INTRODUCTION
Presence of blood in subarachnoid space, termed as subarachnoid hemorrhage (SAH), is always a pathological process. The term ‘aneurisma’ a Greek word, means ‘widening’. Trauma is the most frequent cause of SAH. Nontraumatic SAH accounts for 5 to 10% of all strokes and 5% of all stroke related deaths. The most common etiology of non-traumatic SAH is rupture of a berry aneurysm (80%), followed by rupture of arteriovenous malformation (AVM) (Table 1). Despite advances in diagnostic tools, critical care, and microneurosurgery, rupture of intracranial aneurysm (IA) continues to be a devastating disease. In developing countries, with lack of resources and good public health organization, problems in management are even more severe. Prognosis in patients with SAH depends upon primary hemorrhage and a number of secondary events of which rebleed and vasospasm are most important. Many of the secondary insults, if recognized and treated early, are preventable. Thus physician working in mainstream should be able to suspect, diagnose and refer them appropriately. Early clipping or closure of aneurysm has been shown to improve outcome. It must be kept in mind that clinical monitoring is often inadequate in the setting of coma, sedation and neuromuscular paralysis. Neurointensive care of these patients aims at protocol based monitoring and treatment to have a better outcome.

In this review, we have described clinical presentation, merits of various diagnostic and monitoring methods, medical management and other therapeutic options available in the management of intracranial aneurysms.

EPIDEMIOLOGY
Based on angiographic and autopsy studies, incidence of asymptomatic intracranial aneurysms in general population ranges between 0.5% and 5%. Annual incidence of rupture in patients with known aneurysm is 1.4% to 2.3%. Rupture risk is related to size and site of IA. Worldwide incidence of SAH is about 6-10 per 100,000 of the population each year, varying according to ethnic and geographic characteristics. Exact data for our country is not available. If left untreated, SAH due to rupture of IA carries a mortality of 45% (32-67%) and 25-33% of survivors will have a substantial morbidity. The mean age at presentation
is of 55 years and risk for women is 1.6 times than that of men. According to several epidemiologic studies, 7 to 20% of patients with aneurysmal SAH have a first- or second-degree relative with IA.

Approximately 80 to 85 percent of IA are located in the anterior circulation (Table 2). Common locations of IA are junction of the internal carotid artery and the posterior communicating artery, anterior communicating-artery complex, trifurcation of the middle cerebral artery, junction of vertebral artery and posterior inferior cerebellar artery and bifurcation of the basilar artery. Multiple intracranial aneurysms, usually two or three in number, are found in 20 to 30% of patients.

### PATHOPHYSIOLOGY

Our understanding of the causation, growth and reasons for rupture of IA is quite inadequate. Intracranial arteries are susceptible to aneurysm formation as they lack external elastic lamina and adventitia is very thin. Tunica media is either very thin or absent in the saccular, or berry aneurysm. IA can be either congenital or acquired. Commonest morphological type of IA is saccular or berry aneurysm. Other morphological types are fusiform and dissecting aneurysms. Macroscopically, many intracranial aneurysms, especially those that rupture, have an irregular appearance, with one or more daughter sacs and variable wall thickness. The point of rupture is generally in the dome of the aneurysm. Common risk factors associated with development and rupture of IA have been summarized in Table 3. Most of IA rupture in subarachnoid space. However, it can occur at intraventricular, intracerebral, and subdural locations also.

**Table 2: Locations of intracranial aneurysms**

<table>
<thead>
<tr>
<th>Location</th>
<th>Single aneurysm</th>
<th>Multiple aneurysms</th>
<th>Giant aneurysm</th>
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<tbody>
<tr>
<td>Internal carotid artery</td>
<td>40%</td>
<td>43%</td>
<td>54%</td>
</tr>
<tr>
<td>Anterior cerebral artery complex</td>
<td>32%</td>
<td>21%</td>
<td>10%</td>
</tr>
<tr>
<td>Middle cerebral artery</td>
<td>18%</td>
<td>27%</td>
<td>9%</td>
</tr>
<tr>
<td>Basilar artery</td>
<td>7%</td>
<td>5%</td>
<td>16%</td>
</tr>
<tr>
<td>Vertebral artery</td>
<td>3%</td>
<td>1%</td>
<td>7%</td>
</tr>
</tbody>
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**Table 3: Risk factors associated with development and rupture of IA**

- Age (maximum at 50-59 years), the incidence of hemorrhage increases with age until eighth decade of life
- Gender: F>M in a ratio of 1.6:1.0
- Family history of stroke
- Hypertension including pregnancy-induced hypertension
- Atherosclerosis
- Smoking (more relevant in women)
- A moderate-to-high level of alcohol consumption is an independent risk factor
- Fatty metamorphosis of the liver
- Long-term analgesic use
- Cocaine abuse
- Oral contraceptives
- Size of aneurysm (< 5 mm = 2.5%, 6-10 mm = 41%, 11-15 mm = 87%)
- Location (proximal more likely and intracavernous are least likely to bleed)
- Multiple aneurysms
- Vascular asymmetry in the circle of Willis

reaction in the blood-vessel wall. Extravasated blood and its products in CSF are responsible for development of this dreaded complication. Many spasmogens e.g. oxyhemoglobin, histamine, eicosanoids, endothelin, nitrous oxide and 2-hydroxy-3-methylglutarylcoenzyme have been implicated in the development of vasospasm.

### CLINICAL FEATURES

It is important to realize that more than 50% of the patients are misdiagnosed at first visit to their physician. The common incorrect diagnoses are migraine and tension-type headache (Table 4). Failure to obtain accurate history, absence of neurological deficit at admission and incorrect interpretation of imaging study are common reasons for misdiagnosis. Intracranial aneurysms can present in one of the following ways:

1. **Asymptomatic**: Detected either on investigation of unrelated conditions and while screening for high-risk cases or as co-existence with a ruptured aneurysm (4%). With use of CT and MRI, many more asymptomatic cases will be detected.
2. **SAH (89%)**.
3. **Symptoms other than that of SAH (7-20%)**, e.g. pressure (large or giant IA) on cranial nerves and brain structures, thrombi that embolize distally, and non-specific headache.

Unruptured IA are mostly asymptomatic or cause non-specific local pressure symptoms. Most aneurysmal
Aneurysmal Subarachnoid Hemorrhage

SAH occurs at the time of severe exertion or stress. Prodromal or warning headache from minor blood leakage, referred to as sentinel headache, is present 30-50% of cases but frequently go undetected\textsuperscript{10,11}. Classical presentation of SAH is that of a sudden onset of severe headache, not experienced by the patient earlier. It is often referred to as ‘first and worst’. Commonly, it is accompanied with nausea (77%), vomiting, neck pain (35%), photophobia, and visual blurring. Loss of consciousness at onset is evident in about half of the patients. Approximately 10-25% of patients have seizures at onset.

Onset of SAH is often accompanied by sudden increase in blood pressure, which later becomes labile in presence of increased intracranial pressure. Fever is common after third or fourth day of ictus and is independent of associated infection. Signs of meningeal irritation e.g. neck stiffness, low back pain, bilateral leg pain are seen in upto 80% cases. Neck stiffness is caused by the breakdown of blood products within the subarachnoid space, and develops several hours after the hemorrhage. It is absent in patients who are in deep coma. Other signs on physical examination include diminished level of consciousness and localizing neurological signs e.g. monocular vision loss (ophthalmic artery aneurysm compressing the ipsilateral optic nerve), third-nerve palsy (posterior communicating artery aneurysm), sixth-nerve palsy (increased intracranial pressure), bilateral lower-extremity weakness or abulia (anterior communicating aneurysm), and combination of hemiparesis and aphasia or visuospatial neglect (middle cerebral-artery aneurysm). Pre-retinal hemorrhage (Terson’s syndrome) is seen in up to 5% cases and suggests sudden increase in intracranial pressure. It must be differentiated from commonly seen retinal and subhyaloid hemorrhages. Important neurological complications associated with SAH are vasospasm (46%), hydrocephalus (20%), and rebleeding (7%).

**DIAGNOSIS**

**Computed Tomography (CT)**

A non-contrast CT scanning is the first and most important diagnostic study in evaluation for patients with SAH. It is fast, safe, inexpensive, noninvasive, and widely available. In large number of patients, it obviates the need for lumbar puncture (LP). It also helps in differentiating it from other intracranial lesions as mentioned in Table 4. Extravasated blood is identified as high-attenuated areas. It is desirable to have thin cuts through the base of the brain. CT findings are also graded and are useful in prognostication (Table 5). In case of multiple aneurysms, it may be possible to identify the ones that have bled. Sensitivity of CT scan in detecting SAH depends upon amount of blood leaked and duration of illness at the time of study i.e. 93-98% at 12 hours, 75-80% at day three, 70% at day five, 50 percent at day seven and nearly 30 percent at day fourteen.

**Magnetic Resonance Imaging (MRI)**

The main limitation of MRI is longer acquisition time that is unacceptable in patients with an acute neurological presentation. During acute stage, it is less sensitive than CT study. Modern MRI scanners using

<table>
<thead>
<tr>
<th>Grade</th>
<th>CT scan</th>
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<tbody>
<tr>
<td>1</td>
<td>No blood visualized</td>
</tr>
<tr>
<td>2</td>
<td>A diffuse deposition or thin layer with all vertical layers of blood (interhemispheric fissure, insular cistern, ambient cistern) less than 1 mm thick</td>
</tr>
<tr>
<td>3</td>
<td>Localized clots and / or vertical layers of blood 1 mm or greater in thickness</td>
</tr>
<tr>
<td>4</td>
<td>Diffuse or no subarachnoid blood, but with intracerebral or intraventricular clots</td>
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gradient echo or FLAIR sequences are as sensitive as CT scan during acute stage. However, the main utility of MRI is during subacute or chronic phase of illness when CT findings may have reverted to normal. Diffusion weighted imaging is valuable in diagnosis of ischemia secondary to vasospasm.

**Cerebrospinal Fluid (CSF) Study**

Blood from ruptured aneurysm enters the CSF. In next two to four hours, it is hemolysed to produce oxyhemoglobin. It is relevant to appreciate that this process occurs both in vivo and in vitro. Oxyhemoglobin is then converted to bilirubin by the enzyme hemoglobinase in next 9-15 hours. Thus SAH is characterized by presence of RBCs and xanthochromia in CSF. In the past, CSF study was almost a must in evaluation of suspected SAH. As per current practice, a CT scan is obtained in all patients and LP is done if CT scan findings are negative or equivocal.

Traumatic tap is one of the dilemmas that clinicians face on all occasions. It is a common practice to collect CSF in three to four consecutive tubes and RBC count is done in first and last tube. Diminishing RBC count is a good method for demonstrating traumatic nature of CSF. Crenation of RBCs, and presence of erythrophages lacks sensitivity. Xanthochromia takes few hours to develop and persists for two weeks in all patients with SAH. It must be appreciated that visual inspection alone is not sufficient to evaluate xanthochromia. Spectrophotometer can detect both oxyhemoglobin and bilirubin in CSF and is an excellent test for diagnosing SAH in CT negative patients.

**Imaging of Aneurysm**

Accurate angiographic evaluation of IA is of great importance in planning the management in patients with SAH. Because of its high resolution, digital subtraction angiography (DSA) is the gold standard in imaging cerebral aneurysms. It has a high sensitivity and specificity with false negative results in the range of 5% to 10%. However, it is invasive, expensive, and time-consuming procedure, not available at most of the district centers. Complication rate is upto 1%.

Helical or spiral CT angiography (CTA) is a cheaper noninvasive and faster technique with three-dimensional images. It can be performed along with routine CT study. CTA has a sensitivity of 67 to 100% and specificity of 50 to 100%. Disadvantages include low spatial resolution and poor demonstration of the small aneurysms (<3-5 mm), internal carotid aneurysms, and posterior circulation aneurysms. Three-dimensional CTA and CT dynamic studies are emerging techniques in this field. CTA must be employed with caution in patients with impaired renal function as a large bolus of contrast material is administered.

MR angiography (MRA) is another diagnostic study that carries no risk. It is one of the best investigations for demonstration of a thrombus in the aneurysmal sac. It can detect lesions as small as 2-3 mm in diameter. However, MRA cannot be performed in patients who have been clipped for earlier SAH. In addition, spatial resolution of MRA is slightly inferior to CTA.

**Monitoring in Patients with SAH**

Diagnosis of cerebral vasospasm and other complications are far from satisfactory. Unexplained alteration in sensorium and/or appearance of fresh neurological signs and symptoms raises the possibility of vasospasm, hydrocephalus, hyponatremia, subclinical seizures and other systemic complications.

**Clinical Monitoring**

Clinical grading scales with Hunt and Hess Scale and the World Federation of Neurological Surgeons Scale are commonly used to describe neurological condition at admission and considered to be good prognostic predictors (Table 6). The latter is preferable as it uses combination of Glasgow Coma Scale and the presence of focal neurological signs.

**Intracranial Pressure (ICP) Monitoring**

The main determinant of cerebral blood flow (CBF) is cerebral perfusion pressure (CPP), which in turn is the difference between mean arterial pressure (MAP) and ICP. Aim of ICP monitoring is to maintain adequate CPP. Common causes of raised ICP in SAH are sudden spurt of blood in subarachnoid space, reaction of brain and meninges to extravasated blood, hydrocephalus, diminished compliance of brain and cerebral edema. In critically ill patients, routine procedures such as turning or suctioning can produce deleterious elevations of ICP. ICP monitoring, pressure wave analysis and therapeutic drainage of CSF are possible with indwelling intraventricular catheters.

**Transcranial Doppler Ultrasound (TCD)**

Through the cranial window major cerebral arteries around circle of Willis are mapped with a low-frequency (2 MHz) pulsed wave probe. It detects elevated flow...
velocities in the basal cerebral arteries suggesting vasospasm. TCD is a bedside non-invasive and cheaper procedure that allows serial measurements to identify patients at risk. However, its main limitation is that it is operator dependent.

**Continuous Electroencephalography (EEG)**

It has a limited role in monitoring patients with SAH. Finer details provided by EEG monitoring are often blurred because of artifacts during recording. Its main utility is in detection of non-convulsive seizures.

**Biochemical Markers**

Several serum (S-100, neuron-specific enolase, angiogenic factors, intercellular adhesion molecule) and CSF (S-100, neuron-specific enolase, lipid peroxides, cytokines, angiogenic factors, fibrin and fibrinogen degrading products, CSF endothelin-1, nitric oxide metabolites) markers have been evaluated but final verdict is awaited.

**TREATMENT**

SAH is an emergency and all patients must be stabilised first with maintenance of airway and cardiovascular function. Patients are then transferred to a Neuro ICU and an urgent neurosurgical consultation is obtained. Goals of management at this stage are prevention and treatment of rebleeding and vasospasm, surgical clipping or endovascular occlusion of aneurysm and management of other medical and neurological complications. An outline of treatment has been given in Table 7 and few important points will be discussed.

**General Principles**

Elevated BP must be normalised with IV agents such as labetalol, esmolol or nitroprusside. Once aneurysm has been clipped, elevation of BP can be permitted as a part of triple ‘H’ therapy. Seizures occur in approximately 30% of the patients. In view of the devastating effect of a seizure, prophylactic anticonvulsant must be prescribed for few weeks in all cases. Common medical complications that need careful observation are pulmonary edema in 23% (either cardiogenic or neurogenic), and electrolyte disturbances in 28% of patients. Cardiac abnormalities are common after SAH and include ECG changes, cardiac arrhythmias, elevations of cardiac enzymes, and left ventricular dysfunction. Most of these cardiac abnormalities are temporary.

**Vasospasm**

Patients with SAH are monitored closely with repeated clinical evaluation, CT examination and TCD for development of vasospasm. Two principal approaches to treat vasospasm are hemodynamic augmentation (triple ‘H’ therapy i.e. hypervolemia, hemodilution and induced hypertension) and endovascular reversal. Central venous catheter monitoring is used to maintain CVP around 8-12 mmHg. Fluids used for hypervolemia are 5% albumin and isotonic crystalloids. Mean arterial pressure is maintained around 110 mmHg with the help of vasopressor drugs. Nimodipine is routinely used as prophylaxis for vasospasm and delayed ischemic damage. It is administered orally in a dose of 60 mg every 4 hourly for 21 days. Intravenous nimodipine is given in a dose 1 mg/hour once vasospasm sets in. Attempts have been made to reverse vasospasm with external ventricular drainage and aggressive irrigation of the basal cisterns. Transluminal angioplasty and endovascular or intra-arterial infusion of vasodilator substances (papaverine) or of calcium channel blockers (verapamil, nimodipine or nicardipine) has been tried. Recently, cisternal washing, free radical scavengers, nitric oxide donors, hypothermia, statins and estrogen have been used to prevent vasospasm with encouraging results.

**Hydrocephalus**

Hydrocephalus develops in about 15-20% of patients who have an aneurysmal SAH. Diagnosis is confirmed...
Surgical Treatment

Whether a given aneurysm should be observed, treated surgically, or managed endovascular, remains controversial. Microsurgical placement of a clip across the neck and endovascular coiling are two main therapeutic options for securing a ruptured aneurysm. Surgical clipping has been assessed for a long period and has high acceptability with neurosurgeons. Aneurysms that are not amenable to clipping can be dealt with other sophisticated techniques, such as vascular bypass grafting, hypothermic cardiac arrest, and surgical or endovascular occlusion of the proximal vessel. Current consensus is for early surgery (within 72 hours after the ictus) because of high risk of rebleed in the first week and its effectiveness in preventing vasospasm. Late surgery is complicated by presence of vasospasm and brain edema around the clot.

Endovascular Therapy

In selected cases, endovascular treatment is emerging as a promising alternative to surgical clipping. The goal of endovascular coiling is to thrombose the aneurysmal sac with transarterial placement of small and soft platinum or titanium coils. Elderly patients, patients in poor medical condition, aneurysms at difficult locations, and those associated with large intracerebral hematoma are better treated by an endovascular approach. Aneurysms with wide necks are less amenable to endovascular treatment than those with narrow necks. Though this procedure carries a lower risk, its long-term effectiveness is yet to be proved.

Surgery for Unruptured Intracranial Aneurysm

Choosing surgery for patients with an unruptured intracranial aneurysm is a difficult therapeutic decision. One must weigh the risk of intracranial hemorrhage against the risks associated with surgery. Co-morbid medical conditions, severe cardiac, pulmonary, or renal disease or cancer weighs against prophylactic surgery. Patient’s feelings, experiences, biases, and personal preferences are equally important. Size and site of unruptured aneurysms matters a lot in arriving at a decision.

PROGNOSIS

Nearly 15-20% patients die before admission, and another 40% die during the first month. More than one-third of survivors have major neurological deficits.
Common reasons for death are vasospasm (32%), direct effect of bleed (25%), rebleeding (18%), brain compression and shift (5%), hydrocephalus (4%), myocardial ischemia/arrhythmia, and hyponatremia. The major prognostic factors associated with poor outcome are level of consciousness at admission (Table 6) and amount of blood shown at first CT study (Table 5). The outcome of surgery depended heavily on age. The surgery-related morbidity and mortality at one year is 6.5% for those < 45 years, 14.4% for 45-64 years, and 32% > 64 years. Other prognostic factors related to surgery are experience of surgeon, team and centre; size and location of the aneurysm; and morphologic features of the aneurysm.

CONCLUSION

Non-traumatic subarachnoid hemorrhage (SAH) accounts for 5-10% of all strokes and it has an incidence of 10.5/100000 persons/year. The most common cause of non-traumatic SAH is rupture of an intracranial aneurysm. Other causes include vascular malformations, tumors, and infection. Intensive critical care support and prompt diagnosis with high-resolution CT remain key aspects of good patient management. In patients presenting with a suspected non-traumatic SAH, CT within 12 hours will reliably show 98% of SAH. In patients who present after 12 hours with a negative CT scan, formal CSF spectrophotometry will detect SAH for the next two weeks with a reliability of 96%. The natural history of untreated aneurysmal subarachnoid hemorrhage carries a dismal prognosis. Case fatalities range between 32% and 67%. Today, with improved techniques for coil embolization and clip occlusion of aneurysms, a great majority of patients are successfully treated through the acute phase after SAH. Given the complexity of evaluation, treatment and management of aneurysmal subarachnoid hemorrhage, a team approach to the problem has proved useful.

We are still to answer many questions related to this disease, e.g. epidemiological pattern, reasons for rupture of aneurysm, reasons and best management for vasospasm and rebleed, role of neuroprotection, intracisternal application of thrombolytic therapy, use of biologically active coils and stents for endovascular treatment.

KEY POINTS

- Early diagnosis of SAH is crucial to good results.
- All patients presenting with sudden, severe headache, warrant further investigation

- A CT scan within 12 hours of presentation is 98% sensitive for SAH
- Lumbar puncture must be performed more than 12 hours after presentation.
- Visual analysis of CSF is not acceptable and spectrophotometry detection of bilirubin in CSF is indicative of SAH
- Prompt angiography identifies the cause of SAH.
- Early obliteration of the aneurysm prevents rebleed.
- Early recognition and management of cerebral vasospasm minimizes stroke.

REFERENCES


