Recent Advances

Interventional neuroradiology

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Interventional neuroradiology aims to cure, ameliorate, or stabilise symptoms due to vascular lesions in the brain or spinal cord and their surrounding tissues. The range of lesions amenable to treatment is wide, but the techniques that are applied are comparatively few. The principal approaches include obliterating abnormal vessels by occlusion with various substances, increasing flow in abnormally narrow vessels, and dissolving blockages produced by fresh thrombus with clot dissolving agents; vascular stents are being assessed for their efficacy in treating carotid stenosis and occluding aneurysms. All are based on an understanding of the natural history of the lesions and the balance of the risk and benefits of treatment in each case.

Interventional neuroradiology as a developed specialty is 20 years old and was first concerned with extracranial embolisation of vascular lesions and tumours of the head and neck. One of its main contributions is not technical but in the clinicopathological understanding of intracerebral arteriovenous malformations.

Technical advances

The principal advances have been in the design of catheters and guide wires. Very small diameter catheters with distal tips of variable stiffness are available. There are flow dependent catheters and catheters that run over guide wires to the correct location. Some guide wires can be coated with a hydrophilic substance to ease their passage through the small cerebral vessels. These systems are usually delivered through a parent catheter, which is constantly perfused with heparinised saline. Technical advances in the catheters have meant that interventional neuroradiologists can treat lesions whose nature and natural history is not completely known. This can result in assessment of technical results without a clear view of the overall outcome for the patient.

Interventional neuroradiology in children

Advances in interventional radiology in children have been technical and clinicopathological. The design of catheters has permitted superselective catheterisation directly from the groin. This saves children the extra trauma of having a large parent catheter inserted that needs to be perfused with heparinised saline; each perfusion results in a fluid load in patients whose cardiovascular systems are already compromised. The effects of a high flow vascular lesion on an immature brain when the skull is unfused are becoming clearer.

Three principal types of vascular anomaly are present in children: an embryonic malformation of a

Recent advances in interventional neuroradiology

- New designs of catheters and guide wires permit easier and safer distal catheterisation of vessels
- In children these new designs permit super-selective catheterisation from the groin and avoid the extra trauma of insertion of a large parent catheter requiring perfusion with heparinised saline
- Results from interventional neuroradiology have shown that the arteriovenous malformations that occur in children behave differently from those in adults, partly because of the effect of the lesion on an immature brain in a growing skull; procedures can now be timed to be safe and allow for a child's growth
- A European network now exists among participating neuroradiologists; data on about 1000 cases of arteriovenous malformations in adults a year are pooled, thus increasing understanding of the natural course of such malformations and which treatment is appropriate
- Intracranial tumours can be punctured and the vascular spaces occluded directly with, for example, acrylic glue in an oil based contrast medium
- Endovascular treatments for intracranial aneurysms are available as an alternative to surgery, electrolytically detachable coils are currently being assessed
- Angioplasty is a safe alternative to carotid endarterectomy in the small percentage of patients who are thought to have a stroke as a result of carotid stenosis
- Fibrinolysis may be beneficial in patients with thromboembolic stroke and is probably beneficial in patients with central retinal artery occlusion

deep vein that is the precursor of the vein of Galen, and pial and dural arteriovenous malformations. Arteriovenous malformations of the brain and dura mater have features that differ from those occurring in adults because of their effect on the immature brain and unfused skull.

The vein of Galen is usually the main channel for deep venous drainage of the brain, but in children with malformation of this vein the brain does not have this

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system. Instead blood drains into the same system as the arteriovenous malformation or into collateral vessels through the cavernous sinus once the skull base has grown enough.^{1,2} The vein of Galen drains an arteriovenous malformation in the choroid fissure of the brain, or more distally in the wall of the vein itself (figs 1 and 2). This is a high flow arteriovenous shunt and causes cardiac and multisystem failure.³ Symptoms develop secondarily as a result of disordered water balance in the brain—that is, macrocranial ventriculomegaly,⁴ and herniation of the cerebellar tonsils through the foramen magnum.⁵ Such changes are reversible if the underlying lesion is treated correctly, usually by embolisation with an acrylic based glue in the arteries (fig 2 (centre)). With this approach, neurological outcome is normal for 80% of children who are selected for treatment.⁶

Pial arteriovenous malformations in children should in general be treated as a matter of urgency because their haemodynamic effects on the brain lead to rapid destruction of the brain within weeks, the so called melting brain syndrome.⁷ A protocol for assessment of the child that permits optimum treatment and timing has been developed.⁸

The most important aspects of managing children with such lesions are whether and when to treat. The risks of treating a neonate are greater because of the technical limitations of the procedure and embolisations should be instigated before neurological damage occurs while allowing for some growth of the child. This is the concept of the therapeutic window.⁹

Arteriovenous malformations in adults

The treatments for brain arteriovenous malformations in adults are not new. The options include surgery, radiotherapy, and embolisation, or a combination. The aim of treating such lesions used to be to

remove the risk of life threatening haemorrhage or to relieve headaches, seizures, or neurological deficit without harming the patient. The concept of partial and combined treatments is central to the philosophy of this specialty.

There is a developing understanding of risk factors: the aim of treatment is obviously to be safe and effective. Units that deal with these lesions in large numbers are increasingly aware of the ability of patients to tolerate the lesion and of the warning symptoms and signs that signal a loss of patients' compliance. Many physicians believe that seizures are an acceptable consequence of an arteriovenous malformation. However, the onset or recurrence of seizures may herald important changes in the lesion itself and may reflect venous congestion of the cerebral cortex. Arteriovenous malformations have deleterious effects on the veins and promote kinking, stenosis, and occlusions.⁷

With considered intervention these features can be dealt with and the aim is to return to the symbiotic relationship without harming the mechanisms by which the brain tolerates the lesion. In many patients seizures can be abolished or their frequency diminished.⁹

One of the best ways of developing an understanding of the natural history of arteriovenous malformations is to pool the experience of interventional neuroradiologists into a uniform database. A European network now exists into which participating neuroradiologists contribute. Data on about 1000 cases a year are collected.

Direct embolisation of tumours

Direct puncture of intracranial tumours or those at the base of the skull is possible when embolic material (usually acrylic glue diluted with an oil based contrast medium) is injected. The embolic material fills the vascular spaces in the tumour. This can be used preoperatively or, in the case of frail patients, as a palliative procedure.

Intracranial aneurysms

The surgical treatment of intracranial aneurysms is well established and the outcome of surgery well documented.¹⁰ The aim of the procedure is to eliminate the risk of rebleeding. Intracranial aneurysms are common lesions and controversy exists about their true prevalence and rate of bleeding. One paper quotes a prevalence of 8% of incidental aneurysms in patients at necropsy.¹¹ Other sources suggest that the risk of bleeding of a previously unruptured aneurysm in any one year ranges from 0.1%¹¹ to 1.0%.¹² This risk should be remembered when incidental unruptured aneurysms are discovered and considered for treatment

FIG 1—Left: Magnetic resonance scan of vein of Galen malformation. Note dilated venous pouch (arrow). Right: Scan of same patient after treatment showing that venous pouch has disappeared

FIG 2—Left: Cerebral angiogram (injection into internal carotid artery) showing vein of Galen malformation with abnormal fistulous communication of posterior choroidal vessel to giant venous pouch. Centre: Plain lateral skull radiograph showing glue cast in venous pouch and feeding vessel. Right: Cerebral angiogram after embolisation showing vessel remnant and complete occlusion of shunt

FIG 3—Left: Cerebral angiogram showing aneurysm arising from carotid artery (arrow). Right: Cerebral angiogram showing the aneurysm occluded with coils

as treatment itself is associated with adverse effects. The risk of rebleeding from a ruptured aneurysm is similarly hard to establish because it is highest during the first few days after an ictus; thereafter it falls to the risk of bleeding in an unruptured aneurysm after a (probably fairly short) period of time. A widely quoted figure is a risk of rebleeding of 50% at 6 months,¹² but this includes the time immediately after an ictus, when most rebleeding occurs.

In some cases surgery is not technically feasible or the patient is medically unfit. In such cases interventional neuroradiologists can treat the aneurysm by an endovascular route, placing a superselective catheter into the lumen of the aneurysm and depositing balloons or coils to obliterate it. A predictable series of complications comes with these approaches, including migration of the balloons and coils into the parent vessels, with consequent distal embolisation; irretrievable misplacement of the coil; and regrowth of the aneurysm because of incomplete closure of the lumen. Aneurysms rarely rupture during the procedure. A recently developed platinum coil whose joint with the introducing catheter is detached by electrolysis has shown some promising results.¹³⁻¹⁶ A major advantage is that it can be retracted from the aneurysm if it does not seem to be well sited before electrolysis is started. The soft coils can pack the aneurysm's contours more effectively than the inflatable balloons previously used. The coils cost about £300 each and, depending on the size of the aneurysm, between 4-12 coils are usually used (fig 3). The average overall cost of treating a patient by this method is £4500-5500.¹⁴

Another approach being developed in animal experiments entails placing a stent across the mouth of the aneurysm.¹⁷⁻¹⁹ In dogs intravascular stents placed across the neck of an artificially created aneurysm with thrombosis show continued patency of the parent vessel after 28 days. Such a device relies on the aneurysm occurring on a fairly straight stretch of vessel, but aneurysms tend to occur at vessel bifurcations; however, the possibility of an endovascular approach without entering the lumen of the aneurysm is exciting.

Stroke

Over the past four years international studies have reported a declining incidence of and mortality from stroke. Against this epidemiological background the government is committed to reduce death from stroke by 40% in the year 2000 and to support programmes aimed at implementing this policy.²⁰

In 1990 both the European and North American

symptomatic carotid endarterectomy trials reported that carotid endarterectomy can convey a net benefit in patients who have a greater than 70% stenosis of the carotid artery on the side relevant to transient ischaemic attacks.^{21 22} This subgroup, however, only represent about 2% of patients with stroke.²³

An international, multicentre trial, funded by the NHS Management Executive known as the carotid and vertebral transluminal angioplasty study has been assessing the risks and benefits of carotid and vertebral angioplasty and comparing them with surgical treatments in patients eligible for surgery or best medical treatment in those who are not. Angioplasty is a technique of established benefit in coronary and peripheral vessels, but there has been concern about distal embolisation in the cerebral vessel when treating the carotid artery. Percutaneous transluminal angioplasty has the advantage of avoiding the risk of general anaesthesia and has cost advantages of a short admission and less use of resources because patients' stay is shorter. Recent series have suggested that carotid percutaneous transluminal angioplasty could have a risk of immediate stroke or death similar to that of carotid endarterectomy.²⁴ By 1994, 285 cases of atherosclerotic internal carotid stenosis treated by percutaneous transluminal angioplasty had been reported, with an observed rate of stroke and transient ischaemic attack of less than 5%.²⁵⁻²⁸ Recent analysis of the first 100 patients in the NHS Management Executive's international trial shows no significant difference between the surgical and angioplasty group (A Clifton, personal communication). The complication rates in the European and North American symptomatic carotid endarterectomy trials have been reported as 7.5% and 5.8% respectively.^{21 22} Most of the strokes occurred at the time of operation and about half resulted in death or permanent disability. This risk has to be balanced against that of doing nothing. In the two trials the incidence of disabling and fatal strokes in the territory of the ipsilateral carotid artery in those who were not operated on was 13.1% and 8.4% respectively. When a complication rate of performing angiography of 1-2% is included in the overall risks of performing carotid endarterectomy, the overall risk of invasive treatment approaches that of doing nothing. However, the risks of angiography could be included in the overall risks of angioplasty, provided that diagnosis and treatment were carried out at the same sitting. The margins of benefit remain perilously narrow and could be even smaller if increasing numbers of operators with inadequate experience and caseloads were performing these procedures—a practice all too widespread in medicine.

Clearly, before any technical advances such as stents covered with vein graft or polyfluorotetraethylene²⁹ are incorporated into the interventional neuroradiological armoury, the procedures must be performed in such a way that the increasing technical complexity does not increase the overall risks and effectively remove any net benefit.

Fibrinolysis

Phase III trials in coronary artery fibrinolysis have shown that this technique can save lives in myocardial ischaemia, and this has led to interest in the possible benefits in patients with stroke.

Most ischaemic strokes are caused by thromboembolic occlusion of cerebral vessels. Cerebral intra-arterial fibrinolysis is a method of delivering clot lysing agent directly into the body of the embolus to dissolve it and permit recanalisation of distal thrombosis and reperfusion of ischaemic brain tissue. The aim is to limit the area of cerebral damage and neurological deficit.

Systemic thrombolysis has been tried in randomised studies.³⁰ The results seem to indicate that recanalisation rates exceed those in the placebo group, but they are disappointingly low and the risk of intracranial haemorrhage seems to be increased after treatment.³⁰ Fibrinolytic treatment still needs to correlate with the clinical benefits of the treatment.³¹

Several studies report the use of local intra-arterial fibrinolysis in stroke.³²⁻³⁹ They used urokinase, streptokinase, or recombinant tissue plasminogen activator alone or in combination so cannot be compared directly. Evidence suggests that recanalisation rates measured within minutes to hours after treatment range from 40% to 75%; the spontaneous recanalisation rate was 17% in the first few hours in the placebo groups of a small controlled trial of intravenous cerebral fibrinolysis and 40-80% over days in the non-treated groups. The reports seem to indicate that rapid recanalisation is a marker for improved outcome,³²⁻³⁵ but no study clearly indicates the clinical effectiveness and safety of intra-arterial thrombolysis. Currently, there are no phase III trials underway to address these issues. The correct way to assess this treatment is debatable⁴⁰⁻⁴¹ but clearly some form of objective rather than anecdotal approach is necessary to avoid using a treatment that may end up being of little benefit or even harmful to patients.

Central retinal artery occlusion has a poor outcome for patients, but some evidence suggests that thrombolysis can genuinely be valuable.⁴² A catheter is placed in or close to the origin of the ophthalmic artery and a thrombolytic solution is perfused into it.

Conclusions

Interventional neuroradiology offers powerful treatments, whose applications are still being refined. Although the techniques seem to be minimally invasive compared with neurosurgery, they are in fact risky for the patient and their practice has to reflect this.

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Correction

Ethics committees: impediments to research or guardians of ethical standards?

A typesetter's error occurred in this short report by Professor Alison E While (9 September, p 661). The table cited in the second paragraph under methods and results was omitted and is reproduced below.

Time taken by 43 district ethics committees to reply to letter seeking ethical approval

	No of committees
Time taken to notify outcome (days):	
1-30	8
31-60	14
61-90	7
>90	10
No notification of outcome	4