Figure 1 Early pathophysiology of subarachnoid haemorrhage

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Figure 2 Pathophysiological processes in delayed cortical ischaemia

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Figure 3 Pathophysiological causes of ischaemia

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Figure 4 CT scan and cerebral angiography of SAH

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Figure 5 A management scheme—our approach to SAH and DCI

### Table 1 Drugs in development for treatment of SAH

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<th>Drug class</th>
<th>Putative mechanisms of action</th>
<th>Status</th>
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<td>Statins</td>
<td>Inhibit HMG-CoA reductase, thereby reducing synthesis of cholesterol, geranylgeranylpyrophosphate and farnesylpyrophosphate&lt;sup&gt;122&lt;/sup&gt; Preserve endothelial function via increased synthesis of nitric oxide, and decreased synthesis of endothelin-1 and RhoA Anti-inflammatory effects Antioxidant effect via decreased production of oxygen free radicals and peroxynitrite, and decreased expression of angiotensin receptors and NADPH oxidase Anti-thrombotic actions Vascular protection through decreased expression of matrix metalloproteinases Neuroprotective and neurorestorative action (increased synaptogenesis, increased neurogenesis)</td>
<td>Six randomized clinical trials of statins in patients with SAH&lt;sup&gt;99&lt;/sup&gt; Systematic review of these studies found no effect of statin treatment on poor outcome; mortality was 10% in statin group versus 21% in controls (RR 0.46, 95% CI 0.20-1.06); DCI was significantly reduced in statin group Quality of the studies overall was low to moderate At least two ongoing clinical trials&lt;sup&gt;20,21&lt;/sup&gt; Current recommendation: only administer statins if the patient was already receiving them at time of SAH</td>
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<td>Magnesium</td>
<td>Vasodilatation via antagonism of calcium channels on vascular smooth muscle and increased endothelial cell prostacyclin&lt;sup&gt;256&lt;/sup&gt; Endothelial protection through inhibition of platelet aggregation and decreased production of angiotensin-converting enzyme Protect the blood–brain barrier Reduce cerebral oedema via decreased aquaporin-4 expression Antagonism (N-methyl-D-aspartate receptor antagonism)</td>
<td>Studied in seven randomized clinical trials&lt;sup&gt;127,134&lt;/sup&gt; Meta-analysis reported no effect of magnesium on poor outcome Therapeutic intravenous infusions of magnesium are not recommended for patients with SAH&lt;sup&gt;324&lt;/sup&gt;</td>
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<td>Anti-inflammatory drugs</td>
<td>Prevent vasospasm, inhibit IL-2 production, and prevent T-cell dysfunction (using cyclosporin A)^&lt;sup&gt;311,315&lt;/sup&gt; Inhibit complement activation and inflammation (using FUT-175 (nafamostat mesilate))&lt;sup&gt;339&lt;/sup&gt; Acetylsalicylic acid and thromboxane synthase inhibitors have anti-inflammatory and antiplatelet activity&lt;sup&gt;311,132&lt;/sup&gt; Prevent upregulation of endothelial cell adhesion molecules that allow binding of macrophages and neutrophils (which infiltrate the subarachnoid space, die and degenerate, releasing endothelin-1 and oxygen free radicals)&lt;sup&gt;54&lt;/sup&gt; Corticosteroids have multiple anti-inflammatory actions, mostly on chronic inflammation NSAIDs inhibit cyclo-oxygenase, which decreases prostaglandin synthesis; ibuprofen inhibits expression of endothelial adhesion molecules and reduces subarachnoid inflammation</td>
<td>Literature review concluded that NSAIDs have little measurable benefit for treatment of SAH&lt;sup&gt;434&lt;/sup&gt; Glucocorticoid steroids studied in three SAH trials, but too few patients studied (256) to draw conclusions about efficacy&lt;sup&gt;65&lt;/sup&gt; Randomized controlled trial found no effect of methylprednisolone on angiographic vasospasm or DCI after SAH, but significantly improved outcome at 1 year compared with controls&lt;sup&gt;65&lt;/sup&gt;</td>
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Abbreviations: DCI, delayed cerebral ischaemia; HMG-CoA, 3-hydroxy-3-methylglutaryl coenzyme A; SAH, subarachnoid haemorrhage.