Progress Review

Risk Factors for Subarachnoid Hemorrhage

W.T. Longstreth, Jr., M.D., MPH,* Thomas D. Koepsell, M.D., MPH,‡
Mark S. Yerby, M.D., MPH,*† and Gerald van Belle, Ph.D.§

WHO IS AT INCREASED RISK for a subarachnoid hemorrhage from a ruptured aneurysm? The question apparently dates back to ancient times. Hippocrates described “... when persons in good health are suddenly seized with pains in the head, and straightway are laid down speechless, and breathe with stertor, they die in seven days, unless fever comes on.” 11 Little more was known about subarachnoid hemorrhage until the 18th century when the pathology of this condition was elucidated. 2 In 1718 Dionis described two cases of subarachnoid hemorrhage at autopsy that probably represent the first reported cases. In 1761, Morgagni reported the first unruptured aneurysm found at autopsy, and in 1778 Biumi demonstrated the first case of a subarachnoid hemorrhage caused by a ruptured aneurysm. Once Quincke’s technique of lumbar puncture came into general use early in the 20th century, the clinically suspected diagnosis could be confirmed while the patient was alive.

In 1924 Symonds, who first coined the term spontaneous subarachnoid hemorrhage, synthesized the existing data and produced a detailed description of the clinical syndrome and cerebrospinal fluid findings associated with ruptured intracranial aneurysms. 3 When Moniz introduced cerebral angiography later that decade, 4 the stage was set for surgical intervention. Dott reported the first intracranial surgery for an aneurysm, 5 and Dandy the first clipping. 6 Following the second World War, remarkable developments occurred in the medical and surgical treatment of subarachnoid hemorrhage. 7,8 Recent research has concentrated largely on events that follow the bleed, especially vasospasm and rebleeding. Unfortunately our understanding of the risk factors that precede the bleed remain incomplete.

The estimated incidence of subarachnoid hemorrhage is between 10 and 28 cases per 100,000 persons per year. 2,9-11 An estimated 25,000 new cases of subarachnoid hemorrhage occur each year in the United States, accounting for about 10% of all strokes. 11-14 Most of the bleeding into the subarachnoid space results from ruptured aneurysms; only 4 to 5% are from ruptured arteriovenous malformations. 2,11,15,16 Despite extensive evaluation, 14 to 22% of patients may not have an aneurysm or other identified source for the bleeding. 2,16-18 In some who die early in their course, a massive clot in the subarachnoid space at autopsy prevents discovery of the aneurysm. In others, cerebral angiography fails to show the source of the bleeding, and these patients typically have a good prognosis. 17,18 Age and sex are similar in patients found with and without aneurysms. 16 Thus patients without a source found are presumed to have bled from an aneurysm that clotted or was destroyed at the time of the bleed.

Despite the many medical and surgical developments in treatment for this disease, the case fatality rate for subarachnoid hemorrhage has remained unchanged for the last two to three decades. 9,10 Thus, subarachnoid hemorrhage is both frequent enough and serious enough to qualify as a major clinical and public health problem. Because of the limited ability of currently available therapies to affect the outcome once a bleed has occurred, prevention may be a more effective method for reducing the morbidity and mortality of subarachnoid hemorrhage.

Prevention of subarachnoid hemorrhages depends upon identification of risk factors that can be modified or eliminated. The relation of several factors to subarachnoid hemorrhage has been studied. Some factors such as age or gender cannot be altered but may give a better understanding of pathophysiology. Other factors such as hypertension and the use of oral contraceptives, tobacco, and alcohol may be modified and could have a substantial impact on this disease. Whether a factor affects aneurysm formation, rupture or both will remain unknown until a non-invasive technique to identify aneurysms is widely available.

Table 1 summarizes the potential risk factors that will be discussed.

Age

As with other types of strokes, the incidence of subarachnoid hemorrhage rises steadily with age. 6,11,16,19 Studies that have not found an increase in the oldest age group blame the lack of aggressive evaluation of elderly stroke patients. 2,9 Nonetheless, the rise with age appears less marked than with other types of strokes. 9,20 Patients are affected at an earlier age so that, compared to other types of strokes, the young carry a disproportionate burden of subarachnoid hemorrhage. 11,20 The incidence of subarachnoid hemorrhage in the young is high in Iceland. 21 In this study
and others reviewed in it, 40 to 50% of strokes in people under 35 years were due to subarachnoid hemorrhage. From 1981 to 1982 in New Zealand the incidence of subarachnoid hemorrhage was 8.5 per 100,000 persons per year for the age group 25 to 35 years old. In Rochester, Minnesota over 15 years, 75% of subarachnoid hemorrhages occurred in patients less than 65 years old. The reverse was true for cerebral thrombosis where 75% of strokes occurred in patients 65 years or older. More productivity is lost compared to other types of strokes especially given the relatively young age of those affected and the high mortality rates; about 50% are dead within a month of the bleed. Mortality rates are high even in the younger age groups among whom other types of strokes usually are not fatal.

The mechanism by which the risk of subarachnoid hemorrhage increases with age is unknown. Data from the Framingham study suggest that systolic blood pressure, not diastolic, rises with age in men and women and that the prevalence of isolated systolic hypertension (systolic blood pressure 160 mm Hg or greater and diastolic pressure under 95 mm Hg) also increases with age in men and women. Although these investigators did not specify stroke types, they found that isolated systolic hypertension increased the risk of stroke 2 to 4 times over the control population. They argued that peak systolic pressures could provoke subarachnoid hemorrhage. Other factors that are probably responsible for the increasing incidence of bleeds with age include the increased occurrence of atherosclerosis with altered hemodynamics in the circle of Willis and age-related changes in blood vessels leading to increased fragility. Such factors along with hypertension are known to affect aneurysm formation and rupture in experimental animals, but their effects in humans remain speculative.

Gender

In most epidemiologic studies of subarachnoid hemorrhage women are affected more often than men. Pakarinen's argument that the excess of women in most series simply reflects their greater number in the older age groups has not been supported by more recent studies in which age-specific rates of subarachnoid hemorrhage are higher in women than men. Most other types of strokes show a preponderance in men.

The explanation for bleeds occurring more frequently in women is not apparent. The effects of estrogens on blood vessels have been used to explain the fluctuation of symptoms due to spinal arteriovenous malformation during menses and pregnancy. During pregnancy the incidence of subarachnoid hemorrhage increases with increasing gestational age but is infrequent during labor. Although the fluctuating hormone levels associated with menses affect endometrial spiral arteries, their effects on cerebral vessels and aneurysms remain unknown. Heyman and his associates studied 30 menstruating women with subarachnoid hemorrhage and 24 with cerebral infarction. In 17 of the 30, the onset of the hemorrhage was during the first five days of the menstrual cycle. In the 24 women with cerebral infarction, the onset of the stroke occurred randomly throughout the menstrual cycle. If these preliminary data could be confirmed, they might help clarify the pathophysiology of subarachnoid hemorrhage. Hypertension does not seem to explain the gender difference as elevated blood pressure is more frequent in men than women in most age groups.

Hypertension

As with other forms of stroke, the most widely accepted risk factor for subarachnoid hemorrhage is hypertension. The evidence to support this association is surprisingly limited. Arguments have been made on the basis of large clinical and pathologic series both for and against the association. The conflicting results are not unexpected because such studies deal with selected groups of patients and rely on a retrospective review of records to determine if hypertension was present. Subarachnoid hemorrhage could be the first symptom of previously unrecognized hypertension, and the blood pressure levels after the bleed would not necessarily reflect levels before the bleed. A systematic bias could occur that would tend to minimize the effects of hypertension as a risk factor. For instance, patients dying before receiving medical attention are not included in these studies. If a history of hypertension makes patients more likely to die as a consequence of their subarachnoid hemorrhage, then patients dying before medical attention would be more likely to be hypertensive than patients who survived long enough to be hospitalized. An estimated 8 to 15% of patients with subarachnoid hemorrhage die without receiving medical care. This percentage depends in part on the intensity of pre-hospital emergency care in the community.

Other studies of cohort design have examined the relation between hypertension and subarachnoid hemorrhage. In the Walnut Creek Contraceptive Drug Study, which is discussed in more detail in a later section, Petit and Wingerd found a history of hypertension was almost twice as common in the 11 women who had a subarachnoid hemorrhage than in the control patients who were drawn from the remaining cohort of women aged 18 to 54. The difference however was not statistically significant.

Between 1945 and 1974, 119 patients suffered a subarachnoid hemorrhage in Rochester, Minnesota. Blood pressure was recorded in 98 of these patients before their first subarachnoid hemorrhage although measurements were within 1 year of the bleed in less than 50%. Only 28% of the 98 patients had systolic
blood pressures over 160 mm Hg and only 30% had diastolic blood pressures over 95 mm Hg. These percentages were similar to those in other comparably aged populations. Hypertension prevalence figures for the Rochester population of the same time period were not available.

In another study of patients seen at the Mayo Clinic between 1955 and 1975, 65 patients were identified with unruptured intracranial saccular aneurysms. Hypertension was a significant risk factor for hemorrhagic strokes. Although the Mayo Clinic study did not consider patients with subarachnoid hemorrhage separately, the Framingham study did. The 5,184 people followed for 26 years or more had biennial examinations that included measurement of blood pressure in a standard fashion. Definite hypertension was said to be present when at least two blood pressures recorded during a visit had either systolic pressure of at least 160 mm Hg or diastolic of at least 95 mm Hg. Patients whose blood pressure was under 140/90 mm Hg were considered normotensive. Those with intermediate values were considered to have borderline hypertension. When the 36 patients with subarachnoid hemorrhage were compared to four controls matched to each case for age and sex, these investigators found that hypertension was significantly more common in cases than controls. At sometime before the hemorrhage, 92% of cases had definite or borderline hypertension, in comparison with 79% of controls. The relationship seemed to hold regardless of the measure considered: blood pressure at entry into the study, blood pressure at the last examination before the hemorrhage and mean systolic or diastolic blood pressure of all prior biennial values. The investigators concluded that hypertension was a strong precursor of subarachnoid hemorrhage.

Similar conclusions came from a smaller prospective study of the Japanese town of Hisayama. About 90% of the town's residents over the age of 40 years old were followed with examinations every two years. After 13 years, 103 of the 1,621 subjects had died from stroke, 12 due to subarachnoid hemorrhage. Compared to normotensive subjects, rates of subarachnoid hemorrhage were almost twice as high for subjects with borderline hypertension and almost three times as high for subjects with definite hypertension. Subarachnoid hemorrhages occurred in 4 of 867 normotensive subjects, 3 of 344 subjects with borderline hypertension and 5 of 410 subjects with definite hypertension.

Studies on the treatment of hypertension also lend strength to the association between hypertension and subarachnoid hemorrhage. They seem to confirm the presumptions of Sacco and associates that "more effective control of hypertension . . . may result in a decrease in future occurrence of subarachnoid hemorrhage."

In the Veterans Administration Cooperative Study involving patients with diastolic blood pressures between 115 and 129 mm Hg no subarachnoid hemorrhages occurred. Subarachnoid hemorrhage is encountered more commonly in the studies of mild hypertension; these typically enroll more patients than the earlier studies. Although all these studies show reduction of cerebrovascular complications with control of mild hypertension, some do not reveal how many of the strokes were subarachnoid hemorrhages. In studies giving this detail, some do not reveal how many of the strokes were subarachnoid hemorrhages; none of the bleeds occurred in treated patients, and only one of all the strokes occurred in a treated patient. More information may be forthcoming when the largest of these trials, the Medical Research Council trial in Great Britain, is completed. It has enrolled 17,000 people and plans to accumulate 90,000 person-years of experience.

Taken together, these data support an association between subarachnoid hemorrhage and hypertension. Although still scant, the data from the treatment trials of mild hypertension suggest a causal association. In experimental animals hypertension alone does not cause aneurysms, but when hypertension is combined with procedures to alter hemodynamic stresses in the circle of Willis, aneurysms form. The association between hypertension and subarachnoid hemorrhage will remain difficult to evaluate with complete accuracy. In retrospective studies the relative rarity of subarachnoid hemorrhage, most of the early studies concerned with the treatment of severe hypertension did not encounter patients with subarachnoid hemorrhage or did so infrequently. In the Veterans Administration Cooperative Study involving patients with diastolic blood pressures between 115 and 129 mm Hg no subarachnoid hemorrhages occurred.
hemorrhages are more common than ischemic strokes in younger age groups. The Collaborative Group for the Study of Stroke in Young Women was the first to find in its case-control study that the pill increased the risk of both ischemic and hemorrhagic strokes. Patients with subarachnoid hemorrhage were not analyzed separately.

The cohort studies mounted in the 1960's to evaluate the side effects of oral contraceptives were able to evaluate the occurrence of subarachnoid hemorrhage. Two studies showed that both current and former users were at increased risk for a subarachnoid hemorrhage (table 3). Persistence of risk after discontinuation of the pill has also been described for myocardial infarction. The largest study was the Royal College of General Practitioners' Oral Contraception Study. In over 300,000 woman-years of observation, 20 deaths due to subarachnoid hemorrhage occurred. Of these 20 patients, 3 were never users, 11 were former users and 6 were current users of oral contraceptives. The relative risk for former users was 4.5 (p < 0.05), for current users was 3.2 (p > 0.05) and for ever users was 4.0 (p < 0.05). All but two cases occurred in women over 35 years old.

Although 2 of the 3 smaller cohort studies did not show a significant relation between subarachnoid hemorrhage and oral contraceptives, the third did. The Walnut Creek Contraceptive Drug Study was the smallest of the cohort studies having enrolled 16,759 women. By the end of 1976, 11 cases of subarachnoid hemorrhage had occurred, all confirmed by angiography, necropsy or operation as being due to rupture of a cerebral aneurysm. Two of 11 cases were never users, 5 were former users and 4 were current users of oral contraceptives. The relative risk was 3.5 for former users (p < 0.05) and 6.5 for current users (p < 0.05). Although a history of hypertension was almost twice as common in the 11 cases than the 3956 matched controls, the difference was not statistically significant (95% confidence interval 0.5 to 6.8). In this group of women, use of oral contraceptives and tobacco (see below) were more important risk factors for subarachnoid hemorrhage than hypertension. As in the British study, all but one bleed occurred in women over 35 years old.

Two retrospective case-control studies found small but not significant associations between oral contraceptive use and subarachnoid hemorrhage. These studies were flawed by having included less than half of the eligible population of women dying from a subarachnoid hemorrhage, their failure to consider nonfatal cases and their reliance on chart review for information about oral contraceptive use. Interestingly, both studies did find hypertension to be the major risk factor.

Several mechanisms have been proposed by which oral contraceptives could increase the incidence of subarachnoid hemorrhage. Oral contraceptive use is associated with a rise of systolic and diastolic blood pressure. Others have proposed some as yet unidentified direct action of these hormones on blood vessels that would affect aneurysm formation and rupture. As mentioned in the section on gender these hormones clearly affect endometrial blood vessels, but their effects on cerebral vessels are unknown. Finally, these hormones' effects on the immune system could slow the natural reparative process in the vessel wall.

### Cigarette Smoking

Although cigarette smoking is an important risk factor for coronary artery disease, its role in stroke is less certain. Most of the data linking smoking and subarachnoid hemorrhage have come from studies designed to evaluate the risks of oral contraceptives. The findings of the Collaborative Group for the Study of Stroke in Young Women foreshadowed the findings of subsequent studies. Smoking was not a risk factor for thrombotic strokes but was for hemorrhagic strokes regardless of oral contraceptive status. For women who were not using oral contraceptives the risk of a hemorrhagic stroke was about 2 times greater in those who smoked more than 1 package of cigarettes a day than in those who had never smoked. In oral contraceptive users, the risk was 6 to 7 times greater. Patients with subarachnoid hemorrhage were not analysed separately.

Both the Royal College of General Practitioners' Oral Contraception Study and the Walnut Creek Contraceptive Drug Study had similar results. Smoking was a risk factor for subarachnoid hemorrhage and seemed especially important when the patient was older and used oral contraceptives. In the British study 14 of the 20 cases were smokers, far more than in the controls. In the California study, 8 of the 11 cases were smokers. The relative risk of subarachnoid hemorrhage associated with smoking was 5.7 (p < 0.05), but with smoking and current oral contraceptive use the relative risk was 22 (p < 0.001). No relation was found between oral contraceptive use and smoking. When smoking was controlled for in the analysis, the relation between oral contraceptive use and subarachnoid hemorrhage remained unchanged. Thus smoking and oral contraceptive use appear to be independent risk factors for subarachnoid hemorrhage, and their coexistence in the same individual appears to lead to a particularly dramatic increase in risk.

In the Framingham Study, discussed previously in

<table>
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<tr>
<th>OC User Status</th>
<th>Relative Risk UK Study'84</th>
<th>95% Confidence Interval</th>
<th>Relative Risk US Study'86</th>
<th>90% Confidence Interval</th>
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<tbody>
<tr>
<td>Former</td>
<td>4.5</td>
<td>1.2 to 16.5</td>
<td>5.3</td>
<td>1.3 to 22.0</td>
</tr>
<tr>
<td>Current</td>
<td>3.2</td>
<td>0.6 to 16.3</td>
<td>6.5</td>
<td>1.9 to 22.6</td>
</tr>
</tbody>
</table>

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The table shows the relative risk of subarachnoid hemorrhage associated with oral contraceptive use and smoking in both the UK and US studies. The relative risk for former users was 4.5 (p < 0.05) and 6.5 for current users (p < 0.05) compared to never users. Smoking was a risk factor for subarachnoid hemorrhage with a relative risk of 5.7 (p < 0.05) compared to non-smokers.
the section on hypertension, cigarette smoking was more common in patients with subarachnoid hemorrhage than controls at both entry into the study and at the closest prior examination. Prior to the hemorrhage, 50% of cases smoked 20 or more cigarettes per day compared to 29% of controls (p = 0.03). The effects of smoking seemed greater in women than men.

Other studies including men are limited, although two retrospective studies have suggested an association between smoking and subarachnoid hemorrhage. Bell and Symon reviewed hospital records on 208 patients admitted after a subarachnoid hemorrhage and found that those who had an aneurysm as the source of the bleeding were more often smokers than expected from the general population. The relative risk for current smokers was 3.9 for men and 3.7 for women. Former smokers were not at increased risk. In a study of patients discharged after subarachnoid hemorrhage, Taha and associates found similar results with relative risk of 4.7 for men and 2.6 for women. Again former smokers were not at increased risk. Both studies were seriously flawed by their considering a select population of patients with subarachnoid hemorrhage, by their lack of adequate comparison groups and by their failure to control for other factors such as hypertension.

Smoking-induced elevation of blood pressure might be the mechanism by which smoking promotes subarachnoid hemorrhage. Acutely, with smoking a cigarette, the blood pressure rises significantly, systolic more than diastolic. The acute effects of smoking on the cardiovascular system last about three hours. The time relation between when a cigarette is smoked and when a subarachnoid hemorrhage occurs is unknown. In Taha’s study, those whose subarachnoid hemorrhage originated from a ruptured aneurysm smoked significantly more cigarettes than those with arteriovenous malformations or those in whom no source for the bleed was found. The chronic effects of smoking may be different. Kubota and associates have shown that in otherwise healthy smokers tested after the acute effects of smoking have dissipated, the cerebral blood flow is reduced compared to non-smokers.

These data suggest that cigarette smoking may increase the risk of subarachnoid hemorrhage in both men and women. If the increased risk is due to hypertension, then it should only be present while smoking or in the few hours after. Although smoking is associated with renovascular hypertension, it is not associated with essential hypertension. The risk in former smokers is unknown. The prospective cohort studies did not examine former smokers. Both retrospective studies did not show any excess risk in former smokers, suggesting that the reportedly increased risk of subarachnoid hemorrhage may indeed be acute and reversible. Further studies are needed and should include evaluation of the time relationship and risk in former smokers.

**Alcohol**

Several studies have suggested that alcohol consumption is related to stroke. Based on a forensic series of 130 patients, Secher-Hansen proposed a relation between alcohol and subarachnoid hemorrhage although head trauma was thought to play a role. Most of the recent work linking alcohol consumption and subarachnoid hemorrhage comes from studies by Hillbom and Kaste in Finland. In 172 patients with subarachnoid hemorrhage who survived the first 24 hours, they found 22% of the patients had been intoxicated (consuming 80 grams of alcohol or more in a few hours) and 19% were heavy drinkers (consuming more than 5 drinks per day almost daily). These percentages were said to be more than expected in a general Finnish population. Finally, 41% of the patients who had been intoxicated in the 24 hours preceding their subarachnoid hemorrhage were still intoxicated at the time of their bleed. Several mechanisms may exist to explain this association including hypertension, increased cerebral blood flow and hemostatic changes.

Reasonable criticisms have been leveled at this poorly controlled study. A select population of patients with subarachnoid hemorrhage is compared with a general population from a different time period, and ascertainment of data on alcohol consumption was different in cases and controls. A better controlled study is underway to evaluate the relation between alcohol consumption and stroke, but whether it will contain a sufficient number of patients with subarachnoid hemorrhage is unknown. In the Framingham Study, prior alcohol consumption was not found to be related to the occurrence of subarachnoid hemorrhage.

Several studies have shown a direct relation between the amount of alcohol consumed and elevated blood pressure. When alcohol consumption is stopped, the blood pressure may return to normal. Most cohort studies that have looked at adverse health outcomes of drinkers have found an excess of stroke deaths. Klatsky and associates suggested that their failure to find a relationship was due to the youth of their cohort. In these studies most of the association between alcohol and stroke can be explained by controlling for hypertension but not by controlling for smoking.

Most of these studies did not specify types of strokes. In the Honolulu Heart Study alcohol consumption was associated with fatal and nonfatal intracranial hemorrhage and not thromboembolic strokes. The relationships remain significant in this cohort study of Hawaiian men of Japanese descent even after controlling for the effects of hypertension. Similar conclusions came from an autopsy study of the men who died during the follow-up period. Hypertension, cigarette smoking and alcohol use were significant risk factors for death from a hemorrhagic stroke. In these reports from the Honolulu Heart Study, less than half of the patients with intracranial hemorrhage had subarachnoid hemorrhage. These investigators did not do separate analyses because they stated that patients with subarachnoid hemorrhage and intracerebral hemorrhage had similar mean values of study factors, differing only with respect to left ventricular hypertrophy as determined by electrocardiogram.

These data tentatively suggest that alcohol con-
The most likely mechanism relates to the association of hypertension and alcohol consumption. Former drinkers whose blood pressure returns to normal should no longer be at risk. In experimental animals alcohol can have direct vasoactive effects on blood vessels that might increase the chance of vessel rupture and might lead to a commensurate elevation of blood pressure.

Further studies are needed that quantify the risk of subarachnoid hemorrhage in current drinkers, former drinkers and teetotalers.

**Other Factors**

Many other factors may be associated with subarachnoid hemorrhage (table 4).

<table>
<thead>
<tr>
<th>Possible Mechanism</th>
<th>Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>coarctation of the aorta, polycystic kidney disease, stimulant drug use, exercise</td>
</tr>
<tr>
<td>Vessel fragility</td>
<td>Marfan’s syndrome, pseudoxanthoma elasticum, Ehlers-Danlos syndrome, familial</td>
</tr>
<tr>
<td>Altered hemodynamics in the circle of Willis</td>
<td>atherosclerosis, fibromuscular dysplasia, arteriovenous malformations, moya-moya disease</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>pituitary tumors, influenza A, low cholesterol, antithrombotic agents</td>
</tr>
</tbody>
</table>

In experimental animals hemodynamic factors in the circle of Willis can promote aneurysm formation. Such a mechanism may explain the association of subarachnoid hemorrhage with fibromuscular dysplasia, atherosclerosis, arteriovenous malformations, and moya-moya disease. Other miscellaneous conditions that have been reported associated with subarachnoid hemorrhage include pituitary tumors, influenza A infections, and possibly low cholesterol. Factors affecting hemostasis such as anticoagulants or antiplatelet agents have not been studied systematically.

**Population Trends**

Stroke mortality has been falling in several countries since the earlier part of this century. Data from the Mayo Clinic have suggested that the fall is due to the falling incidence of stroke rather than an improved case fatality rate. The fall preceded the availability of effective measures to treat hypertension and the awareness of the need to treat it. The fall in stroke incidence and mortality thus probably involves factors other than the medical treatment of hypertension. That factors other than hypertension are operating is also suggested by the data on subarachnoid hemorrhage. The investigators from the Mayo Clinic have argued that if the fall of stroke incidence and mortality is due to hypertension control and hypertension is a risk factor for subarachnoid hemorrhage, then the incidence of subarachnoid hemorrhage should be falling as well. They found that the incidence from 1945 to 1975 was stable. They concluded that hypertension may not be a risk factor for subarachnoid hemorrhage. An alternative explanation is that hypertension control may not be the only factor leading to a fall in stroke incidence and that other factors such as use of oral contraceptives, cigarettes and alcohol have influenced the incidence of subarachnoid hemorrhage. For instance a reduced risk of subarachnoid hemorrhage resulting from control of hypertension might be offset by an increased risk resulting from increased alcohol consumption, which has been the trend in the United States since 1960. The divergent trends for subarachnoid hemorrhages and other strokes could be explained by the above factors having different risks for different types of stroke.

In New Zealand and Finland the incidence of subarachnoid hemorrhage has fallen during the 1970’s especially for women. In New Zealand, during this time cigarette smoking and oral contraceptive use have declined in women. The mortality rate for subarachnoid hemorrhage in the United States also began to fall in the mid-1970’s more for women than men. Data on incidence of subarachnoid hemorrhage in the United States is unknown, but if the case fatality rate is constant as has been shown in two studies, then the incidence like the mortality rate is also falling. Explanation for these trends remains unknown, but their existence suggests that factors exist whose alteration
could substantially influence the incidence, and thus morbidity and mortality, of subarachnoid hemorrhage.

**Conclusion**

Despite subarachnoid hemorrhage being a well-recognized clinical and pathological entity for over two centuries, knowledge of its risk factors remains meager. Hypertension is the most widely accepted risk factor, but the supporting evidence is by no means unambiguous. Nevertheless, the studies that are best designed to evaluate this relationship do support the contention that hypertension is an important risk factor for subarachnoid hemorrhage. As in experimental animals however it may be one of several important factors and not necessary or sufficient in itself to produce subarachnoid hemorrhage.24

Literature exists suggesting a role for several other factors that could be modified to bring about a reduction in the incidence of subarachnoid hemorrhage. These factors include the use of oral contraceptives, cigarettes and alcohol. Further studies are needed to evaluate these and other risks. Such studies would optimally be population based and akin to the study proposed by Bonita and associates.9 Studies examining only survivors could lead to erroneous conclusions. For instance, a factor that increased a patient’s chances of surviving the initial bleed would be found more commonly in survivors and incorrectly thought to be a risk factor for subarachnoid hemorrhage. Also, differences between acute and chronic exposures and current and former exposures for such factors as oral contraceptives, cigarettes and alcohol would need to be anticipated (table 5). With medical and surgical developments having little impact on the case fatality rate,9,10 studies of risk factors have perhaps the greatest chance of reducing the incidence of this devastating disease.

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