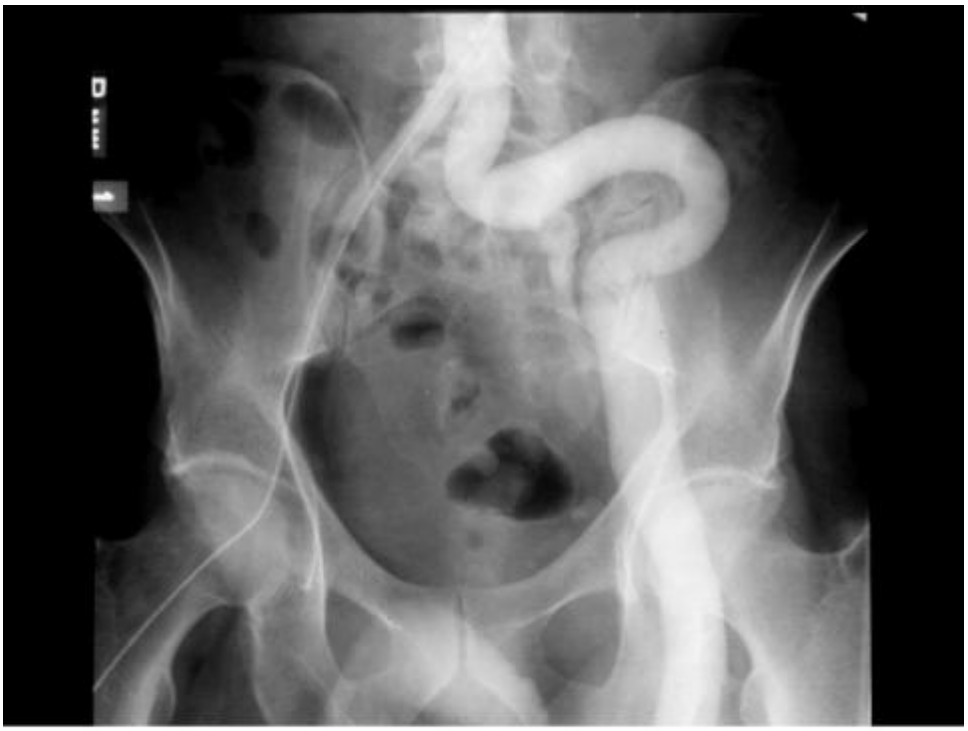
ANEURYSMS AND AORTIC DISSECTION

NORMAL, PHYSIOLOGIC REGULATION OF ARTERIAL DIAMETER

Arteries must provide adequate supply of blood to meet the demands of the tissues they perfuse in as efficient a manner as possible. They accomplish this by altering their diameter to meet demand. Regulation of diameter in response to changes in flow is mediated by the endothelium. Flowing blood rubs against cells lining the vessel wall, creating a shear force that pushes the surface membrane in the direction of flow. When shear is increased or decreased (due to increased or decreased flow, respectively) the endothelium generates vasoactive and growth regulatory molecules that cause the vessel to dilate, in the case of increased flow, or constrict, in the case of decreased flow. As a result, arteries dilate when flow is increased until shear is reduced to normal, physiologic levels. Conversely, arteries constrict when flow and shear are decreased until shear is again normalized. The result is the ideal arterial diameter to minimize the amount of energy the heart needs to exert to pump blood through the vascular system. Both developing and mature arteries increase in diameter when supplying organs that are increasing in size (for example, organs growing during maturation) and decrease diameter when supplying tissues that are atrophying (for example, the iliac artery decreases in diameter following amputation of the limb it supplies). They respond similarly to changes in flow due to other causes, such as increased flow in fistulas created for dialysis access or trauma to adjacent arteries and veins (Figure 1).



This angiogram was taken 25 years after the patient suffered a gunshot wound to the left groin, which created a fistula between the superficial femoral artery and vein. Increased flow through the left iliac system caused it to dilate over the years to four times its normal diameter. The iliac vein was similarly dilated.

Figure 1

Arteries increase their diameter by growing in all directions and thus they also lengthen. This causes the vessel to become tortuous (the enlarged iliac artery in Figure 1 is a good example). This occurs both in healthy and aneurysmal segments that dilate. Tortuosity makes it challenging to determine the true diameter of the vessel since cross-sectional imaging in a plane that transects the artery at an angle will exaggerate the measured maximal diameter. The geometry is the same as when tube-shaped vegetables, like carrots, are sliced diagonally to create elliptical segments, which are much wider on long axis than the true diameter of the tube. In this case, the shortest diameter of the ellipse most closely approximates the true diameter. It is wise, therefore, when measuring diameter with ultrasound to use a longitudinal view taken along the axis of the artery. Similarly, sagittal and coronal views are useful on CT scanning to determine diameters that may be affected by an improper scan plane when transverse, axial images are used.

Change in arterial diameter in response to flow is initially an active one caused by relaxation or contraction of smooth muscle cells in the arterial wall and is nearly instantaneous. It can be appreciated by making a tight fist to restrict flow through the hand for as little as ten seconds and then opening the hand. The skin, initially white due to reduced blood flow, immediately becomes pinker than the opposite hand due to rapid vasodilatation. A marked increase in radial artery flow can be detected as a high frequency, monophasic signal using a Doppler flow detector. This post-ischemic reperfusion response, and the resulting high velocity, monophasic flow pattern, is both rapid and temporary in this example, but can be prolonged, for example, after successful reperfusion of a chronically ischemic limb, which causes prolonged hyperemia.

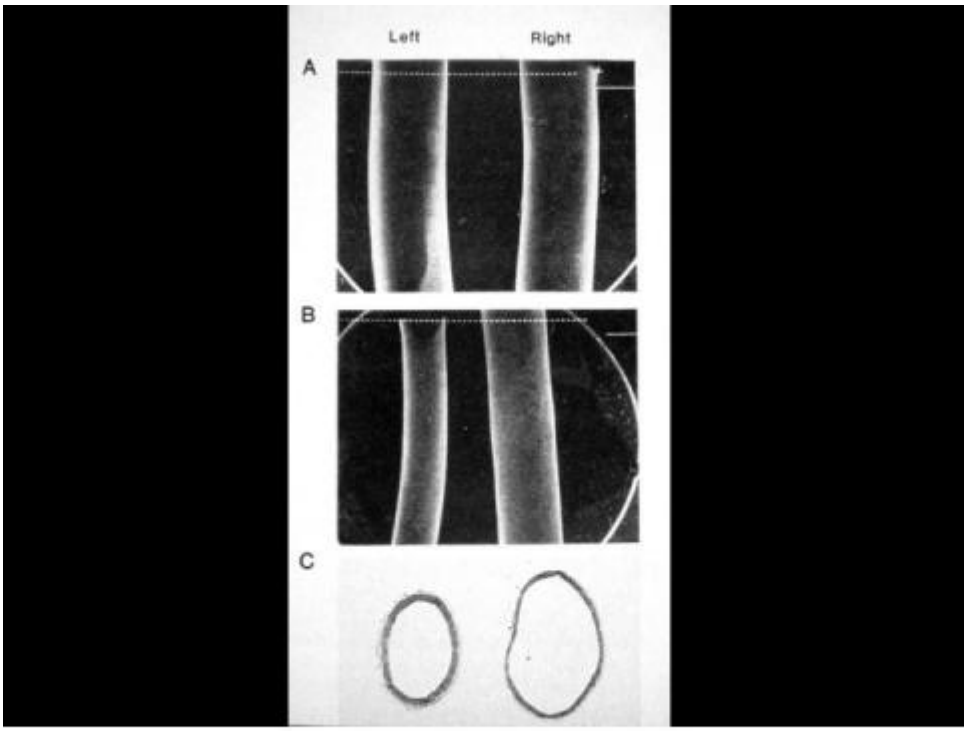
Chronic changes in flow cause remodeling of the vessel wall structure to the new diameter. This remodeling is caused by prolonged action of the same molecules that are responsible for acute diameter changes since in addition to their vasoactivity, they affect smooth muscle cell function (such as proliferation and matrix deposition, Table 1).

Table 1: Regulation of Vessel Tone and Wall Structure

Examples of Vasodilators and Vasoconstrictors
Vasodilators – Antiproliferative
Nitric oxide
Prostacyclin
Vasoconstrictors – Pro-proliferative
Angiotensin II
Platelet Derived Growth Factor (PDGF)
Endothelin

The rapid response to changes in flow is a vasomotor process. Long-term flow changes cause vessel wall remodeling. This has been shown in an experiment by Langille (Figure 2). The outflow of the left carotid artery of a rabbit was decreased 30% by ligating the external carotid artery. As a result, the diameter

decreased to a level that maintained normal shear force on the endothelium. Initially this response could be reversed by application of vasodilators that cause the smooth muscle cells to relax. However, after several weeks the wall remodeled and vasodilators had little effect.



The carotid ligation experiment. A) left and right carotid before ligation, B) carotids after ligation on the left, C) histologic cross sections.

Figure 2

AORTIC ANEURYSM

The aorta is the mother of all arteries. It is about 3 centimeters in diameter at the aortic root and narrows slightly as it descends to its bifurcation into the common iliac arteries. This large vessel, particularly in the thorax, has a higher content of elastin than the more peripheral, muscular arteries. The high elastin content allows it to dilate and act as a capacitor during systole, storing energy so it can maintain flow as it returns to normal diameter during diastole. The most life-threatening diseases of the aorta are caused by processes that weaken the wall and cause it to become aneurismal (dilated).

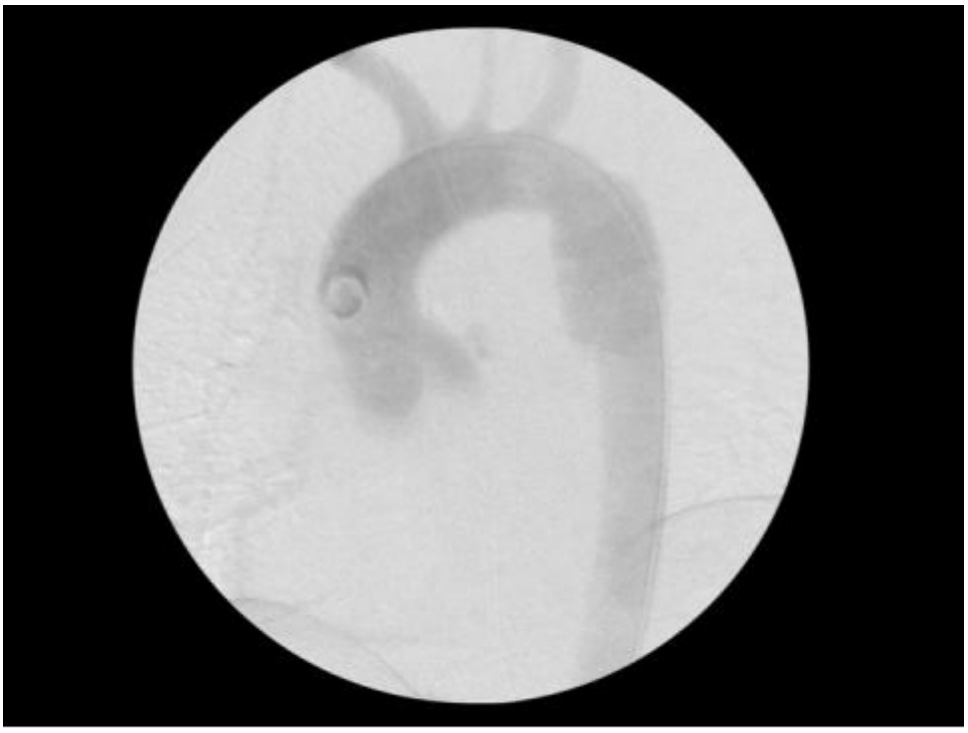
Definition of Aneurysm

An aneurysm is localized widening of a vessel by at least 50% of the normal diameter. This term applies equally to veins and arteries, although venous aneurysms are far less common than arterial aneurysms. Diffuse enlargement of the arteries is referred to as arteriomegaly. A true aneurysm is a widening of the blood vessel itself, and thus involves all layers (intima, media, and adventitia). A pseudoaneurysm, or false aneurysm, refers to a leak out of the artery into a surrounding hematoma that stays in contact with the artery lumen, resulting in a pulsating mass, indistinguishable from a true aneurysm on physical examination. The intima and media are always disrupted; sometimes the adventitia remains intact, containing the bleeding. The most commonly encountered pseudoaneurysms are those that form at catheter puncture sites if the artery continues to bleed after the catheter is removed. On duplex exam a jet of blood can often be detected entering the pseudoaneurysm from the injured native artery. The size of the pseudoaneurysm and the width and length of the “neck” connecting it to the artery dictates the treatment, which is prolonged direct pressure as long as the vessel can be compressed between the skin

and a bony structure beneath, which is not possible for puncture sites in the subclavian artery or femoral punctures that are too high (above the inguinal ligament). If this maneuver fails, small femoral pseudoaneurysms may simply be monitored whereas larger or symptomatic pseudoaneurysms may be treated by injection of thrombin if the neck is favorable or arterial repair for large pseudoaneurysms with broad necks. Leaking puncture sites in more central vessels, like the subclavian artery, may require placement of an endograft.

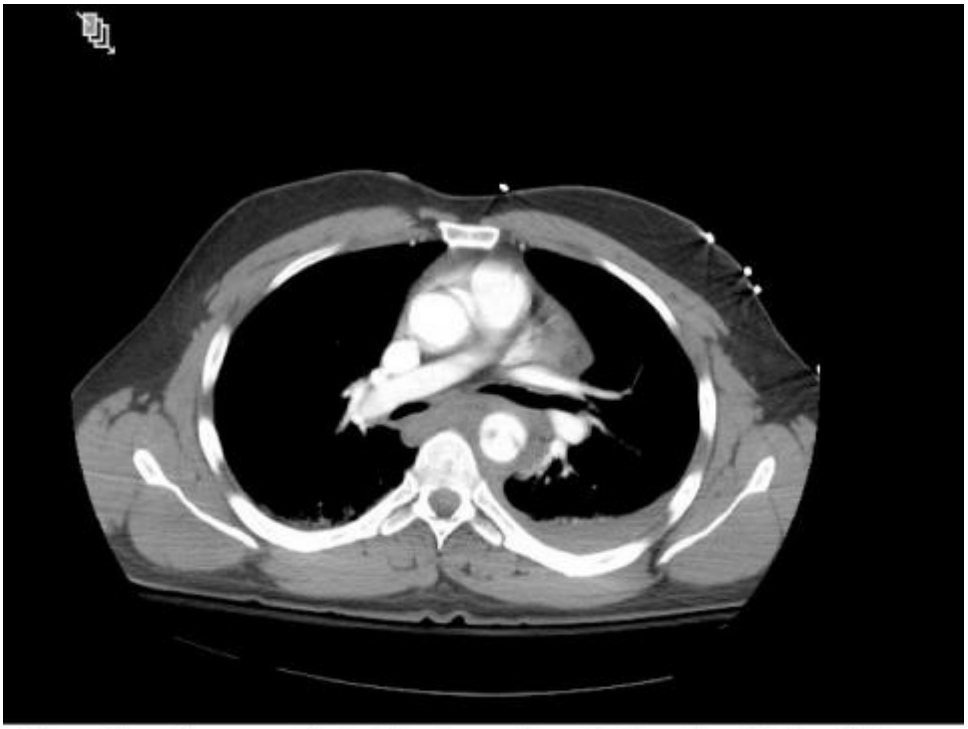
Pseudoaneurysms can also occur months to years following bypass grafting, particularly where grafts are sewn into arteries, most commonly Dacron grafts to the common femoral artery. In this case, bleeding results from the break-down of the suture line due to suture disruption, weakness of the artery wall, or infection. If asymptomatic, these do not always need treatment. Indications for repair include development of local pain, symptoms from compression of the femoral nerve or vein, signs of infection, size (3-4 cm), or embolization of mural thrombus.

Following blunt trauma, such as sudden deceleration injury in motor vehicle accidents, the thoracic aorta can tear where it is tethered by the ligamentum arteriosum, just beyond the subclavian takeoff (Figures 3 and 4). In this case, the pseudoaneurysm may be contained by an intact adventitia. On chest x-ray the mediastinum appears to be widened. Repair is often accomplished by placing and endovascular stent graft as soon as possible since free rupture can occur at any time.



A traumatic aortic tear. Note the widening of the first part of the descending aorta.v

Figure 3



CT scan from the same patient with a traumatic aortic dissection. The line of dissection can be seen across the ascending and descending aorta. There is mediastinal blood surrounding the descending aorta.

Figure 4

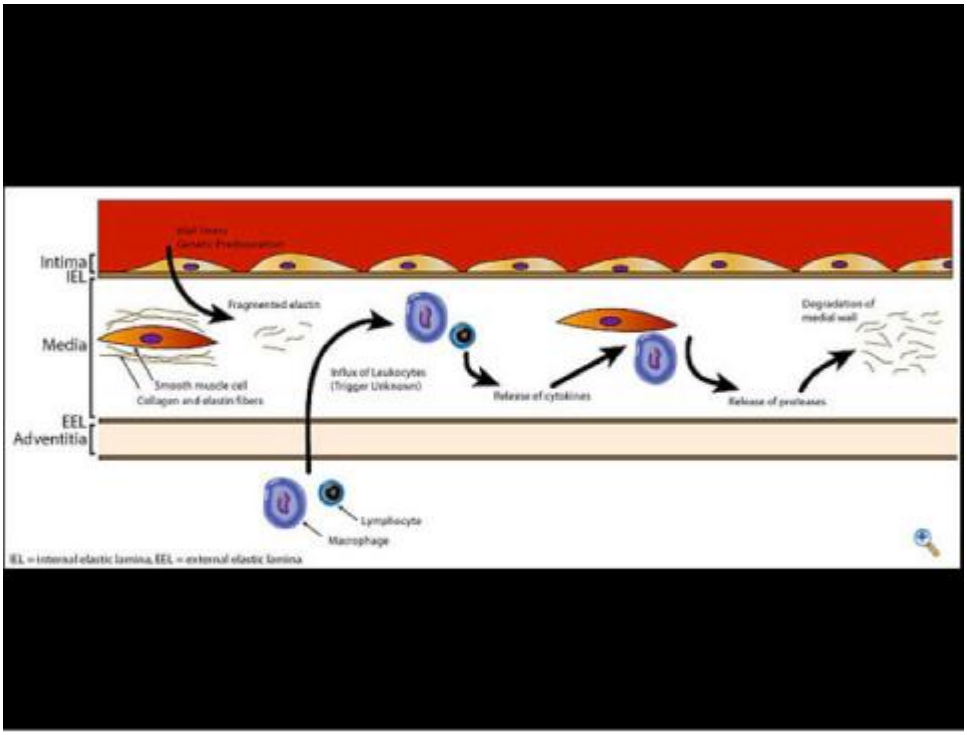
PATHOPHYSIOLOGY

The most common cause of peripheral arterial aneurysms has been considered to be atherosclerosis, but there are many differences between aneurysmal degeneration of the arterial wall and occlusive atherosclerosis. Both share many risk factors, such as smoking, hypertension and male gender. However, in aneurysm disease the wall thins and loses elastin and collagen. There is a heritable component to this process, suggesting a genetic abnormality of matrix metabolism. Aneurysm patients tend to be taller and older than patients with occlusive disease and their arteries in general tend to be larger. Finally, aortoiliac occlusive disease is present in no more than 25% of patients with an abdominal aortic aneurysms (AAA). Other causes of aneurysm include collagen vascular disorders, dissection, infection, and vasculitis (Table 2).

Table 2: Causes of Aneurysm

Degeneration of the wall (atherosclerosis)
Collagen vascular disorders
Marfan syndrome
Ehlers-Danlos syndrome
Dissection
Infection (mycotic)
Salmonella
Staphylococci
Streptococci
Tuberculosis
Syphilis
Fungi

Degenerative aneurysm formation involves four main processes: 1) proteolytic degradation of the wall, 2) inflammation, 3) wall stress, 4) genetic predisposition. Degradation is caused by the action of matrix metalloproteinase proteinases (MMPs) produced by macrophages and aortic smooth muscle cells. Macrophages and lymphocytes can been seen across the entire aneurysm wall. Production of cytokines by these inflammatory cells may stimulate the smooth muscle cells to produce MMP's (Figure 5). The fact that abdominal aortic aneurysms tend to form a centimeter or two below the origin of the renal arteries and extend into the iliac arteries suggests that particular flow patterns or the composition of the wall, which becomes less elastic and more muscular in this region, contribute to aneurysm formation. Once the wall diameter increases, wall tension increases according to the Law of LaPlace (tension equals pressure times diameter). Thus, there is a positive-feedback loop as widening of the artery increases wall stress (tension per millimeter of wall thickness), which increases the stretching force on the wall. There is a genetic component to development of AAA. Siblings of patients with AAA have an increased risk of AAA themselves, and Rh-negative individuals are at lower risk.



Pathogenesis of degenerative aneurysms (illustration courtesy of BS Knipp, U of Mich)

Figure 5

Aneurysms caused by collagen vascular disorders tend to occur in younger patients and to involve the thoracic aorta more commonly than the abdominal aorta. Infection can involve the arterial wall, particularly in atherosclerotic plaques. Such mycotic aneurysms may result after an episode of bacteremia following dental work, cholecystitis (associated with Salmonella), or other infections. Prior to development of penicillin, syphilis was a common cause of thoracic, mycotic aneurysm. Vasculitis, such as giant cell arteritis and Takyaksu's arteritis, may cause aneurysms of medium-sized arteries, but more commonly cause stenosis or occlusion.

Aneurysms are most commonly found in the infrarenal aorta and adjacent common iliac arteries and to a much lesser extent in the thoracic aorta and the femoral or popliteal arteries. Even less common are mesenteric, renal, and splenic aneurysms. (Berry aneurysms occur at bifurcations of cerebral arteries and are due to an inherited weakness of the wall, which is unrelated to aneurysm development elsewhere.) Aneurysms are asymptomatic until complications develop. They may compress adjacent structures, usually nerves or veins, causing pain, numbness, weakness, or venous congestion (this is particularly true of popliteal aneurysms), but these symptoms are rare. Abdominal aneurysms can occasionally rupture into the adjacent vein (usually the inferior vena cava) causing an acute arteriovenous fistula. This causes a marked increase in cardiac output, elevated heart rate, and possibly high-output congestive heart failure. Also rare, but usually fatal, is formation of a primary aortoenteric fistula between the aneurysm and small bowel, typically the duodenum, which overlies the neck of the aneurysm. This may cause an initial, small "herald" bleed as the mucosa becomes friable, followed at a variable interval by massive and often fatal upper GI bleed. Aortoenteric fistulae are much more common in their secondary form, when the proximal suture line of an aortic graft erodes in the adjacent duodenum following open surgical repair of an aneurysm.

Mural thrombus is a common finding on imaging of aneurysms. Thrombus forms along the wall where flow is relatively stagnant due to flow separation: most flow goes down the center of the vessel and does

not fill in the areas near the lateral wall. For this reason, arteriograms, which only demonstrate flowing blood in the vessel lumen, can look completely normal in an aneurismal segment of artery (although the astute observer may notice the absence of lumbar and other branches that should be present but are occluded by the luminal thrombus).

Mural thrombus can break off and embolize, causing ischemia in the more distal vasculature. This is an uncommon event with abdominal aortic aneurysms, which lie at the back of the abdominal wall and are not subject to flexion, but is the primary cause of morbidity in patients with popliteal aneurysms, which are located at the knee and subject to frequent flexion and extension. Popliteal aneurysms rarely rupture, and when they do there is no threat to life since massive bleeding cannot occur in the popliteal space. However, limb loss due to embolism can occur with popliteal aneurysms and is the reason that these aneurysms are treated. Thus, it is particularly important to document the presence or absence of mural thrombus when imaging popliteal aneurysms.

DIAGNOSIS

It is desirable to diagnose aneurysms before they become symptomatic since the first symptom may lead to loss of life or limb. Physical examination should always include palpation of the abdomen and popliteal spaces for pulsatile masses. In thin persons, a prominent aortic pulse may confused with an aneurysm. This may also occur in elderly patients, whose aortas may be elongated and tortuous without being aneurysmal. As mentioned earlier, angiograms show only the flow lumen and therefore often do not demonstrate aneurysms. Since abdominal aneurysms can erode into the spine, patients may present with back pain. Lumbar spine x-rays in these patients may show the outline of the enlarged and calcified aortic wall. Detailed anatomic information is required to plan endovascular aneurysm repair (repair with stent grafts); currently computerized tomography scanning is the best method of obtaining this information.

Ultrasound is the diagnostic tool of choice because it is accurate, noninvasive, and relatively inexpensive. Mural thrombus does not contribute to the strength of the wall and thus should not be included in measurements of wall diameter. Guidelines from the U.S. Preventive Services Task Force recommend that men aged 65 to 75 who have ever smoked should have a single screening abdominal ultrasound for AAA. This recommendation is based on a balance of the benefit of finding and preventing aneurysm rupture versus the expense of screening and the potential harm of false positive screening examinations. The task force continues to review the effectiveness of one-time screening by analysis of subpopulations based on risk factors such as family history, age, smoking history, and race/ethnicity. Some patients with a family history of ruptured AAA reasonably seek screening for reassurance. Because iliac, aortic, and popliteal aneurysms often occur in the same individuals, patients with an aneurysm in one location should have ultrasound screening to rule out aneurysms in the others.

Treatment

As suggested by the Law of LaPlace and the fact that the aortic wall continues to thin as it expands, abdominal aortic aneurysms are increasingly prone to rupture as they enlarge. Repair is urgent in patients with leaking or ruptured aneurysms. This group may present with the classic triad of abdominal pain, hypotension, and a palpable, pulsatile abdominal mass and should be taken immediately to the operating room. Impending rupture is suggested by the sudden onset of back or abdominal tenderness or tenderness on palpation of the aneurysm and should prompt consideration of immediate repair. With contained rupture, the intact retroperitoneum prevents massive bleeding. The patient experiences sudden onset of abdominal pain and syncope but has an obtainable blood pressure on arrival in the

emergency room. Free rupture occurs when the retroperitoneum breaks and bleeds freely into the peritoneal cavity. These patients typically do not have an obtainable blood pressure if they survive the trip to the emergency room, and mortality is very high.

The annual incidence of rupture by size has been estimated as follows:

Less than 4.0 cm in diameter – 0%

4.0 cm to 4.9 cm in diameter – 0.5% to 5%

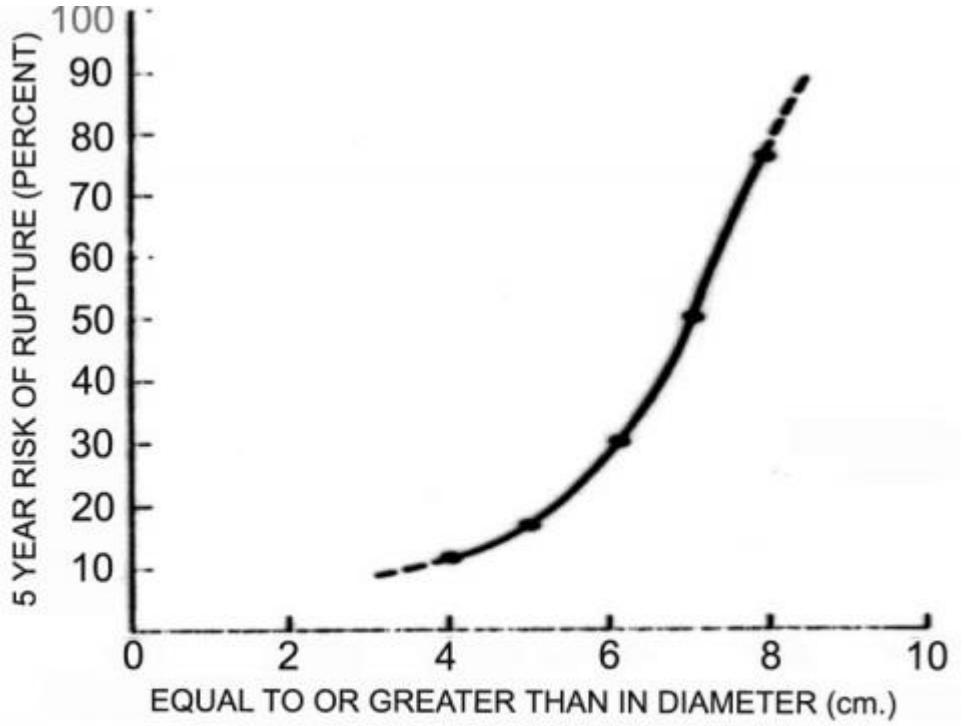
5.0 cm to 5.9 cm in diameter – 3% to 15%

6.0 cm to 6.9 cm in diameter – 10% to 20%

7.0 cm to 7.9 cm in diameter – 20% to 40%

8.0 cm in diameter or greater – 30% to 50%

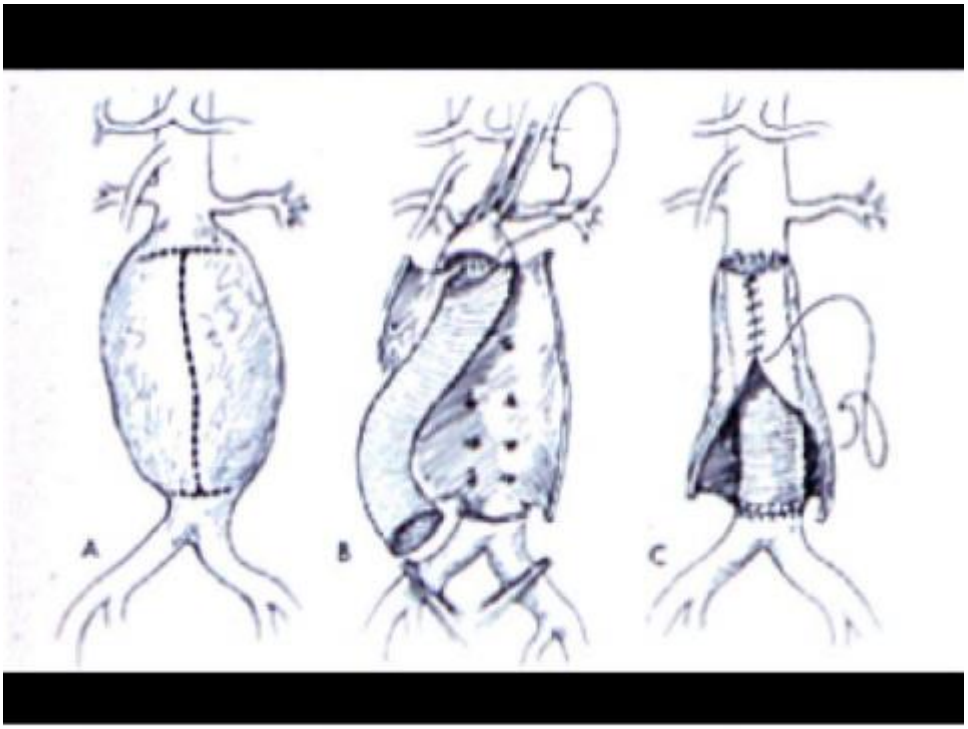
As a general rule, elective surgical repair is indicated when aortic aneurysms exceed 5.5 cm diameter. Risk of rupture sharply increases above this size. Studies comparing early repair with watchful waiting in patients with 4.5 to 5.5 cm aneurysms has shown equivalent mortalities. However, many patients required repair during observation as their aneurysms enlarged or became symptomatic. The decision to treat must be individualized. Persons with aneurysms less than 4.5 cm in diameter should be followed yearly with ultrasound and those with aneurysms from 4.5 to 5.4 cm should be followed every six months. Young persons (under the age of 65 or so) with aneurysms that are 5.0 cm may deserve early repair since their aneurysms, on average, will increase 3 mm per year and their overall health and ability to tolerate repair will diminish as they age. Women should be treated at a smaller aneurysm size (4.5 to 5.0 cm) because they have a higher mortality than men for the same size aneurysm, possibly because their arteries are smaller in general and so the same size aneurysm represents a relatively greater enlargement in women than in men, but this is just speculation. Since there is a genetic component to aneurysm disease, patients who have a family history of aneurysm rupture may be treated earlier. These patients are usually aware of the dire consequences of aneurysm rupture and therefore seek early treatment. For many patients, knowing that they have an aneurysm that could rupture is like living with a ticking time bomb. For them, repair can return peace of mind.



It has long been recognized that the risk of rupture increases with abdominal aortic aneurysm size, as shown in this somewhat dated graph. More recent estimates of rate of rupture are given in the text.

Figure 6

Traditional aneurysm repair involves abdominal surgery to replace the diseased aorta with a Dacron tube, which can be bifurcated to extend to the iliac or femoral vessels if necessary to bypass all diseased segments (Figure 7). This is a major operation that requires a lengthy recovery period and carries significant morbidity and mortality. In the 1990's stent grafts were developed by covering large metal stents with a fabric to prevent blood flow out of the device, allowing it to bypass the diseased segments. Because the devices are placed through catheters inserted in the groin they are referred to as endografts. Placing devices across abdominal aortic aneurysms, referred to as EVAR (endovascular aneurysm repair) revolutionized treatment of AAA, both electively and for ruptures. The procedure is minimally invasive and thus less traumatic. Patients can go home and resume normal activities as soon as the day following an elective repair. Survival after rupture is much higher when EVAR can be used. The devices need to be able to seal against the vessel wall at their top and bottom end to fully exclude the aneurysm and thus require relatively normal arterial anatomy at these locations. Thus, not every patient can have an EVAR. Successful repair usually results in thrombosis of the aneurysm sac followed by decrease in its size.



Traditional aneurysm repair involves an abdominal operation. The aorta is clamped above and below the aneurysm, which is then opened. Any patent lumbar arteries are oversewn, and a Dacron tube is sewn in to replace the diseased segment. The aneurysm sac is then closed over the Dacron tube.

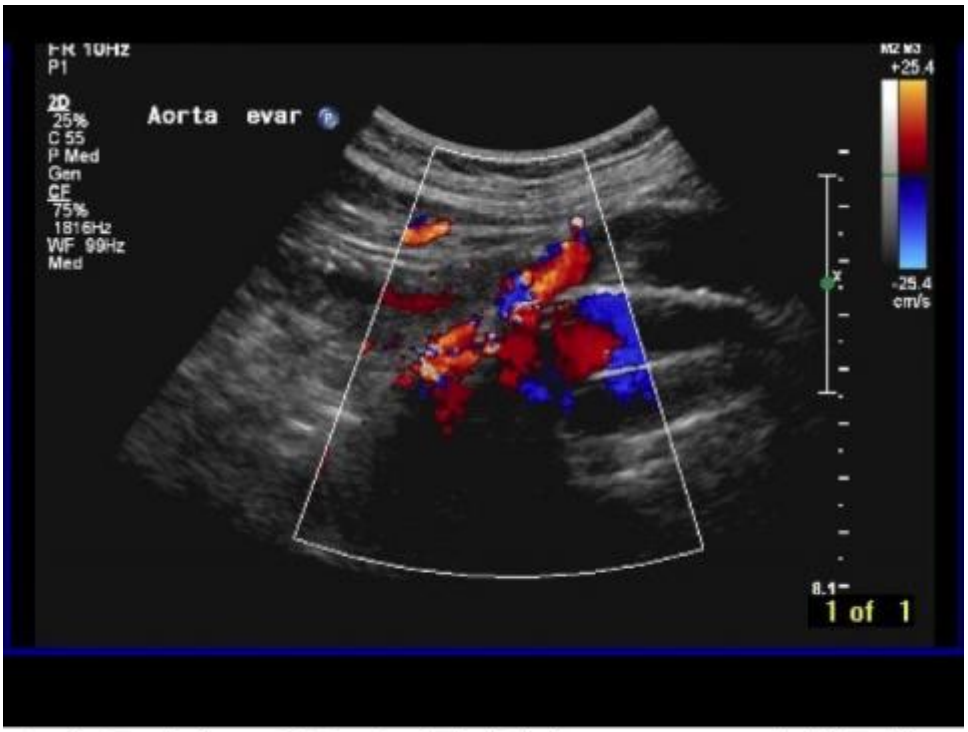
Figure 7

Follow-up of EVAR is necessary to assure that the device remains in proper position, does not fracture, that the aneurysm does not expand, and that there are no endoleaks (blood entering the aneurysm sac). There are several possible types of leaks (Table 3). Type I is a leak at a proximal or distal fixation site. These require immediate treatment since the aneurysm is not excluded from aortic blood flow. Type II leaks result from patent lumbar, sacral, or mesenteric branches from the aneurysm that continue to feed blood into it. Usually two vessels are patent with flow going from one to the other. Single patent vessels usually thrombose along with the aneurysm sac since blood ceases to flow. Type II leaks often do not fully pressurize the aneurysm sac and thus can be followed as long as the aneurysm does not enlarge. Type III leaks result from damage to the device or separation of its components. In Type IV, blood leaks through the fabric of the endograft. These are generally temporary until the fabric is sealed by fibrin and are infrequent with current devices. Type V endoleaks are those for which a cause cannot be found on imaging and are sometimes referred to as endopressure.

Table 3: Types of Endoleaks

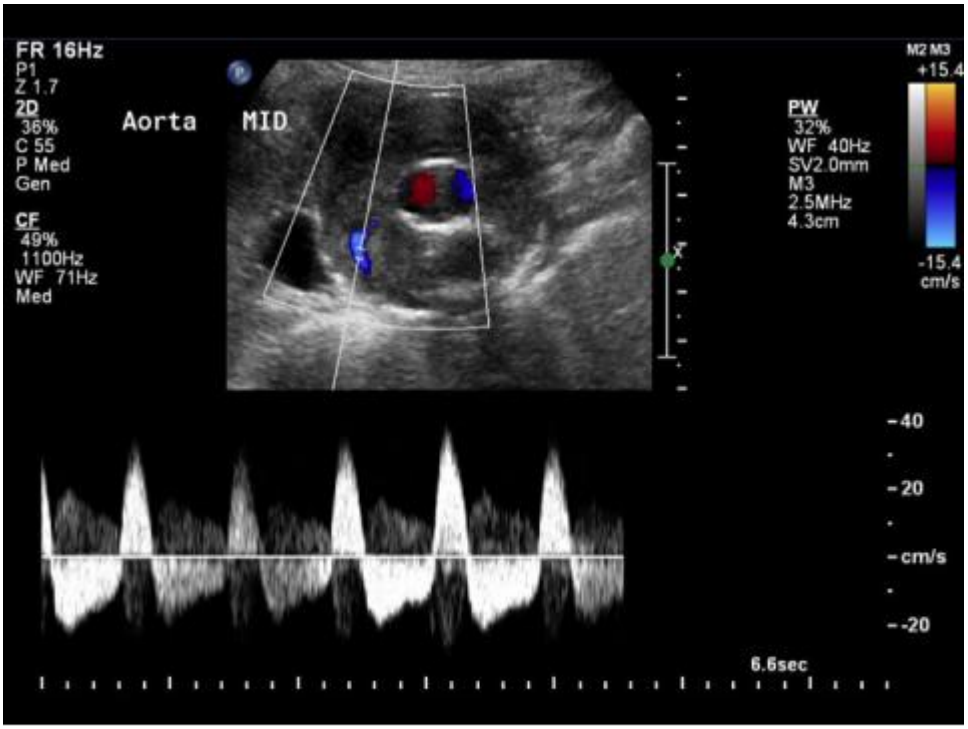
Type I	Leak from the proximal or distal attachment site
Type II	Leak from patent lumbar, sacral, or inferior mesenteric arteries
Type III	Leak from a defect in the device
Type IV	Leak through the device fabric
Type V	Unknown cause

CT scan, with and without contrast, is the gold standard for follow-up studies. It documents aneurysm size and can detect endoleaks, device fracture or migration, and presence of thrombosis or stenosis. Because it is expensive and involves radiation and injection of contrast, duplex scanning is being used to replace it in selective cases. Recommended follow up for EVAR begins with a contrast CT scan at one month. If there is no endoleak, many clinicians will then use duplex scanning with color Doppler to follow the repair at 6 or 12 month intervals, depending on the presence or absence of endoleaks. Scans should document the size of the aneurysm since enlargement indicates failure to exclude the aneurysm and therefore further intervention is required. Also on scanning, renal flow should be noted in case the device encroaches on the renal artery orifices. Patency of graft limbs should be documented as well as any stenosis within the involved vessels. Finally, color Doppler is used to detect the presence of endoleak (Figures 8). Small leaks may be difficult to detect; contrast enhanced scanning may be more sensitive. This may not be a major issue since difficult to detect endoleaks may be of little consequence and are not important if the aneurysm size is stable or decreasing. Type II endoleaks often have a to-and-fro waveform pattern (Figure 9).



A color Doppler image of a Type II endoleak. The large aneurysm sac is visible with the much smaller, echogenic endograft in the center. The graft has flow. The sample volume is in the endoleak (blue) in the lower left of the image. The waveform has the typical to-and-from pattern.

Figure 8



A color Doppler image of a Type I endoleak on longitudinal view. The red jet of blood is seen flowing anteriorly adjacent to the stent graph (white line with dots where the metal struts are located).

Figure 9

AORTIC DISSECTION

Dissection occurs when blood enters the aortic wall through a tear in the intima and forms a false lumen within the media that can impinge on the true lumen causing stenosis or total occlusion. The dissection may start anywhere along the aorta, but most commonly begins beyond the arch vessels, and tends to spiral down into the iliac vessels. This is a different entity than degenerative aneurysms, which rarely dissect. The most common cause of aortic dissection is hypertension. The driving force pushing blood into the wall is the rising pressure gradient between the wall and the lumen as the pressure wave passes through the aorta. Thus, treatment is aimed at reducing hypertension with vasodilators, such as nitroprusside, and the pressure gradient (dP/dT) with beta antagonists. Dissection is also commonly associated with collagen vascular disorders, such as Marfan syndrome, that cause weakening of the wall.

Symptoms and diagnosis

Symptoms of aortic dissection include acute onset of tearing back pain and symptoms associated with occlusion of branch vessels. Involvement of carotid arteries could lead to stroke, of renal arteries to acute renal failure or exacerbation of hypertension, of superior mesenteric and celiac arteries to mesenteric ischemia, and of iliac and acute lower extremity arteries to limb ischemia. Occlusion of the subclavian arteries causes decreased upper extremity blood pressure, which may confound the underlying diagnosis of hypertension. Dissection of the ascending aorta is an immediate threat to life due to widening of the aortic root, which causes acute aortic insufficiency, occlusion of coronary arteries causing acute myocardial ischemia, or dissection into the pericardium causing pericardial tamponade. Diagnosis is generally by CT scan with contrast, which demonstrates a true ad false lumen, with the true lumen compressed and narrowed by the blood in the false lumen. The aortic wall is weakened and can rupture or become aneurysmal. Echocardiography can identify cardiac tamponade. The non-invasive vascular laboratory can identify stenosis of occlusions causing extremity ischemia. Blood pressures should be measured in all four extremities. Duplex scanning is useful when there is concern for in significant

stenoses or occlusions of the carotid, iliac, or femoral vessels. Renal and mesenteric flow may also be assessed, although these examinations may be limited by the ability to insonate these deep vessels in acutely ill patients.

Treatment

Treatment of aortic dissection is based on the anatomic location and degree of ischemia. Patients with acute dissection need continuous monitoring and rapid control of blood pressure in an intensive care unit. Intervention is required for dissections involving the ascending aorta and arch (Type I), due to their acute life-threatening nature. Medical therapy (control of hypertension) is used for dissections beyond the arch (Type II). Intervention is required if medical treatment fails to halt symptoms or there are ischemic complications from branch occlusions. Treatment may require surgical replacement of a segment of the aorta (and sometimes of the aortic valve), closing off the entry point of the dissection with an endograft, puncture of the false lumen to allow re-entry into the true lumen (so called fenestration, done angiographically), or bypass from uninvolved arteries to vessels whose origin has been occluded by the dissection.

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