Vasa Vitae - Keeping The Channels Open

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Surgical attitudes to blood vessels through the millennia and leading up to the middle of the twentieth century were, with anecdotal exceptions, limited to life-saving cautery or ligation. The practice of vascular surgery was initiated only in the fifties when arteries and veins - these vasa vitae or vessels of life - were deliberately sought out and reconstructed. Keeping the channels open in order to preserve life, to revitalise an organ or to salvage a limb has been the raison d'être of the vascular surgeon. The objectives of surgical intervention are also its rewards.

The fun and the reward of vascular surgical practice lies in the challenge of dealing with patients with major cardiovascular and other risk factors, in the precision of operative technique and in the generally gratifying outcomes, tempered on occasion by the experience of failure. It is a specialty which has grown enormously in the range and complexity of procedures undertaken. Over a third of the large numbers treated require emergency attention. The ubiquitous presence of diseased blood vessels makes for refreshing changes of clinical and operative scene and also accounts for the close links between vascular surgeons and other doctors. These fortuitous associations generate varied interdisciplinary research programmes which not only straddle the neat boundaries of prescribed research groupings but also extend outwards to the sciences, engineering and so on. It is exactly such collaborative vascular research which has enriched our knowledge of the microcirculation, led to advances in haemodynamic monitoring, introduced the concept of the non-invasive ultrasound investigation, stimulated prosthetic graft development and brought about innovations in surgical instrumentation.

During the seventies, the broadening repertoire of exciting operative procedures in this relatively young specialty, in personal terms, proved both captivating and timely. My objective on being appointed to the very firm where the distinguished surgeons Mr Sinclair Irwin and the late Mr Reginald Livingston had once been my mentors, was the conversion of a general surgery unit with 11% vascular throughput into a dedicated, regional vascular centre and to set up a clinical vascular laboratory. This process of engineered metamorphosis was entirely in keeping with the best progressive traditions of the Royal Victoria Hospital wherein interlinking specialties have evolved to create a favourable milieu for clinical care and research.

This Vascular Surgery Unit at the Royal, one of the first of three or four such centres in the British Isles, has contributed to vascular research and specialist development at international level for two decades. The vascular service at the Royal relies on the combined expertise of vascular surgeons, radiologists, anaesthetists, nursing staff and laboratory personnel. This team provides a tertiary regional service covering the entire spectrum of vascular disease.

In a very busy clinical vascular laboratory, over 4,000 studies are undertaken annually. The Vascular Surgery Unit is licensed to provide specialist vascular training over the final two-year span. In research it is represented on national bodies and is also involved in international projects. A regional Northern Ireland Vascular Registry (NIVASC), in which other vascular surgeons in the province participate, is in its second year of operation and joins half-a-dozen other such national registries extant in Europe. The Royal Victoria Hospital, with its clinical profile and facilities is well placed to meet the challenges at the threshold of the new millennium.

If these vivid lines from Shakespeare

'...but when we have stuffed
These pipes and these conveyances of our blood
With wine and feeding. we have supper souls
Than in our priest-like fasts...'

Menenius
Coriolanus V.I.

seem to extol the spiritual dividends of gluttony, then they also appear a trifle prescient about recent knowledge of the health-giving properties of red wine. On the other hand, they do not, by any stretch of the imagination, demonstrate an understanding of the best
way of escaping the onset of atherosclerosis. That knowledge, relatively recently acquired, is being accelerated by crucially important observations which will undoubtedly shape therapy in the early years of the next millennium.

New information is constantly expanding our knowledge of the pathophysiology of injury to the arterial flow surface. We now know that fluid shear stresses promote the release of platelet-derived growth factor (PDGF) and basic fibroblast growth factor (bFGF)\(^1\) and regulate the expression of adhesion molecules,\(^2\) all of which have pathophysiological relevance to the process of development of intimal hyperplasia. Equally, the epidemiology and pathogenesis of atherosclerosis is being unravelled by the addition of new pieces to a complex jigsaw. In studies at the Karolinska, autoantibodies against oxidised LDL,\(^3\) endothelial cells and cardiolipin \(^4\) were found to be associated with early onset of peripheral arterial disease. An Australian group has shown that raised serum lipoprotein(a) in association with elevated LDL cholesterol is a significant determinant of the extent of carotid atheroma.\(^5\) The spotlight on elevated homocysteine as a risk factor in the progression, not only of premature and widespread arterial disease but, interestingly, also of venous thrombosis,\(^6\) may in future merit its inclusion in the routine thrombophilia screen. The observed dose-dependent atherogenic effects of alcohol consumption on carotid arteries\(^7\) may give pause to the current enthusiasm for a prophylactic glass of wine.

The complex morphogenesis of the fibrous cap on an atherosclerotic plaque eventually leading to erosion and the dangerous consequences of plaque haemorrhage, rupture and thromboembolism has caught the imagination of investigators on both sides of the Atlantic. The accumulation of activated mast cells around the fibrous cap\(^8\) and the production of matrix-degrading metalloproteinases (MMPs) which induce collagen breakdown destabilise the fibrous cap,\(^9\) the thinness of which determines its vulnerability. A fibrous cap at such risk, can now be detected by ‘attenuation-slope mapping’, of plaque using a sophisticated intravascular ultrasound probe.\(^10\) The discovery of Chlamydia pneumoniae in atherosclerotic plaque\(^11\) and a possible causal relationship is a fascinating mystery which awaits clarification.

The landmark Scandinavian Simvastatin Survival Study (4S) convincingly proved that the lowering of cholesterol prolongs life in patients with established coronary artery disease.\(^12\) Clinical research reports of the value of pravastatin, lovastatin, and other statins leave one with the impression that a specific statin attuned to each permutation of lipid abnormalities will probably come on line. The exciting observation of carotid plaque regression in women receiving oestrogen replacement therapy\(^13\) offers a seductive avenue for a large-scale controlled study, the practicalities of which are already under consideration. Vast quantities of research data in this area are accumulating which will catalyse the development of new modalities of treatment aimed at arresting and reversing the march of atherosclerosis.

In the years ahead, molecular genetic and gene therapy will be mobilised in the task of vitiating major risk factors such as hyperlipidaemic disorders and diabetes, both of which accelerate the advance of arterial disease. Recombinant DNA technology has already been used experimentally to modify endothelial and vascular smooth muscle cell expression.\(^14\) In this way, intimal hyperplasia developing at prosthetic graft anastomoses with the host artery, might be suppressed sufficiently to prevent occlusion of the lumen and graft failure. In time, miniaturised endovascular delivery techniques might well be employed to treat a particular diseased segment of artery but before that goal is realised several hurdles of technique, safety and efficacy in using gene therapy will have to be faced.

New operative techniques will undoubtedly herald the new millennium but their implementation should be dependent on objective appraisal. In the past, vascular operations originated in three main ways: through argument based on knowledge of the pathophysiology, empirically through successful experiment or on the strength of results of a controlled trial, and thirdly, on the pragmatic basis that it works.\(^15\) Thus a priori knowledge that emboli from carotid plaque and thrombus produced acute neurological and ocular events, persuaded surgeons to proceed with carotid endarterectomy. Around the world, excessive zeal by a few to operate even when the case for surgery was not convincing, has been matched by the therapeutic nihilism of some neurologists grounded on the Descartian assertion that carotid artery disease as such did not exist. The North American Symptomatic Carotid Endarterectomy Trial (NASCET)\(^16\) and the European Carotid Surgery Trial (ECST)\(^17\) simultaneously concluded that surgery for symptomatic carotid stenosis of 70% or more was preferable to best medical treatment in reducing the rate of stroke and mortality. That position is founded

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on the presumption that selection of patients follows careful assessment and that surgical technique is meticulous. The advantage of patch angioplasty in reducing the incidence of recurrent stenosis has been increasingly appreciated. Transcranial Doppler monitoring of middle cerebral artery flow perioperatively provides objective assurance of the safety of surgery. Surgeons should continue to perform this operation only if their audited morbidity and mortality figures remain within the bounds of best reported practice.

It is predicted that two major international trials into which I have entered cases, namely the Asymptomatic Carotid Surgery Trial (ACST) and the Asymptomatic Carotid Stenosis Risk of Stroke (ACSSR) Study will provide important answers. The former is likely to confirm that surgery, in good hands, is preferable to best medical treatment, while the latter is likely to show that certain plaque characteristics are associated with a higher incidence of stroke. Certainly, accumulating evidence of the natural history of carotid atheroma would lead one to anticipate the recommendation that surgery is worthwhile even in the asymptomatic carotid patient.

Diagnostic imaging of the cerebrovascular tree has evolved over the years. Carotid angiography which carries a small but finite risk has been displaced to some extent by colour flow Duplex scans. It must be admitted, however, that during the occasional carotid operation one would have given anything for a set of clear cerebrovascular angiography films in place of the necessarily limited ultrasound image. Nevertheless, it is not just the image or the flow data but the capacity of the Duplex scan to characterise plaque, in terms of echodensity or more unstable echolucency, which has enhanced its popularity. Precise computer-assisted plaque characterisation will eventually be the norm in evaluating the degree of plaque instability.

Evidence-based treatment supported by sustained audit of outcome should be the touchstone of ideal vascular practice. Acute carotid ischaemic stroke represents a scenario which challenges the clinician to act quickly to prevent disaster. The American trial of intravenous tissue plasminogen activator (pt-PA) aimed at arterial clot lysis within three hours of onset of stroke resulted in 50% of patients having minimal disability or none at three months, but the dilemma lies in the knowledge that this benefit was bought at the cost of a 6.4% incidence of symptomatic intracranial haemorrhage. The results of the European Co-operative Acute Stroke Study (ECAS) and that of an Italian trial have been comparatively discouraging, but further study in this area is bound to continue.

In the United States the activities of many cardiologists have been attenuated in the wake of constraints placed by the flourishing HMO systems. Not to be outdone by such reversals, some of them have mobilized their costly, but otherwise redundant equipment, to perform angioplasties and stenting procedures on patients with carotid artery disease. The assessment and selection of these patients for treatment and the outcomes, however, ought to be submitted to the detailed scrutiny generally accorded to carotid endarterectomy by vascular surgeons. If carotid angioplasty is to gain acceptance, data based on standardised protocols must first be produced and, if deemed appropriate, a randomised double-blind controlled trial comparing it with carotid endarterectomy should follow.

Severe vertebrobasilar insufficiency (VBI) has hitherto received scant surgical attention but operations to improve vertebral artery flow are being undertaken more often. A detached distal vertebral artery may be transposed directly into the common carotid artery or, alternatively, a skeletonised external carotid artery may be mobilised and anastomosed to the distal vertebral artery.

The quality of surface ultrasound in revealing plaque on the walls of the arch of the aorta and great vessels has been superseded by transoesophageal echocardiography (TOE) which, being safe, portable and accurate, may become the investigation of choice in acute traumatic aortic disruption. Data reconstruction from spiral CT scans already provides 3-D images of aortic dissection and of thoraco-abdominal aneurysms. Both (TOE) and the more invasive technique of intravascular ultrasound will continue to compete with CT in the diagnosis of thoracic aortic dissection.

Operative reconstruction of the great vessels for atheroma or Takayasu's disease, aimed at preventing stroke, blindness, and upper limb ischaemia, will still be necessary. The occasional practice of balloon angioplasty of stenotic lesions at the origin of the great vessels is not risk-free. The safety margins in surgery for thoraco-abdominal aneurysms have slowly improved: a mortality rate of 5% and a paraplegia rate of 1.5% reported from Houston by Joseph Coselli can hardly be excelled. Epidural spinal cord protection, increasing preference for a 'clamp-and-repair' approach and the selective use of partial bypass may
have contributed to a better outcome.

Endovascular repair of infrarenal aortic aneurysms was perceived as an exciting development in that it offered an alternative form of treatment for the high risk patient with the added bonus of a shorter stay. 3-D multiplane reformatting from spiral CT scans and virtual reality software can be used to plan the procedure. James May of Sydney, a key exponent, acknowledges that the technique creates its own problems. Two major operative risks are micro-embolisation of clot from within the aneurysm and failure of the procedure itself requiring conversion to conventional surgery. Late dangers include delayed rupture, leaks into the aneurysm sac and even dislodgement of the proximal end of the stent graft as the aorta dilates. Clearly, this procedure requires to be monitored, but as entry into available registries is voluntary, failures may go unrecorded. One clear and recognised indication for endoluminal stenting is aortic dissection for which it is safer than conventional surgery. Premature conclusions regarding endoluminal aneurysm repair places vascular surgeons under pressure from potential consumers, and it has also spawned a proliferation of competing and sometimes unreliable products. These influences may induce some surgeons to join the bandwagon simply to 'enhance' their centres regardless of the phenomenal expense involved. The timeless axiom of 'primium non nocere', ie ‘first do no harm’, ought to be kept in mind before initiating any change. That can only come after disciplined evaluation through well controlled studies using standardized protocols based on an intention to treat. Progress in technological support is also required and therefore the precise indications for endovascular aneurysm repair will become clearer well after the year 2000.

One apparently simple but elusive question on surgery for abdominal aortic aneurysms is the optimal diameter at which operation should be undertaken to preempt rupture. A recent Canadian study has confirmed prejudices that aneurysms exceeding 5 cm diameter require surgery and that intervention in those of lesser size should depend on their rate of enlargement. Recent papers have highlighted the appearances of the 'crescent sign', a high-attenuating peripheral crescent observed on an unenhanced CT scan, which signals impending rupture and therefore demands urgent intervention. An increased turnover of Type III collagen in the aneurysm wall may reflect the rate of degradation and may turn out to be a useful marker of the rate of enlargement. Research into elastase and collagenase in aneurysm wall activity will probably continue in desultory fashion well into the next century. A few surgeons have attempted laparoscopic aorto-iliac surgery: this expensive and potentially disastrous procedure which requires up to seven ports and lasts approximately 7-8 hours has little hope of being accepted in the foreseeable future. Surgery for renal artery stenosis, for both ostial and non-ostial atherosclerotic lesions as well as for fibromuscular hyperplasia, has been replaced almost completely by balloon angioplasty and stent insertion but we must keep our eye open for recurrent stenosis in the longer term. An interventional approach also bodes well for the management of symptomatic mesenteric arterial lesions.

Hypercoagulability is observed in up to 40% of vascular patients although the nature of the underlying problem is not always identified with ease. Factor V resistance to activated protein C, attributable to a single point mutation is now recognised as the most frequent offender. Undoubtedly other such abnormalities will come to light. Catheter-guided intra-arterial thrombolysis has secured its place in the management of some patients presenting with an acutely ischaemic limb. In acute occlusion of bypass grafts, lytic therapy, sometimes as a prelude to balloon or operative angioplasty, is also well established. Nonetheless, in either instance, if the vascular surgeon believes that the time taken for effective lysis will compromise viability, he should proceed immediately to surgery.

Angioscopically-directed thrombo-emolectomy is an attractive technique in ensuring more complete clearance of clot but its application may wane as intraoperative adjuvant thrombolytic techniques become more refined and less frequently complicated by bleeding, stroke, ischaemia-reperfusion injury, limb loss and even mortality. Using the isolated thrombolysis perfusion technique pioneered by Tony Comerota of Philadelphia, effectively high local levels can be attained while the risks of systemic problems remain negligible. In resolving doubt as to the viability of ischaemic muscle, positron emission tomography (PET) scans using [18F] fluoro-2-deoxyglucose (FDG) uptake have shown high accuracy but this innovative approach is very cumbersome and for the present has to remain no more than a research tool.

The severely disabled claudicant deserves bypass surgery but in the ordinary case doctors are drifting to promising exercise rehabilitation programmes.

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Carnitine (propionyl-L-carnitine), a naturally occurring compound, which removes excess acetyl co-enzyme A and improves oxidative metabolism, is especially effective in claudication and may become a valuable adjuvant. Even more intriguing has been the experimental demonstration of the biological response to ischaemia of angiogenesis or neovascularisation in which the mitogenic potential of acidic fibroblast growth factor (aFGF) can be enhanced by heparin which is a cofactor for aFGF. The possible clinical impact of accelerating the development of collateral flow using this concept of ‘therapeutic’ angiogenesis in patients with limb ischaemia ought to become clearer during the next decade.

The large calibre Dacron graft used in aorto-femoral bypass operations represents an unparalleled success story for lengthy occlusions. Balloon angioplasty, possibly along with stenting, works well in a good proportion of short-segment iliac occlusive lesions. In the femoro-popliteal region the success rate of angioplasty is modest and it often has to be repeated; whereas vein bypass grafts of short length have the best patency rates on record and ought to be the first line of treatment. At infrageniculate level angioplasty tends to be no more than a temporising measure. In general, however, the vascular radiologist is proving to be an increasingly valuable ally in the battle to keep the channels open. Stent grafts of polytetrafluoroethylene to replace lengthy femoro-popliteal occlusions is a new but rather clumsy solution to a problem eminently dealt with by the vascular surgeon. Fortunately, as in the past, many such innovations become fashionable but fail to displace well tried operations and are consigned swiftly to the waste-bin of obsolescence.

Femoro-distal bypass surgery in patients with critical lower limb ischaemia, many of them with diabetes and some with Buerger’s disease, have been rewarded by improving rates of limb salvage. After over two decades of disillusionment with a variety of small-calibre prosthetic grafts surgeons are turning increasingly to the original gold standard of autogenous vein, harvesting it from the upper limb if necessary. In-situ vein grafts or reversed vein grafts, the valves of which require to be disrupted by a valvulotome, allow a better match of calibre of vein to host vessel at each end and therefore became popular in long bypasses. This technique of vein grafting led to the introduction of myriad techniques for disabling vein valves, including angioscopically-guided valvulotomy. After mature reflection and having noted the incidence of failure, especially of small-diameter in-situ bypass grafts, vascular surgeons are showing a renewed faith in the well-tried and tested reversed vein graft. In the anastomotic field, fine clips may in time replace polypropylene suture while fibrin glues and sealants which reduce suture line bleeding are now available. Spinal cord stimulation is being used in an attempt to relieve pain in extreme cases of lower limb ischaemia but this expensive device should not be used indiscriminately until it is first subjected to the rigours of a randomised trial.

Surveillance of limb bypass grafts using colour flow Duplex scans to pick up early signs of stenosis in vein grafts or of intimal hyperplasia at prosthetic graft anastomoses has been one of the many functions of the clinical vascular laboratory. These changes, usually discovered in a modest proportion of cases within a year of implantation, allow the opportunity for corrective surgery to preempt graft failure. There is much debate on the value of ultrasound surveillance but the view is held, not surprisingly from the cold-blooded perspective of cost-effectiveness, that it is not worth while. It should be appreciated that prompt intervention to prolong graft patency can save a limb, and also that early postoperative evidence of normality of a graft does not bestow perpetual patency on it.

Much more desirable, of course, is an effective deterrent against intimal hyperplasia. Vascular literature is replete with reports on restenosis of arterial grafts and the complex pathophysiological mechanisms involved in smooth muscle cell proliferation and matrix deposition observed in intimal hyperplasia. Various drugs such as heparin, calcium channel blockers and angiotensin-converting enzyme (ACE) inhibitors have been employed to discourage this process. Less appealing strategies include the interposition of vein cuffs and collars between prosthesis and host artery, and the more disturbing measure of intravascular low-dose irradiation. Encouraging research work using matrix metalloproteinase activity inhibitors, photodynamic therapy and others await the test of time.

Low molecular weight heparin (LMWH) is safe, effective and convenient and has almost completely displaced the use of unfractioned heparin in deep vein thrombosis prophylaxis. The peroperative physical measures of intermittent pneumatic compression of the calf used by some surgeons is being superseded by the surprisingly effective impulse foot-pump. In acute deep vein thrombosis, colour flow Duplex scans of the major channels are accurate and informative but venography will still remain important in the detailed
imaging of calf vein tributaries. Advances in MRA technology will in due course offer a fresh alternative to current diagnostic imaging of the venous system. Thrombolysis in instances of ilio-femoral vein thrombosis perhaps protected by a caval filter has the attractive potential for clearing clot early enough to preserve valve function while also expediting discharge from hospital. When contraindications to lysis exist, surgical thrombectomy and construction of a temporary arteriovenous fistula is the best available alternative.32

In the management of post-thrombotic lower limb venous hypertension, valve reconstruction and valve transposition techniques have been refined and will be increasingly applied. The durability of the much-vaunted technique of endoscopic subfascial ligation of incompetent perforators in promoting ulcer healing, so far unproven, can only be established by a proper controlled trial. In vein trunk compression syndromes, usually a feature of advanced cancer, stents carefully placed by the skilled interventional radiologist have brought profound relief.

Management of the non-operative aspects of vascular disease, which in this country is largely the responsibility of the vascular surgeon, falls within the discipline of angiology, a specialty which has been successfully nurtured in several European countries. Some angiologists even undertake interventional vascular procedures, a technical role which in most British centres is exercised by our radiology colleagues. This collaborative relationship between vascular surgeons and radiologists is set fair for the next millennium as long as it is rooted on the immutable premise that optimal care of the vascular patient as a whole remains the pre-eminent consideration. A case should be made for the enlargement of this team to include a physician with a specific interest in vascular disease.

Looking ahead to the future of vascular surgery one could conceivably become preoccupied rather fruitlessly by the inequities and the underfunding of health care in general. These concerns however, seem, ephemeral, particularly when viewed against the ethos of service, immeasurable devotion, compassion, sacrifice and, not least, the optimism, which have steered this great hospital through two long centuries, and which will doubtless sustain it in the years to come.

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