Inherited and acquired risk factors have been associated with the formation of intracranial aneurysms (Table 1). Familial clustering of these aneurysms may occur with no other history of hereditary disease. The incidence of intracranial aneurysms is between 8 and 9 percent in persons with two or more relatives who have had a subarachnoid hemorrhage. Compared with other family members, the siblings of affected persons have a higher risk of developing aneurysmal subarachnoid hemorrhage.

Various hereditary connective tissue disorders have been associated with the formation of aneurysms, presumably as a result of the weakening of vascular walls. One study found that intracranial aneurysms may develop in 10 to 15 percent of patients with polycystic kidney disease, an autosomal dominant condition. Although Marfan syndrome was previously identified as a risk factor for aneurysms, a recent detailed study found no significant relationship. Coarctation of the aorta, fibromuscular dysplasia, and pheochromocytoma have been associated with intracranial aneurysms, most
likely because of the elevated blood pressures
that occur in these conditions.3

Recent data have shown that age over 50
years, female gender, and current cigarette
smoking are risk factors for intracranial
aneurysm.9 Since 1984, cocaine use has been
linked to the formation and rupture of
aneurysms. This association is thought to be
due to increased turbulence of blood flow
and repeated, transient bouts of hyperten-
sion. Among cocaine users, aneurysms have
been found in significantly younger patients
and in vessels with a smaller diameter.10

Infections from bacterial or fungal coloniza-
tion of vessel walls, head trauma, and intra-
cranial neoplasms or neoplastic emboli are
rare causes of intracranial aneurysms.

Pathophysiology

Intracranial aneurysms are classified as sac-
cular, fusiform, or dissecting. Approximately
90 percent are saccular (berry aneurysms).11
Saccular aneurysms are responsible for most
of the morbidity and mortality caused by
subarachnoid hemorrhage.11

Saccular aneurysms develop from defects in
the muscular layer (tunica muscularis) of
arteries. Alterations in the internal elastic
membrane (lamina elastica interna) of cere-
bral arteries are thought to weaken vessel
walls and render them less resistant to
changes in intraluminal pressure.12 These
changes most frequently develop at sites of
vessel bifurcation, where blood flow is most
turbulent and shear forces against the arterial
wall are greatest13 (Figure 1).

Saccular aneurysms most frequently form in first-
and second-order arteries originating from the cerebral arterial circle (circle of
Willis) at the base of the brain. Multiple
aneurysms develop in 30 percent of affected
patients.14

Fusiform aneurysms develop from ectatic,
tortuous cerebral arteries, most often in the
vertebrobasilar system, and can reach several
centimeters in diameter. Patients with fus-
iform aneurysms characteristically present

### TABLE 1
Risk Factors for Intracranial Aneurysm

<table>
<thead>
<tr>
<th>Inherited risk factors</th>
<th>Other risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal dominant polycystic kidney disease</td>
<td>Age over 50 years</td>
</tr>
<tr>
<td>Type IV Ehlers-Danlos syndrome</td>
<td>Female gender</td>
</tr>
<tr>
<td>Pseudoxanthoma elasticum</td>
<td>Current cigarette smoking</td>
</tr>
<tr>
<td>Hereditary hemorrhagic telangiectasia</td>
<td>Cocaine use</td>
</tr>
<tr>
<td>Neurofibromatosis type 1</td>
<td>Infection of vessel wall</td>
</tr>
<tr>
<td>Alpha-antitrypsin deficiency</td>
<td>Head trauma</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
<td>Intracranial neoplasm or neoplastic emboli</td>
</tr>
<tr>
<td>Fibromuscular dysplasia</td>
<td>Hypertension*</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>Alcohol*</td>
</tr>
<tr>
<td>Klinefelter’s syndrome</td>
<td>Oral contraceptive pill use*</td>
</tr>
<tr>
<td>Tuberculous sclerosis</td>
<td>Hypercholesterolemia*</td>
</tr>
<tr>
<td>Noonan’s syndrome</td>
<td></td>
</tr>
<tr>
<td>Alpha-glucosidase deficiency</td>
<td></td>
</tr>
</tbody>
</table>

*—The significance of the association is still being studied.
Information from reference 3.

The Authors

CHARLES VEGA, M.D., is assistant professor and associate residency program director in the Department of Family Medicine at the University of California, Irvine, College of Medicine. Dr. Vega received his medical degree from the University of Wisconsin Medical School, Madison, and completed a family medicine residency at the University of California, Irvine.

JEREMIAH V. KWOON, M.D., is a resident in the Department of Family Medicine at the University of California, Irvine, College of Medicine. He received his medical degree from the Medical College of Wisconsin, Milwaukee.

SEAN D. LAVINE, M.D., currently is assistant professor of neurologic surgery and radiology, and director of endovascular neurosurgery at Columbia University College of Physicians and Surgeons, New York, N.Y. Previously he was assistant clinical professor of neurosurgery and director of cerebrovascular and endovascular neurosurgery at the University of California, Irvine, College of Medicine. Dr. Lavine received his medical degree from Cornell University Medical College, New York, N.Y. He completed a residency in neurosurgery and a fellowship in endovascular neurosurgery and interventional neuroradiology at the University of Southern California, Los Angeles.

Address correspondence to Charles Vega, M.D., University of California, Irvine, College of Medicine, Department of Family Medicine, 101 The City Dr., Bldg. 200, Rte. 81, Room 512, Orange, CA 92868 (e-mail: cpvega@uci.edu). Reprints are not available from the authors.
with symptoms of cranial-nerve or brain-stem compression, but the symptoms are not commonly associated with subarachnoid hemorrhage.\textsuperscript{14}

Dissecting aneurysms are the result of cystic medial necrosis or a traumatic tear of an artery. Like dissecting aneurysms elsewhere in the body (e.g., dissecting aortic aneurysms), they form as blood courses through a false lumen while the true lumen is collapsed upon itself.\textsuperscript{12}

**Clinical Presentation**

Most intracranial aneurysms are asymptomatic and remain undetected until the time of rupture. Subarachnoid hemorrhage, a medical emergency, remains the most common initial clinical presentation. It was the first symptom in 58 percent of patients in one series.\textsuperscript{15} A history of the abrupt onset of a severe headache of atypical quality (“the worst headache of my life”) is typical of subarachnoid hemorrhage. Headache onset may or may not be associated with brief loss of consciousness, nausea and vomiting, focal neurologic deficits, or meningismus.

Despite the characteristic history, subarachnoid hemorrhage is frequently misdiagnosed. Nearly one half of patients present with milder symptoms caused by a “warning leak” before full rupture of the aneurysm.\textsuperscript{16}

A case-record review of 111 patients re-
ferred to a tertiary care center for the management of unruptured aneurysm found that only 41 percent of the aneurysms produced symptoms (Table 2). In most of these patients, symptoms persisted beyond two weeks and were more likely to occur in patients with larger aneurysms located in the posterior circulation.

**Imaging**

Current neuroimaging techniques for intracranial aneurysms include intra-arterial digital subtraction angiography, magnetic resonance angiography, computed tomographic angiography, and transcranial Doppler ultrasonography. Although intra-arterial digital subtraction angiography is the gold standard, it is an invasive test with a 1 percent risk of transient neurologic complications and a 0.5 percent risk of permanent neurologic complications. Caution must be exercised in using magnetic resonance imaging in a patient with a history of surgery, because surgical clips may pose a threat to the patient during the test. The sensitivity and specificity of imaging modalities are presented in Table 3.

**Risk of Aneurysmal Rupture**

Given the high mortality rate associated with ruptured intracranial aneurysms, determining the likelihood of rupture is critical to management decisions. Before 1998, several large studies found annual rupture rates of 1.4 to 1.9 percent for intracranial aneurysms; rates of rupture were higher when aneurysms were larger than 10 mm in diameter, symptomatic, or located in the posterior circulation.

Although larger aneurysms have consistently been shown to be at higher risk for rupture, smaller aneurysms should not be overlooked. In one series of 25 patients, intracranial aneurysms were less than 5 mm in diameter at the time of rupture in five patients and less than 9 mm in diameter in 11 patients. Hence, vigilant surveillance and neurosurgical referral are necessary in all patients with intracranial aneurysms.

---

**TABLE 2**

**Symptoms of Unruptured Aneurysms in 111 Patients**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Number of affected patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute</strong></td>
<td></td>
</tr>
<tr>
<td>Severe headache</td>
<td>7</td>
</tr>
<tr>
<td>Transient ischemia</td>
<td>7</td>
</tr>
<tr>
<td>Seizures</td>
<td>3</td>
</tr>
<tr>
<td>Oculomotor nerve palsy or vision loss</td>
<td>2</td>
</tr>
<tr>
<td><strong>Chronic</strong></td>
<td></td>
</tr>
<tr>
<td>Noncatastrophic headache of different character than previous headaches</td>
<td>18</td>
</tr>
<tr>
<td>Chronic loss of vision</td>
<td>10</td>
</tr>
<tr>
<td>Unilateral optic neuropathy</td>
<td>7</td>
</tr>
<tr>
<td>Motor weakness or cranial neuropathy not involving the eye</td>
<td>4</td>
</tr>
<tr>
<td>Facial pain</td>
<td>3</td>
</tr>
</tbody>
</table>

*—Only 41 percent of the aneurysms caused symptoms.

Information from reference 17.
The findings of the International Study of Unruptured Intracranial Aneurysms (ISUIA)\textsuperscript{21} were published in 1998. To date, the ISUIA is the largest retrospective evaluation of the risk of aneurysmal rupture. Examination of 2,621 patient records at 53 medical centers over 7.5 years yielded average annual rupture rates below those of previous estimates. Aneurysms less than 10 mm in diameter had an average annual rupture rate of 0.05 percent in patients with no history of subarachnoid hemorrhage; however, the rupture rate was 10 times higher for aneurysms of a similar size in patients with a history of subarachnoid hemorrhage. The annual rupture rate for larger aneurysms approached 1 percent.

The ISUIA data suggest that aneurysms with a diameter of 10 mm or more are at critical risk for rupture. The study findings also make a strong case for differentiating patients with aneurysms and a history of subarachnoid hemorrhage from those without such a history. Surveillance of patients from the ISUIA is ongoing and will help to define the risk of aneurysmal rupture over time.

**Treatment of Intracranial Aneurysms**

Patients with suspected or confirmed asymptomatic or symptomatic intracranial aneurysms should be referred to a neurosurgeon. The two options for invasive treatment are open craniotomy and endovascular treatment.

### Table 3

<table>
<thead>
<tr>
<th>Modality</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnetic resonance angiography</td>
<td>69 to 100</td>
<td>75 to 100</td>
</tr>
<tr>
<td>Computed tomographic angiography</td>
<td>85 to 95</td>
<td>Not reported</td>
</tr>
<tr>
<td>Transcranial Doppler ultrasonography</td>
<td>50 to 91</td>
<td>87.5</td>
</tr>
</tbody>
</table>

Information from reference 3.

The risk of aneurysmal rupture appears to be higher in patients with a history of subarachnoid hemorrhage.
and the experience of the surgeon were risk factors for decreased function after surgery.

ENDOVASCULAR TREATMENT

Endovascular treatment for intracranial aneurysms has developed over the past decade. The Guglielmi detachable coil system is the only device that the U.S. Food and Drug Administration has labeled for endovascular treatment of ruptured and unruptured aneurysms. In this treatment, microwires are custom-fitted to occlude the vessel abnormality.

Some studies suggest that endovascular treatment of aneurysms may result in less procedural morbidity and mortality than conventional surgical techniques. In one series, however, only 54 percent of aneurysms were completely occluded by the procedure. It is not clear whether an aneurysm must be completely occluded to protect the patient against rupture, and data on long-term outcomes for endovascular treatment are lacking.

One ongoing study is comparing outcomes in patients with unruptured aneurysms who are treated with surgery versus coiling. Results from this study are not yet available.

Screening for Intracranial Aneurysms

Given the serious consequences of intracranial aneurysmal rupture and the emergence of new technologies that could aid in diagnosis and treatment before rupture, the prospect of screening is intriguing. In recent years, the literature has given some attention to the subject.

Screening of asymptomatic patients without risk factors does not appear to provide any benefits. Asymptomatic patients are defined by the absence of symptoms noted in Table 2. The relatively low incidence of intracranial aneurysms, their relatively low rate of rupture, and the potential complications of management make screening of asymptomatic patients inappropriate for the prevention of morbidity and mortality. Similarly, screening of patients with acquired risk factors, such as smoking or alcohol abuse, is not recommended. [Evidence level C, consensus/expert guidelines]

Screening of patients with a positive family history of ruptured intracranial aneurysm is controversial. Patients with one affected first-degree relative should be differentiated from those with more than one such relative. In one study, screening was performed in patients with first-degree relatives who had an aneurysmal subarachnoid hemorrhage: 4 percent of these patients were found to have intracranial aneurysms, most of which were less than 5 mm in diameter. Of these patients, 18 underwent surgery, and

<table>
<thead>
<tr>
<th>Time after surgery</th>
<th>History of subarachnoid hemorrhage</th>
<th>Mortality rate (%)</th>
<th>Disability rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 days</td>
<td>Yes</td>
<td>0</td>
<td>13.7</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>2.3</td>
<td>15.3</td>
</tr>
<tr>
<td>1 year</td>
<td>Yes</td>
<td>1</td>
<td>12.1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>3.8</td>
<td>12</td>
</tr>
</tbody>
</table>

11 had decreased neurologic function after the procedure. The study found that although screening in this patient population increased estimated life expectancy by 2.5 years, it also resulted in an average of 19 years of neurologic morbidity.26

Based on data such as these, the Stroke Council of the American Heart Association does not recommend screening for aneurysms in patients who have only one first-degree relative with aneurysmal subarachnoid hemorrhage.21

The issue of screening in patients who have two or more family members with intracranial aneurysms is more complicated. Although several studies27,28 have advocated the use of screening in this patient population, the conclusions were based on higher aneurysmal rupture rates than the ISUIA study found. A more recent analysis29 indicated that screening does not reduce significant morbidity or mortality in these patients. Therefore, the decision on whether or not to screen for intracranial aneurysms in patients who have two or more first-degree relatives with documented subarachnoid hemorrhage is best decided on a case-by-case basis.21

A definitive recommendation may emerge as more is learned about the risk of intracranial aneurysmal rupture and as the techniques for diagnosing and managing intracranial aneurysms improve.

Screening should also be considered in patients with rare conditions (e.g., autosomal dominant polycystic kidney disease) that are associated with an increased risk of aneurysms.7 However, the decision to screen these patients should be based on their overall health.

In patients with a history of aneurysmal subarachnoid hemorrhage, the annual rate of new aneurysm formation is between 1 and 2 percent, and the risk of aneurysmal rupture appears to be increased.30 Therefore, surveillance of these patients with magnetic resonance angiography or intra-arterial digital subtraction angiography may be justified.23

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REFERENCES

12. Selman WR, Tarr RW, Ratcheson RA. Intracranial Aneurysms