

# 1) Disorders of the Arterial System – Dr. Amanj

## I. ANATOMY

Blood is delivered from the heart to the organs and tissues by the arterial system.

Arteries may be categorized as large, medium-sized, or small. The smallest Arteries that connects to the capillaries are termed arterioles.

The histologic characteristics of the arterial wall are largely dependent on the size of the vessel. The large arteries must withstand the greatest stress and pressure and therefore contain considerable elastic tissue in their walls. The medium-sized arteries have less elastic tissue and more smooth muscle. At the level of the arteriole, elastic tissue is scant or absent. Collagen is present in all parts of the arterial system, the collagen ratio becoming dominant as the arteries become smaller.

Collateral circulation is of primary importance in all aspects of medicine, particularly in surgery. All organs have some collateral circulation, although it varies greatly in different tissues and organs. The subclavian artery can usually be ligated safely in the first portion, such as in the performance of a subclavian-pulmonary anastomosis for congenital cyanotic heart disease (Blalock operation), since the collateral circulation around the shoulder is excellent. Moreover, three of the four major arterées of the stomach (the left and right gastric and the left and right gastric epiploic) can be ligated without significant ischemia.

Some arteries, such as the coronary, renal, and retinal arteries, have an inadequate natural collateral circulation. Acute occlusion of these vessels is usually followed by serious ischemia or infarction, and such arteries are referred to as end arteries.

Time involved in occlusion of an artery is of considerable significance. For example, with slow, progressive occlusion of an artery, there is ample time for collateral vessels to develop and become larger. (that is why more damages occur in acute occlusions than in acute on chronic occlusions)

## II. PHYSIOLOGY OF THE ARTERIAL SYSTEM

The normal arterial wall consists of three layers: the intima, the media, and the adventitia. Endothelial cells are a confluent monolayer of thin, flattened, rhomboid-shaped cells lining the intimal surface of all blood vessels. Smooth muscle cells are found within the media in association with a matrix of connective tissue components (collagen, elastin, and occasional fibroblasts). The intima consists of a single layer of endothelial cells resting on a thin basal lamina. The intima and media are separated by a definite basal lamina in arteries; the demarcation between the intima and the media is less clearly defined in veins. There is a very slow turnover of both endothelial and medial smooth muscle cells in uninjured vessels.

In the adult human, the net mass of the endothelium is equivalent to approximately 1% of body mass and has a surface area of approximately 5000 sq. m. In many respects, the endothelium fulfills all the definitions of an organ, and perhaps it should be considered as such. Normal endothelial cells maintain a delicate balance in the vasculature between:

1. Growth promotion and inhibition,
2. Vasoconstriction and vasodilation,
3. Blood cell adherence and nonadherence,
4. Anticoagulation and procoagulation.

In these ways, the endothelium controls vasomotor tone, regulates vascular structure, maintains blood fluidity, and mediates both inflammatory and immunologic responses.

Smooth muscle cells are the principal cells found in the media of a vessel. They are embedded in a matrix of connective tissue elements and provide mechanical and structural support to the vessel. Physiologically active smooth muscle cells and the extracellular matrix provide intrinsic vascular dimensions and tone. In addition to their vasoreactive characteristics, smooth muscle cells are capable of synthesizing and secreting elements of the extracellular matrix, particularly proteoglycans. The biologic roles of the proteoglycans are diverse, including mechanical support functions, cell adhesion, motility, and proliferation.

## **MAINTENANCE OF VASCULAR TONE**

Seven families of compounds have been associated with endothelium-mediated vasomotor responses: prostanoids, nitric oxide (NO) and nitric oxide-containing compounds, oxygen free radicals, endothelins, angiotensins, smooth muscle cell hyperpolarization factors, and other, as yet uncharacterized, endothelium-derived constriction factors.

## **COAGULATION**

The endothelium plays a role in both the procoagulant and anticoagulant pathways. It synthesizes several factors: protein S, factor V, tissue factor, plasminogen activators (PAs), and plasminogen activator inhibitors (PAIs); in addition, the endothelium contributes to the proteoglycan pool, which influences coagulation and regulates platelet activation and adherence by producing prostacyclin (PGI<sub>2</sub>), nitric oxide (NO), and thromboxane A<sub>2</sub> (TXA<sub>2</sub>).

## **INFLAMMATORY AND IMMUNOLOGIC RESPONSES**

Due to its strategic position, the endothelium is important in the mediation and modulation of both inflammatory and immunologic responses. The process of cell adherence, cell activation, and cell migration involves an interplay between the expression of adhesion molecules by the endothelial cells, leukocyte activation, and local cytokine activity.

## **VASCULAR WALL MODELING**

In addition to the variety of extracellular matrix proteins that are produced by the endothelium, the endothelial cells also produce several regulatory substances that can be either growth promoting or growth inhibiting. Endothelial cells synthesize platelet-derived growth factor (PDGF), basic fibroblast growth factor (bFGF), and insulin-like growth factor 1 (IGF-1). The best characterized growth factor is PDGF, which is composed of the two polypeptide chains A and B.

## **ARTERIAL SUBSTITUTES**

### **INTRODUCTION:**

The explosive growth in arterial surgery over the last 45 years has in large part been dependent on the increased use of arterial substitutes. It has been estimated that in the United States alone, over 350,000 synthetic arterial grafts are implanted each year; the number of peripheral autogenous vein grafts exceeds 200,000 per year. This large use of arterial grafts indicates that development of the optimal arterial substitute is of great clinical importance. However, critical review of the present results of arterial grafting leads to the conclusion that the ideal arterial substitute has not yet been developed.

The optimal arterial substitute **should**:

- (1) be strong, inexpensive, and capable of lasting the life of the patient;
- (2) be easily and permanently attachable to the host vessel;
- (3) be biocompatible with the host and have a nonthrombogenic luminal surface;
- (4) resist infection;
- (5) be readily available in appropriate sizes;
- (6) remain patent without subsequent intervention; and
- (7) have viscoelastic properties similar to those of a normal artery.

An ideal vascular graft **should not**

- (1) leak blood or serous fluid with restoration of flow;
- (2) degenerate chemically or physically with time;
- (3) incite an abnormal proliferative response from the native vessel or surrounding tissue;
- (4) promote thrombus formation or be a source of embolic material;
- (5) occlude when flexed; or
- (6) damage blood components.

No currently available arterial substitute approaches these requirements; hence the large amount of clinical and basic research devoted to the development and evaluation of vascular grafts.

## HISTORICAL ASPECTS

In 1906, Carrel and Guthrie first reported successful implantation of venous autografts into the arterial systems of dogs. They observed that these autografts underwent rapid structural change consisting primarily of a marked thickening of the connective tissue in the adventitia and media. They also noted improved patency when the calibers of the vein and the artery to which it was anastomosed were similar. This was soon followed by clinical use of the popliteal vein for arterial reconstruction after popliteal aneurysm excision by Goyanes in 1906.

The first use of a saphenous vein graft in popliteal artery reconstruction after popliteal aneurysm excision in the United States was by Bernheim in 1915.

The first successful arterial allograft was reported by Hoepfner in 1903.

## EVALUATION OF ARTERIAL SUBSTITUTES

Patency is the most important end-point in the evaluation of the clinical performance of any arterial substitute.

It is critical to distinguish between primary and secondary patency and assisted primary patency.

- **Primary patency** is that achieved without any additional graft-directed procedures.
- **Secondary patency** refers to grafts that have been maintained patent by one or more additional graft-directed procedures, regardless of whether the graft thrombosed prior to revision. If a later operation involves only the inflow or outflow of the graft and not the anastomoses of the graft or the graft itself, the graft may still be regarded as primarily patent.
- **Assisted primary patency**, a disputed term in limited use, refers to secondarily patent grafts that undergo revision prior to actual graft thrombosis.

The concepts of primary, assisted primary, and secondary patency are all important. Primary patency reflects the natural history of individual arterial substitutes. Secondary patency is an indicator of the long-term functional effectiveness of a graft. Assisted primary patency has come to be an indicator of the effectiveness of a clinical follow-up program to detect failing grafts prior to thrombosis. Clearly, however, primary patency is the most important factor in assessing the true overall value of a graft.

## ALLOGRAFTS

### Arterial Allografts

Arterial allografts were the first widely used arterial substitutes. Early results were encouraging, and it was soon recognized that tissue viability was not essential for successful grafting, provided the vessels were properly preserved. This realization, in combination with increasing demand for allografts, led to the establishment of human arterial banks in the late 1940s, freeze-drying being the most popular method of allograft preservation.

Arterial allografts rapidly lose endothelium. A platelet-fibrin coagulum forms on the exposed basement membrane and slowly undergoes fibrous organization. This process begins in anastomotic sites and is frequently incomplete in the central area of the allograft, leaving this area permanently covered with only a fibrin coagulum and prone to ulceration.

Allograft walls become less cellular with time. Progressive thinning of the wall, with loss of collagen and fragmentation of elastic fibers, typically occurs after several years. Similar degenerative changes affect both muscular and elastic arterial allografts, but they occur much more rapidly with the former. Thus, allografts of the aorta, composed predominantly of collagen and elastin, have been associated with fewer complications (thrombosis, calcification, aneurysm formation, rupture) and longer graft function than femoral artery allografts, which contain a large component of smooth muscle and elicit a more prominent rejection reaction. However, with the exception of short segment repairs for aortic coarctation, even aortic allografts have disappointing long-term results. They have a high closure rate after only a few years, occasionally accompanied by dilatation and/or rupture.

With the high incidence of complications, arterial allografts have been abandoned in favor of more satisfactory arterial substitutes. Allografts, however, occupy an important place in the history of vascular surgery.

## **Saphenous Vein Allografts**

Saphenous vein allografts from human cadavers generally have proved unsatisfactory in clinical practice. Initial encouraging reports were quickly overwhelmed by numerous studies demonstrating a high failure rate in the first postoperative year, as well as late aneurysmal degeneration.

Like arterial allografts, venous allografts are normally antigenic and elicit an immunologic rejection response by the host. Microscopic analysis of failed saphenous vein allografts reveals areas of wall necrosis and intimal disruption.

Cryopreservation alone does not alter allograft immunogenicity, and the suggestion by some that cryopreservation may enhance vein allograft function has not been confirmed. However, the ability to preserve veins, coupled with advances in immunosuppression, may eventually lead to the establishment of practical antigen-defined allograft vein banks.

Currently, however, saphenous vein allografts have no significant clinical application. The only vascular allograft that has enjoyed widespread use is the umbilical vein allograft.

## **Umbilical Vein Allografts**

Umbilical vein allografts have been used primarily for lower extremity revascularizations and were developed as an alternative to autogenous vein. The grafts are prepared from human umbilical cords and are subjected to glutaraldehyde tanning and multiple ethanol extractions and are externally reinforced with a polyester mesh tube.

This conduit has a bursting high pressure and is essentially nonantigenic.

A clinical experience has been reported primary patency rates of 70% and 50% at 1 and 5 years for femoropopliteal grafts and 50% and 25% at 1 and 5 years for femorotibial grafts.

Randomized prospective evaluation of umbilical vein grafts compared with polytetrafluoroethylene (PTFE) grafts (discussed later) indicates comparable patency rates for both grafts when used as below-knee femoropopliteal bypasses.

Umbilical vein grafts have several disadvantages that have precluded widespread clinical use. The grafts exhibit degenerative changes over time and are prone to the development of aneurysms. They are technically difficult to implant, and the intima is easily damaged by clamps or attempts at thrombectomy. Infection of umbilical vein conduits requires their removal, and reoperative dissections are often difficult.

At present, umbilical vein grafts have no well-defined role in the modern practice of vascular surgery, and they are used with decreasing frequency.

## **XENOGRAFTS**

Unmodified arterial xenografts were used clinically in the early 1950s. These grafts elicited a prominent host immunologic reaction, leading to severe damage to the graft wall. Their use was associated with a high incidence of thrombosis and rupture, and it soon became obvious that unmodified arterial xenografts were not suitable for clinical use.

Rosenberg and associates produced modified xenografts by treating bovine carotid arteries with the proteolytic enzyme ficin, followed by tanning with dialdehyde starch. The result was an almost nonantigenic, collagenous tube that was devoid of smooth muscle and elastic tissue but possessing the same tensile strength as a normal artery.

Modified xenografts were used frequently as arterial substitutes from the mid-1960s to mid-1970s but did not produce satisfactory clinical results, particularly in infrainguinal reconstructions.

These grafts exhibited poor long-term patency rates of about 40% 3 to 6 years following implantation. In addition, aneurysms occurred in 3% to 6% of grafts, usually several years after placement.

Moreover, clinical use of these grafts was associated with an unacceptable infection rate of 3% to 7%, several times that associated with other arterial substitutes.

Nevertheless, bovine xenografts have proved to function satisfactorily as hemodialysis access shunts and remain the preferred conduit for this purpose in some centers. They currently have no other well-defined role.

## AUTOGRAFTS

### Arterial Autografts

The clinical use of arterial autografts was introduced by Wylie in 1965. Proponents of autografts cite their numerous advantages, including retention of viability associated with the maintenance of an intact intrinsic blood supply during grafting, absence of aneurysmal degeneration, resistance to infection, preservation of normal flexibility at points of joint motion, and possession of growth potential when used in pediatric patients. The obvious disadvantage is a lack of availability, including inadequate length of arteries for most potential applications.

The clinical use of arterial autografts is restricted primarily to coronary artery bypass grafting, renal artery bypass in children, and arterial substitutes in infected surgical fields.

Radial arteries have been used as free grafts in coronary bypass surgery, but their use has been largely unsuccessful due to early graft closure associated with florid intimal proliferation. However recent studies showed that patency rate of radial artery is nearly similar to that of internal mammary artery.

Currently, however, the internal mammary artery is frequently used as a conduit in coronary bypass surgery.

There is general agreement that children requiring renal artery reconstruction should have arterial autografts. The internal iliac artery has proved to be a suitable conduit, and its use obviates the high incidence of late aneurysmal graft dilatation in this age group when saphenous vein grafts are used. Iliac artery autografts have also proved to be remarkably effective in a limited number of adult patients undergoing renal vascular surgery.

Use of the internal iliac artery is, however, limited in the adult population by its frequent involvement with advanced atherosclerosis. The external iliac artery may also be used as an arterial autograft, but it generally requires prosthetic replacement of the autograft donor site.

Arterial autografts are occasionally used to bridge short arterial defects in infected or contaminated surgical fields that preclude the use of synthetic grafts.

### Venous Autografts

Venous autografts have proved to be the most successful and clearly the most clinically important small-caliber arterial substitutes. They are the preferred graft for infrainguinal arterial reconstruction. The greater saphenous vein, lesser saphenous vein, cephalic and brachial veins, and superficial femoral and internal jugular veins have all been used as bypass conduits.

**Greater Saphenous Vein.** Greater saphenous vein autografts are by far the most widely used autogenous vascular graft in modern vascular surgery and are currently the standard with which all other small-caliber arterial substitutes are compared.

The normal greater saphenous vein averages 70 to 80 cm. in adult men. It begins at the medial malleolus at the junction of the medial marginal and internal malleolar veins. This vein is quite superficial in the leg but lies close to the deep fascia in the thigh. It is a single vessel in the thigh in 75% of patients; contains 8 to 12 bicuspid valves, mainly below the knee; and averages 5.5 mm. in diameter. The luminal surface consists of a monolayer of endothelial cells. The media is composed of an inner layer of longitudinally arranged smooth muscle cells and an outer layer of circumferentially oriented smooth muscle cells. The outer adventitial layer is composed of a loose mixture of collagen and elastic tissue.

The saphenous vein has been used as a replacement for small and medium-sized arteries in all parts of the body, with most being used for coronary artery bypass grafts and for lower extremity bypass of occluded superficial femoral, popliteal, and tibial arteries. Other less frequent uses include upper extremity bypass, as well as mesenteric and renal artery bypass. The coronary, mesenteric, and renal results are described in other sections and are generally excellent.

Lower extremity bypasses using autogenous saphenous vein may be performed using one of two basic techniques.

1. **Reverse:** An appropriate length of vein may be removed from either the ipsilateral or the contralateral lower extremity; it is then reversed in direction to permit arterial flow in the direction of the venous valves and sutured in place, usually in an end-to-side configuration.
2. **In situ,** an intact ipsilateral vein of adequate quality may largely be left in its anatomic position and the valves destroyed using one of a variety of intraluminal devices, followed by similar proximal and distal arterial anastomoses. This technique has been termed in situ saphenous vein bypass. Both techniques are currently widely employed and generally produce similar results.

The primary patency of reversed femoropopliteal saphenous vein autografts ranges from 80% to 90% at 1 year, 55% to 86% at 5 years, and 38% to 46% at 10 years

A patient's continued cigarette smoking and the use of a small vein (less than 4 mm. after gentle distention) both decrease long-term patency. Curiously, vein graft patency appears to be slightly higher in diabetic patients. 38 The role of antiplatelet drugs in enhancing vein graft patency is unproven, although considerable anecdotal evidence supports their use.

Large series of in situ vein bypass initially suggested that the technique resulted in superior patency rates compared with the reversed vein technique. 18 Modern series of reversed vein bypasses, however, have demonstrated similar or superior patency rates to in situ bypasses in grafts to the popliteal and tibial arteries. 38 Clearly, reversed vein grafting is applicable to larger numbers of patients, because many patients do not have an intact ipsilateral saphenous vein, which is mandatory for an in situ bypass.

Veins implanted into the arterial system that remain patent inevitably undergo significant thickening. This process, which has been termed "arterialization" of vein grafts, produces medial and subintimal fibrous hyperplasia, the result is a variable thickening of the vein wall and obliteration of the lumen.

A number of other pathologic changes have been noted in vein grafts causing stenosis.

- Clamp trauma may produce transmural fibrosis.
- Fibrosis of the venous valves
- Suture narrowing caused by improper suture ligation of venous side branches.

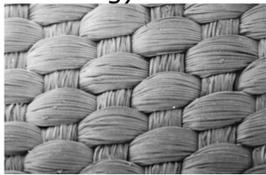
## PROSTHETIC GRAFTS

### Textile Grafts

The hypothesis was then proposed that a fine mesh fabric would result in similar healing and thus function as a satisfactory arterial substitute.

Dacron and Teflon grafts are manufactured by weaving or knitting multifilament texturized yarns.

Each process has advantages and disadvantages. Woven grafts must be tightly interlaced to prevent slippage and fraying of the yarn. This compact structure of the graft produces small interstices and low porosity. These grafts leak minimally at the time of implantation but are somewhat stiff and difficult to handle. In addition, the tight configuration of the graft theoretically reduces the potential for the development of a living neointima by connective tissue ingrowth through the graft interstices (see the following).



**Figure 50-10**

**Close-up photograph (×50) of a woven Dacron prosthetic vascular graft. This graft is relatively impervious to blood because of the tightness of the weave.**



**Figure 50-11**

**Close-up photograph (×50) of a knitted Dacron prosthetic vascular graft. The large openings between the knitted yarns make this graft relatively permeable to blood, and the graft must be preclotted before use in order to fill the interstices with fibrin.**

Knitted grafts are softer and more compliant than woven grafts, and the knit can be varied. The looser the knit, the more elastic and porous the graft. They have been widely used in vascular surgical operations below the diaphragm because of their excellent handling characteristics, including softness and lack of fraying at cut ends.

Knitted grafts are quite porous, between 1200 and 1900 ml. per cm. per minute, and must be preclotted prior to implantation.

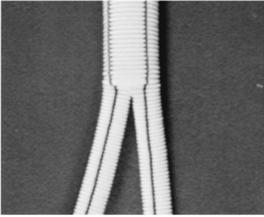
(Porosity for graft applications is defined as the amount of water that will pass through 1 sq. cm. of graft wall per minute under a hydrostatic driving pressure of 120 mm. Hg.)

Porous grafts must be used with great caution in patients with platelet or coagulation defects. A tightly woven graft is preferred in this setting. Woven grafts are also generally preferred in repairs of the thoracic aorta to limit hemorrhage through the graft interstices, especially in operations requiring full heparinization and cardiopulmonary bypass.



**Figure 50-12**

**Photograph (×50) of the external surface of a woven double velour Dacron graft. The striking difference in the surface texture compared with that of a standard knitted or woven Dacron prosthesis (Figs. 50-10 Figs. 50-10 and 50-11 50-11) is obvious. The velour configuration promotes rapid fibrous anchoring of the graft to surrounding tissues.**



**Figure 50-13**

**Photograph of a standard knitted Dacron bifurcation graft. The crimp pattern is clearly seen. The stripes aid the surgeon in proper graft positioning and diminish the likelihood of unrecognized axial rotation of the graft limb when placed in the aortofemoral position.**



**Figure 50-14**

**Angiogram of an aortofemoral knitted bifurcation Dacron graft. The graft extends from the infrarenal aorta to the common femoral arteries.**

Clinical Applications of Textile Grafts. The knitted Dacron graft has been the most frequently used prosthetic arterial graft during the past 30 years. Woven Dacron grafts have traditionally been used primarily in those settings in which interstitial bleeding would present major problems, but the addition of velour surfaces has prompted widespread application of woven grafts.

Textile-fabricated Teflon grafts are presently used infrequently, but they generally appear to function satisfactorily, especially in large artery applications.

Five- and 10-year patencies have been reported as high as 91% and 66%, respectively,

### **Polytetrafluoroethylene (PTFE) Grafts**

PTFE is a fluorocarbon polymer, is not a textile but rather a semi-inert polymer consisting of solid nodes of PTFE with interconnecting small fibrils.

PTFE grafts are available with external ring supports to avoid compression in subcutaneous locations and kinking with angulation. Wall thickness may be varied, with thin-walled grafts preferred for infrainguinal bypasses. Thick-walled grafts function well as hemodialysis shunts

Clinical Applications of PTFE Grafts. PTFE grafts are available in a wide variety of sizes and configurations suitable for almost any arterial reconstructive procedure. They have been used most widely for construction of extra-anatomic bypasses and as a substitute for autogenous vein in infrainguinal bypasses.

Externally supported PTFE axillofemoral grafts provide 5-year patency rates of about 70%.

Disadvantages; Penetration of PTFE grafts by needles may cause alteration of the polymeric structure and subsequent graft disruption when the anastomosis is stressed by shoulder elevation or arm abduction in case of axillo-femoral bypass graft.

PTFE grafts have performed poorly, however, in comparison with saphenous vein when used as bypass conduits to the below-knee popliteal and tibial arteries or in situations in which there is poor distal runoff.

## **Prosthetic Graft Healing**

Shortly after prosthetic graft implantation, a thin layer of fibrin is deposited on the luminal surface. In grafts with high flow, the thickness stabilizes at about 1 mm. and is well tolerated. In a low-flow environment, however, the fibrin layer frequently continues to increase in thickness, proceeding to luminal occlusion.

## **Complications of Prosthetic Grafting**

The most frequently observed prosthetic graft complications include:

- Anastomotic neointimal hyperplasia,
- Graft infection,
- Graft failure caused by fiber disruption or stretching,
- Perigraft seromas,
- Anastomotic false aneurysms.

**Neointimal Hyperplasia.** This process is similar to that described for saphenous vein grafts and is present at both proximal and distal anastomoses. Clinically, the distal anastomotic process appears to be more significant and is frequently implicated as a cause of prosthetic graft failure. Both textile and PTFE grafts are affected.

**Graft Infection.** Infection is one of the most feared complications of prosthetic grafting. *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Escherichia coli* are the most frequently isolated organisms. The incidence is about 1.5% to 2.5%; it is slightly lower when the graft is completely intra-abdominal and higher when a groin anastomosis is present. Aortic graft infections may be associated with an operative mortality of 10% to 25% and an amputation rate of 15% to 20%.

**Graft Failure.** Two distinct types of Dacron graft failure have been described.

1. Gradual, diffuse graft dilatation, caused by expansion of the knit rather than elongation or weakening of individual fibers.
2. Dropped stitch in the manufacturing process, or fiber degeneration. This type of defect usually causes localized holes and leaks, with the potential for false aneurysm formation. These are termed false aneurysms.

**Perigraft Seroma.** A perigraft seroma is a sterile collection of clear fluid within a nonsecretory pseudomembrane surrounding a prosthetic vascular graft. It usually occurs in association with extra-anatomic bypasses, that is, an axillofemoral or femorofemoral graft.

**False aneurysm** occurs when there is leak from the anastomotic sites which will be contained by the surrounding tissues forming a fibrous capsule around it.