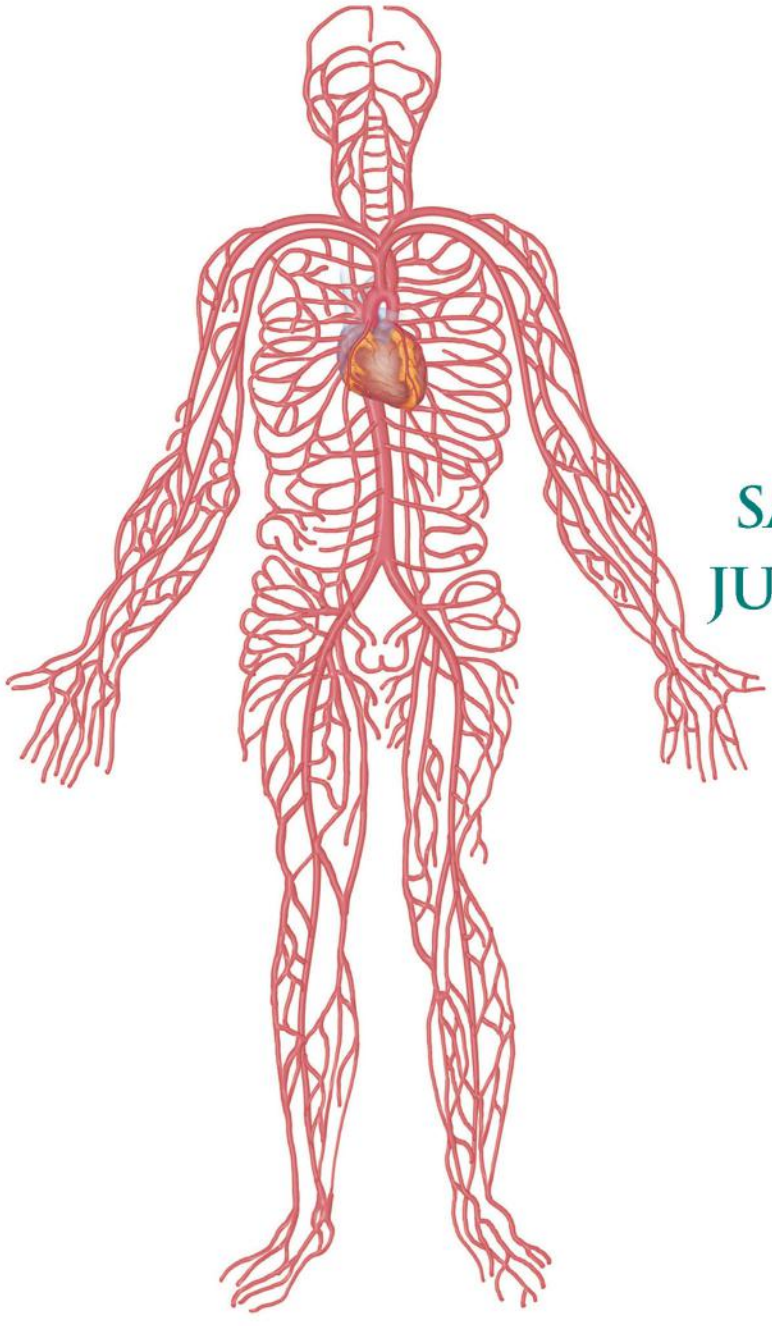
VASCULAR SURGERY

PRINCIPLES AND PRACTICE

FOURTH EDITION



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This one is for Ellie, Sam and Camille.

Samuel Eric Wilson

For Dr. Carlos and Ana Jimenez, my parents and inspirations for my medical career.

Juan Carlos Jimenez

I have four people who have supported my career throughout and who deserve an acknowledgement: my wife Carol and my associates Jackie Simpson, Julie Harris and Jamie McKay.

Frank J. Veith

To my three mentors, Jetmund Engeset, Vaughan Ruckley and Peter Bell.

A. Ross Naylor

Contents

Preface

When the first edition of *Vascular Surgery: Principles and Practice* was planned three decades ago, we could not have anticipated the revolution that was about to occur in vascular surgery. On reflection, the changes brought by endovascular methods evolved progressively from 'Jeffersonian research' – the application of innovation to solve practical problems. Beginning with Dotter's recanalization experiments in dilation of obstructed arteries and his human application, leading to Gruentzig's critical balloon catheter modifications, the stage was set for rapid advancement. Peripheral arterial stents were made from stainless steel and nitinol, and percutaneous angioplasty began to replace bypass operations for arterial occlusive disease. Endovascular repair of aortic aneurysms was the most dramatic advance reducing operative mortality to one quarter of open repair and reducing hospitalization to 1 or 2 days.

Throughout all of this change, vascular surgeons, more than any other surgical specialty, have supported their practice with rigorous clinical trials. For example, in occlusive disease percutaneous angioplasty was compared to bypass operation and carotid endarterectomy to medical management. In aneurysmal disease, repair was randomized to observation for small aortic aneurysms and endovascular to open repair. Some specialties having major changes to less invasive technology have seen numbers of procedures multiply, whereas having well-defined indications for intervention, as in aneurysm repair and carotid endarterectomy, has not led to proliferation in these procedures. More than anything, this signifies the need for vascular surgeons to remain involved in research – both basic and clinical – ultimately ensuring the public health.

Vascular surgery continues to evolve. No doubt questions such as the role of carotid stenting, repair of type II endoleaks, prevention of myointimal hyperplasia or designing a better arterial replacement will be answered in the next decade.

The goal of this text is to set out current standards in practice. We recognize these may change in the years ahead, but the methods we describe have been selected to last for the remainder of this decade. Proven patient management is emphasized, relying heavily on clinical trial research. Procedures are described and an atlas of open procedures included, but it is not a text of personal operative descriptions. Rather the discussions are directed at diagnosis, indications, methods of intervention and expected outcomes. We hope this work will be useful for the practicing vascular surgeon, resident in training or anyone inquiring into our field.

Indeed, the reader will find vascular surgery has evolved dramatically since the first edition of this text was published in 1987. Vascular surgery has seen a remarkable transformation from a specialty which dealt with the natural history of vascular disease and its treatment primarily by open procedures to a specialty which has kept the focus it had while mastering the major components of improved imaging and endovascular treatments. This fourth edition of *Vascular Surgery: Principles and Practice* has incorporated these advances while maintaining the specialty's past assets. Since natural history and open surgery will always be a component of optimal care for patients with vascular diseases, this mix of the old and the new will make this edition a valuable resource for all vascular surgeons and others interested in the optimal care of vascular patients.

Lastly, we thank the authors who have given so generously of their time, knowledge and experience, which made this book possible.

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SECTION I

Assessment of Vascular Disease

1

The evolution of vascular surgery

JAMES C. STANLEY

CONTENTS

Contemporary vascular surgery evolved slowly over many years with notable exceptions that catapulted new paradigms into clinical practice. Most landmark contributions occurred during the last half of the twentieth century, resulting from a better understanding of the physiologic consequences of vascular disease, the availability of heparin anticoagulation, the introduction of synthetic grafts, the development of non-invasive testing, an improved anatomic imaging and the maturation of technical skills in complex open surgical and endovascular procedures. Although vascular surgery had its beginning in many other disciplines, it has evolved into a finite specialty with a defined body of knowledge and established standards of practice. The history of vascular surgery is best addressed by reviewing three specific time periods: antiquity to the end of the nineteenth century, the early twentieth century and the last half of the twentieth and the early twenty-first century.

A select group of listings of landmark contributions have been created as a reference to the historical events affecting certain aspects of vascular surgery, including aortic occlusive disease (Table 1.1); nonanatomic revascularization of the lower extremities (Table 1.2); femoral, popliteal and tibial arterial occlusive disease (Table 1.3); aortic aneurysms (Table 1.4); femoral and popliteal artery aneurysms (Table 1.5); splanchnic and renal arterial disease (Table 1.6); cerebrovascular disease recognition and basis for treatment (Table 1.7); cerebrovascular disease–surgical treatment (Table 1.8); and venous disease (Table 1.9).

Many of the aforenoted events represent first-time accomplishments in the specialty; others were simply benchmark contributions to the care of patients with vascular diseases. Many clinicians and clinical scientists have added both depth and breadth to our knowledge of vascular surgery but are not included in the aforenoted listings because of this review's brief nature. Four earlier historical works have been published that offer additional insight into the evolution vascular surgery.[1–4]

ANTIQUITY TO THE END OF THE NINETEENTH CENTURY

Arterial disruptions due to trauma and ruptured aneurysms were confronted by the ancients, whose earliest vascular surgical procedures related to controlling bleeding from these vessels.[3] Perhaps, the first recorded reports on this topic were from India, where Sushruta used hemp fibres for blood vessel ligations around 700 BC.[5] Celsus made an important contribution in the first century, when he ligated vessels both above and below the site of injury and then transected the involved vessel so that it might retract from the wound, thus lessening the risk of hemorrhage which often accompanied wound infections. A century later, Galen had ligated many vessels and Antyllus ligated both entering and exiting vessels of an aneurysm, but infection continued to compromise such efforts.

Venous disease was also well recognized by the ancients, including Hippocrates, who recommended treating venous varicosities with compressive dressings and avoidance of standing.[3] Celsus used bandages and plasters to treat venous ulcerations in the first century and Galen suggested multiple ligations as a therapeutic intervention in the second century. Little change occurred in the management of venous disease over the next 1500 years.

The dark ages of European history witnessed few advances in vascular surgery. It wasn't until the sixteenth century that Ambroise Pare successfully ligated vessels in the battlefields at Danvilliers and used stringent agents to lessen wound

infections.[6] This was a major contribution in the treatment of controlling hemorrhage from arteries and veins.

During the eighteenth century, considerable efforts were extended to the treatment of aneurysms, led by John Hunter, who made many extraordinary contributions to the scientific classification and treatment of vascular diseases.[7–10] One of his more noteworthy accomplishments involved ligation of the femoral artery for the treatment of a popliteal artery aneurysm. This procedure provided the impetus for his interest in the relevance of the collateral circulation in the extremities.

During the ensuing nineteenth century, many other physicians described arterial ligature in the management of aneurysms. One of the most inventive of those practitioners was Ashley Cooper,[11,12] a student of Hunter, who ligated the carotid artery for an aneurysm in 1805.[13] The patient subsequently died, but he undertook a second successful ligation for the same disease 3 years later in 1808.[14] Cooper also ligated the aorta for an iliac artery aneurysm and treated a femoral artery aneurysm by ligation during this same era. Shortly thereafter, in 1817, Valentine Mott ligated the innominate artery for a subclavian aneurysm.[15] Mott also ligated the common iliac artery for an external iliac artery aneurysm in 1820. His work, performed in New York City, was some of the earliest vascular surgery undertaken in the United States.

Rudolph Matas was a widely recognized contributor to vascular surgery towards the end of the nineteenth century.[16] In 1888, he successfully performed a brachial artery aneurysm endoaneurysmorrhaphy.[17] His technique of ligating the entering and exiting vessels from within the aneurysm proved essential in preserving collateral vessels and maintaining the viability of distal tissues. Matas applied this procedure to the treatment of aortic aneurysms in the next century.

Chronic occlusive disease came to the forefront during the nineteenth century, when Barth described claudication for the first time in 1835, affecting a patient with an aortic thrombosis.[18] His report went unrecognized for many decades, but clearly established the concept that arterial obstructions could cause chronic symptoms amenable to later reconstructive procedures.

In 1896, a critical contribution to the understanding of vascular diseases came about with Wilhelm Roentgen's initial discovery of x-rays,[19] followed 3 months later by an actual arteriogram performed in an amputated upper extremity.[20] It would be decades before the usefulness of arteriography would become apparent in clinical practice.

Jaboulay and Briau successfully performed an end-to-end reanastomosis of the carotid artery in 1896.[21] This was remarkable, given the previously held belief that sutures placed in a vessel would result in its early thrombosis. John Murphy, a year later in 1897, described a successful end-to end arterial anastomosis of a femoral artery that had been injured with a gunshot wound with development of a pseudoaneurysm.[22] His case followed considerable experimental work with vascular anastomoses in both canine and bovine subjects and set the stage for subsequent advances in the succeeding century.

EARLY TWENTIETH CENTURY

Alexis Carrel, a student of Jaboulay, had an early interest in vascular anastomoses.[23,24] Carrel came to the United States shortly after the turn of the century and joined Charles C. Guthrie in the Department of Physiology at the University of Chicago.[25,26] These two individuals took the concept of inserting a vein into the arterial circulation and demonstrated that such was feasible in animal experiments.[27–29] Together they co-authored 28 papers. This work was the basis of Carrel's receiving the Nobel Prize in Medicine and Physiology in 1912.

Given an awareness of the novelty of successful vascular anastomoses performed in the laboratory, Jose Goyanes resected a patient's popliteal artery aneurysm and replaced it with a popliteal vein graft in 1906.[30] This was considered the first clinically successful arterial reconstruction using a vein graft.

The treatment of aortic aneurysms at the beginning of the twentieth century continued to involve non-reconstructive procedures. Instillation of large amounts of wire into an aneurysm as a means of inducing thrombosis and external wrapping to limit aneurysmal expansion proved inadequate and was soon discarded as acceptable therapy. Rudolph Matas, who successfully ligated the infrarenal aorta for the treatment of an aortic aneurysm in 1923,[31] reported his life's experience in 1940 with 62 similar operations for aneurysms with a commendable mortality of only 15%.[32] Although the natural history of untreated aortic and peripheral aneurysms became better defined during the early twentieth century, adequate treatment would not become commonplace until the second half of the century.

The management of lower extremity ischemia advanced quickly towards the end of the first half of the twentieth century. In 1946, Juan Cid dos Santos undertook a number of extensive endarterectomies for arteriosclerotic arterial occlusions.[33,34] He is often credited as the founder of arterial endarterectomy, although similar procedures had been performed earlier by Bazy and colleagues for aortic occlusive disease.[35] Endarterectomy was a landmark contribution to the evolution of vascular surgery.

In 1948, Jean Kunlin performed a successful femoropopliteal bypass with reversed autogenous saphenous vein and established a therapeutic approach that continues to present times.[36] William Holden, 6 months following Kunlin's achievement, was first in the United States to perform a lower extremity bypass with vein,[37] and his success was followed by that of many others.

Although not directly related to treating lower extremity ischemia, the surgical therapy of thoracic isthmic coarctations during the early mid-twentieth century established

the feasibility of clamping the aorta and undertaking its operative reconstruction. Clarence Crafoord, in 1944, first resected the coarcted segment and reconstructed the aorta with an end-to-end anastomosis.[38] Robert Gross did the same in 1945,[39] and in 1948 he replaced the coarcted aortic segment with a homograft.[40,41] These achievements allowed others to treat aortoiliac occlusive disease later with much greater confidence.

Attention to diseases of the distal aorta followed Rene Leriche's 1923 report on the clinical manifestations of thrombotic occlusion of the arteriosclerotic aortic bifurcation.[42] His experience with the treatment of this disease was later described in a widely heralded report of 1948.[43] The treatment of aortoiliac occlusive disease by operative means progressed rapidly thereafter during the last half of the century.

Recognition of diseases affecting the renal artery during the first half of the twentieth century would wait many years before they were successfully treated surgically. Harry Goldblatt, in elegant studies performed in the 1920s and 1930s, documented that renal artery constrictions in experimental animals caused hypertension.[44] In 1938, the clinical relevance of his observations became apparent when Leadbetter and Burkland removed a small ischemic kidney in a child with renal artery occlusive disease and cured his severe hypertension.[45] Unfortunately, the next few decades saw many kidneys removed without benefit, namely, because the careful selection of patients having a renin-mediated form of hypertension was undeveloped and vascular procedures for reconstructing the renal arteries were non-existent.

The classic description of occlusive disease of the splanchnic arteries causing intestinal angina was proposed in J. Englebert Dunphy' s classic paper of 1936.[46] He recognized the importance of postprandial abdominal pain as a manifestation of arteriosclerotic narrowings of the major arteries to the gut and noted its potential to eventuate in intestinal infarction. As was the case with renal artery disease, many years would pass before the successful vascular surgical treatment of intestinal angina occurred.

During the first half of the twentieth century, the role of the extracranial internal carotid artery as a cause of stroke received little attention. There were a number of reasons for this. First, cerebral angiography, initially performed by Egas Moniz in 1927,[47] was not to be used as a diagnostic test for many decades to come. Second, neck vessels were rarely examined during routine autopsy studies, and the existence of extracranial carotid artery arteriosclerosis was usually overlooked. In fact, the most commonly perceived cause of a cerebrovascular accident during the mid-century was thrombosis of the middle cerebral artery, with no understanding that thromboembolism from the region of the carotid bulb often played a role in the occlusive process.

The treatment of venous diseases was one of the mainstays of practice among physicians during the first half of the twentieth century. Varicose veins were known to have plagued man since antiquity, and external compression continued to be the basis of most therapies at the close of the century. A noteworthy contribution in that regard was the plaster dressing introduced by Unna, which became the forerunner of the dressing carrying his name a century later.[48] In 1905, Keller undertook stripping of extremity veins[4] and Babcock in the same time period developed an intraluminal stripper for vein removal.[49]

John Homans subsequently made many observations that advanced our understanding of venous disease. During the century's second decade, he emphasized the importance of saphenofemoral vein ligation in the prevention of varicosities.[50,51] A little more than 20 years later, in 1938, Robert Linton described the importance of incompetent communicating veins and subsequently developed a technique for subfascial ligation of these perforating veins.[52] More direct surgical interventions on the veins themselves to prevent venous hypertension would await another 3 decades.

The lethal nature of pulmonary emboli was well known in the early twentieth century, and prevention of this complication of venous thrombosis became important. In 1934, Homans advocated femoral vein ligation to prevent pulmonary embolism.[53] By 1945, ligation of the inferior vena cava (IVC) was reported by Northway, Buxton and O'Neill as a means of preventing fatal pulmonary embolism.[54,55] Ligation of the cava for prevention of septic emboli had been reported a few years earlier.[56]

A major advance in the evolution of vascular surgery during the early twentieth century was the introduction of translumbar aortography in 1929 by Reynaldo dos Santos.[57] Imaging of blood vessels was to prove essential to the continued advancement of vascular surgery. A second major advance was the use of heparin anticoagulation to prevent perioperative thromboses that affected the vast majority of vascular interventions during the very early twentieth century. Although heparin had been discovered in 1918 by Jay McLean in W. H. Howell's laboratory,[58] it was not purified and readily available for use until the 1930s and 1940s. It was only then that its value in treating arterial thromboses became widely recognized.[59,60]

Thus, the first half of the twentieth century witnessed the ability to approximate injured vessels, removal of arteriosclerotic plaque by the technique of endarterectomy and replacement of chronically diseased arteries with bypass grafts, all under the influence of anticoagulation. These achievements laid the foundation for the many advances of the last half of the twentieth century in vascular surgery.

THE LAST HALF OF THE TWENTIETH CENTURY AND THE EARLY TWENTY-FIRST CENTURY

More recent times have been born witness to profound changes in the practice of vascular surgery. These events are best discussed by addressing the individual contributions unique to specific disease entities.

Aortoiliac arteriosclerotic occlusive disease

Treatment of arteriosclerotic aortic disease was first successfully undertaken by Jacques Oudot in 1950 with a homograft replacement of a thrombosed aortic bifurcation.[61,62] With the recognition of homograft degeneration and the initial use of synthetic grafts, this form of aortic reconstruction fell into disuse.

Although the earliest aortoiliac endarterectomy may have been performed by Bazy and colleagues,[35] this technique was first undertaken in 1951 in the United States by Norman Freeman[63] and shortly thereafter popularized by his former colleague in practice, Edwin Wylie.[64,65]

The introduction of synthetic bypass grafts for the management of aortic diseases changed treatment dramatically, and for the next 40 years, these grafts, serving as aortofemoral bypasses, were the most common means of treating aortoiliac occlusive diseases.[66–73]

Nonanatomic revascularization procedures also evolved during the 1950s and 1960s for the treatment of aortoiliac occlusive lesions in high-risk situations. These unconventional interventions were used most often in reoperations for an infected or failed earlier bypass, avoidance of a hostile abdomen or concerns about the operative hazards of a more extensive procedure. Many types of nonanatomic procedures were developed over a short period of time.

The first of these nonanatomic reconstructions was by Jacques Oudot in 1951, who performed a crossover ilioiliac arterial bypass.[74] Subsequently, Norman Freeman used an endarterectomized superficial femoral artery in 1952 to perform a femorofemoral arterial crossover bypass.[75] An iliac artery to contralateral popliteal artery bypass was constructed by McCaughan and Kahn in 1958.[76] However, little attention was paid to these operations by most practitioners in the earlier days of contemporary vascular surgery.

It was in the 1960s that nonanatomic procedures became popular, after reports by Veto of a femorofemoral arterial crossover bypass in 1960,[77]as well as by Blaisdell and Hall of an axillofemoral bypass using a synthetic graft in 1962.[78]An important contribution to the latter procedure came from Lester Savage, who in 1966 added a crossover femorofemoral arterial bypass to a unilateral axillofemoral bypass as a means of revascularizing both lower extremities.[79] Although unrelated to the primary treatment of aortoiliac occlusive disease, the performance of an obturator bypass, first reported by Guida and Moore in 1969,[80] allowed lower extremity revascularizations with avoidance of an otherwise hostile groin area.

Endovascular interventions provided the most important major advance in the treatment of aortoiliac occlusive disease during the last quarter of the twentieth century, becoming widely used in the 1990s. This technology evolved from the pioneering work of Charles Dotter who reported on percutaneous coaxial dilation of peripheral arteries in 1964[81] and Andreas Gruentzig, who introduced percutaneous twin-lumen balloon angioplasty in 1974.[82] Treatment of iliac artery stenoses by balloon dilation markedly reduced the frequency with which open aortobifemoral bypass procedures were undertaken, and the use of balloon-assisted intraluminal stents developed by Palmaz in 1988[83] lessened the risk of complications associated with dissections. The rapid application of stent technology to angioplasty of iliac artery lesions followed during the next decade.[84]

Infrainguinal arteriosclerotic occlusive disease

Jean Kunlin reported 17 patients who had undergone autogenous vein lower extremity revascularizations in 1951.[85] Just 3 years after, he performed the first such operation. This was followed by similar bypass procedures in the United States by many surgeons including Julian, Lord, Dale, DeWeese, Linton, Darling and Szilagyi that confirmed the utility of reversed saphenous vein femoropopliteal reconstructions. Extension of vein graft procedures to the more distal infrageniculate arteries was first reported by Palma, who undertook a femorotibial bypass in 1956.[86] This too was followed with similar revascularizations by many others.

The use of the saphenous vein in situ after rendering its valves incompetent was first reported by Karl Hall in 1962.[87] This technology saw limited use until 1979, when Robert Leather and his colleagues introduced a new valve cutter for in situ revascularizations.[88] Subsequently, the procedure became widely used during the next decade.

Table 1.1 Aortic and aortoiliac occlusive disease.

Reynaldo dos Santos	1929	Translumbar aortography
Clarence Crafoord	1944	Thoracic coarctation resection, aortic reanastomosis
Rene Leriche	1948	Treatment of thrombotic occlusion of atherosclerotic aortic bifurcation, first described in 1923
Robert Gross	1949	Homograft replacement of thoracic aortic coarctation
Jacques Oudot	1950	Homograft replacement of thrombosed aortic bifurcation
Norman Freeman	1951	Aortoiliac endarterectomy; followed shortly thereafter in 1951 by Wylie, who popularized the open technique first described by Bazy and colleagues in 1949
Julio Palmaz	1988	Balloon-assisted stenting of arterial stenoses

Table 1.2 Nonanatomic revascularization of the lower extremities.

Jacques Oudot	1951	Ilioiliac bypass
Norman Freeman	1952	Femorofemoral bypass with endarterectomized superficial femoral artery
J.J. Mccaughan Jr., S. F. Kahn	1958	Iliopopliteal bypass
R. Mark Veto	1960	Femorofemoral bypass
F. William Blaisdell, A.D. Hall	1962	Axillofemoral bypass
Lester Sauvage	1966	Axillobifemoral bypass
P.M. Guida, S.W. Moore	1969	Obturator bypass

Table 1.3 Femoral, popliteal and tibial arterial occlusive disease.

Joao Cid dos Santos	1946	Femoral endarterectomy
Jean Kunlin	1948	Reversed autogenous saphenous vein femoral popliteal bypass
Eduardo Palma	1956	Femoral–tibial bypass with vein
Karl Hall	1962	In situ saphenous vein bypass
Thomas Fogarty	1963	Balloon-catheter embolectomy
Charles Dotter	1964	Percutaneous angioplasty (coaxial)
	1969	Percutaneous arterial endograft (experimental)
Peter Martin	1971	Extended profundoplasty
Herbert Dardik	1976	Use of human umbilical vein grafts in lower extremity revascularizations
Robert Leather	1979	In situ saphenous vein bypass popularized with introduction of new valve cutter
Dierk Maass	1982	Percutaneous expandable endoprosthesis
John Simpson	1985	Percutaneous transluminal atherectomy
Adair Bolia	1989	Percutaneous subintimal arterial recanalization

Although some have questioned the advantage to these reconstructions, their use in many distal revascularization procedures appeared valid.

An alternative biologic graft for use instead of autogenous vein was the tanned human umbilical vein, reported initially by Herbert Dardik in 1976.[89] Late aneurysmal changes in these grafts led to their eventual disuse. Although utilization of Dacron grafts for lower extremity reconstructions waned with the success of vein revascularizations, the introduction of extruded polytetrafluoroethylene (PTFE) grafts caused a resurgence in synthetic graft use for the treatment of lower extremity ischemia. In two hallmark papers, John Bergan, Frank Veith, Victor Bernhard and their colleagues demonstrated the utility of PTFE grafts for femoropopliteal reconstructions, with lesser benefits when used for distal infrageniculate procedures.[90,91]

The importance of the profunda femoris artery was initially reported in 1971 by Peter Martin, who described an extended profundoplasty as a means of improving blood flow to the ischemic extremity.[92]Although unrelated to his report, the importance of the profunda femoris artery in completing the distal anastomosis of an aortofemoral bypass was well recognized during the same time period, and an extension of the graft limb onto this vessel became standard practice.

The endovascular approach in managing lower extremity peripheral arterial occlusive became popular around the turn of the century. The spectrum of these less-invasive interventions ranged from simple balloon angioplasty of a focal superficial femoral artery stenosis to more complex subintimal recanalizations that were proposed by Adair Bolia in 1989.[93] Subsequently, catheter-directed mechanical atherectomy for more severe occlusive disease was introduced by John Simpson in 1985.[94] A variety of such devices are now used in contemporary practice to remove obstructing arteriosclerotic plaque. Percutaneous placement of a prosthetic graft, initially proposed by Dotter in 1969,[95] became clinically relevant in 1982 with the publication by Maass on the use of catheter-implanted expandable endografts.[96] Later, stenting both diseased vessels and endografts with self-expanding devices was advanced by Rabkin's 1989 report on the use of nitinol stents in humans.[97]

Embolic arterial occlusions of the lower extremity

One of the major advances in vascular surgery was introduced in Thomas Fogarty's 1963 report on balloon-catheter extractions of thromboembolic material from distant

vessels.[98] Given the risks of open procedures for saddle aortic emboli that often followed a myocardial infarction and the difficulties in removing emboli originating from atrial fibrillation in the smaller arteries of the leg, the ability to remove occlusive material through a femoral artery under local anaesthesia must be considered a sentinel contribution to the discipline of vascular surgery.

Aortic aneurysms

The lethal nature of aortic aneurysms led to many direct therapeutic advances, once clamping of the aorta was recognized to be tolerable and the postoperative management of these patients became better. Charles Dubost was the first to successfully treat an abdominal aortic aneurysm in 1951.[99] He replaced the aneurysm with a thoracic aortic homograft in a relatively complex procedure. Shortly thereafter, in 1953, Michael DeBakey and Denton Cooley replaced a thoracic aortic aneurysm with a similar homograft.[100] These reconstructions occurred during a time of considerable interest in the use of homografts for a variety of vascular procedures. The inevitable degenerative changes affecting these conduits led to their later abandonment in the clinical practice of aortic surgery, although in contemporary times they have been used in cases of infection when replacing the aorta.

Aortic aneurysm treatment changed dramatically shortly after Arthur Voorhees, Arthur Blakemore and Alfred Jaretzki reported the successful implantation of Vinyon-N cloth grafts in animals in 1951.[72] Two years later, in 1953, they used this type of graft in a patient with a ruptured aortic aneurysm who subsequently died of a myocardial infarction. However, their case was made, and in 1954 they described the use of this type of synthetic graft in 17 patients.[101] Unfortunately, this nylon material proved too brittle. Conduits constructed of Teflon and Dacron were subsequently developed, with the latter being popularized by DeBakey in the mid-1950s. Operative refinements involved lessening the risk of graft-enteric erosions by covering the implanted graft with the aneurysm shell, which in earlier times was usually excised in toto, and using synthetic sutures rather than silk, which with its deterioration led to late anastomotic separations of the graft from the vessel and eventual development of pseudoaneurysms. An important innovation in the therapy of aortic aneurysmal disease was the 1974 reported success of E. Stanley Crawford in using intraluminal grafts rather than bypass grafts to treat thoracoabdominal aneurysms that involved the renal and splanchnic arteries.[102]

The most important advance in aortic surgery during recent decades followed the publication by Volodos in 1988 on the use of an endograft to treat a traumatic aneurysm of the aorta.[103] This work and its implication to clinical practice went relatively unnoticed until 1991 when Juan Parodi reported using an endograft to treat an abdominal aortic aneurysm.[104] These former contributions, especially Parodi's, revolutionized the management of aortic aneurysms, and the subsequent decade witnessed many contributions to this new paradigm of vascular surgery. In 1994, this technology expanded the use of endografts in the treatment of ruptured abdominal aortic aneurysms.[105] A major and necessary improvement in the endovascular treatment of abdominal aortic aneurysms was modular prostheses, introduced by Chuter in 1994.[106,107] One of the most

Table 1.4 Aortic aneurysms.

Rudolph Matas	1923	First successful ligation for treatment of abdominal aortic aneurysm; unsuccessful attempt by Ashley Cooper in 1817
Charles Dubost	1951	Homograft replacement of abdominal aortic aneurysm
Arthur Voorhees, Arthur Blakemore, Alfred Jaretzki	1952	Development of synthetic graft (Vinyon-N) in experimental subjects; first clinical results with these grafts reported in 1953
Michael DeBakey, Denton Cooley	1953	Homograft replacement of thoracic aortic aneurysm
Michael DeBakey	1955	Repair of abdominal aortic aneurysm with prosthetic grafts
E. Stanley Crawford	1974	Intraluminal graft repair of thoracoabdominal aneurysms
Nicholas Volodes	1988	Endograft treatment of traumatic thoracic aortic aneurysm
Juan Parodi	1990	Endograft treatment of abdominal aortic aneurysm
Timothy Chuter	1994	Modular endograft treatment of aortic aneurysm
Syed Yusuf	1994	Endograft treatment of ruptured aortic aneurysm

Table 1.5 Femoral and popliteal artery aneurysms.

Ashley Cooper	1808	Femoral aneurysm ligation (patient lived 18 years)
Jose Goyanes	1906	Popliteal aneurysm excision, replaced with vein (first vein bypass graft used in clinical practice)
Michael Marin	1994	Endovascular stent–graft exclusion of popliteal artery aneurysm

valuable applications of this technology was the placement of endovascular stent grafts in the treatment of degenerative thoracic aortic aneurysms, as initially reported by Michael Dake in 1994.[108] It is an understatement to note that endovascular interventions have had a major impact on patient care and indeed the very definition of vascular surgery.

The common association of femoral and popliteal artery aneurysms with aortic aneurysms, especially in male patients, was clearly established in the last half of the twentieth century.[109–111] Their clinical management during recent decades was advanced by lytic therapy for thrombosed popliteal artery aneurysms before the operative bypass and aneurysm exclusion was performed. Endovascular placement of an endoluminal graft to exclude a popliteal aneurysm was first reported by Marin and his colleagues in 1994,[112] although the exact circumstances have not been defined when this technology is best pursued.

Renal artery occlusive disease

The first renal artery endarterectomy was performed by Norman Freeman in 1953,[113] a procedure popularized later by Edwin Wylie and his colleagues.[114] Nevertheless, aortorenal bypass using autogenous saphenous vein, first performed by Marion S. DeWeese in 1958, was subsequently more widely used than endarterectomy.[115] Stoney and his colleagues favoured using autologous iliac artery for reconstructing the renal arteries,[116] and DeCamp's first successful nonanatomic renal revascularization by a splenorenal bypass in 1957 offered yet another alternative means of renal revascularization.[117]

Despite these early contributions, the surgical treatment of renal artery occlusive disease was uncommon until after a series of publications from the Cooperative Study of Renovascular Hypertension in the mid-1970s.[118–122] Shortly thereafter, large surgical series appeared which firmly established the appropriateness of operation for renovascular hypertension.[123,124] During the same time period, a definitive classification of renal artery occlusive disease followed two publications, one in 1971[125] and the other in 1975.[126]

Andreas Gruntzig and his colleagues reported the first successful percutaneous balloon dilation of an arteriosclerotic renal artery occlusive lesion in 1978.[127] This technology had caused major changes in the management of renovascular hypertension by the close of the twentieth century. Continued clinical experience confirmed that endovascular-performed angioplasty is preferred for the treatment of most adult fibrodysplastic renal artery disease. Although the use of stents is technically efficacious in treating many arteriosclerotic ostial stenoses, this technology has received little support from a number of prospective trials including a recent study by Cooper and his colleagues in 2014 comparing percutaneous transluminal angioplasty to drug therapy alone.[128] However, considerable controversy surrounds a potential bias in many of the former studies regarding patient selection entering the trials.

Splanchnic artery occlusive disease

Acute intestinal ischemia, usually a consequence of embolism to the superior mesenteric artery, continued to be a lethal illness throughout latter half of the twentieth century. Klass in 1951 was the first to successfully treat acute intestinal ischemia by performance of a superior mesenteric artery embolectomy.[129] The operative treatment of both acute and chronic intestinal ischemia leading to today's endarterectomy and bypass procedures was subsequently advanced by Shaw and Mikkelsen with their colleagues in the late 1950s.[130,131] Additional experience during the last few decades of the twentieth century

Table 1.6 Splanchnic and renal arterial disease.

Renal artery disease		
Harry Goldblatt	1929	Established importance of renal artery occlusion and secondary hypertension
W.F. Leadbetter, G.E. Burkland	1938	Nephrectomy for renovascular hypertension (first treated case of renovascular hypertension)
Norman Freeman	1953	Renal artery endarterectomy
Marion DeWeese	1959	Aortorenal bypass with autogenous vein
Andreas Gruntzig	1978	Percutaneous renal artery balloon dilation
Splanchnic artery disease		
J. Englebert Dunphy	1936	Description of chronic intestinal ischemia
J. Klass	1951	Superior mesenteric artery embolectomy
R.S. Shaw, E.P. Maynard	1958	Operative treatment of acute and chronic intestinal ischemia
W.P. Mikkelsen	1959	Operative treatment of chronic intestinal ischemia
J. Furrer	1980	Percutaneous balloon angioplasty of the superior mesenteric artery

affirmed the generally accepted tenets that aortomesenteric bypasses with synthetic grafts were preferable to vein graft reconstructions and that multiple vessel revascularizations were more likely to provide greater long-term benefits than single-vessel reconstructions.

As has been evident in other vascular territories, endovascular therapy has become part of the therapeutic armamentarium in treating splanchnic arterial occlusive disease. The first percutaneous angioplasty in the treatment of chronic intestinal ischemia was reported by Furrer and Gruntzig and their colleagues in 1980.[132] The surgical management of intestinal ischemia due to splanchnic arteriosclerosis must be considered somewhat anecdotal compared to treatment of other vascular diseases. In fact, no large clinical studies exist that properly compare the differing therapeutic options. The same conclusion applies to the therapy of many splanchnic artery aneurysms, with few definitive experiences reported since two widely quoted reviews were published in the 1970s.[133,134]

Cerebrovascular disease

Miller Fisher reported autopsy findings in 1951 that for the first time presented irrefutable evidence that extracranial carotid artery bifurcation arteriosclerosis was likely to be a common cause of a stroke.[135] This led to a series of remarkable advances in the surgical treatment and prevention of stroke. The first reported operation for carotid artery stenotic disease was in 1951 by Raul Carrea, Mahelz Molins and Guillermo Murphy, who resected the affected carotid artery and reanastomosed the internal carotid artery to the external carotid artery.[136] Three years later, in 1954, Felix Eastcott, George Pickering and Charles Rob reported a similar procedure with resection of the diseased carotid bifurcation and a reanastomosis of the internal carotid artery to the common carotid artery.[137] In 1953, the first conventional carotid endarterectomy was performed by Michael DeBakey.[138] One year later, in 1954, Davis, Grove and Julian reported having performed the first innominate artery endarterectomy,[139] and in 1958,

Table 1.7 Cerebrovascular disease: recognition and basis for treatment.

Egas Moniz	1927	Cerebral angiography.
Miller Fisher	1951	Post-mortem exam of 373 patients suggested arteriosclerosis of the extracranial carotid artery bifurcation might be a common cause of cerebrovascular accident.
Henry Barnett	1991, 1998	NASCET documented benefit of surgical therapy for symptomatic stenotic lesions greater than 50%.
Robert Hobson	1993	Surgical benefit documented for select treatment of asymptomatic carotid artery stenosis.
James O'Toole	1993	Asymptomatic carotid artery study documented surgical benefit for asymptomatic lesions greater than 70%.
J.S. Yadav	2004	Randomized trial comparing carotid artery stenting and endarterectomy in high-risk patients.

Table 1.8 Cerebrovascular disease: surgical treatment.

Raul Carrea, Mahelz Molins, Guillermo Murphy	1951	Resected arteriosclerotic carotid, with external to internal carotid reanastomosis (first operation for carotid stenotic disease)
Michael DeBakey	1953	Carotid artery endarterectomy
H.H.G. (Felix) Eastcott, George Pickering, Charles Robb	1954	Resected carotid bifurcation, with common carotid to internal carotid reanastomosis
C. Lyons, G. Galbraith	1956	Subclavian–carotid artery bypass
J.B. Davis, W.J. Grove, O.C. Julian	1954	Innominate artery endarterectomy
Michael DeBakey, George Morris, G.L. Jordan, Denton Cooley	1957	Innominate–subclavian–carotid arterial bypass
Stanley Crawford, Michael DeBakey, William Fields	1958	Vertebral artery endarterectomy and bypass
M. Gazi Yasargil, Hugh A. Krayenbuhl, Julius H. Jacobson II	1970	Extracranial–intracranial arterial bypass
Klaus D. Mathias	1977	Percutaneous angioplasty of carotid artery stenosis
Donald Bachman, Robert Kim, Klaus D. Mathias	1980	Percutaneous angioplasty of subclavian artery stenosis

E. Stanley Crawford, Michael DeBakey and William Fields reported endarterectomy as a means of treating vertebral artery occlusive disease.[140]

The benefits of treating cerebral ischemic syndromes with a bypass were also first recognized during the mid-1950s. Lyons and Galbraith in 1956 performed a subclavian-to-carotid artery bypass,[141] and in 1958, Michael DeBakey and his associates reported an innominate artery to subclavian and carotid arterial bypass.[142] A vertebral artery bypass was also reported by Crawford, DeBakey and Fields that same year. A more dramatic approach to these diseases was by an extracranial–intracranial arterial bypass, championed by Yasargil and his colleagues in the early 1970s.[143] This has been used infrequently following a still-controversial clinical study of the technique published by Henry Barnett and his colleagues in 1989.[144]

One of the most important effects on the surgical treatment of carotid artery arteriosclerosis resulted from a series of well-designed and well-conducted prospective clinical studies initially published in the 1990s that better defined the indication for endarterectomy procedures. The first, the North American Symptomatic Carotid Endarterectomy Trial (NASCET), led by Henry Barnett, was published initially in 1991 and updated in 1998.[145,146] These studies documented the benefit of carotid endarterectomy in lessening the risk of subsequent stroke in patients with symptomatic stenotic lesions greater than 50%. Two other studies, one from Europer[147] and the other from veterans' hospitals in the United States,[148] supported the NASCET conclusions.

The beneficial effects of carotid endarterectomy in preventing stroke in patients with asymptomatic carotid stenoses greater than 70% was subsequently reported by James O'Toole and Robert Hobson.[149,150] Although some may dispute the details of any of these studies, the benefits of a carefully performed carotid endarterectomy in a properly selected patient were definitively established.

Carotid endarterectomy at the conclusion of the twentieth century was the most common vascular operation performed in the United States, but it was soon to be challenged by percutaneous endovascular interventions. The first angioplasty for carotid artery disease was reported in 1977 by Mathias,[151] but it wasn't acclaimed to be an appropriate alternative to endarterectomy until decades later when a number of clinical trials were reported; perhaps, the most influential being published in 2004 and 2008 by Yadav and colleagues.[152,153] At the close of the last century, the introduction of percutaneous carotid artery dilation and stenting was touted as a reasonable alternative to carotid endarterectomy. However, its exact role in the clinical arena has yet to be clearly established.

Less controversy exists regarding endovascular dilation and stenting of the proximal subclavian artery for the treatment of vertebrobasilar symptoms evident in the subclavian steal syndrome. Percutaneous angioplasty of subclavian stenoses was first reported in 1980 by Bachman and Kim[154] and Mathias.[155] Although these initial procedures involved balloon dilation alone, the use of stenting in succeeding years became part of most interventions.

Venous disease

Prevention of embolization and venous hypertension arising from deep venous thromboses led to a number of important surgical interventions during the last half of the twentieth century. Although ligation of the IVC had been performed earlier for prevention of pulmonary embolism and often was used as the treatment of choice for septic emboli, the morbidity of this therapy was considerable.

In 1958, Marion S. DeWeese was the first to partially interrupt the vena cava for the prevention of pulmonary emboli, using a suture plication technique.[156,157] In 1967, Kazi Mobin-Uddin introduced an umbrella device to trap emboli in transit.[158,159] His remarkable innovation was followed by Lazar Greenfield's conical vena cava filter,[160] which was initially placed through the jugular vein with an open procedure but was later inserted percutaneously through a femoral vein route. Subsequently, other caval devices have been developed to trap emboli from the lower body veins. The reduction in fatal pulmonary embolism using vena cava filters represents a major accomplishment of vascular surgeons.

Treatment of venous hypertension in the last half of the twentieth century focused on both direct venous reconstructive surgery and less-invasive procedures for interrupting incompetent perforating veins. In 1952, Jean Kunlin performed a saphenous vein bypass of an obstructed external iliac artery vein,[161] and 6 years later, Eduardo Palma performed a saphenofemoral vein crossover bypass.[162] A more distal decompressive procedure, a saphenopopliteal vein bypass, was accomplished by Husni in 1970.[163]

Endovascular disobliteration of thrombosed extremity veins with subsequent catheter-based dilation, usually with stenting, is a direct means of reducing venous hypertension but has had limited applicability in clinical practice. However, endovascular interventions for obstructions affecting the more major veins have been pursued in cases of severe venous hypotension. The first stenting of the vena cava in such a setting was reported in 1986 by Gianturco and his colleagues.[164]

Reducing elevated venous pressures in the lower extremity by reconstructing the vein's valves was introduced by Robert Kistner, who successfully performed venous valvuloplasty procedures,[165,166] and Taheri who was the first to undertake transplantation of a venous valve.[167] Hauer in 1985 reported on the endoscopic interruption of incompetent perforating veins that contributed to elevated venous pressures at the ankle.[168] Durable treatment of venous hypertension and its complications, including cutaneous ulcerations, continues to challenge the current clinical skills of physicians.

Surgical elimination of lower extremity varicose veins by means other than stripping was advanced after a 1944 report on foam sclerotherapy,[169] with the later development of various sclerosing agents. Subsequently, an early form of radiofrequency ablation was introduced

Table 1.9 Venous disease.

Prophylactic prevention of pulmonary embolism		
John Holmans	1934	Femoral vein ligation
O. Northway, Robert Buxton, E. O'Neill	1944	IVC ligation
Marion S. DeWeese	1958	Suture plication of the IVC
Kazi Mobin-Uddin	1967	Transvenous IVC umbrella filter
Lazar J. Greenfield	1974	Percutaneous IVC conical–strut filter
Correction of venous hypertension		
Robert Linton	1938	Subfascial division of incompetent perforating veins
Jean Kunlin	1952	Saphenous vein bypass of obstructed external iliac vein
Eduardo Plama	1958	Saphenofemoral vein crossover bypass
E.A. Husni	1970	Saphenopopliteal vein bypass
Robert Kistner	1975	Valvuloplasty
S.A. Taheri	1982	Vein–valve transplant
G. Hauer	1985	Endoscopic interruptions of incompetent perforating veins
C. Charnsangavej	1986	Endovascular stenting of the vena cava
Removal of varicose veins		
W.W. Babcock	1905	Intraluminal stripper for vein removal
John Homans	1916	Saphenofemoral vein ligation
E.J. Orbach	1944	Foam sclerotherapy
M. Politowski	1966	Radiofrequency venous ablation
C. Bone	1999	Laser venous ablation

in 1966[170] followed by laser venous ablation in 1999.[171] Both interventions have been part of the endovascular approach to the contemporary management of venous disease.

THE FUTURE

The diagnosis of vascular disease in the early decades of the current millennium is likely to evolve dramatically with genetic testing that will identify patients at risk for various arteriosclerotic occlusive disorders, matrix problems leading to aneurysms and other vascular diseases. This will revolutionize the selection of patients for early interventions, both medical and surgical, and will affect vascular surgery more than any other advance since the introduction of contemporary imaging techniques, vascular grafts and heparin anticoagulation.

The practice of vascular surgery, especially in industrial nations during the early decades of the twenty-first century, will be impacted by increasing costs of health care, a greater number of patients needing treatment as the population ages and the involvement of third parties in controlling affordable medical practice. Given society's greater medical literacy and availability of the internet, there will also be an increasing patient demand for better care in relation to outcomes. Vascular surgery, because of its easily documented clinical end points, should be the beneficiary of evidence-based care.

Finally, there will be complementary and competing practices in the new millennium. This will likely result in the establishment of true multidisciplinary care and the elimination of those disciplines unable to adapt to new paradigms of practice. Vascular surgery can ill afford to not adapt to change. This relates to training and certification in a bureaucratic era, where benefits of treatment, and surgical intervention in particular, must outweigh the risk of alternative therapies. Durable benefits must be afforded patients. The evolution of vascular surgery has been one of enormous success. The challenge now is how to best enhance and advance the knowledge base and practice patterns enacted by our discipline's forebears.

REFERENCES

1. Barker WF. A history of vascular surgery. In: Moore WF, ed. *Vascular Surgery: A Comprehensive Review*, 5th ed. Philadelphia, PA: Saunders, 1998, pp. 1–19.
2. Dale WA, Johnson G Jr., DeWeese JA. *Band of Brothers: Creators of Modern Vascular Surgery*. Chelsea, MI: BookCrafters, 1996.
3. Friedman SG. *A History of Vascular Surgery*. New York: Futura, 1989.
4. Thompson JE. History of vascular surgery. In: Norton JA, Bollinger RR, Chang AE, Lowry SF, Mulvihill SJ, Pass HI, Thompson RW, eds. *Surgery: Basic Science and Clinical Evidence*. New York: Springer-Verlag, 2001, pp. 969–985.
5. Prakash UBS. Sushruta of ancient India. *Surg Gynecol Obstet*. 1978;146:263–272.

6. Hamby W. *The Case Reports and Autopsy Records of Ambrose Pare*. Springfield, IL: Charles C. Thomas, 1960.
7. Chitwood WR Jr. John and William Hunter on aneurysms. *Arch Surg*. 1977;112:829–836.
8. Lambert. Extract of a letter from Mr. Lambert, surgeon at Newcastle Upon Tyne, to Dr. Hunter; giving an Account of a new Method of treating an Aneurysm. Read June 15, 1761. *Med Obs Inq*. 1762;2:360.
9. Perry MO. John Hunter-triumph and tragedy. *J Vasc Surg*. 1993;17:7–14.
10. Schlechter DC, Bergan JJ. Popliteal aneurysm: A celebration of the bicentennial of John Hunter's operation. *Ann Vasc Surg*. 1986;1:118–126.
11. Brock RC. The life and work of Sir Astley Cooper. *Ann R Coll Surg Engl*. 1969;44:1.
12. Rawling EG. Sir Astley Paston Cooper, 1768–1841: The prince of surgery. *Can Med Assoc J*. 1968;99:221–225.
13. Cooper A. A second case of carotid aneurysm. *Med Chir Trans*. 1809;1:222–233.
14. Cooper A. Account of the first successful operation performed on the common carotid artery for aneurysm in the year 1808 with the postmortem examination in the year 1821. *Guy's Hosp Rep*. 1836;I:53–59.
15. Rutkow JM. Valentine Mott (1785–1865) the father of American vascular surgery: A historical perspective. *Surgery*. 1979;85:441–450.
16. Cordell AR. A lasting legacy: The life and work of Rudolph Matas. *J Vasc Surg*. 1985;2:613–619.
17. Matas R. Traumatic aneurysm of the left brachial artery. *Med News Phil*. 1888;53:462.
18. Barth. Observation d'une Obliteration Complete de 1·aorte Abdominale Recuillie Dans le Service de M Louis, Suivie de Reflections. *Arch Gen Med*. 1835;8:26–53.
19. Roentgen WK. Ueber eine neue Art von Strahlen. *Nature*. 1896;53:274.
20. Haschek E, Lindenthal OT. Ein Beitrag zur praktischen Verwerthung der Photographie nach Roentgen. *Wien Klin Wochenschr*. 1896;9:63.
21. Jaboulay M, Briau E. Recherches Experimentales Sur la Suture ct al Greffe Arterielle. *Lyon Med*. 1896;81:97–99.
22. Murphy JB. Resection of arteries and veins injured in continuity-end-to-end suture-experimental and clinical research. *Med Res*. 1897;51:73.
23. Carrel A. La Technique Operatoire des Anastomoses Vasculaires et de la Transplantation des Visceres. *Lyon Med*. 1902;98:850.
24. Carrel A, Moullard J. Anastomose Bout a Bout de la Jugulaire et de la Caroticle Primitive. *Lyon Med*. 1902;99:114.
25. Edwards WS, Edwards PD. *Alexis Carrel, Visionary Surgeon*. Springfield, IL: Charles C. Thomas, 1974.
26. Harbison SP. The origins of vascular surgery: The Carrel-Guthrie letters. *Surgery*. 1962;52:406–418.
27. Carrel A, Guthrie CC. Uniterminal and Biterminal Venous Transplantations. *Surg Gynecol Obstet*. 1906;2:266–286.
28. Carrel A, Guthrie CC. Resultats du 'Patching' desArteres. *C R Soc Biol*. 1906;60:1009.
29. Guthrie CC. *Blood Vessel Surgery and Its Applications*. London, UK: Longmans Green, 1912.
30. Goyanes J. Nuevos Trabajos de Cirugia Vascular. Substitution Plastica de las Arterias por las Venas, 0 Arterioplastia Venosa, Applicada, como Nuevo Metodo, al Tratamiento de los Aneurismas. *El Siglo Med*. 1906 September;346:561.
31. Matas R. Aneurysm of the abdominal aorta at its bifurcation into the common iliac arteries. A pictorial supplement illustrating the history of corinne D, previously reported as the first recorded instance of cure of an aneurysm of the abdominal aorta by ligation. *Ann Surg*. 1940;112:909–922.
32. Matas R. Personal experiences in vascular surgery: A statistical synopsis. *Ann Surg*. 1940;112:802–839.
33. dos Santos JC. Sur la Desobstruction des Thromboses Arterielles Anciennes. *Mem Acad Surg*. 1947;73:409–411.
34. dos Santos JC. From embolectomy to endarterectomy or the fall of a myth. *J Cardiovasc Surg*. 1976;17:113–128.
35. Bazy L, Hugier J, Reboul H et al. Techniques des 'Endarterectomies' or Arterities Obliterantes Chroniques des Membres Inforieures, des Iliaques, et de L' aorte Abdominale Inferieur. *J Chir*. 1949;65:196–210.
36. Kunlin J. Le Traitement de L'arterite Obliterante par la Greffe Veineuse. *Arch Mal Coeur*. 1949;42:371.
37. Holden WD. Reconstruction of the femoral artery for arteriosclerotic thrombosis. *Surgery*. 1950;27:417–422.
38. Crafoord C, Nylin G. Congenital coarctation of the aorta and its surgical treatment. *J Thorac Surg*. 1945;14:347–361.
39. Gross RE. Surgical correction for coarctation of the aorta. *Surgery*. 1945;18:673–678.
40. Gross RE, Hurwitt ES, Bill AH Jr., Pierce EC II. Preliminary observations on the use of human arterial grafts in the treatment of certain cardiovascular defects. *N Engl J Med*. 1948;239:578–579.
41. Gross RE. Treatment of certain aortic coarctations by homologous grafts: A report of 19 cases. *Ann Surg*. 1951;134:753–758.
42. Leriche R. Des Obliterations Arterielles Hautes (Obliteration de la Terminaison de l'aorte) Comme Cause des Insuffisancces Circulatoires des Membres lnferieurs. *Bull Mem Soc Chir*. 1923;49:1404–1406.
43. Leriche R, Morel A. The syndrome of thrombotic obliteration of the aortic bifurcation. *Ann Surg*. 1948;127:193–206.
44. Goldblatt H, Lynch J, Hanzal RF, Summerville WW. Studies on experimental hypertension. I. The production of persistent elevation of systolic blood pressure by means of renal ischemia. *J Exp Med*. 1934;59:347–379.
45. Leadbetter WF, Burkland GE. Hypertension in unilateral renal disease. *J Urol*. 1037;39:661–726.

46. Dunphy JE. Abdominal pain of vascular origin. *Am J Med Sci*. 1935;192:109–113.
47. Moniz E. L'encephalographic Arterielle son Importance dans la Loalisation des Tumeurs Cerebrales. *Rev Neurol*. 1927;2:72–90.
48. Unna PG. Ueber Paraplaste: Eine neue Form medikamentoser Pilaster. *Wien Med Wschr*. 1895;46:1854.
49. Babcock WW. A new operation for the extirpation of varicose veins. *N Y Med J*. 1907;86:153–156.
50. Homans J. The operative treatment of varicose veins and ulcers, based upon a classification of these lesions. *Surg Gynecol Obstet*. 1916;22:143–158.
51. Homans J. The etiology and treatment of varicose ulcer of the leg. *Surg Gynecol Obstet*. 1917;24:300–311.
52. Linton RR. The communicating veins of the lower leg and the operative treatment for their ligation. *Ann Surg*. 1938;107:582–593.
53. Homans J. Thrombosis of the deep veins of the lower leg causing pulmonary embolism. *N Engl J Med*. 1934;211:933–997.
54. Northway O, Buxton RW. Ligation of the inferior vena cava. *Surgery*. 1945;18:85–94.
55. O'Neill EE. Ligation of the inferior vena cava in the prevention and treatment of pulmonary embolism. *N Engl J Med*. 1945;232:641–646.
56. Collins CG, Jones JR, Nelson WE. Surgical treatment of pelvic thrombophlebitis. *New Orleans Med Surg J*. 1943;95:324–329.
57. dos Santos R, Lamas A, Pereirgi CJ. L'arteriographie des Membres de L'aorte et ses Branches Abdominales. *Bull Soc Nat Hir*. 1929;55:587.
58. Howell WH. Two new factors in blood coagulation-heparin and proantithrombin. *Am J Physiol*. 1918;47:328–341.
59. Murray G. Heparin in surgical treatment of blood vessels. *Arch Surg*. 1940;40:307–325.
60. Murray GWG, Best CH. The use of heparin in thrombosis. *Ann Surg*. 1938;108:163–177.
61. Oudot J. La Greffe Vasculaire dans les Thromboses du Crrefour Aortique. *Presse Med*. 1951;59:234–236.
62. Oudot J, Beaconsfield P. Thrombosis of the aortic bifurcation treated by resection and homograft replacement: Report of five cases. *Arch Surg*. 1953;66:365–374.
63. Freeman NE, Leeds FH. Vein inlay graft in treatment of aneurysm and thrombosis of abdominal aorta: Preliminary communication with report of 3 cases. *Angiology*. 1951;2:579–587.
64. Wylie EJ Jr., Kerr E, Davies O. Experimental and clinical experiences with the use of fascia lata applied as a graft about major arteries after thromboendarterectomy and aneurysmorrhaphy. *Surg Gynecol Obstet*. 1951;93:257–272.
65. Wylie EJ. Thromboendarterectomy for arteriosclerotic thrombosis of major arteries. *Surgery*. 1952;32:275–292.
66. DeBakey ME, Cooley DA, Crawford ES, Morris CG Jr. Clinical application of a new flexible knitted dacron arterial substitute. *Arch Surg*. 1957;74:713–724.
67. Edwards WS, Tapp S. Chemically treated nylon tubes as arterial grafts. *Surgery*. 1955;38:61–70.
68. Julian OC, Deterling RA, Dye WS, Bhonslay S, Grove WJ, Belio ML, Javid H. Dacron tube and bifurcation prosthesis produced to specification: II. Continued clinical use and the addition of microcrimping. *Arch Surg*. 1957;78:260–270.
69. Sauvage LR, Berger K, Wood SJ, Nakagawa Y, Mansfield PB. An external velour surface for porous arterial prostheses. *Surgery*. 1971;70:940–953.
70. Szilagyi DE, France LC, Smith RF, Whitcomb JG. Clinical use of an elastic dacron prosthesis. *Arch Surg*. 1958;77:538–551.
71. Voorhees AB Jr. The development of arterial prostheses: A personal view. *Arch Surg*. 1985;120:289–295.
72. Voorhees AB Jr., Jaretzki A, Blakemore AH. The use of tubes constructed from vinyon "N" cloth in bridging arterial defects: A preliminary report. *Ann Surg*. 1952;135:332–336.
73. Wesolowski SA, Dennis CA, eds. *Fundamentals of Vascular Grafting*. New York: McGraw-Hill, 1963.
74. Oudot J. Un Deuxiemecas de Greffe de la Bifurcation Aortque Pour Thrombose da la Fourche Aortique. Mem. *Acad Chir*. 1951;77:644–645.
75. Freeman NE, Leeds FH. Operations on large arteries: Application of recent advances. *Calif Med*. 1952;77:229–233.
76. Mccaughan JJ Jr., Kahn SF. Cross-over graft for unilateral occlusive disease of the iliofemoral arteries. *Ann Surg*. 1960;151:26–28.
77. Yetto RM. The treatment of unilateral iliac artery obstruction with a trans-abdominal subcutaneous femorofemoral graft. *Surgery*. 1962;52:342–345.
78. Blaisdell FW, Hall AD. Axillary-femoral artery bypass for lower extremity ischemia. *Surgery*. 1963;54:563–568.
79. Sauvage LR, Wood SJ. Unilateral axillary bilateral femoral bifurcation graft: A procedure for the poor risk patient with aortoiliac disease. *Surgery*. 1966;60:573–577.
80. Guida PM, Moore SW. Obturator bypass technique. *Surg Gynecol Obstet*. 1969;128:1307–1316.
81. Dotter CT, Judkins MP. Transluminal treatment of arteriosclerotic obstruction: Description of a new technique and a preliminary report of its application. *Circulation*. 1964;30:654–670.
82. Gruentzig AR, Hopff H. Perkutaner Rekanalisation Chronischer Arterieller Verschluss mit Einem Neuen Dilatations Katheter. *Dtsch Med Wschr*. 1974;99:2502.
83. Palmaz JC, Tio FC, Schatz RA, Alvarado R, Res C, Garcia O. Early endothelialization of balloon-expandable stents: Experimental observations. *J Intervent Radiol*. 1998;3:119–124.

84. Palmaz JC, Richter G, Noeldge G et al. Intraluminal stenting of atherosclerotic iliac artery stenosis: Preliminary report of a multicenter study. *Radiology*. 1998;168:727–731.
85. Kunlin J. Le Traitement de L'ischemie Arteritique par la Greffe Veineuse Longue. *Rev Chir*. 1951;70:206.
86. Palma EC. The treatment of arteritis of the lower limbs by autogenous vein grafts. *Minerva Cardioangiol Eur*. 1960;8:36–49.
87. Hall KV. The great saphenous vein used in situ as an in arterial shunt after extirpation of the vein valves. *Surgery*. 1962;51:492–495.
88. Leather RP, Powers SR Jr., Karmody AM. The reappraisal of the in situ saphenous vein arterial bypass: Its use in limb salvage. *Surgery*. 1979;86:453–461.
89. Dardik H, Miller N, Dardik A, Ibrahim IM, Sussman B, Silvia M, Berry M, Wolodiger F, Kahn M, Dardik I. A decade of experience with the glutaraldehyde-tanned human umbilical cord vein graft for revascularization of the lower limb. *J Vasc Surg*. 1988;7:336–346.
90. Bergan JJ, Veith FJ, Bernhard VM, Yao JST, Flinn WR, Gupta SK, Scher LA, Samson RH, Towne JB. Randomization of autogenous vein and polytetrafluoroethylene grafts in femoral distal reconstruction. *Surgery*. 1982;92:921–930.
91. Veith FJ, Gupta SK, Ascer E, White-Flores S, Samson RH, Scher LA, Towne JB, Bernhard JJ. Six-year prospective multicenter randomized comparison of autologous saphenous vein and expanded polytetrafluoroethylene grafts in infrainguinal arterial reconstructions. *J Vasc Surg*. 1986;3:104–114.
92. Martin P, Renwick S, Stephenson C. On the surgery of the profunda femoris artery. *Br J Surg*. 1971;55:539–542.
93. Bolia A, Brennan J, Bell PR. Recanalization of femoro-popoliteal occlusions: Improving success rate by subintimal recanalization. *Clin Radiol*. 1989;40:325.
94. Simpson JB, Johnson DE, Thapliyal HV, Marks DS, Braden LJ. Transluminal atherectomy: A new approach to the treatment of atherosclerotic vascular disease. *Circulation*. 1985;72(Suppl. 2):111–146.
95. Dotter CT. Transluminally-placed coilspring endarterial tube grafts: Long-term patency in canine popliteal artery. *Invest Radiol*. 1969;4:327–332.
96. Maass D, Kropf L, Egloff L, Demierre D, Turina M, Senning A. Transluminal implantation of intravascular "double helix" spiral prostheses: Technical and biological considerations. *ESAO Proc*. 1982;9:252–256.
97. Rabkin JK. New types of technology in roentgenosurgery. IX. All-Unions Konress-Uber Frotschritte in der Roentgen-Chirurgie. Moskau, Russia, 1989.
98. Fogarty TJ, Cranley JJ, Krause RJ, Strasser ES, Hafner CD. A method for extraction of arterial emboli and thrombi. *Surg Gynecol Obstet*. 1963;116:241–244.
99. Dubost C, Allary M, Oeconomos N. Resection of an aneurysm of the abdominal aorta: Reestablishment of the continuity by preserved human arterial graft, with results after six months. *Arch Surg*. 1952;64:405–408.
100. DeBakey ME, Cooley DA. Successful resection of aneurysm of thoracic aorta and replacement by graft. *J Am MedAssoc*. 1953;152:673–676.
101. Blakemore AH, Voorhees AB Jr. The use of tubes constructed from vinyon "N" cloth in bridging arterial defects experimental and clinical. *Ann Surg*. 1954;140:324–334.
102. Crawford ES. Thoracoabdominal aortic aneurysms involving renal, superior mesenteric and celiac arteries. *Ann Surg*. 1974;179:763–772.
103. Volodos NL, Karpovich IP, Shekhanin VE, Troian VI, Iakovenko LF. A case of distant transfemoral endoprosthesis of the thoracic artery using a self-fixing synthetic prosthesis in traumatic aneurysm. *Grudn Khir*. 1988;6:84–86.
104. Parodi J, Palrnaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. *Ann Vasc Surg*. 1991;5:491–499.
105. Yusuf SW, Whitaker SC, Chuter TAM, Wenham PW, Hopkinson BR. Emergency endovascular repair of leaking aortic aneurysm (letter). *Lancet*. 1994;344:1645.
106. Chuter TAM. Transfemoral aneurysm repair (DM Thesis). Nottingham, UK: University of Nottingham, 1994.
107. Scott RAP, Chuter TAM. Clinical endovascular placement of bifurcated graft in abdominal aortic aneurysm without laparotomy. *Lancet* 1994;343:413.
108. Dake MD, Miller DC, Semba CP, Mitchell RS, Walker PJ, Liddell RP. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. *N Engl J Med*. 1994;331:1729–1734.
109. Diwan A, Sarkar R, Stanley JC, Zelenock GB, Zelenock GB, Wakefield TW. Incidence of femoral and popliteal artery aneurysms in patients with abdominal aortic aneurysms. *J Vasc Surg*. 2000;31:863–869.
110. Graham LM, Zelenock GB, Whitehouse WM Jr., Erlandson EE, Dent TL, Lindenauer SM, Stanley JC. Clinical significance of arteriosclerotic femoral artery aneurysms. *Arch Surg*. 1980;115:502–507.
111. Whitehouse WM Jr., Wakefield TW, Graham LM, Kazmers A, Zelenock GB, Cronenwett JL. Limb threatening potential of arteriosclerotic popliteal artery aneurysms. *Surgery*. 1983;93:694–699.
112. Marin ML, Veith FJ, Panetta TF, Cynamon J, Bakal CW, Suggs WD, Wengerter KR, Barone HD, Schonholz C, Parodi JC. Transfemoral endoluminal stented graft repair of a popliteal artery aneurysm. *J Vasc Surg*. 1994;19:754–757.

113. Freeman NE, Leeds FH, Elliot WG, Roland SI. Thromboendarterectomy for hypertension due to renal artery occlusion. *J Am Med Assoc*. 1954;156:1077–1079.
114. Wylie WJ, Perloff DL, Stoney RJ. Autogenous tissue revascularization techniques in surgery for renovascular hypertension. *Ann Surg*. 1969;170:416–428.
115. Stanley JC. Surgical treatment of renovascular hypertension. *Am J Surg*. 1997;174:102–110.
116. Stoney RJ, DeLuccia N, Ehrenfeld WK, Wylie WK. Aortorenal arterial autografts: Long-term assessment. *Arch Surg*. 1981;116:416–422.
117. DeCamp PT, Snyder GH, Bost RB. Severe hypertension due to congenital stenosis of artery to solitary kidney: Correction by splenorenal arterial anastomosis. *Arch Surg*. 1957;75:1023–1026.
118. Bookstein JJ, Abrams HD, Buenger RE, Reiss MD, Lecky JW, Franklin SS, Bleifer KH, Varady PD, Maxwell MH. Radiologic aspects of renovascular hypertension. Part 2. The role of urography in unilateral renovascular disease. *J Am Med Assoc*. 1972;220:1225–1230.
119. Bookstein JJ, Abrams HL, Buenger RE, Reiss MD, Lecky JW, Franklin SS, Bleifer KH, Varady PD, Maxwell MH. Radiologic aspects of renovascular hypertension. Part 3. Appraisal of arteriography. *J Am Med Assoc*. 1972;221:368–374.
120. Bookstein JJ, Maxwell MH, Abrahams HL, Buenger RE, Lecky J, Franklin SS. Cooperative study of radiologic aspects of renovascular hypertension: Bilateral renovascular disease. *J Am Med Assoc*. 1977;237:1706–1709.
121. Foster JH, Maxwell SS, Bleifer KH, Trippel OH, Julian OC, DeCamp PT, Varady PD. Renovascular occlusive disease: Results of operative treatment. *J Am Med Assoc*. 1975;231:1043–1048.
122. Franklin SS, Young JD, Maxwell MH, Foster JH, Palmer JM, Cerny J, Varady PD. Operative morbidity and mortality in renovascular disease. *J Am Med Assoc*. 1975;231:1148–1153.
123. Foster JH, Dean RH, Pinkerton JA, Rhamy RL. Ten years experience with surgical management of renovascular hypertension. *Ann Surg*. 1973;177:755–766.
124. Ernst CB, Stanley JC, Marshall FF, Fry WJ. Autogenous saphenous vein aortorenal grafts: A ten-year experience. *Arch Surg*. 1972;105:855–864.
125. Harrison EG Jr., McCormack LJ. Pathology classification of renal arterial disease in renovascular hypertension. *Mayo Clin Proc*. 1971;46:161–167.
126. Stanley JC, Gewertz BL, Bove EL, Sottiurai V, Fry WJ. Arterial fibrodysplasia: Histopathologic character and current etiologic concepts. *Arch Surg*. 1975;110:551–556.
127. Gruntzig A, Kuhlmann U, Vetter W, Lutolf U, Meier B, Siegenthaler W. Treatment of renovascular hypertension with percutaneous transluminal dilatation of a renal-artery stenosis. *Lancet*. 1978;1:801–802.
128. Cooper CJ, Murphy TP, Cutlip DE, Jamerson K, Henrich W, Reid DM, Cohen DJ, for the CORAL Investigators. Stenting and medical therapy for atherosclerotic renal-artery stenosis. *N Engl J Med*. 2014;370:13–22.
129. Klass J. Embolectomy in acute mesenteric occlusion. *Ann Surg*. 1951;134:913–917.
130. Shaw RS, Maynard EP. Acute and chronic thrombosis of the mesenteric arteries associated with malabsorption: Report of two successful cases treated by thromboendarterectomy. *N Engl J Med*. 1958;258:874–878.
131. Mikkelsen WP, Zaro JA. Intestinal angina: Report of a case with preoperative diagnosis and surgical relief. *N Engl J Med*. 1959;260:912–914.
132. Furrer J, Gruntzig A, Kugelmeier J, Goebel N. Treatment of abdominal angina with percutaneous dilatation of an arteria mesenterica superior stenosis. *Cardiovasc Intervent Radiol*. 1980;3:43–44.
133. Deterling RA. Aneurysm of the visceral arteries. *J Cardiovasc Surg*. 1971;12:309–322.
134. Stanley JC, Thompson NW, Fry WJ. Splanchnic artery aneurysms. *Arch Surg*. 1970;101:689–697.
135. Fisher M. Occlusion of the internal carotid artery. *Arch Neurol Psychiatry*. 1951;65:346–377.
136. Carrea R, Molins M, Murphy G. Surgical treatment of spontaneous thrombosis of the internal carotid artery in the neck: Carotid-carotideal anastomosis: Report of a case. *Acta Neurol Latinoamer*. 1955;I:71–78.
137. Eastcott HHG, Pickering GW, Rob CG. Reconstruction of internal carotid artery in a patient with intermittent attacks of hemiplegia. *Lancet*. 1954;2:994–996.
138. DeBakey ME. Successful carotid endarterectomy for cerebrovascular insufficiency: nineteen year follow-up. *J Am Med Assoc*. 1975;233:1083–1085.
139. Davis JB, Grove WJ, Julian OC. Thrombotic occlusion of the branches of the aortic arch, Martorell's syndrome: Report of a case treated surgically. *Ann Surg*. 1956;144:124–126.
140. Crawford ES, DeBakey ME, Fields WS. Roentgenographic diagnosis and surgical treatment of basilar artery insufficiency. *J Am Med Assoc*. 1958;168:514.
141. Lyons C, Galbraith G. Surgical treatment of atherosclerotic occlusion of the internal carotid artery. *Ann Surg*. 1957;146:487–498.
142. DeBakey ME, Morris GC, Jordan GL, Cooley DA. Segmental thrombo-obliterative disease on branches of aortic arch. *J Am Med Assoc*. 1958;166:998–1003.
143. Yasargil MC, Krayenbuhl HA, Jacobson JH II. Microneurosurgical arterial reconstruction. *Surgery*. 1970;67:221–233.
144. Extracranial intracranial Bypass Study Group. Failure of extracranial-intracranial anterior bypass to reduce the risk of ischemic stroke. *N Engl J Med*. 1985;313:1191–1200.

145. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med*. 1991;325:325–453.
146. Barnett HJ, Taylor DW, Eliasziw M et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. *N Engl J Med*. 1998;339:1415–1425.
147. European Carotid Surgery Trialists' Collaborative Group. MRC European carotid surgery trial: Interim results for symptomatic patients with severe (70–99%) or with mild (0–29%) carotid stenosis. *Lancet*. 1991;337:1235–1243.
148. The Veterans Affairs Cooperative Studies Program 309 Trialist Group, Mayberg MR, Wilson SF, Yatsu F, Weiss DG, Messina L, Hershey LA. Carotid endarterectomy and prevention of cerebral ischemia in symptomatic carotid stenosis. *J Am Med Assoc*. 1991;266:3259–3295.
149. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. *J Am Med Assoc*. 1995;273:1421–1428.
150. The Veterans Affairs Cooperative Study Group, Hobson RW II, Weiss DG, Fields WS, Goldstone J, Moore WS, Towne JB, Wright CB. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. *N Engl J Med*. 1993;328:221–227.
151. Mathias K. A new catheter system for percutaneous transluminal angioplasty (PTA) of carotid artery stenoses. *Fortschr Med*. 1977;95:1007–1011.
152. Yadav JS, Wholey MH, Kuntz RE et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med*. 2004;351:1493–1501.
153. Gurm HS, Yadav JS, Fayad P et al. Long-term results of carotid stenting versus endarterectomy in high-risk patients. *N Engl J Med*. 2008;358:1572–1579.
154. Bachman DM, Kim RM. Transluminal dilatation for subclavian steal syndrome. *Am J Roentgenol*. 1980;135:995–996.
155. Mathias K, Staiger J, Thron A, Spillner G, Heiss HW, Konrad-Graf S. Percutaneous transluminal dilation of the subclavian artery. *Dtsch Med Wochenschr*. 1980;105:16–18.
156. DeWeese MS, Hunter DC Jr. A vena cava filter for the prevention of pulmonary emboli. *Bull Soc Int Chir*. 1958;1:1–19.
157. DeWeese MS, Kraft RO, Nichols KW. Fifteen-year clinical experience with vena cava filter. *Ann Surg*. 1973;173:247–257.
158. Mobin-Uddin K, Smith PE, Martinez LD, Lombardo CR, Jude JR. A vena cava filter for the prevention of pulmonary embolus. *Surg Forum*. 1967;18:209–211.
159. Mobin-Uddi K, McLean R, Bolooki H et al. Caval interruption for prevention of pulmonary embolism: Long-term results of a new method. *Arch Surg*. 1969;99:711–715.
160. Greenfield LJ, Peyton MD, Brown PP, Elkins RC. Transvenous management of pulmonary embolic disease. *Ann Surg*. 1974;180:461–468.
161. Kunlin J. The reestablishment of venous circulation with grafts in cases of obliteration from trauma or thrombophlebitis. *Mem Acad Clin*. 1953;79:109.
162. Palma EC, Esperon R. Vein transplants and grafts in the surgical treatment of the post phlebitis syndrome. *J Cardiovasc Surg*. 1960;1:94–107.
163. Husni EA. In situ saphenopopliteal bypass graft for incompetence of the femoral and popliteal veins. *Surg Gynecol. Obstet*. 1970;2:279–284.
164. Charnsangavej C, Carrasco CH, Wallace S, Wright KC, Oyawa K, Richli W, Gianturco C. Stenosis of the vena cava: preliminary assessment of treatment with expandable metallic stents. *Radiology*. 1986;161:295–298.
165. Kistner R. Surgical repair of a venous valve. *Straub Clin Proc*. 1968;34:41–43.
166. Kistner R. Surgical repair of the incompetent femoral vein valve. *Arch Surg*. 1975;110:1336–1342.
167. Taheri SA, Lazar L, Elias S, Marchand P, Heffner R. Surgical treatment of postphlebitic syndrome with vein valve transplant. *Am J Surg*. 1982;144:221–224.
168. Hauer G. The endoscopic subfascial division of the perforating veins-preliminary report. *Vasa*. 1985;14:59–61.
169. Orbach EJ. Sclerotherapy of varicose veins-utilization of an intravenous air block. *Am J Surg*. 1944;66:362–366.
170. Politowski M, Zelazny T. Complications and difficulties associated with electrocoagulation treatment of varices of lower extremities. *Pol Przegl Chir*. 1966;38:519–522.
171. Bone C. Tratamiento Endoluminal de las Varices con Laser de Diodo: Studio preliminary. *Rev Patol Vasc*. 1999;5:35–46.

2

Pathophysiology of human atherosclerosis

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CONTENTS

Atherosclerosis is a degenerative process of the major human elastic and muscular arteries. It is characterized by the formation of intimal plaques consisting of lipid accumulations, smooth-muscle and inflammatory cells, connective tissue fibres and calcium deposits. Morbidity associated with atherosclerosis arises from plaque enlargement or degeneration. Plaque enlargement may obstruct the lumen, resulting in stenosis and impairment of blood flow. Sudden obstruction of the lumen may result from the dissection of blood from the lumen into or under the plaque or hemorrhage within the plaque from vasa vasorum. Plaque ulceration may result in embolization of plaque elements or thrombus formation on the disrupted intima. Thrombosis may also occlude atherosclerotic vessels without obvious plaque disruption due to local modifications of flow. Finally, atrophy of the media, often associated with atherosclerotic disease, may result in weakening of the artery wall with aneurysmal dilatation, mural thrombosis and rupture.

Atherosclerosis is a generalized disorder of the arterial tree associated with a number of recognized predisposing risk factors, including altered serum lipid and lipoprotein profiles, hypertension, cigarette smoking, diabetes mellitus and lifestyle. However, the clinical expression of atherosclerosis tends to be focal, with clinical symptoms caused by localized interference with circulation occurring in several critical sites. In addition, the morphologic features underlying morbidity and mortality vary somewhat depending on location. In the coronary arteries, for example, stenosis and thrombosis tend to reduce flow or cause sudden catastrophic occlusion, principally at the site of lesion formation, while at the carotid bifurcation, plaque ulceration and thrombosis often cause characteristic symptoms by embolization to distal cerebral vessels. Extensive disease, often with multiple focal occlusive stenoses, is characteristic of peripheral vascular disease of the lower extremities, while aneurysm formation is a major feature of abdominal aortic disease. While there is a large body of descriptive clinical and experimental knowledge with regard to the general appearance of atherosclerotic lesions, the precise initiating and perpetuating pathogenic mechanisms in human beings remain obscure, and the factors which determine human lesion composition, rate of lesion enlargement, lesion organization and lesion disruption remain to be elucidated.

In this chapter, we discuss both the structural features of the artery wall and the hemodynamic factors which may relate to the pathogenesis, localization and disruption of plaques, and we review the principal features of human lesion composition and configuration. These considerations should help to provide insight into the clinical consequences of differences in plaque localization and composition and serve as a basis for the critical evaluation of currently available methods for the quantitative assessment of human lesions.

STRUCTURE OF THE ARTERY WALL

The artery wall consists of three concentric layers or zones. From the lumen outward, these are the intima, the media and the adventitia (Figure 2.1).

Intima

The intima extends from the luminal endothelial lining to the internal elastic lamina. The endothelium is formed by a continuous monolayer of flat, usually elongated polygonal cells, which tend to be aligned in the direction of blood flow. In areas of slow, reversing or nonlaminar flow, endothelial cells tend to assume a less clearly oriented configuration.[1] Edges of adjacent endothelial cells overlap, with the downstream edges of most endothelial cells overriding their immediate downstream neighbours much like the shingles on a roof. Cytoplasmic bridges, surface ridges and microvillus projections as well as interendothelial gaps, stomata or open junctions between endothelial cells have been described. These features are, however, largely absent from vessels which have been fixed while distended and which have not been manipulated prior to fixation.[2] A protein coating, the glycocalyx, overlies the luminal surface. Immediately beneath the endothelium is a closely associated fibrillar layer, the basal lamina. This structure is thought to form a continuous bond between the endothelial cells and the subendothelial connective tissue matrix. Numerous focal attachments are also present between endothelial cells and the underlying internal elastic lamina,[3] while less prominent focal attachments are also formed with other fibres in the intima. The extensive basal lamina provides a supple, pliable junction well adapted to permit bending and changes in diameter or configuration associated with pulse pressure without disruption or detachment of the endothelium. The focal, tight, relatively rigid junctions may prevent downstream slippage or telescoping, which could result from the shear stresses imposed by blood flow. Between the basal lamina and the internal elastic lamina, the intima in most locations normally contains a few scattered macrophages, smooth-muscle cells and connective tissue fibres.

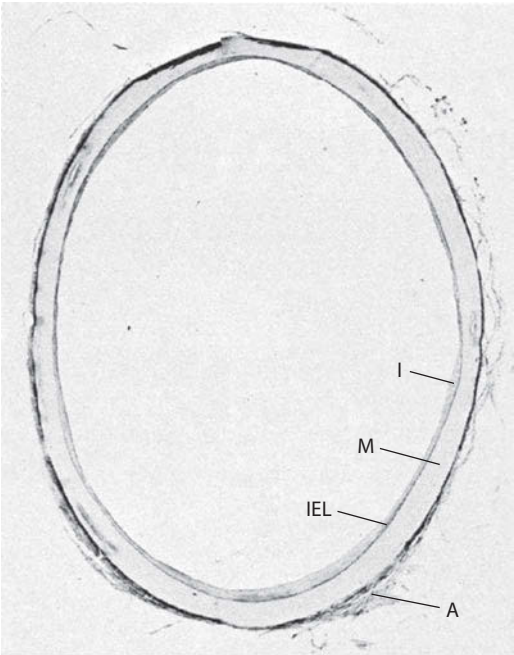

Figure 2.1 Transverse section of a normal human superficial femoral artery. Note intima (I), media (M) and adventitia (A). The intima and media are separated by the internal elastic lamella (IEL).

Since the endothelial cell layer is the immediate interface between the bloodstream and the underlying artery wall, it is subjected to normal forces exerted by blood pressure and to shearing or drag forces resulting from blood flow. Experimentally, imposed shearing stresses in excess of 400 dyn/cm^2 in canine aortas have resulted in morphologic evidence of endothelial injury or disruption and in increased endothelial permeability.[4] Other observations have failed to reveal evidence of endothelial injury in areas normally subjected to comparable or higher levels of shear stress,[5] suggesting that endothelial cells may withstand relatively high shearing stresses without ill effect in some locations (Figure 2.2).

Endothelial cells exposed to continuous high-flow conditions, such as in arteries supplying an arteriovenous fistula, are activated, whereas the endothelial cells in arteries with decreased flow are inactivated. Endothelial activation is characterized by lumen protrusions, increase of cytoplasmic organelles, abluminal protrusions, basement membrane degradation, internal elastic lamina degradation and sproutings in the capillaries. These are ultrastructurally comparable to angiogenesis. Endothelial inactivation is characterized by the decrease of endothelial cell number with apoptosis, which is ultrastructurally comparable to angioregression.[6,11]

The endothelial layer has been considered to function as a thrombosis-resistant surface as well as a selective interface for diffusion, convection and active transport of circulating substances into the underlying artery wall. Endothelial cells play a critical role in the physiology and pathophysiology of vascular disorders.[7] They respond

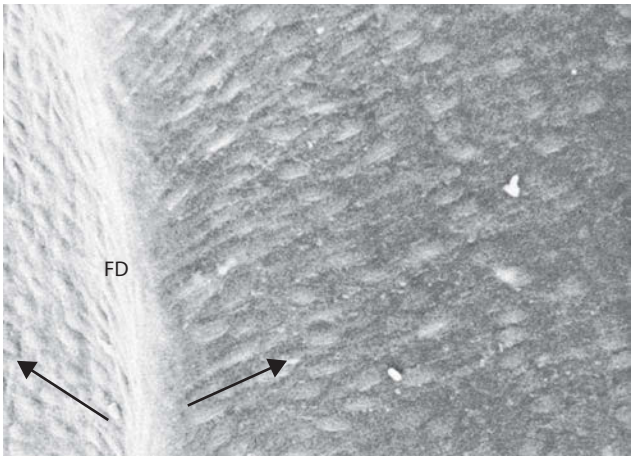

Figure 2.2 Scanning electron micrograph of a monkey aortic ostial flow divider (FD). The FD is an area subjected to high shear stress. The endothelial cells are intact and elongated in the direction of flow with no disruption. Arrows indicate direction of blood flow.

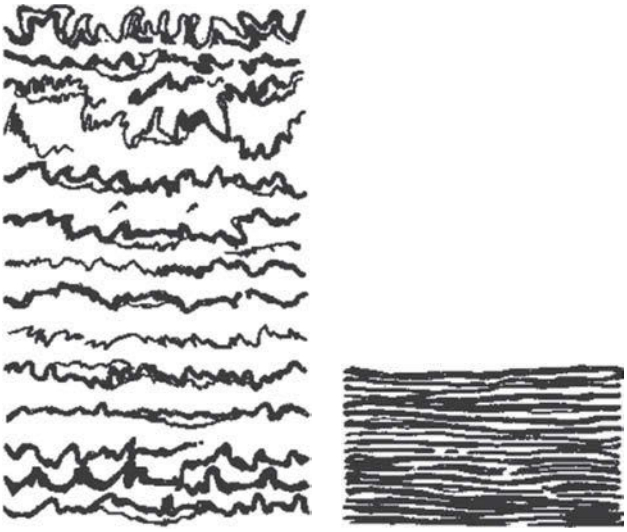

Figure 2.3 Tracing of elastic fibres in transverse sections of rabbit aortic media. (a) A transverse section of a collapsed aorta demonstrating wavy elastic lamellae and increased thickness of each lamellar unit and increased total thickness of the media. (b) A rabbit aorta fixed while distended. Note the straight elastic fibres and thickness of the media.

to hemodynamic stresses and may transduce an atheroprotective force[8] by regulating the ingress, egress and metabolism of lipoproteins and other agents that may participate in intimal plaque initiation and progression.[9,10] Endothelial cells have been shown to participate in an array of metabolic and biosynthetic functions related to thrombosis, prostaglandin formation and smooth-muscle contraction.[11] Detachment of endothelial cells with persistence of the basal lamina does not necessarily result in occlusive thrombus formation. Although a layer of thrombocytes appears to deposit on the denuded basal lamina, large aggregates and fibrin deposits may require the exposure of collagen fibres and other deeper mural components.[12]

Media

The media extends from the internal elastic lamina to the adventitia. Although an external elastic lamina demarcates the boundary between media and adventitia in many vessels, a distinct external elastic lamina may not be present, particularly in vessels with a thick and fibrous adventitial layer. The outer limit of the media can nevertheless be distinguished in nearly all intact arteries, for in contrast to the adventitia, the media consists of closely packed layers of smooth-muscle cells in close association with elastin and collagen fibres. Elastic fibres of the media are predominantly wavy or undulating on cross sections of collapsed arteries but appear as relatively straight bands or lamellae in fully distended vessels (Figure 2.3). The smooth-muscle cell layers are composed of groups of similarly oriented cells, each surrounded by a common basal lamina and a closely associated interlacing basketwork of collagen fibrils, which tighten about the cell groups as the media is brought under tension.[13] This configuration tends to hold the groups of cells together and prevents excessive stretching or slippage. In addition, each cellular subgroup or fascicle is encompassed by a system of similarly oriented elastic fibres. Focal tight attachment sites between smooth-muscle cells and elastic fibres are normally abundant. In the aorta, the juxtaposition of similarly oriented musculoelastic fascicles results in the appearance on transverse sections of layers of continuous elastic lamellae and intervening smooth-muscle layers. In addition to the pericellular network of fine collagen fibrils, thicker, crimped collagen bundles weave between adjacent lamellae. The elastic fibres are relatively extensible and allow for some degree of compliance; they recoil during the cardiac cycle and tend to distribute mural tensile stresses uniformly. The thick collagen fibre bundles provide much of the tensile strength of the media and, because of their high elastic modules, limit distension and prevent disruption (Figure 2.4).

The aortic elastin lamella and its corresponding smooth-muscle layer has been termed a lamellar unit. With increasing mammalian species size, the adult aortic radius increases, with a corresponding increase in medial thickness and in the number of transmural lamellar units (Figure 2.5).[14] The total tangential tension exerted on the wall is closely approximated by the product of the distending pressure and the radius (law of Laplace). Since aortic pressure is similar for most adult mammals and individual medial layers tend to be of similar thickness regardless of

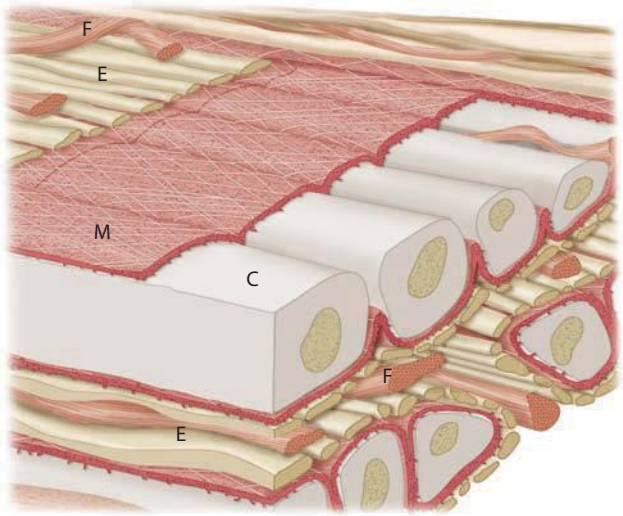

Figure 2.4 Diagrammatic representation of the microarchitecture of the media of the aortic wall. The long axes of the smooth-muscle cells (C) are oriented circumferentially or perpendicular to the long axis of the artery. Each cell is surrounded by a matrix (M) consisting of basal lamina and a fine meshwork of collagen fibrils. Groups or layers of smooth-muscle cells are surrounded by circumferentially oriented elastic fibres (E), which appear as almost continuous sheets on transverse section of the artery. Wavy collagen bundles (F) course between the successive facing elastic fibre layers. (Adapted from Clark JM and Glagov S, *Arteriosclerosis*, 5, 19, 1985. With permission.)

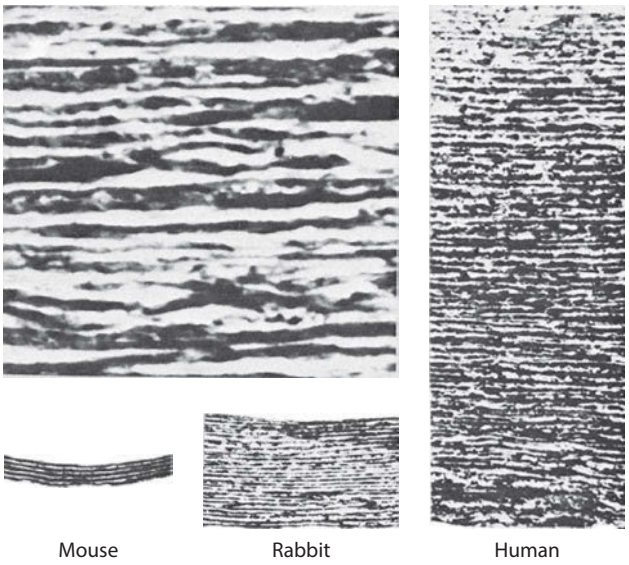

Figure 2.5 Aortic lamellar architecture in three mammals. With increasing species size, the aortic radius increases. There is a corresponding increase in medial thickness due to an increase in the number of medial lamellar units. (A) Higher-power view of transverse section of media demonstrating lamellar architecture.

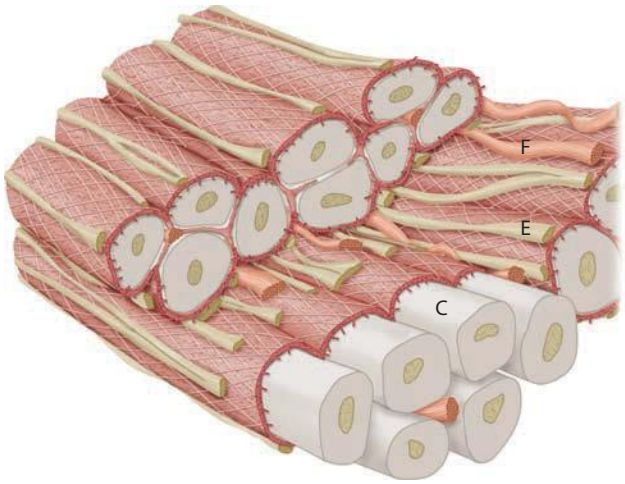

Figure 2.6 Diagrammatic representation of microarchitecture of the wall of a muscular artery. The long axes of the smooth-muscle cells (C) of the media are oriented circumferentially or perpendicular to the long axis of the artery. Cells are surrounded by a matrix of basal lamina and collagen fibrils. Elastin fibre systems (E) are less prominent. Collagen bundles (F) are interspersed. Compared to elastic arteries (see Figure 2.4), muscular arteries have a greater number of smooth-muscle cells and relatively fewer collagen and elastin fibres. (Adapted from Clark JM and Glagov S, *Arteriosclerosis*, 5, 19, 1985. With permission.)

species, there is a very nearly linear relationship between adult aortic radius and the number of medial fibrocellular lamellar units. On the average, the tangential tension per aortic lamellar unit is close to 2000 dyn/cm.

Smaller *muscular arteries* contain relatively less collagen and elastin and more smooth-muscle cells than the aorta and the proximal, larger elastic arteries. The musculoelastic fascicles, which are very prominent in elastic arteries, are also present in muscular arteries and are generally aligned in the direction of the tensile forces (Figure 2.6). However, because of the preponderance of smooth-muscle cells, they are less clearly demarcated and the layering of the media is less distinct.[15] Medial thickness and the number of layers is nevertheless closely related to the radius, and the average tension per layer tends to be constant for homologous vessels in mammals.[16] In addition, the relative proportion of collagen and elastin varies between muscular and elastic arteries. The media of the proximal aorta and that of the major brachiocephalic elastic arteries contain a larger proportion of elastin and a lower proportion of collagen than the abdominal aorta or the distal peripheral vessels.[17] The proximal major vessels are therefore more compliant than the abdominal aorta but also are more friable and prone to tear with suturing.

Medial smooth-muscle cells, in addition to synthesizing the collagen and elastin fibres, which determine the mechanical properties of the aortic wall, are actively engaged in metabolic processes that contribute to wall tone and may be related to susceptibility to plaque formation.[18]

Under conditions of increased pulse pressure, increased wall motion and increased wall tension, which exist proximal to an aortic coarctation, medical smooth-muscle cell metabolism is increased, as is plaque formation.[19] Conversely, when wall motion, pulse pressure and smooth-muscle cell metabolism are decreased, as in areas distal to a severe arterial stenosis, intimal plaque formation is inhibited, despite the continued presence of strong atherogenic stimuli such as marked hyperlipidemia.[20] In vitro studies have revealed that cyclic stretching of smooth-muscle cells grown on elastin membranes results in increased biosynthetic activity,[21] and acute arterial injury experiments have revealed that an intact, metabolically active media may be required for intimal plaque formation.[22] The composition and microarchitecture of the media are designed to ensure stability, whereas the metabolic state of the media appears to be an important factor in the pathogenesis of atherosclerotic lesions.

Adventitia

Although the boundary between media and adventitia is usually distinct, even in the absence of a well-defined external elastic lamina, the outer limit of the adventitia may be difficult to identify, for it is often continuous with the surrounding perivascular connective tissues. Although the aorta and pulmonary trunk are normally invested by relatively little adventitial fibrous connective tissue and are closely associated with mediastinal or retroperitoneal adipose tissue and lymph nodes, the adventitia of some of the major arteries, such as the renal and mesenteric branches, are composed of prominent layers of elastic and collagen fibres and may be thicker than the associated media. Compared to the media, cells in the adventitia are relatively sparse and most are fibroblasts. For the normal aorta, removal of the adventitia has little effect on static pressure–volume relationships. In muscular arteries, however, where connective tissue fibres are relatively sparse in the media and smooth-muscle contraction may regulate vessel diameter and play a role in maintaining circumferential tensile support, a thick, structured adventitia may serve to provide significant tethering and axial tensile support, prevent excessive dilatation and dampen the cyclic changes in tangential tension associated with the pulse pressure wave. In instances where a large, intimal atherosclerotic plaque overlies an atrophic media, a thickened adventitia may be the principal mural structural component of the artery wall (see Figure 2.7). During carotid or femoral endarterectomy, the entire intima and extensive portions of remaining media may be removed, leaving only the adventitia to provide support.

The adventitia is also the primary source of vasa vasorum and may play a prominent role in arteritis and periaortitis[23] as well as in the inflammatory component of atherosclerosis.[24] Adventitial responses may also be important in the artery wall response to balloon injury and angioplasty.[25,26]

Figure 2.7 Transverse section of superficial femoral artery. Note the prominent adventitial (A) thickening and vasa vasorum (arrow) penetrating through media (M) into plaque (P).

ARTERY WALL NUTRITION

The adventitia of all of the major elastic and muscular arteries contains vasa vasorum – i.e., small arteries, arterioles, capillaries and venous channels – which are presumed to participate in the nutrition of the artery wall. Except for the aorta, however, precise relationships among vasa supply, vessel location, diameter, wall thickness and architecture have not been established. The aortic media is nourished directly from the lumen and may also be perfused by means of vasa vasorum from the adventitial side. Passage through the lining endothelium is apparently sufficient to nourish the inner 0.5 mm of the adult mammalian aortic media, which corresponds to approximately 30 medial fibrocellular layers.[27] Thus, the aortic media of a small mammal such as the rat or rabbit, which is less than 0.5 mm thick and has fewer than 30 medial lamellar layers, contains no medial vasa vasorum and is nourished largely from the intimal side. Large mammals such as pigs, sheep and horses have an aortic media with more than 30 medial lamellar layers. The inner 30 aortic layers in such species are avascular, but the remaining outer medial lamellar units contain vasa vasorum (Figure 2.8). Aortic vasa vasorum arise from major arterial branches close to their origins and usually enter the media at right angles. Within the media, the vasa tend to be oriented axially in

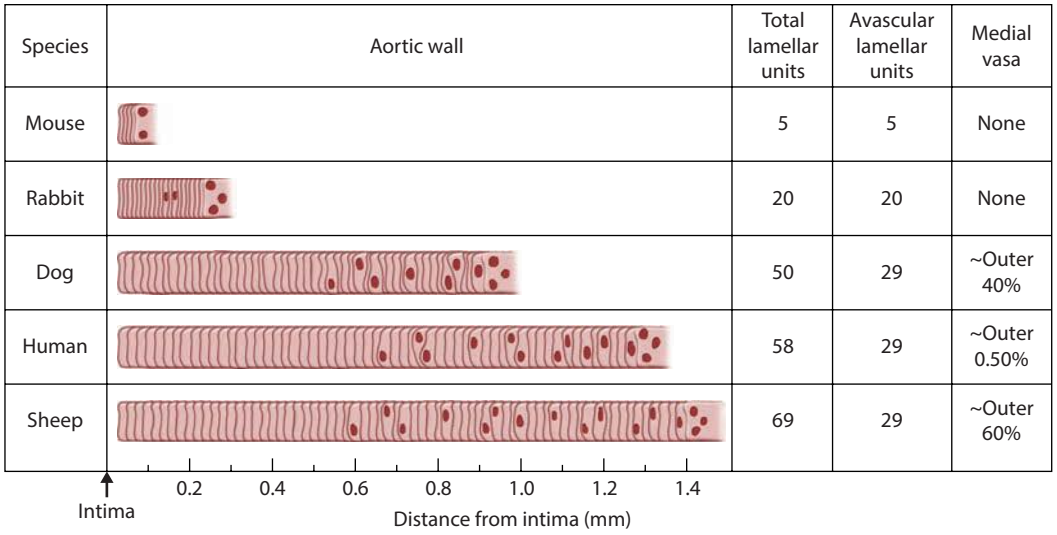

Figure 2.8 Relationship between aortic medial lamellar architecture and vasa vasorum blood supply to outer portion of the media in different species. (Reproduced from Glagov S, Hemodynamic risk factors: Mechanical stress, mural architecture, medial nutrition and the vulnerability of arteries to atherosclerosis, in: Wissler RW and Geer JC, eds., *The Pathogenesis of Atherosclerosis*, Williams & Wilkins, Baltimore, MD, 1972, pp. 166–199. With permission.)

several branching levels. The average tension per medial lamellar unit for aortas that contain medial vasa tends to be somewhat higher than for aortas without vasa, suggesting that the presence of nutritive vessels within the media permits each lamellar unit to function at a somewhat higher level of tensile stress. The human abdominal aorta appears to be exceptional when compared to aortas of other mammals, since it is more than 0.5 mm thick but contains fewer than 30 layers.[28] It is not furnished with medial vasa vasorum, although the estimated tensile stress per layer is in the range of those aortas with medial vasa (Figure 2.9). The implication of this situation with respect to atherosclerosis and aneurysm formation is discussed in the following text. Although mural stresses and deformations associated with hypertension may impair medial vasal flow,[29] the details of aortic media microarchitecture, which permit intramural vasa vasorum to remain open under normal conditions despite the cyclic

Comparison of human thoracic and abdominal aorta

	Diameter (mm)	Wall thickness (cm)	Lamellar units (LU)		Tension		
			Number	Thickness (mm)	Total (dyn/cm)	Per LU (dyn/cm)	Stress (dyn/cm^2)
Thoracic	17	9.5×10^{-2}	56	0.017	117,000	2095	122×10^4
Abdominal	13	7.3×10^{-2}	28	0.026	89,000	3180	122×10^4

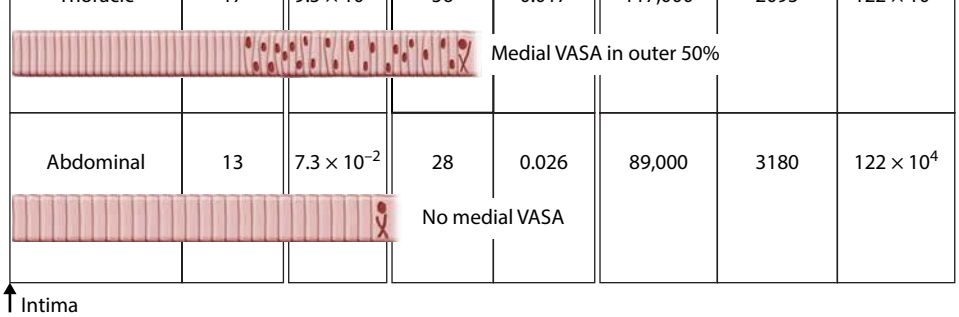

Figure 2.9 The human thoracic aorta has medial vasa vasorum in the outer lamellae, and each lamellar unit supports approximately 2095 dyn/cm. The human abdominal aorta, however, has 28 lamellar units and has no medial vasa, and each lamellar unit supports about 3180 dyn/cm. This architectural difference may be important in the vulnerability of the abdominal aorta to atherosclerosis and aneurysm formation. (Reproduced from Glagov S, Hemodynamic risk factors: Mechanical stress, mural architecture, medial nutrition and the vulnerability of arteries to atherosclerosis, in: Wissler RW and Geer JC, eds., *The Pathogenesis of Atherosclerosis*, Williams & Wilkins, Baltimore, MD, 1972, pp. 166–199. With permission.)

compressive and shearing stresses within the artery wall, have not been clarified. Vasa vasorum have been identified in atherosclerotic arteries and, in particular, within atherosclerotic plaques. Although vasa vasorum in atherosclerotic plaques have been supposed to underlie disruptive lesion hemorrhages,[30] relationships among lesion size, composition and complications and the presence of vasa vasorum are not clear.

AGE-RELATED CHANGES IN THE ARTERY WALL

Focal intimal thickenings, including cushions or pads at or near branch points, have been observed in infants and fetuses. Many of these tend to be modified and incorporated into the media during growth, and most are therefore likely to represent local changes in vessel wall organization related to redistributions of tensile stress associated with developmental changes in diameter, length and geometric configuration.[31]

Progressive fibrocellular diffuse intimal thickening, on the other hand, proceeds from infancy to old age, differing considerably in both extent and degree in different locations in the arterial tree.[32,33] This process tends to be more or less uniform about the vessel circumference and is not limited to areas about branch ostia, bifurcations or the inner aspects of curves. Although the component cells tend to be oriented axially in straight portions of arteries, the organization and composition of thickened intima resemble to some extent that of the underlying media (Figure 2.10). The lumen may not, however, be significantly narrowed by this process, for, while the condition may produce an artery wall with an intima thicker than the media, the process tends to be concentric, accumulation of lipid is not a prominent feature, there is no focal stenosis and the vessel lumen may actually be larger than normal. Diffuse intimal thickening is, nevertheless, especially evident in those vessels that tend to be susceptible to clinically significant atherosclerotic disease.[34] There is, however, little evidence to indicate that diffuse intimal thickening is necessarily a precursor of the formation of atherosclerotic lesions. With advancing age, the internal elastic lamina of the aorta and of the large arteries may show gaps, splits and fragmentation as well as calcium salt deposits. In addition, neoformation of elastin within the thickened intima or in plaques may result in the accumulation of many layers of elastic fibres in the intima.

In general, arteries tend to increase in diameter, elongate and become tortuous with age. Age-related changes include intimal and medial thickening, arterial calcification and increased deposition of matrix substances, thus leading to increased wall stiffness that significantly contributes to an increase in systolic blood pressure.[35]

Diffuse, apparently irreversible enlargement, when marked, is called ectasia. The common form of diffuse and extensive ectasia of the aorta and large arteries parallels a relative overall increase in matrix fibre accumulation,[36]

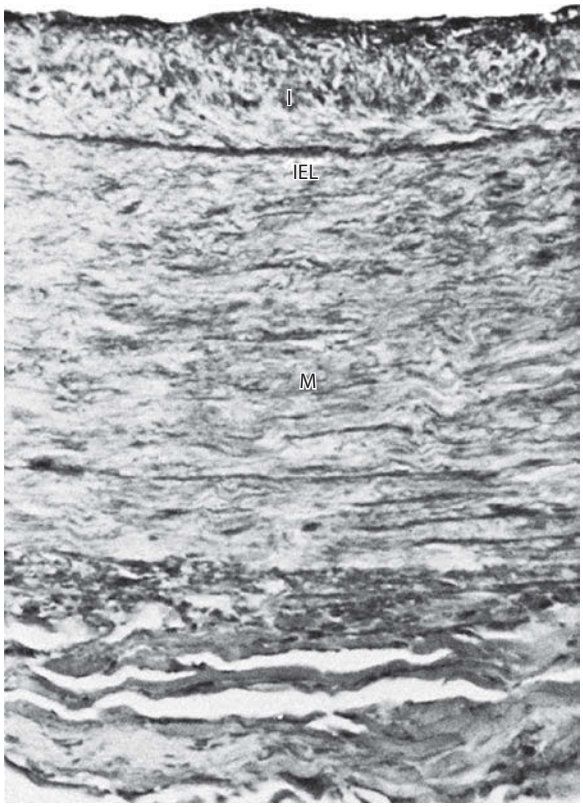

Figure 2.10 Transverse section of coronary artery of an 18-year-old accident victim demonstrating diffuse intimal thickening (I). Note that the organization and composition of the thickened intima resembles the underlying media (M). IEL represents the internal elastic lamina.

including an increase in collagen content, a decrease in elastin content, a calcification of the elastic fibres and a decrease in compliance of the wall. While elongation and tortuosity of the vessel may be quite marked, the diffuse and extensive form of moderate ectasia is not necessarily associated with serious consequences. When complications occur, they are generally attributable to associated atherosclerosis and/or the formation of aneurysms.[37]

STRUCTURE OF ATHEROSCLEROTIC LESIONS

Atherosclerotic lesions may begin in childhood or adolescence and enlarge progressively over years or decades without associated symptoms. Although intimal plaques are evident in arteries of nearly all adults coming to autopsy in much of the world, little is known concerning the factors which determine individual differences in plaque morphology or govern the gradual or sudden transition from asymptomatic plaques to those which enlarge sufficiently to cause obstruction to flow, ulcerate or induce occlusive thrombosis or aneurysm formation. On the basis of morphologic appearance and composition, human lesions are usually classified as *fatty streaks* or fibrous 'raised' *plaques*. Transitional forms have also

been identified. While fatty streaks are not associated with symptoms, raised plaques are more complex and are associated with the alterations which underlie circulatory compromise.

Fatty streaks

Fatty streaks are relatively flat, fairly well-demarcated patches or minute yellow foci which may appear soon after birth and are seen on the luminal surface of most aortas of individuals over the age of 3 years (Figure 2.11).[38] Fatty streaks are found with increasing frequency between the ages of 8 and 18, becoming most numerous around puberty. These formations are not, however, limited to young persons and may be seen at any age adjacent to or even superimposed upon fibrous plaques. Fatty streaks consist largely of intimal lipid-laden cells (foam cells) and variable quantities of matrix materials beneath an intact endothelium. The extent to which fatty streaks are precursors of subsequent complex, fibrous, progressive atherosclerotic lesions remains unresolved.[39] There is evidence that many human fatty streaks may be evanescent, for the distribution of fatty streaks seen in young individuals does not coincide entirely with the distribution of fibrous plaques seen later in life. It has also been found that cells in human fatty streaks are not monotypic with respect to isoenzyme content[40] but that advanced lesions are composed of cells which contain extensive regions of cellular monotypia.[41] These findings have suggested that focal events occurring in some fatty streaks may result in cellular proliferation with the persistence of lesions and the subsequent formation of the more complex fibrous plaques, while other fatty streaks resolve.

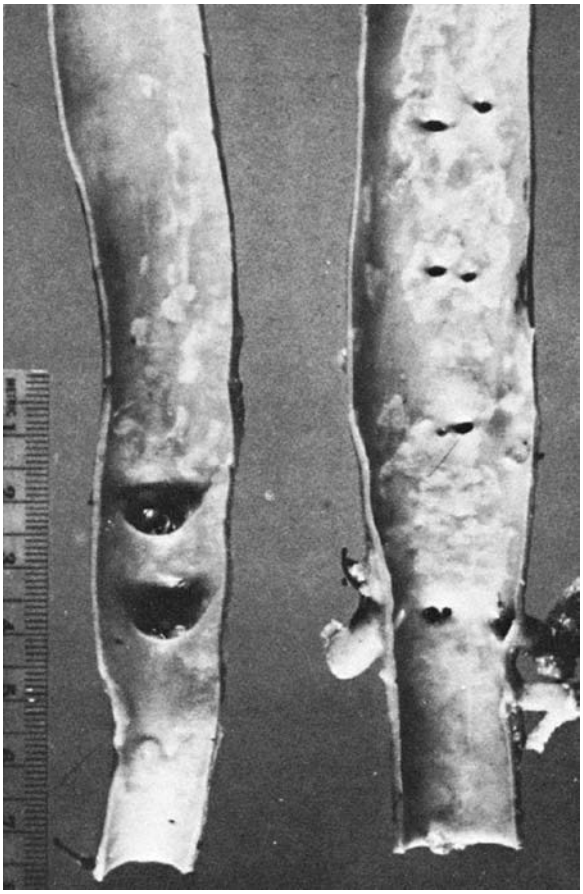

Figure 2.11 Fatty streaks in aorta of 45-year-old patient.

Intimal thickening can reflect an adaptive response to diminish lumen calibre under conditions of reduced flow or can be a response designed to augment wall thickness when tensile stress increases.[42,43] Focal intimal thickenings have been observed in infants and fetuses at or near branch points and probably represent local remodelling of vessel wall organization related to growth and the associated redistribution of tensile stress.[44] Diffuse fibrocellular intimal thickening can occur as a more generalized phenomenon without a clear relationship to branches or curves and may result in a diffusely thickened intima that is considerably thicker than the media. Lipid accumulation is not a prominent feature in such intimal thickening, and the lumen remains regular and normal or slightly larger than normal in diameter.[33] Although there is little direct evidence that diffuse intimal thickening is a precursor of lipid-containing atherosclerotic plaques, both intimal thickening and plaques tend to occur in similar locations, and intimal thickening is most evident in vessels that are especially susceptible to atherosclerosis.[34,45] Evidence has also been presented that diffuse forms of intimal thickening do not develop uniformly and that foci of relatively rapid thickening undergo dystrophic changes, which give rise to necrosis and other features characteristic of plaques.[46] The relationship of these findings to usual atherosclerosis remains to be defined.

Fibrous plaques

Fibrous plaques do not usually appear until the second decade of life and may not become the predominant lesion type until the fourth decade. The endothelial lining appears to be intact over most uncomplicated lesions, i.e., lesions without evidence of disruption, ulceration, hemorrhage or thrombus formation. Although plaque composition varies considerably with respect to the relative proportions of the usual lesion components, a predominant mode of composition and organization can be discerned. There is frequently a relatively compact zone of connective tissue fibres and smooth-muscle cells immediately beneath the endothelium known as the fibrous cap (Figure 2.12). Deeper in the central portion of the plaque and beneath the fibrous cap is a zone of variable composition and consistency known as the *necrotic core* or *centre*. It contains amorphous debris, lipid-containing cells with morphologic and functional characteristics of either smooth-muscle cells or macrophages,[47] extracellular lipids including droplets and cholesterol crystals,