm and emphasized that failure in locating an aneurysm at autopsy did not exclude its existence. Symonds[36] demonstrated that subarachnoid hemorrhages of unexplained origin are often caused by aneurysms that are not found since they frequently are minute and may be imbedded deeply in the clot.

It has long been realized that the aneurysmal dilatation or sac is a weak area in the vessel wall and is prone to rupture. Eppinger[9] pointed out that this weakness was congenital and due to defects in the elastic tissue of the vessel. Turnbull in 1918 and more recently Forbus[11] demonstrated the presence of local defects in the media of cerebral arteries at the apices of the angles formed by arterial branching or bifurcation. Forbus found local areas in which the media was completely absent in the cerebral arteries of each of 12 cases in which aneurysms were found. Moreover, he found similar defects in the cerebral arteries of 25 out of 33 cases in which there was no aneurysm. Defects of media were found in one of two stillborn infants examined. Since defects were equally frequent in children and adults, he concluded there was a factor in addition to the weakened vascular wall that was instrumental in aneurysm development. He then demonstrated physiologically that increases in pressure were greatest at the points corresponding with bifurcation angles in the arteries. He suggested that the evolution of aneurysms in such areas is largely due to mechanical factors consisting of increased intravascular pressure, normally developed at the bifurcation, exerted against the congenitally weak arterial wall in the same area. Histologically, the sequence of events is that the muscular defect in the media is the basis of dilatation, and that degeneration of the internal elastic lamina due to continued over-stretching is the final stage in the production of the aneurysm. Glynn[14] examined ten cases with aneurysms of the circle of Willis and 15 with normal circles and concluded that medial defects per se were not the primary factor but that the concentration of the elastic

tissue is in the internal elastic lamina in the cerebral arteries instead of being spread throughout the coats as it is in other vessels thereby permitting greater vulnerability to injury and degeneration.

Dandy[7] agreed that most aneurysms were of congenital origin but he did not believe that they could occur only at the bifurcation of vessels where the various investigators had found defects in the vessel wall. He studied the embryogenesis of the intracranial vascular tree and concluded that these congenital defects could also occur at sites where embryonic vessels or vascular buds had developed but later disappeared. He strongly denied that all aneurysms were junctional. He believed that they occurred at sites of weakness resulting from embryonic vessel formation. More recently Bassett[5] has added evidence to confirm this. Whether the weakness of the wall is always congenital, however, is strongly debated. Ellis regarded arteriosclerosis as a primary cause of aneurysms. Others (Symonds[36], Strauss et al[34], Tuthill[37]) have agreed with this. Tuthill postulated a local fatty degeneration of the media in association with elastic tissue changes. He criticized Forbus' findings because the media defects could conceivably be caused by artifacts from imbedding and staining the tissues. Richardson and Hyland examined vessels with the possibility in mind of producing artifacts by twisting the tissue and they concluded Tuthill to be wrong and agreed with Forbus that the defects were real.

Ayer believed that most aneurysms were congenital because he found involvement in several members of one family and also found aneurysms in each of maternal cousins. Woltman and Sheldon described a subarachnoid hemorrhage occurring in a patient with congenital stenosis of the isthmus of the aorta and reported this condition to be associated with cerebral aneurysms.

Riggs and Rupp pointed out that the lack of a significant increase in number of aneurysms in older age individuals largely eliminates systemic disease such as arteriosclerosis, hypertension, etc., as primary etiologic factors. Failure by them to find aneurysms in a large series of children under 10 years of age lends confirmation to the theory of Forbus that miliary aneurysms as such are not of congenital origin but that structural defects of embryonic origin in the arterial wall are fundamentally related to the development of aneurysms. They found that 86% of aneurysms lie in the region of arterial bifurcation where there is a potential source of increased arterial tension. Precipitating factors - Strauss and Tarachow[35] studied 105 cases of subarachnoid hemorrhage and came to the conclusion that extrinsic factors such as exercise or straining were not as important as intrinsic factors in the production of subarachnoid hemorrhage. But neither extrinsic or intrinsic factors were very important in their opinion. In a series of 34 patients with subarachnoid hemorrhage, Strauss, Globus, and Ginsburg[34] found as possible precipitating agents, cardiovascular disease in three, hypertension in two, syphilis in two, eclampsia in one, exertion in two, emotion in three, alcoholism in one, and trauma in two. In a series of 64 patients, Sahs and Keil[30] found marked exertion in 10, mild exertion in 32, and no precipitory factor in 22. Richardson and Hyland[27] found that the majority of their patients were enjoying good health when their hemorrhage occurred and that they had no evidence of an underlying disease at the time of examination. In their series of 118 cases, the only condition which was found with sufficient frequency to render it significant was hypertension and this was found in only 13% of their cases. They also found that the activity of the patient at the time of hemorrhage was of little importance in determining its onset. Wolf et al[45] stated that the majority of their 46 patients were engaged in ordinary work when rupture took place. In 37 of 45 cases Wilson et al[44] found no precipitating factor, in 8 there was a history of alcoholic debauch, mild exertion, or argument. They concluded that it was impossible to tell if these factors play any causative role; they felt that they

were probably coincidental.

Symptoms and Signs of Subarachnoid Hemorrhage

The onset of symptoms in patients with subarachnoid hemorrhage is usually abrupt but occasionally mild premonitory symptoms may exist for several hours or days. These include mild headaches, vertigo, visual disturbances, and ataxia. They are probably due to recurrent small leakages from the aneurysm. Richardson and Hyland[27] concluded from their clinicopathological studies that the rupture of an aneurysm sac probably is a gradual process with stretching, hemorrhagic dissection and mild recurrent leakage.

The most common initial symptom is a generalized excruciating headache (Ingvar[17]) which tends to predominate over the occipital region and may extend down over the back of the neck. Occasionally the headache may be localized to one occipital, parietal, or frontal region. Headache is the first symptom in about 80% of patients. It may be accompanied by vomiting and in about 5% of patients vomiting is the initial symptom. Loss of consciousness occurs as the initial symptom in approximately 10% of patients. Symonds[36] stated that this loss of consciousness, even with small hemorrhages, is due to the shock of the bursting vessel with effects similar to cerebral concussion. Other symptoms that rarely occur initially but often occur sometime during the illness are vertigo, visual disturbances, convulsions, irrationality, chills, speech disturbances, and pains in the back and extremities. Actually all symptoms can be divided into (1) those of a general nature due to generalized increased intracranial pressure and to blood diffused throughout the subarachnoid space, and (2) those of a focal nature due to the local involvement of structures either by the hemorrhage or its associated aneurysm. The site and the amount of the hemorrhage determines the sequence and degree of symptoms. Symptoms of a focal nature will be discussed later along with the focal signs.

As the symptoms, so also the signs may be divided into those of a general and those of a focal nature. The general signs are due to blood spreading through the cerebrospinal fluid and are similar to an aseptic meningitis. They include nuchal rigidity, mental retardation, generally diminished reflexes, low grade fever, and leukocytosis. In addition to these signs of meningitis, there may occur (1) evidence of blood in the cerebrospinal fluid, (2) ophthalmoscopic abnormalities, and (3) renal abnormalities. When performing a spinal puncture on a patient suspected of having a subarachnoid hemorrhage, the fluid should be collected successively in three bottles. The concentration of blood if a subarachnoid hemorrhage is present should be the same in each bottle. The spinal fluid has three characteristics: (1) an even admixture of blood with cerebrospinal fluid, (2) absence of coagulum, and (3) xanthochromic supernatant fluid. None of these three features is observed in cerebrospinal fluid contaminated by accidental injury to veins during a lumbar puncture. The concentration of blood is due (1) to the severity of the hemorrhage, and (2) to the situation of the ruptured vessel. Blood extravasated into one of the basal cisterns will find its way more readily to the lumbar region than will blood extravasated from a vessel over the cerebral surface or in the lateral ventricles. Symonds found that the fine trabeculations permeating the subarachnoid space tend to promote coagulation of blood at and around the point of leakage. This tendency to promote clotting is most apparent in the cases of cortical or ventricular hemorrhage owing to the obstacles of diffusion. In the cases of severe basal hemorrhage, however, the blood spreads out before clotting has time to occur so that the subarachnoid space over the cerebrum and down into the lumbar region becomes filled with a thin layer of blood. In the early stages after the subarachnoid hemorrhage, the number of leukocytes in proportion to the erythrocytes is similar to blood. Later there is an increase in leukocytes (especially P.M.N's, large mononuclears, and eosinophils and later lymphocytes)

and a small increase in leukocytes may still be observed when the erythrocytes have disappeared from the fluid. All this is associated with an increase in bile pigment in the blood and urine. In the series of Richardson and Hyland[27] evidence of fresh blood, shown by the presence of erythrocytes disappeared in periods varying from four to nineteen days (average nine days) after onset. They found xanthochromia may develop in 12 hours, usually it develops in 24 hours, but may not be found for 3 to 4 days after onset. The cerebrospinal fluid returned to normal in 10 to 39 days (average 20 days). Strauss et al[34] found the cerebrospinal fluid to contain no blood in 2 of 34 cases of verified subarachnoid hemorrhage.

The ophthalmoscopic abnormality characteristic of subarachnoid hemorrhage is a subhyaloid extravasation of blood which occurs in 10% of cases. The blood dissects forward in the optic nerve and appears beneath the retina. Papilledema may also be present. Griffith, Jeffers, and Fry[15] commented on the infrequency of papilledema (10%) in spite of the high cerebrospinal fluid pressure so commonly present in patients with subarachnoid hemorrhage. They concluded from experimental work that blood in the spinal fluid, if in sufficient amounts, tends to block the perineural spaces of the optic nerve and so prevent the development of papilledema.

The presence of massive albuminuria in subarachnoid hemorrhage was first noted by Widal in 1903. It has been postulated that this albuminuria may be due to a lesion in the brain stem. Focal signs produced in patients with subarachnoid hemorrhage are due either to local pressure on adjacent regions by the extravasated blood or to extension of the blood into the adjacent brain tissue with disruption of function of the corresponding part. Richardson and Hyland[27] found in their series that aneurysms rarely attain size sufficient to compress adjacent structures. However, it is well established that the pressure exerted by an unruptured aneurysm occasionally may cause a severe neurologic defect. Jefferson[18] has reported clinical syndromes produced by carotid trunk aneurysms. He divided them into those occurring in the subclinoidal portion which are symptomatic by involvement of the extraocular nerves and of the trigeminal nerve and into those occurring in the supraclinoidal portion. The supraclinoidal aneurysms arise from the carotid artery in the region of the ophthalmic or posterior communicating or at the final bifurcation of the main trunk into anterior communicating and middle cerebral arteries. With these lesions, visual loss is more common and is due to compression of the optic nerve or of the optic tract, chiasm or radiations. Jefferson was able to find records in the literature of only 66 examples of disturbance of vision by aneurysm in addition to the 12 cases of his own. This, of course, does not include visual loss from subhyaloid hemorrhage as described earlier. Additional signs of unruptured aneurysms in this region are anosmia, somnolence, visceral and sympathetic disturbances, and dyspituitarism.

Unruptured aneurysms of the anterior communicating and anterior cerebral arteries may also produce visual disturbances, usually by pressure on the chiasm or optic nerve. Similar to those on the carotid artery, these aneurysms may, if sufficiently large, compress the extraocular nerves or hypothalamos.

Unruptured aneurysms on the middle cerebral artery seldom, if ever, produce symptoms. They usually are relatively small and do not compress the adjacent structures sufficiently to be symptomatic.

Aneurysms may occur on the basilar artery or its branches. Pressure may be produced on the brain stem and on the cranial nerves in the posterior fossa. These must be differentiated from cerebellopontine angle tumors, primary tumors of the brain stem, and chordomas.

The significance of these unruptured aneurysms is the similarity they bear to neoplasms. Symptoms are produced by pressure from the gradually expanding mass and differentiation may be possible only by angiography or surgery.

Aneurysms may rupture and the blood remain confined to the region immediately surrounding the aneurysm, even to the extent that no evidence of the hemorrhage can be found in the lumbar spinal fluid. Focal symptoms produced by such a hemorrhage are similar to those described above for large unruptured aneurysms.

Richardson and Hyland[27] found in 70% of their cases that blood extravasated into the cerebral substance. Courville and Olson[6] also described the frequent occurrence of intracerebral hemorrhage occurring secondary to subarachnoid bleeding. Although they were unable to ascertain in their patients any characteristic clinical syndrome of such extravasation, others (Gull[16], Albright[2], Symonds[36]) have observed a correlation between sequence of symptomatology and location of an aneurysm. Invasion of the frontal lobes by hemorrhage usually results from ruptured aneurysms of the anterior cerebral, anterior communicating, or middle cerebral arteries. When this occurs, the symptomatology depends upon the site and extent of the hemorrhage. The frontal lobe is penetrated much more frequently via its medial surface by hemorrhage from anterior cerebral and anterior communicating artery aneurysms and such hemorrhages may penetrate into both frontal lobes. When cerebral penetration does occur, Courville[6] has found the blood tends to follow fiber tracts. With frontal lobe involvement a contralateral hemiparesis is the commonest manifestation and this may vary from a slight weakness to severe hemiplegia. The paresis is frequently confined to or is maximal in one leg. Aphasia may result if the dominant hemisphere is involved. Intellectual impairment may occur; it differs from that observed during the acute stages of the subarachnoid hemorrhage in that it is more severe and tends to persist. Involvement of the ipsilateral arm and/or leg may result from a herniation of the temporal lobe into the incisura (Moore and Bockman[23]).

Hemorrhage into the temporal lobe usually results from rupture of aneurysms located at the carotid bifurcation or along the middle cerebral artery. If the lesion is on the dominant side, an aphasia may develop. Extension of the hemorrhage posteriorly in the lobe produces visual field defects. The hemorrhage may dissect medially to involve the internal capsule giving rise to a hemiplegia. Sensory, as well as motor tracts, are usually involved.

Cranial nerve palsies are frequent in patients with aneurysms and are due to the close proximity of some cranial nerves to the internal carotid artery and its major branches. The 3rd, 4th, and 6th nerves are most frequently involved. The 5th nerve is less often involved and when it is there usually is pain in one or more of its divisions. Other cranial nerves less frequently involved are the 2nd, 7th and 8th. There may be a residual paralysis of the affected nerve after recovery from the other symptoms of the hemorrhage.

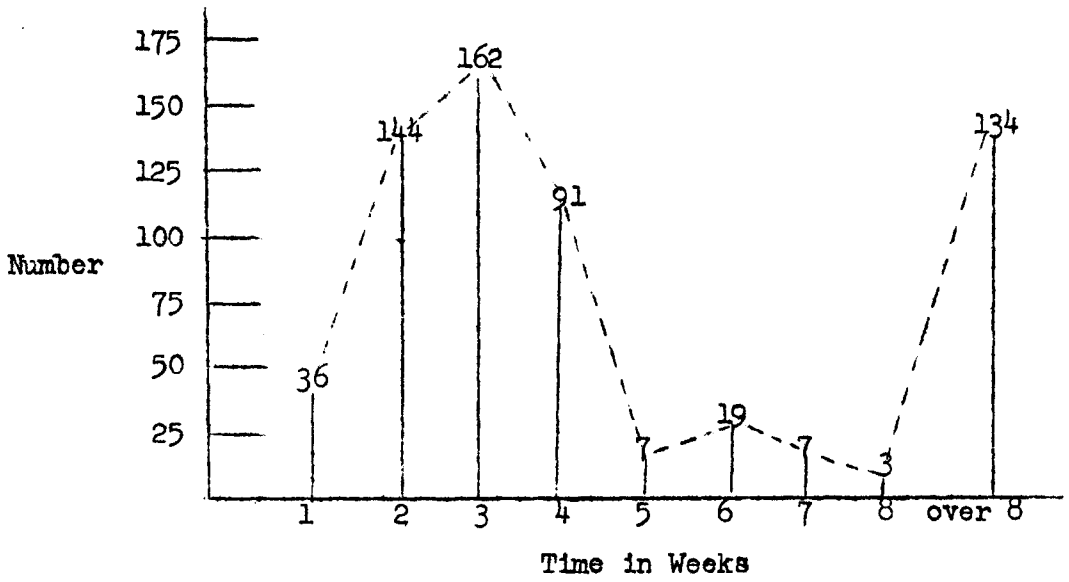
Prognosis

The prognosis in patients with subarachnoid hemorrhage has been poor both relative to mortality and morbidity. Reports in the literature on the mortality rate for the initial attack vary considerably. Most of the reports are of hospitalized cases and in many of them no consideration is given to patients expiring prior to admission. Sahs and Keil[30], however, have emphasized that clinics obtaining patients from long distances have lower mortality rates because the patients expire prior to reaching the hospital. Wolf et al[45] reported a 29% mortality rate for the initial attack but others have had a much higher rate. Magee[20] noted 35% mortality in 150 patients, Richardson and Hyland[27] 52% in 118 patients, and Hamby[16a] 45% in 98 patients. In over 500 cases collected from the literature by the authors, the mortality rate for the initial attack was 44.3%. Twenty-eight of the 69 cases of subarachnoid hemorrhage seen at the University of Minnesota were in the initial attack; the mortality for the initial attack was 32%.

Of those who survive the initial sub-

arachnoid hemorrhage, the probability of a recurrent hemorrhage occurring is very great. Wolf[45] reported 52% had recurrent attacks, Magee[20] reported 33%, and Hamby[16a] reported 50.5%. In 603 cases collected from the literature who survived the initial attack, 51.5% had recurrent attacks. Almost all authors agree that the prevalent time for the recurrent attack is in 2 to 4 weeks after the initial attack. In the 603 cases collected from the literature, the greatest number had recurrence during the second and third week. (See Graph 2).

In the University of Minnesota series the frequency was 57% and the time of



Graph 2

Subarachnoid Hemorrhage Interval Before Recurrence

recurrence varied from one day to 2 years with the majority recurring during the second to fourth week.

The mortality rate for recurrent attacks is higher than for those with initial attacks. Wolf[45] found a 40% mortality rate, Magee[20] 64% and Hamby[16a] 72% for patients with recurrent attacks. In the University of Minnesota series the mortality for recurrent attacks was 34%.

There are certain factors which have been found to unfavorably affect the prognosis. They are (1) history of previous attacks, (2) multiple hemorrhages while in hospital, (3) mental disturbances occurring after the attack, (4) unconsciousness during and following attack and, (5) convulsions during attack. The last three factors are dependent directly on the severity of the bleeding. Of 62 cases with loss of consciousness sometime during the attack, Richardson and Hyland[27] found a 62% mortality. The longer the period of unconsciousness, the poorer the prognosis. The age of the patient does not affect the mortality rate according to most observers (Hamby[16a], Martland[21]) although Richardson and Hyland found the average age to be 10 years higher in the fatal cases. Similarly, hypertension was not a significant factor in mortality (Wolf[45], Richardson and Hyland[27], Hamby[16a]). It seemed to be equally prevalent in those that recovered as in those that expired. There are reports in the literature (Sahs and Keil[30]) stating prognosis is influenced by both age and hypertension but any increase in mortality is rather minimal as suggested by Hamby who found hypertension in 21% of patients who recovered and 24% of patients who died.

In the University of Minnesota series, the factors that seemed to influence mortality were unconsciousness at the onset of the attack and hypertension. Of 40 patients with unconsciousness at the onset, 22 (55%) died and of 21 patients with hypertension, 10 (45%) died. Factors that did not seem to influence mortality were activity at time of onset, the presence of severe neurological signs, and the presence of premonitory headaches. The morbidity of patients suffering subarachnoid hemorrhage is very great. Wolf et al stated that 20% of patients with subarachnoid hemorrhage who survive show severe neurologic sequelae. Magee reported 32% of their survivors to be permanently disabled. Sahs and Keil reported 24 (37.5%) of 64 patients to have sequelae. Of these 24, six had a hemiparesis or hemiplegia, 11 had ocular palsies, 3 had visual field defects, 2 aphasias, and 2 some other type of defect. In the University of Minnesota series there were 66 patients who survived and upon whom follow-up studies were obtained. The neurological sequelae in this series is given in Chart I and is compared with the sequelae found in 21 patients upon whom an operation was performed for a vascular lesion. The interesting fact is that irrespective of whether the lesion was attacked surgically, the frequency of sequelae was essentially unchanged. By operation, however, the mortality rate was reduced from 33% to 4.9%.

Chart I

Subarachnoid Hemorrhage - Sequelae

	Without Surgery (66)		With Surgery (21)	
Sequelae	No.	Percent	No.	Percent
Hemiplegia	7	15.8	3	15.0
III N. Palsy	-	--	2	10.0
Blind	-	--	1	5.0
Aphasia	2	4.5	-	--
Convulsion	2	4.5	-	--
Psychotic Behavior	2	4.5	-	--
Headache and Vertigo	6	14.7	-	--
Homonymous Hemianopia	1	2.2	-	--
Deaths	22	33.	1	4.9

Treatment

The treatment of patients with subarachnoid hemorrhage has changed drastically in the past 5 to 10 years. The reason for this change has been improved methods of diagnosis (better recognition of the clinical syndromes and angiography) and greater knowledge of the surgical management of intracranial aneurysms. Many of the older therapeutic procedures have been retained and are still of value, but because of the present day tendency to perform angiograms early and to eradicate the aneurysm surgically, there is less tendency to carry out expectant waiting. Providing it is not possible to localize the site of hemorrhage all the known non-operative measures may be required so they are included in this report.

1. Bed rest - should not be less than 6 to 8 weeks unless surgery is done. Patients with hypertension probably should be at rest somewhat longer but there is no conclusive proof that this is necessary. No patient with hemorrhage and who has not had his aneurysm treated surgically should be allowed up until free for at least 4 weeks of such symptoms as headache, stiff neck, vertigo, etc. (Richardson and Hyland).

2. Sedation - should be adequate to relieve any activity on the part of the patient but not to suppress respiration or to cloud mental state. Many authors have warned against the use of morphine.

3. Elevate head of bed - for purposes of diminishing intracranial blood pressure.

4. Hypertonic solutions intravenously - to diminish intracranial extravascular tension. This is, on the other hand, considered by some authors to be contra-indicated because any reduction in intracranial tension will remove pressure against a bleeding vessel so that a recurrence or continuation of bleeding occurs.

5. Spinal drainage - Ayer[3] strongly opposed repeated drainage of bloody cerebrospinal fluid because a reduction of intracranial pressure may permit recurrence or continuation of the hemorrhage. However, Merritt[22] advocated frequent lumbar punctures, reducing the pressure to half the initial pressure. He believed one should do two or more punctures daily for the first 3 to 6 days and then once daily for as long as there is evidence of blood or increased pressure. Richardson and Hyland doubt that cerebrospinal fluid drainage is an essential part of the treatment. They disagree with Bagley's[4] work on the effects of blood in the subarachnoid space. Bagley found in experimental hemorrhages in dogs that meningeal adhesions and cortical damage might follow if the blood is permitted to remain in the cerebrospinal fluid. Richardson and Hyland believe that breakdown products of hemoglobin can be adequately dealt with in the subarachnoid space and give as evidence to support this the absence of such changes in their autopsy material.

Sometimes during this conservative method of treatment it is feasible to further investigate the patient in regard to the existence of an aneurysm. Cerebral angiography should be undertaken. The question that arises is just when is the optimum time for the angiography. There are numerous opinions on this, varying from the almost total nihilism of Sahs et al[30] to the enthusiasm of Wechsler[38]. It is now well recognized that angiography can be accomplished without significant mortality or morbidity even in patients of precarious general condition. In short, the trauma of angiography is so inconsequential that it should not delay the procedure. However, it is of little value to ascertain the exact location of an aneurysm if the general condition of the patient precludes any operative interference. Therefore, angiography should be performed no sooner than one can feasibly perform a craniotomy. Until the patient is in good enough condition for operation, there is no justifiable reason to perform angiography, As a general rule, patients with subarachnoid hemorrhage are in good enough condition to withstand operation within a few days after the hemorrhage.

The second question that arises is how long may one safely procrastinate before definitive investigation and therapy are instituted. In an attempt to answer this, cases were collected from the literature and tabulated in graph 2 in which the interval before recurrent hemorrhage occurs is shown. It is obvious that the frequency of recurrences is greatest beginning the second week after the initial hemorrhage. Therefore, angiography should be performed as soon after the hemorrhage as the patients can possibly tolerate an operation and should not be delayed beyond the second week after hemorrhage. To delay longer invites disaster.

The most prevalent sites of occurrence of intracranial aneurysms are reasonably well established. In Chart II is shown the location of 608 aneurysms collected from the literature and of 46 aneurysms in the University of Minnesota series.

The treatment of intracranial aneurysms depends almost entirely on the location of the aneurysm. If the lesion is located far peripherally in the vascular system, it is not imperative that a determination of the circulatory capabilities of the cerebral vessels be made, but if

Chart II

Collected Cases

Location	No.	Percent
Ant. Comm.	92	13.6
Ant. Cerebral	63	9.9
Ophthalamic	3	.6
Middle Cerebral	168	25.2
Int. Carotid	170	25.6
Post. Comm.	23	3.9
Post. Cerebral	18	3.3
Basilar	103	15.3
Sup. Cerebellar	1	.2
Ant. Inf. Cerebellar	5	.9
Post.Inf. Cerebellar	8	1.5
Total	654	100.0

the lesion is located on or near the internal carotid artery, in which event a carotid ligation may be necessary, then the circulatory capabilities require investigation. The easiest method of doing this is digital compression of the carotid artery in the neck (Matas test). Dandy[7] stated that in his experience digital compression of the internal carotid artery in the neck for 10 minutes without symptoms such as dizziness, paresis, or sensory changes never failed to indicate correctly whether the vessel could be ligated safely. It has been the policy in this clinic, whenever feasible, to occlude the surgically exposed carotid artery in the neck for 10 to 20 minutes prior to consideration of ligation. Even with this practice, the advent of neurological sequelae are not entirely eliminated because these can also result from vascular thrombosis in the occluded artery. There are two principle causes for cerebral complications secondary to carotid artery ligation: (1) cerebral ischemia from inadequate collateral circulation through the circle of Willis, and (2) progressive cerebral vascular thrombosis and embolism. In the former, the symptoms usually develop during the 10 to 20 minutes that one digitally compresses the artery (the value of the Matas test), and in the latter the symptoms develop 12 to 48 hours after ligation. Both Dandy[7] and Bassett[5] have written of the congenital abnormalities in the cerebral circulation and Dandy believes the tolerance of an individual to carotid artery occlusion is dependent upon the congenital or acquired difference. In the collateral circulation in the circle of Willis, and upon the age of the individual; older people, especially with pronounced arteriosclerosis, tolerate occlusion poorly because of the diminished calibre of the arterial lumen. An example of this is the case of a 71 year old woman with an aneurysm on the internal carotid artery. Compression of the common carotid artery produced a feeling of syncope and possibly of numbness in the contralateral arm. An angiogram performed on the contralateral side while the ipsilateral carotid artery was compressed revealed no filling of the ipsilateral middle cerebral. The ipsilateral anterior cerebral filled poorly and numerous constrictions consistent with those due to arteriosclerotic placques were visualized on this vessel. It was concluded that the poor filling was secondary to the arteriosclerosis and that ipsilateral carotid artery ligation was contraindicated. In Dandy's series of 105 ligations there was less than 4% immediate complications and less than 2% late complications. In this clinic 17 ligations have been performed with two (11%) immediate and one (5%) late complications. In all these patients the sequelae was transient. In an attempt to prevent the late complications due to progressive thrombosis in the carotid, patients have been heparinized and then given dicumarol. Whether this has been of appreciable avail has not been determined definitely because of the small number of cases and the relative infrequence of this complication. The frequency of vascular thrombosis is considered to be related to the damage incurred to the intima (Dandy[7]).

It is the policy in this clinic to wrap the carotid artery in fascia at the time of ligation so that when the ligature is drawn tightly, the damage to the intima is minimized. Another advantage in this method is the easy removal of the suture in case complication should arise. In one patient in the University of Minnesota series who developed late sequelae, the ligature around the carotid was removed.

No definite improvement could be noticed except that the neurologic deficit did not increase thereafter.

The practice of partially occluding the carotid artery at the first operation, then reoperating upon the patient at a later date and completely occluding it has certain theoretical advantages. It should prevent or diminish the frequency of immediate complications from ischemia but contrarily it theoretically increases the possibility of producing an arterial thrombosis with its late onset of complications. Dandy was convinced that an adequate collateral circulation could be established by partially occluding the internal carotid artery (reducing the lumen about one-half) and then in 7 to 10 days accomplishing a total occlusion. It is very probable that if a patient has a normally developed circle of Willis the collateral circulation is consistently adequate. However, Dandy found a high frequency of anomalous vascular formations in this region and concluded that cerebral ischemia was often due to inadequate collateral circulation through an inadequately developed anastomosing (communicating) artery. The practice of occluding the carotid in steps may permit the development of an adequate blood flow. In this clinic partial occlusion of the carotid has not been done to date but certainly should be considered if the appropriate situation should arise.

The location of the aneurysm determines the surgical procedure to be instituted. Aneurysms may be treated by (1) ligating the neck of the sac, (2) trapping the aneurysm between two clips, (3) trapping the aneurysm between a ligature in the neck and an intracranial clip. There have been other procedures advocated such as packing with muscle the immediate vicinity of the aneurysm so that the hemorrhage may not recur, opening the aneurysm and inserting a piece of muscle, cauterizing the aneurysm, and surgically excising the aneurysm with a plastic repair of the entering artery. None of the latter methods have found even temporary favor because either they have failed to prevent secondary rupture of the vessel or have been technically inadvisable. The policy in this clinic has been to attempt ligation of the neck of the aneurysm. If this is not possible, the aneurysm is trapped between a clip distally and a carotid artery ligature proximally.

In the University of Minnesota series there have been 4 patients with aneurysms involving the infraclinoidal portion of the internal carotid artery. These have been tested by ligation of the internal carotid or of the external and common carotid artery in the neck and then performing a craniotomy with placement of a silver clip distal to the aneurysm. The latter clip, of course, is to prevent reflux of blood into the aneurysm from either the anterior or posterior communicating arteries. The one exception to the above treatment was the case of a 65 year old woman in which only a carotid ligation was performed. It was anticipated performing the second procedure of intracranial ligation but when she was relieved of her symptoms, she declined the operation. She has been followed for over 2 years and has remained symptom free.

One of the complications that might ensue following this method of ligating the carotid artery intra and extracranially is that this also traps the ophthalmic artery. Compromise of the blood flow through this vessel may result in loss of vision. This is infrequent, however, because sufficient collateral circulation is maintained through the external carotid system. It did not occur in this series. There was one patient who died as a result of compression and thrombosis of an aneurysm on the infraclinoidal portion of the artery. At the time of surgery the lesion was not recognized as an aneurysm but rather was thought to be a meningioma. A large piece of the aneurysm was excised and during the closure of this rent, it was felt that the patient expired due to compromising the flow through the carotid.

There were 7 patients with aneurysms located at the junction of the internal carotid and posterior communicating

artery or between this site and the junction of the internal carotid with the anterior communicating artery. The importance of these two vessels, of course, is the part they play in the collateral circulation. Three of the aneurysms in this location have been treated by ligation of the neck of the aneurysm. In 4 patients it was impossible to ligate the neck of the aneurysm because of its width. In these cases the carotid was ligated in the neck and the carotid artery ligated intracranially distal to the aneurysm. An attempt was always made to maintain collateral circulation through the anterior communicating artery to the ipsilateral middle cerebral artery. A case representing such a problem occurred in this series. The aneurysm was at the junction of the internal carotid and the posterior communicating artery. The internal carotid was ligated in the neck and also intracranially. A postoperative angiogram revealed the maintained blood flow through the anterior communicating into the middle cerebral artery.

There were 9 patients treated for aneurysms located peripheral to the anterior communicating artery, i.e., out on either the anterior or middle cerebral artery. Ligation of one anterior cerebral artery can be done without apparent neurological deficit providing the systemic blood pressure is maintained, but ligation of the middle cerebral is likely to be followed by death or at least by a paresis or paralysis of the contralateral face and arm, and occasionally of leg. When the aneurysm is located in the dominant hemisphere, there is considerable question of whether surgical attack should be proposed because of the probability of development of an aphasia. Aneurysms in this location are extremely hazardous to treat. According to Dandy[7] there probably is less likelihood of curing a middle cerebral artery aneurysm, at least without extreme neurologic deficit, than in the case of any other aneurysm of the brain. It seems that he was not including those aneurysms located in the basilar artery but his statement reflects the results expected in treating middle cerebral artery aneurysms.

There has been only one aneurysm of the posterior cerebral artery in this series and that was in a 16 month old child. In this patient the aneurysm was located about in the midline just above the pineal gland. It received its blood supply from branches from both the right and left posterior cerebral artery. Following intracranial clipping of these vessels the patient's general condition improved. A follow-up x-ray revealed the clip on one side had slipped off but an angiogram subsequently performed on that side failed to fill the aneurysm. It was concluded that the vessel had been thrombosed. Even so it is contemplated to re-clip the vessel at a later date.

There was one patient in this series with an aneurysm on the ophthalmic artery. It was treated with livation of the vessel and the patient made an uneventful recovery.

There were no patients in this series treated for aneurysms located on the vertebral-basilar arterial system. The apparent infrequence of aneurysms in this location is due to (1) the difficulty in clinically recognizing such a lesion, and (2) the difficulty in demonstrating angiographically the exact location of the lesion. The latter is undoubtedly due to inexperience with vertebral angiography; both difficulties should in the future be resolved. Dandy stated in 1948 that he knew of no successful outcome from operative attacks upon an aneurysm located in the posterior fossa but he held out hopes that those located on accessible and relatively non-vital vessels such as the posterior-inferior cerebellar or one of the vertebrals may, in the future, be successfully attached.

The results in the series of aneurysms treated surgically at the University of Minnesota Hospitals are shown in Chart III. The operative mortality rate of 4.9% probably is not significant because of the smallness of the series. Dandy in a series of 105 aneurysms experienced a 25% mortality rate. When one considers the prognosis of these patients if left untreated, it becomes immediately evident

that an attempt to cure them is justified.

Chart III

Intracranial Vascular Abnormalities Treated Surgically

Location Aneurysm	No.Cases	Died	Mortality %	Complications		
				Convulsion	Hemiparesis	III N.
Internal Carotid						
Infraclinoidal	4	1	14	-	-	-
Supraclinoidal	7	-	-	1	1	-
Ant. Cerebral	4	-	-	-	-	-
Middle Cerebral	4	-	-	-	1	-
Ophthalmic	1	-	-	-	-	-
Posterior Cerebral	1	-	-	-	-	-
Total	21	1	4.9	1	2	-

Summary

1. The causative agent in the majority of patients with subarachnoid hemorrhages is an arterial aneurysm.

2. The eventual mortality rate for the primary and recurrent hemorrhages is 80% if no attempt is made to eradicate the aneurysm.

3. An attempt should be made to locate and surgically eradicate the aneurysm as soon after the hemorrhage as the patient's general condition will permit a craniotomy. To procrastinate beyond the second week after the hemorrhage invites disaster because of the greater frequency of recurrent hemorrhage at that time.

4. Relatively poor general condition of a patient is no contraindication for angiography.

5. Intracranial aneurysms can be treated surgically with considerable success.

Bibliography

1. Adie, W. J.
Permanent hemianopia in migraine and subarachnoid hemorrhage.
Lancet 219:237, '30.

2. Albright, F.
The syndrome produced by aneurysm at or near the junction of the internal carotid artery and the circle of Willis.
Bull. Johns Hopkins Hosp. 44:215, '29.

3. Ayer, W. D.
So-called spontaneous subarachnoid hemorrhage.
Am.J.Surg.,26:143, '34.

4. Bagley, C.
Blood in the cerebrospinal fluid. Resultant functional and organic alterations in the central nervous system.
Arch.Surg. 17:18, '28.

5. Bassett, R. C.
Intracranial aneurysms. I. Some clinical observations concerning their development.
J.Neurosurg. 6:216, '49.

6. Courville, C. B. and Olsen, C. W.
Miliary aneurysm of the anterior communicating artery.
Bull.Los Angeles Neurol.Soc. 3:1,'38

7. Dandy, W. E.
Intracranial arterial aneurysms.
Comstock Pub.Co.,Inc.,Publisher, '47, Ithaca, N. Y.

8. Dunning, H. S.
Intracranial and extracranial vascular accidents in migraine.
Arch.Neurol.& Psychiat.48:396, '42

9. Eppinger, H.
Pathogenesis (Histogenesis und aetiologie) der aneurysmen einschliesslich der aneurysma equi verminosum.
Arch.f.Clin.Chir.35:1, 1887.

10. Fearnsides, E. G.
Intracranial aneurysms.
Brain. 39:224, '16.

11. Forbus, W. D.
On the origin of miliary aneurysms of the superficial cerebral arteries.
Bull.Johns Hopkins Hosp.47:239, '30.

12. Froin, G.
Les hemorragies sous arachnoidiennes et le micanisme de l' hematolyse en general.
These de Paris, '04, No.113, Steinheil, Paris.

13. Gintrac, E.
Maladies de l' appariel nerveau.
Paris, Germer-Bailliere, publisher, 1869.

14. Glynn, L. E.
Medial defects in the circle of Willis and their relation to aneurysm formation.
J.Path.and Bact. 51:213, '40.

15. Griffith, J. B., Jeffers, W. A. and Fry, W. E.
Papilledema associated with subarachnoid hemorrhage. An experimental and clinical study.
Arch.Int.Med. 61:880, '38.

16. Gull, W.
Cases of aneurism of the cerebral vessels.
Guy's Hosp.Rep. 5:281, 1859.

16a. Hamby, W. B.
Intracranial aneurysms of internal carotid artery and its branches.
J.Internat.Coll.Surgeons, 5:216,'42.

17. Ingvar, S.
Sur les hemorragies meningees.
Nouv.icon de la Salpetriere 23:313, '16-'18.

18. Jefferson, G.
Compression of the chiasma, optic nerves, and optic tracts by intracranial aneurysms.
Brain, 60:444, '37.

19. Leriche, R.
Principes actuels de la chirurgie des aneurysmes.
J.Chir.62:85, '46.

20. Magee, C. G.
Spontaneous subarachnoid hemorrhage.
Lancet: 245:497, '43.

21. Martland, H. S.
Spontaneous subarachnoid hemorrhage and congenital 'Berry' aneurysms of the circle of Willis.
Am.J.Surg.43:10, '39.

22. Merritt, H. H.
The Diagnosis and treatment of vascular lesions in the brain.
Med.Clin.N.Am.22:577, '38.

23. Moore, M. T. and Bockman, A. A.
Ruptured aneurysm of the left anterior cerebral artery with production of ipsilateral cerebral signs.
Arch.Neurol.and Psychiat.46:1057, '41.

24. Noran, H. H.
Intracranial vascular tumors and malformations.
Arch.Path.39:393, '45.

25. Norlen, G.
Arteriovenous aneurysms of the brain.
Report of ten cases of total removal of the lesion.
J.Neurosurg. 6:475, '49.

26. Ponfick, E.
Ueber embolische aneurysmen, nebst Bermerkungen über das acute Herzaneurysma (Herzgeshwür).
Virchows Arch.F.path.Anat. 58:528, 1873.

27. Richardson, J. C. and Hyland, H. H.
Intracranial aneurysms.
Medicine 20:1, '41.

28. Riggs, H. E. and Rupp, C.
Miliary aneurysms. Relation of anomalies of the circle of Willis to aneurysm formation.
J.Neuropath.and Exp.Neurol.,1:442, '42.

29. Rogers, L.
Ligature of arteries, with particular reference to carotid occlusion and the circle of Willis.
Brit.J.Surg.35:43, '47.

30. Sahs, A. L. and Keil, P. G.
Subarachnoid hemorrhage caused by ruptured intracranial aneurysm.
Am.Heart J.26:645, '43.

31. Sands, I. J.
Diagnosis and management of subarachnoid hemorrhage.
Arch.Neurol.and Psychiat. 46:973,'41.

32. Schmidt, M.
Intracranial aneurysms.
Brain: 53:489, '30.

33. Schorstein, J.
Carotid ligation in saccular intracranial aneurysms.
Brit.J.Surg. 28:50, '40.

34. Strauss, I., Globus, J. H. and Ginsburg, S. W.
Spontaneous subarachnoid hemorrhage, Its relation to aneurysm of cerebral blood vessels.
Arch.Neurol. and Psychiat. 27:1080, '32.

35. Strauss, I. and Tarachow, S.
Prognostic factors in spontaneous subarachnoid hemorrhage.
Arch.Neurol.and Psychiat. 38:239, '37.

36. Symonds, C. P.
Spontaneous subarachnoid hemorrhage.
Quart.J.Med. 18:93, '24.

37. Tuthill, C. R.
Cerebral arteries in relation to arteriosIcerosis.
Arch.Path.16:453, '33.

38. Wechsler, D.
Textbook of clinical neurology.
W.B.Saunders Co., pub., Philadelphia, p.556, '39.

39. Wichern, H.
Klinische Beiträge zur Kenntnis der Hirnaeurysmen.
Deut.Zeit.f.Nervenheilk, 44:220,'12.

40. Widal, F.
Le Diagnostic De L' hemorragie meningee.
La Prerse Medicale, 44:413, '13.

41. Wilks, S.
Sanguinous meningeal effusion, spontaneous and from injury.
Guy's Hosp.Rep.5:119, 1859.

42. Wilks, S.
Lectures on diseases of the nervous system.
Delivered at Guy's Hosp.. 2nd edition, London, J.and A. Churchill, 1883.

43. Wilson, S. A. K.
Neurology.
The Williams and Wilkins Co., pub., Baltimore, '40.

44. Wilson, G., Rupp, C. and Bartle, H.
Ruptured aneurysms of the circle of Willis. A clinicopathologic study of 45 cases.
Trans.Am.Neurol.Assoc.,68:140, '42.

45. Wolf, G. A. Jr., Goodell, H. and Wolff, H. G.
Prognosis of subarachnoid hemorrhage and its relation to long term management.
J.A.M.A. 129:715, '45.

46. Woltman, H. W. and Shelden, W. D.
Neurologic complications associated with congenital stenosis of the isthmus of the aorta.
Arch.Neur.& Psychiat.17:303, '27.

II. MEDICAL SCHOOL NEWS

Coming Events

March 6-8 - Continuation course in Gastro-Intestinal Diseases for General Physicians.

March 27-29 - Continuation course in Dermatology for General Physicians.

April 10-12 - Continuation course in Pediatrics for Specialists.

* * *

Continuation Course in Gastro-Intestinal Diseases

A continuation course in Gastro-Intestinal Diseases for General Physicians will be presented at the Center for Continuation Study March 6, 7, and 8. The course will open with a presentation on "Some Current Concepts of Gastro-Intestinal Physiology" by Dr. Nathan Lifson, Professor of the Department of Physiology. Dr. Raymond N. Bieter, Professor and Head of the Department of Pharmacology will discuss "Newer Drugs Acting on the Gastro-Intestinal Tract".

Clinical and full-time members of the staff of the medical school will complete the faculty of the course. Emphasis will be placed on the diagnosis and management of gastro-intestinal disorders most frequently confronting the general physician.

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Faculty News

Hal Downey, Professor Emeritus of the Department of Anatomy, has returned to his office at the University of Minnesota after spending the fall quarter as consulting hematologist at the Mayo Clinic.

Dr. Maurice Visscher, Professor of Physiology, has recently been elected as a member of the Board of Directors of the National Society for Medical Research. The National Society for Medical Research has been active in promoting conditions for such research in recent years. Its activities have offered an effective opposition to the anti-vivisection societies.

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Drs. Horns and Aagaard to Attend Conference on Audio-Visual Education

Dr. Howard L. Horns and Dr. George N. Aagaard will be attending a conference on Audio-Visual Education conducted by the Association of American Medical Colleges at the University of Illinois in Chicago on Friday, March 3. The purpose of the conference will be to prepare plans for the development and usage of all types of audio-visual materials in the teaching programs of cardiovascular diseases in the medical schools.

III. UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS

February 26 - March 4, 1950

No. 279

Sunday, February 26

9:00 - 10:00 Surgery Grand Rounds; Station 22, U. H.

10:30 - 11:00 Surgical Conference; Rm. M-109, U. H.

Monday, February 27

8:00 - Fracture Rounds; A. A. Zierold and Staff; Ward A, Minneapolis General Hospital.

9:00 - 9:50 Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H.

9:00 - 10:50 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; M-109, U. H.

10:00 - 12:00 Neurology Rounds; A. B. Baker and Staff; Station 50, U. H.

11:00 - Pediatric Rounds; Erling Platou; Sta. I, General Hospital.

11:00 - 11:50 Physical Medicine Seminar; E-101, U. H.

11:00 - 11:50 Roentgenology-Medicine Conference; Veterans Hospital.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Eustis Amphitheater, U. H.

12:00 - 1:00 Physiology Seminar; Studies in Accurate Blood pH Determination; E. B. Brown; 214 M. H.

12:15 - 1:20 Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.

12:30 - 1:20 Pathology Seminar; Visceral and Systemic Lesions in Scleroderma with Case Reports; Jim Jaeck; 104 I. A.

12:30 - 1:30 Surgery Problem Case Conference; A. A. Zierold, C. Dennis and Staff; Small Classroom, Minneapolis General Hospital.

1:30 - 2:30 Surgery Grand Rounds; A. A. Zierold, C. Dennis and Staff; Minneapolis General Hospital.

1:30 - 2:30 Pediatric-Neurological Rounds; R. Jensen, A. B. Baker and Staff; U. H.

4:00 - Medical-Surgical Conference; Deep Phlebitis; C. V. Kusz; Bldg. I, Main Conference Room, Veterans Hospital.

4:00 - Public Health Seminar; Subject to be announced; 113 Medical Sciences.

4:00 - Pediatric Seminar; Somato-Psycho Pathology; Dr. Bussman; 6th Floor West, Child Psychiatry, University Hospitals.

Monday, February 27 (Cont.)

5:00 - 5:50 Clinical Medical Pathologic Conference; Todd Amphitheater, U. H.

5:00 - 6:00 Urology-Roentgenology Conference; D. Creevy, O. J. Baggenstoss and Staffs; M-109, U. H.

Tuesday, February 28

8:15 - 9:00 Roentgenology-Surgical-Pathological Conference; Craig Freeman and L. G. Rigler; M-109, U. H.

8:30 - 10:20 Surgery Conference; Small Conference Room, Bldg. I, Veterans Hospital.

9:00 - 9:50 Roentgenology Pediatric Conference; L. G. Rigler, I. McQuarrie and Staffs; Todd Amphitheater, U. H.

10:30 - 11:50 Surgical Pathological Conference; Lyle Hay and E. T. Bell; Veterans Hospital.

11:00 - Contagion Rounds; Forrest Adams; Sta. L, General Hospital.

12:30 - Pediatric-Surgery Rounds; Drs. Stoesser, Wyatt, Chisholm, McNelson and Dennis; Sta. I, Minneapolis General Hospital.

12:30 - 1:20 Pathology Conference; Autopsies; J. R. Dawson and Staff; 102 I. A.

1:30 - 2:30 Pediatric Psychiatry Conference; R. A. Jensen and Staff; 6th Floor, West Wing, U. H.

1:00 - 2:30 X-ray Surgery Conference; Auditorium, Ancker Hospital.

2:00 - 2:50 Dermatology and Syphilology Conference; H. E. Michelson and Staff; Bldg. III, Veterans Hospital.

3:15 - 4:20 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U. H.

3:30 - 4:20 Clinical Pathological Conference; Staff; Veterans Hospital.

4:00 - 5:00 Physiology-Surgery Conference; Anemia after Lateral Intestinal Anastomoses; Robert Toon; Eustis Amphitheater.

4:00 - 5:00 Pediatric Rounds on Wards; I. McQuarrie and Staff; U. H.

5:00 - 6:00 Prophyrin Seminar; C. J. Watson, Samuel Schwartz, et al; Powell Hall Amphitheater.

5:00 - 6:00 X-ray Conference; Presentation of Cases by Ancker Hospitals Staff; Drs. Lipschultz & Mosser; Todd Amphitheater, U. H.

Wednesday, March 1

8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-109, U. H.

8:30 - 9:30 Clinico-Pathological Conference; Auditorium, Ancker Hospital.

8:30 - 10:00 Orthopedic-Roentgenologic Conference; Edward T. Evans; Room 1AW, Veterans Hospital.

8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker; Veterans Hospital.

11:00 - Pediatric Rounds; Erling Platou; Sta. I, General Hospital.

11:00 - 12:00 Pathology-Medicine-Surgery Conference; Medicine Case; O. H. Wangensteen, C. J. Watson, and Staffs; Todd Amphitheater, U. H.

12:00 - 1:00 Radio-Isotope Seminar; Report on Current Literature on Radio-Active Isotopes; E. Gasteiger; 113 Medical Sciences.

12:15 - Staff Meeting; Main Classroom, General Hospital.

3:00 - Pediatric Rounds; C. J. Huenekens; Sta. I, General Hospital.

3:30 - 4:30 Journal Club; Surgery Office, Ancker Hospital.

4:00 - 5:00 Infectious Disease Rounds; Veterans Hospital, Main Conference Room, Bldg. I.

5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; E-101, U. H.

Thursday, March 2

8:30 - 10:20 Surgery Grand Rounds; Lyle Hay and Staff; Veterans Hospital.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; M-109, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:50 Surgery-Radiology Conference; Daniel Fink and Lyle Hay; Veterans Hospital.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Todd Amphitheater, U. H.

11:30 - Pathology Conference Clinic; Main Classroom; General Hospital.

11:30 - 12:30 Clinical Pathology Conference; Steven Barron, C. Dennis, George Fahr, A. V. Stoesser and Staffs; Large Classroom, Minneapolis General Hospital.

12:00 - 1:00 Physiological Chemistry Seminar; Displacement Chromatography of Amino Acids by Resins; Esther Freier; 214 M. H.

1:00 - 1:50 Fracture Conference; A. A. Zierold and Staff; Minneapolis General Hospital.

2:00 - 3:00 Errors Conference; A. A. Zierold, C. Dennis and Staff; Large Classroom, Minneapolis General Hospital.

4:15 - 5:00 Bacteriology and Immunology Seminar; Production of Riboflavin by Eremothecium Ashbyii; Mr. Norman Lawrence; 214 M. H.

4:30 - 5:20 Ophthalmology Ward Rounds; Erling W. Hansen and Staff; E-534, U. H.

5:00 - 6:00 X-ray Seminar; Thoracic Surgery Cases; Thomas Kinsella and Nathan K. Jenson; Todd Amphitheater, U. H.

7:30 - 9:30 Pediatrics Cardiology Conference and Journal Club; Review of Current Literature 1st hour and Review of Patients 2nd hours; 206 Temporary West Hospital.

Friday, March 3

8:30 - 10:00 Neurology Grand Rounds; A. B. Baker and Staff; Station 50, U. H.

9:00 - 9:50 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:20 Medicine Grand Rounds; Veterans Hospital.

10:30 - 11:50 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Department, U. H.

11:00 - Pediatric Rounds; Erling Platou; Sta. I, General Hospital.

11:00 - 12:00 Surgery-Pediatric Conference; C. Dennis, O. S. Wyatt, A. V. Stoesser, and Staffs; Minneapolis General Hospital.

11:45 - 12:50 University of Minnesota Hospitals General Staff Meeting; Palliative Roentgen Therapy in Malignant Disease; Jack Friedman; Powell Hall Amphitheater.

12:00 - 1:00 Surgery Clinical Pathological Conference; Clarence Dennis and Staff; Large Classroom, Minneapolis General Hospital.

1:00 - 1:50 Dermatology and Syphilology Conference; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.

1:00 - 3:00 Pathology-Surgery Conference; Auditorium, Ancker Hospital.

1:00 - 2:50 Neurosurgery-Roentgenology Conference; W. T. Peyton, Harold O. Peterson and Staff; Todd Amphitheater, U. H.

3:00 - 4:00 Neuropathology Conference; F. Tichy; Todd Amphitheater, U. H.

3:00 - 6:00 Demonstrations in Cardiovascular physiology; M. B. Visscher, et al; 301 M. H.

4:00 - 5:00 Clinical Pathological Conference; A. B. Baker; Todd Amphitheater, U. H.

Friday, March 3, (Cont.)

4:15 - 5:15 Electrocardiographic Conference; Coronary Insufficiency and Infarct; E. Simonson; 106 Temp. Bldg., Hospital Court, U. H.

5:00 - 6:00 Otolaryngology Seminar; Review of Current Literature; Dr. Frey; Discussor, Dr. Goltz; Todd Memorial Room, U. H.

Saturday, March 4

7:45 - 8:50 Orthopedics Conference; Wallace H. Cole and Staff; M-109, U. H.

8:00 - 9:00 Surgery Literature Conference; Clarence Dennis and Staff; Small Classroom, Minneapolis General Hospital.

8:30 - 9:30 Surgery Conference; Auditorium, Ancker Hospital.

9:00 - 11:30 Psychiatry Conference; Use and Abuse of Sedatives; Dr. Simon; Powell Hall Amphitheater, U. H.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; E-221, U. H.

9:00 - 10:30 Pediatric Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater, U. H.

9:00 - 11:30 Surgery-Roentgenology Conference; Todd Amphitheater, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:00 - 12:50 Obstetrics and Gynecology Grand Rounds; J. L. McKelvey and Staff; Station 44, U. H.

11:00 - Contagion Rounds; Forrest Adams; Sta. L, General Hospital.

11:00 - 12:00 Anatomy Seminar; The Segmental Anatomy of the Middle Lobe of the Lung; Edward A. Boyden; A Review of Drinker's Pulmonary Edema and Inflammation; Ronald M. Ferry; 226 I. A.