Carotid and vertebral artery dissection

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INTRODUCTION
Carotid and vertebral artery dissections are potentially disabling and yet probably under-diagnosed, and mainly seem to affect young and middle-aged people (Bogousslavsky et al. 1987). Our review focuses on the mechanisms, possible underlying causes, clinical manifestations, diagnostic tools, treatment and prognosis of both carotid and vertebral dissection.

EPIDEMIOLOGY
Cervical artery dissection accounts for up to 20% of strokes in patients under 30 years of age (Bogousslavsky et al. 1987). The incidence of carotid dissection is about 2–3 per 100 000 per year (Schievink et al. 1993; Giroud et al. 1995); the incidence of cervical dissection must be higher because these figures do not take into account vertebral dissection (about 25% of all dissections), dissections without ischaemic events (20% of extracranial dissections) or asymptomatic dissections. Furthermore, dissections may be overlooked because the clinical manifestations resolve spontaneously and are not necessarily familiar to many emergency physicians. Most studies report either no sex predilection or a female predominance. The mean age is between 39 and 45 years. This young age may be in part due to diagnostic bias because the dissection imaging protocol is applied less frequently in older people.

PATHOPHYSIOLOGY
Cervical dissections are thought to arise from an intimal tear and so penetration of circulating blood into the vessel wall and the formation of an intramural haematoma. In addition, some dissections may be due to a primary intramural haematoma (Schievink 2001). Subintimal dissection tends to cause luminal narrowing or occlusion, whereas subadventitial dissection may cause a dissecting aneurysm (Guillon et al. 1999). Combined forms with stenosis and aneurysmal dilatation occur. There are three main consequences of dissection:

• Retinal or brain ischaemia caused by embolization of thrombus overlying the dissection to the retinal artery or the intracranial vessels (Benninger et al. 2004). Less frequently, if the collateral circulation is insufficient, hypoperfusion may lead to haemodynamically induced infarction.
Compression or stretching, due to the enlarged artery and any aneurysm, causes local symptoms such as pain, Horner’s syndrome and cranial nerve palsies.

Subadventitial rupture of the dissected artery, mostly the intracranial vertebral, can cause subarachnoid or intracerebral haemorrhage. This may be because the wall of the intracranial segment is thinner than that of the extracranial arteries.

In 15–20% of patients, multivessel cervical artery dissections occur simultaneously (Mas et al. 1985; Schievink et al. 1994a); it is unclear whether these patients represent a distinct group with particular predisposing intrinsic factors or precipitating events leading to a transient arteriopathy. In some cases renal infarcts due to simultaneous renal artery dissection may occur, with acute abdominal pain and an increased ESR (Amarenco et al. 1994).

AETIOLOGY
The cause of cervical artery dissections is largely unexplained. It most likely involves an underlying abnormality of the vessel wall (Brandt et al. 2001) as well as triggering factors such as trauma or infection (Mokri 1990; Guillon et al. 2003).

Intrinsic (genetic) factors
In at least some patients an underlying arteriopathy or an anatomic variant of the arteries predisposes to vessel dissection. Reports of familial carotid dissection and dissection associated with vessel tortuosity, fibromuscular dysplasia, intracranial aneurysms, aortic root enlargement, alpha 1-antitrypsin deficiency and hereditary connective tissue disorders such as Ehlers-Danlos syndrome vascular type, Marfan’s syndrome, autosomal dominant polycystic kidney disease and osteogenesis imperfecta type I all support the concept that predisposing genetic disorders play some role in pathogenesis (Schievink et al. 1994b). Skin biopsies of patients with carotid dissection have shown ultrastructural abnormalities in the dermal connective tissue, including enlarged or irregular collagen fibrils and pronounced elastic fibre fragmentation, suggesting a predisposing systemic disorder (Brandt et al. 1998). In an ultrasound study, common carotid artery diameter change during the cardiac cycle was significantly higher in carotid dissection cases than in controls. These findings all suggest that a generalized defect of the extracellular matrix is present in at least some patients with spontaneous carotid dissection. However, extensive genetic studies for mutations in extracellular matrix molecules have been negative (Grond-Ginsbach et al. 1999). Hyperhomocystinaemia may be a risk factor for carotid dissection (Gal-lai et al. 2001) and migraine has been reported to be associated with carotid dissection in two case-control studies (D’Anglejan et al. 1989;
Tzourio et al. 2002). This, and another study that demonstrated a highly significant association between migraine and the activity of serum elastase (Tzourio et al. 2000), supports the hypothesis that some underlying disease of the arterial wall and its extracellular matrix could be a predisposing condition for both migraine and cervical artery dissection.

Extrinsic (environmental) factors
There are clearly dissections of traumatic origin following serious head or neck injury. Furthermore, dissections have been reported after mild or trivial trauma, and after various ‘normal’ activities such as sneezing, coughing and forced head turning (Table 1) (Mokri 1990). However, the role of mild trauma in the pathogenesis of dissections is questionable and the differentiation between spontaneous and traumatic dissection is somewhat artificial.

Table 1 Activities that may cause minor trauma to the arteries in the neck and that are associated with cervical artery dissection

| Driving a car: | car accident (e.g. whiplash injury), turning the head while driving |
| Sporting activities: | skiing, rugby, swimming, cycling, riding, scuba diving, judo, yoga, trampoline |
| Medical procedures: | neck extension during anaesthesia or surgery, endotracheal intubation, bronchoscopy, chiropractic manipulation |
| Pregnancy: | delivery, postpartum |
| Various other activities: | sneezing, coughing, sexual activity, vomiting |
| Speed activities: | roller coaster |
| Daily activities: | prolonged phone call, shaving, teeth brushing, ceiling painting |

CLINICAL PRESENTATION

Dissection of the internal carotid artery
Neck and facial pain, headache, unilateral pulsatile tinnitus, Horner’s syndrome, amaurosis fugax, retinal infarction and anterior circulation ischaemia may all occur in isolation, or in various combinations (Table 2). The classical symptom complex of unilateral headache and/or neck pain and an ipsilateral Horner’s syndrome followed by ischaemic symptoms from the ipsilateral hemisphere or retina occurs in less than one-third of patients (Schievink 2001). Local warning symptoms are described in many cases and allow early diagnosis and treatment before cerebral complications occur (Biousse et al. 1995). However, diagnosis is often delayed, especially when only local symptoms occur initially.

Local symptoms
The most common is head pain with acute onset. It is usually a prominent and early manifestation, most frequently localized in the periorbital and fronto-temporal regions and/or in the upper anterolateral cervical region, ipsilateral to the dissection (Biousse et al. 1994; Silbert et al. 1995). Occasionally patients may complain of occipital headache, entire hemicrania or bilateral pain (21%). In 17% of the patients the pain involves the neck, face and head simultaneously (Biousse et al. 1994). In more than 70% the pain is severe. Occasionally the pain is both sudden and 

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and severe, like a thunderclap, mimicking subarachnoid haemorrhage. It can also mimic an attack of migraine, or cluster headache.

Dissection with stenosis may lead to pulsatile tinnitus due to propagation of a bruit from the distal carotid stenosis, but in only about one-quarter of patients (Silbert et al. 1995).

**Local signs**

Ipsilateral Horner’s syndrome is reported in up to 50% of patients. It is due to disturbance of the sympathetic fibres within the carotid wall and is often incomplete (Hart & Easton 1983). A painful Horner’s syndrome of acute onset is almost pathognomonic of carotid dissection. Carotid dissection also leads to cranial nerve palsies in more than 10% of patients (Mokri et al. 1996). The hypoglossal nerve is the most commonly affected, followed by cranial nerves IX, X, XI and V, and we have observed unilateral dysgeusia in some patients. The involvement of various combinations of nerves has been described. The oculomotor and facial nerves may be involved in rare cases. One possible mechanism leading to cranial nerve palsy is compromise of the vasa nervorum. Direct compression of the cranial nerves by the mural haematoma is another plausible explanation.

**Cerebral ischaemia**

The frequency of cerebral ischaemic symptoms varies from 50% to 90%, mainly depending on patient selection and delay to diagnosis. Ischaemic stroke without any preceding warning symptoms may occur. But often local symptoms, amaurosis fugax and/or transient cerebral ischaemic attacks precede the stroke. Most cerebral infarcts are located in the middle cerebral artery territory and occur within the first week of local symptom onset. Later strokes, more than 1 month after the first local symptom or the first TIA, are extremely rare (Bioussé et al. 1995). Carotid dissection with ischaemic events is more frequent with > 80% stenosis, occlusion or intracranial obstruction, and is less frequent with Horner’s syndrome and cranial nerve palsy, than dissection without ischaemic events (Baumgartner et al. 2001).

**Retinal ischaemia**

Amaurosis fugax ipsilateral to the affected carotid artery, due to embolism or impaired blood flow to the retina, is a frequent warning symptom of stroke. It is very suggestive of dissection when associated with acute ipsilateral facial pain or headache in a young subject. Persisting visual loss due to central retinal artery occlusion or anterior ischaemic optic neuropathy is rare (Bioussé et al. 1998).

**Intracranial carotid artery dissection**

This is uncommon and mainly affects healthy young adults less than 30 years old (Bassetti et al. 1994). Usually patients present with ischaemic symptoms in the anterior circulation territory associated with sudden and severe headache. Rarely subarachnoid haemorrhage may occur. However, the diagnosis is difficult because there are no specific symptoms of intracranial carotid artery dissection. When there is subarachnoid haemorrhage present, this can easily be misdiagnosed as aneurysmal and associated with severe spasm of the distal internal carotid artery. The prognosis is thought to be worse than in patients with extracranial carotid dissection but this may be because of publication bias in favour of autopsy cases, largely because of the difficulty of making the diagnosis during life.

**Vertebral artery dissection**

The typical clinical manifestation is posterior neck pain or occipital headache or both, usually more marked on the side of the dissection, followed often after a time delay, by posterior circulation ischaemia (Table 3). It is often associated with major or minor neck or head trauma.

**Local symptoms**

Occipital headache or posterior neck pain or both are a prominent and early finding in most patients (Mokri et al. 1988). The pain is predominantly unilateral and ipsilateral to the dissected artery, but can also occur bilaterally (Sturzenegger 1994). However, in only about 50% of patients is the pain described to be of an unusually worrying intensity and character.

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**Table 2**  Clinical findings in patients with carotid artery dissection

<table>
<thead>
<tr>
<th>Local symptoms or signs</th>
<th>Ischaemic manifestations</th>
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<tr>
<td>Fronto-temporal headache, facial pain,</td>
<td>Amaurosis fugax</td>
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<tr>
<td>anterior neck pain</td>
<td>Retinal infarction (rare)</td>
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<tr>
<td>Horner’s syndrome</td>
<td>TIA</td>
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<tr>
<td>Pulsatile tinnitus</td>
<td>Ischaemic stroke (mainly in the middle cerebral artery territory)</td>
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<tr>
<td>Cranial nerve palsies (mainly cranial nerves IX to XII)</td>
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**Table 3**  Ischaemic manifestations

- Amaurosis fugax
- Retinal infarction (rare)
- TIA
- Ischaemic stroke (mainly in the middle cerebral artery territory)

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Local signs
Even in vertebral dissection patients with neck pain, clinical examination does usually not reveal impaired neck mobility. This is important because the pain is sometimes so severe that the patient is reluctant to have their neck moved and this can be mistaken for torticollis. Spinal epidural haematoma or proximal paresis of an arm due to cervical root impairment, mostly at the C5–C6 level, are rare consequences (Crum et al. 2000). Cervical nerve roots may be compressed or stretched by arterial enlargement due to subadvential mural haematoma or a dissecting aneurysm. Another explanation may be ischaemia of the nutrient artery to the spinal root, originating from the anterior or posterior radicular arteries.

Ischaemic symptoms
More than 80% of patients develop posterior circulation ischaemia (Schievink et al. 1994a). Lateral medullary infarction (Wallenberg’s syndrome) is common, consisting of ipsilateral Horner’s syndrome, sensory disturbance on the ipsilateral face, nystagmus, ipsilateral limb ataxia and pain loss in the contralateral hemibody. Other manifestations include cerebellar, thalamic, pontine, and posterior cerebral artery ischaemia (Mokri et al. 1988). The intradural vertebral artery supplies the rostral cervical spinal cord while the middle cervical spinal segments are perfused by radicular branches of the extradural vertebral artery; therefore, embolic or haemodynamic infarction of the cervical spinal cord may occur as a rare complication of vertebral artery dissection (Crum et al. 2000).

Intracranial vertebral artery dissection
This is rare and usually severe. It may be purely intracranial or due to the upward extension of an extracranial vertebral dissection.
It occurs mostly spontaneously and presents often with posterior headache or neck pain and either posterior circulation ischaemia or subarachnoid haemorrhage (SAH) (Hosoya et al. 1999). It may extend to the basilar artery. This means that aneurysmal SAH should be ruled out by appropriate investigations before starting any antithrombotic treatment for the dissection (see below).

INVESTIGATIONS
Investigations should be performed as an emergency when dissection is suspected, but it must be remembered that each of the following investigations may be normal, stressing the frequent need for combining investigations.

Catheter angiography
Catheter angiography has been the diagnostic method of choice for many years. The main findings of cervical artery dissections are not specific and include mostly irregular, long luminal narrowing (string sign), occlusion and aneurysmal dilatation (Figs 1 and 2). Occlusions due to carotid dissection have typically but not invariably a tapered flame-like or rat's tail appearance (Fig. 3). Pathognomonic findings such as a double lumen or an intimal flap are seen in only a minority of patients. Carotid dissection usually starts about 2–3 cm distal to the origin of the internal carotid artery and usually does not extend to the intracranial segment of the artery, probably because the canal in the petrous bone limits any extension of the dissection. In contrast, atherosclerotic lesions are almost invariably located at the carotid bifurcation, the origin of the internal carotid artery or in the carotid siphon. In dissection without luminal narrowing, catheter angiography may be normal and the dissection can only be proven by MRI.

In vertebral artery dissection the angiographic findings often include luminal narrowing extending over a few centimetres, a double lumen appearance, tapered occlusion or aneurysm formation. Although some authors report a predilection in the V3 segment, vertebral dissection may occur in any segment of the artery.

MRI, MRA and CT of the neck
MRI in combination with MRA is a reliable, non-invasive method for the diagnosis of carotid and vertebral dissection. Axial MRI of the neck can demonstrate the intramural haematoma itself and is therefore replacing catheter angiography as the diagnostic gold standard (Auer et al. 1998). However, false positive findings due to high signal intensity from the perivascular venous plexus, or haemorrhage into an atheromatous plaque, are possible pitfalls of cervical MRI (Bloem & Lammers 1999). The intramural haematoma is typically visualized as a crescentic, semilunar, hyperintense signal within the vessel wall. T1-weighted imaging with
fat-suppression distinguishes the surrounding tissue from the haematoma (Figs 4 and 5). Therefore, an agreed dissection protocol including T1 fat suppression is needed to distinguish surrounding tissue from a true intramural haematoma. However, the characteristic hypointense signal is not always seen in the first 3–4 days so the diagnosis may be overlooked if the patient is seen early on in the disease.

Magnetic resonance angiography (MRA) can show luminal stenosis, occlusion or intimal flaps. And, in recent reports, multisection CT angiography has been described as a sensitive and accurate technique for the diagnosis of cervical artery dissections (Chen et al. 2004).

Brain imaging and the CSF
Brain MRI should be performed in all patients with clinical symptoms suggesting cervical artery dissection, either to visualize clinically evident infarcts or to detect clinically silent brain lesions. CT and MRI show that most infarcts related to carotid dissection are territorial rather than in boundary zones, and are therefore more likely due to thromboembolism than haemodynamic mechanisms (Benninger et al. 2004). In the case of multi-territory infarction, patients should be screened for multivessel dissections and cardiac embolism. In patients with intracranial dissection, particularly vertebral, subarachnoid haemorrhage has to be ruled out by CT or MRI (flair and gradient echo sequences) and if necessary by lumbar puncture.

Ultrasound
In addition to cervical MRI and brain imaging, we use extracranial and transcranial duplex ultrasound in the early phase of investigation of cervical artery dissections. In carotid dissection more than 90% of patients show flow abnormalities, typically a patent carotid bifurcation and proximal internal carotid artery without major atherosclerotic plaque but with an absent or dampened systolic flow signal. With stenotic carotid dissection an accelerated flow in the high cervical part of the carotid artery can be recorded. Specific findings – including intimal flap, double lumen and intramural haematoma as shown in Fig. 6 – are not frequently seen. In vertebral dissection, abnormal flow is detected with ultrasound in about 70–80% of patients (Sturzenegger et al. 1993). A major shortcoming of ultrasound is lack of specificity, stressing the need for confirmation of the diagnosis by MRI/MRA.

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In patients with hypertension, renal ultrasound is performed to screen for renal artery stenosis.

DIFFERENTIAL DIAGNOSIS
A first attack of cluster headache, typically presenting with severe unilateral facial pain and an ipsilateral Horner's syndrome, is a possible differential diagnosis of carotid dissection, but this is often associated with other autonomic signs such as lacrimation, conjunctival injection, and rhinorrhea, and it resolves within 1–3 hours.

Another important differential diagnosis is migraine. To confuse the situation, a flurry of typical migraine attacks with aura, photophobia and phonophobia, nausea and vomiting has been reported in carotid dissection, particularly when there is severe stenosis or occlusion with haemodynamic compromise (Olesen et al. 1993). Such cases of symptomatic migraine may proceed to cerebral infarction and are usually misdiagnosed as ‘migrainous infarcts’. Clues to the diagnosis of dissection are the Horner’s syndrome and a sudden severe headache recognized by the patient as different from their usual attacks of migraine.

Musculoskeletal neck pain is often difficult to distinguish from the pain of vertebral dissection, although in patients with dissection physical examination does not usually reveal any impairment of neck mobility (Sturzenegger 1994). Cervical manipulation in such patients may have catastrophic consequences with upward extension of the dissection and sometimes lethal brain stem infarction (Mas et al. 1989). We therefore recommend avoidance of cervical manipulation, and imaging the brain and cervical region with M R T1 fat-suppression techniques in patients with unusual occipital headache or neck pain, especially in association with any symptoms of posterior circulation ischaemia.

TREATMENT
To date, there are no randomised trials or evidence-based guidelines for the treatment of cervical dissection, which has to be decided on a case-by-case basis. Our usual practice is intravenous heparin or low molecular weight heparin for 1–2 weeks followed by oral warfarin with a target international normalized ratio of 2.0–3.0 for 3–6 months. We then either stop all antithrombotic treatment if the artery has completely normalized on ultrasound and/or M RA, or we switch to antiplatelet therapy such as aspirin 100 mg daily for long-term prevention when there is an underlying arterial disease such as fibromuscular dysplasia, or residual occlusion or stenosis of the dissected artery.

This therapeutic regimen is mainly based on pathophysiological considerations and clinical experience (Schievink 2001). Brain imaging suggests that more than 90% of infarcts are due to artery-to-artery embolism and only in rare cases to haemodynamic compromise. And transcranial ultrasound has shown microemboli in the middle cerebral artery in more than half of the patients with carotid dissection; these signals are markedly reduced by intravenous heparin and some patients have decreased rates of microemboli on aspirin. On the other hand, in some patients heparin can increase the intramural haematoma leading to occlusion of the dissected carotid artery, and heparin does not prevent all strokes (Dreier et al. 2004). Whenever there is any suspicion of haemodynamic ischaemia, we leave patients recumbent until the cerebral haemodynamics measured by transcranial ultrasound and/or perfusion M RI improve (Bioussé et al. 1995).

For intracranial dissection we avoid anticoagulants because of the potential danger of subarachnoid haemorrhage, although there are no controlled trials or case series. In patients with acute ischaemic stroke following cervical artery dissection and marked neurological deficits, thrombolysis has been shown to be feasible (Arnold et al. 2002). However, patients present only exceptionally within 3 hours of symptom onset. Endovascular treatment with balloon dilatation and stenting has been used successfully in selected patients with progressive or fluctuating symptoms of ischaemia despite anticoagulants (Cohen et al. 2003).

We do not believe any special advice is required with respect to normal activities or vaginal delivery.

PROGNOSIS
Clinical functional outcome mainly depends on the initial stroke severity. The long-term prognosis of cervical artery dissection is favourable in the majority of patients. Recurrence is uncommon but may occur at the same location or in another location of the same artery, or in a different artery. Several studies have reported a less than 1% annual rate of recurrent dissection and stroke (Kremer et al. 2003; Touzé et al. 2003). This recurrence rate was not significantly
CONCLUSIONS
• In recent years carotid and vertebral artery dissections have been diagnosed more frequently, probably because new imaging techniques are more reliable and they are certainly less invasive.
• The cause of cervical artery dissections is largely unexplained but probably involves a combination of genetic and environmental factors such as trauma or infection.
• Patients with cervical artery dissection are mostly young or middle-aged adults; dissection still occurs in older people, but is less likely to be detected given less aggressive investigation in this age group.
• In carotid artery dissection neck and facial pain, headache, pulsatile tinnitus, Horner’s syndrome, amaurosis fugax, retinal infarction and anterior circulation ischaemia occurs in various combinations.
• A sudden unilateral headache or facial pain with ipsilateral Horner’s syndrome, transient monocular blindness or tinnitus is highly suggestive of carotid dissection, particularly in the young.
• The typical clinical manifestations of vertebral artery dissection are neck pain or occipital headache or both, followed often after a time delay by posterior circulation ischaemia.
• Any sudden headache perceived by a migraineur as different from his or her usual migrainous headache should be investigated on an emergency basis – it might be a dissection.
• A sudden headache, like a thunderclap (with or without subarachnoid haemorrhage), or neck pain may be the only symptom of carotid or vertebral dissection.
• Each investigation (ultrasound, MRA, CT and catheter angiography) may be normal, stressing the need for combining investigations.
• Our current treatment is intravenous heparin followed by oral warfarin, although there are no data from controlled trials. The use of heparin is based on a consensus and not on evidence.
• Early diagnosis and treatment of dissections presenting with purely local symptoms and signs may prevent ischaemic stroke.
• The long-term prognosis of cervical artery dissection is favourable in the majority of patients. Recurrence of dissection, or recurrent strokes, are uncommon.