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Coronary Angioplasty

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The concept of transluminal angioplasty—enlargement of the lumen of a stenotic vessel by a catheter technique—was first proposed by Dotter and Judkins in 1964 (1). Their idea was to advance a spring-coil guidewire across an atherosclerotic arterial stenosis. As this guidewire remained in place, it would serve as a rail over which a series of progressively larger rigid dilators could be advanced to enlarge the vessel lumen. Although this technique proved to be effective in peripheral arteries, the need to insert large-caliber rigid dilators through the arterial puncture (and the high shear forces applied by the dilators as they crossed the atherosclerotic lesion) ultimately limited the clinical application of this “Dotter” technique. In 1974, Gruentzig (2) modified the technique, by replacing the series of rigid dilators with an inflatable nonelastomeric balloon mounted on a comparatively smaller catheter shaft. The balloon catheter could be introduced percutaneously with minimal trauma, advanced easily across a vascular stenosis in its smaller (collapsed) state, and then inflated with sufficient force to enlarge the stenotic lumen. Although others had speculated about the possibility of balloon dilatation, Gruentzig was the first to develop it into a practical device, and perfect it as a usable clinical tool. Within 4 years he and his colleagues (3) had performed a series of experiments in animals, cadavers, peripheral arteries, and the coronary arteries of patients undergoing bypass surgery, culminating in their performance of the first percutaneous balloon angioplasty of a stenotic coronary artery in a conscious human (September 16, 1977).

Although the new technique of balloon angioplasty was viewed with skepticism by most, a small number of cardiologists around the world recognized the great potential it might hold (4). In 1979 they met to form a registry of all coronary angioplasty cases worldwide under the sponsorship of the National Heart, Lung, and Blood Institute (NHLBI). That registry grew to 3,000 cases by 1981, although no more than 1,000 angioplasties were performed in any given year during that period. From these humble beginnings, progressive improvements in equipment and technique have produced dramatic growth in percutaneous transluminal coronary angioplasty (PTCA), transforming it into a major therapeutic modality that is used to benefit large numbers of patients with ischemic syndromes caused by anatomically suitable coronary artery lesions (5) (Fig. 23.1). Roughly 35% of the 1.4 million people who undergo diagnostic cardiac catheterization each year are referred for revascularization by catheter-based techniques exceeding the number referred for revascularization by bypass surgery. Despite a progressive broadening in its clinical and anatomic indications, the success rate for coronary angioplasty has risen to 98%, with a procedural mortality rate and an emergency bypass rate each less than 1%.

FIG. 23.1.

Growth in the number of coronary angioplasty procedures between 1979 and 1991 is shown by the bottom (stippled) band, increasing from less than 1,000 per year in 1979–1981 to more than 300,000 per year in 1991. This was similar to the annual number of bypass operations (cross-hatched band). The number of annual catheterizations has now grown to approximately 1.4 million, with one of three patients who undergo diagnostic cardiac catheterization being referred for coronary angioplasty, compared with one of four being referred for bypass surgery. CABG, coronary artery bypass grafting; PTCA, percutaneous transluminal coronary angioplasty. (From American College of Cardiology; see also Bittl JA. Advances in coronary angioplasty. N Engl J Med 1996;335:1290.)

Much of the improvement over the past 6 to 8 years, however, has come from the introduction of new adjunctive technologies such as atherectomy and stent implantation (see Chapters 24 and 25), as well as refinements in anticoagulant and antiplatelet pharmacology. Newer devices are now used in more than 80% of coronary interventions, so that stand-alone plain old balloon angioplasty (POBA) has become a minority interventional procedure. But balloon predilation or postdilation still plays an important adjunctive role in almost all such procedures (5), and the roots for our understanding of the strengths and weaknesses of any percutaneous coronary
intervention lie in the history of balloon angioplasty. The intent of this chapter is to examine the basic equipment, strategy, results, and current indications of balloon angioplasty, indicating the situations in which newer stent and atherectomy devices have become dominant through their ability to address the previous limitations of stand-alone balloon angioplasty (6). Even more importantly, this chapter makes it clear that the evolution of catheter-based intervention is continuing, at an ever-increasing pace. The coronary interventionalist must have strong grounding in these fundamental principles, as well as the flexibility to master rapidly changing techniques and indications as they develop, if his or her patients are to receive the greatest benefits of safety, predictability, and durability from percutaneous coronary intervention.

**EQUIPMENT**

A coronary angioplasty system consists of three basic components (Fig. 23.2): (a) a guiding catheter, which provides stable access to the coronary ostium, a route for contrast administration, and a conduit for the advancement of the dilatation equipment; (b) a leading guidewire that can be passed through the guiding catheter, across the target lesion, and well into the distal coronary vasculature to provide a rail over which a series of therapeutic devices can be advanced; and (c) a nonelastomeric balloon dilatation catheter filled with liquid contrast medium. Technologic advances lead to refinements in specific equipment each year, so any detailed description of current products would be outdated too soon to be of value here, but some general principles hold true.

**FIG. 23.2.**

Components of the coronary angioplasty system. The original Gruentzig fixed guidewire balloon (A) is compared with the steerable guidewire system (B). Although both are advanced through a guiding catheter positioned in the coronary ostium, neither the wire shape nor its orientation could be changed once the original Gruentzig catheter was introduced, whereas the steerable design allows the guidewire to be advanced, withdrawn and reshaped, and steered independently of the balloon catheter to select the desired vessel. Once in place in the distal vessel beyond the target lesion, the guidewire serves as a rail over which the angioplasty balloon or other device can be advanced. (From Willerson JT, ed. Treatment of heart diseases. New York: Gower Medical, 1992.)

**Guiding Catheters**

Guiding catheters remain a crucial component in PTCA. Compared with the small lumens, minimal torque control, and sharp edges of the crude initial Teflon guiding catheters, current designs more closely emulate the performance of catheters used for diagnostic coronary angiography. To allow passage of therapeutic instruments, however, guiding catheters must have a lumen diameter at least twice that of a typical diagnostic catheter (e.g., 0.080-inch [2 mm] vs. 0.040-inch [1 mm]). To achieve this lumen in a catheter whose outer diameter is 8F (2.7 mm, or 0.107-inch), the wall thickness must be less than 0.010-inch (0.5 mm). Yet the catheter must still incorporate a Teflon liner to reduce friction, metal or plastic braid to transmit torque and provide sufficient stiffness to offer “backup” support during device advancement, and a smooth outer coating to resist thrombus formation. The complexity of this design goal requires use of special materials whose properties are typically varied along the length of the catheter to optimize the balance between support and flexibility at each point. Most guiding catheters now also include a very soft material in the most distal 2 mm of the catheter to reduce the chance of vessel trauma during engagement of the nontapered tip. Current guiding catheters are available in shapes similar to conventional Judkins and Amplatz curves, as well as a wide range of custom shapes, such as hockey-stick, multipurpose, and Voda (7), that are designed to ease engagement or provide better support for balloon advancement.

Although 9F guiding catheters predominated in the early 1980s, 8F (2.7 mm) catheters are in common use today. Improvements in catheter design have enabled routine lumen diameters of 0.088 inches in 8F guiding catheters to facilitate passage of bulkier devices such as stents and Rotablator burrs. Smaller (7F and even 6F) guiding catheters are also available, with a more restricted inner diameter (0.076 inches or 1.9 mm), well suited to the current generations of balloon catheters and bare-mounted stents and ideal for use from alternative access sites such as the radial artery (see Chapter 4). Larger (9F and 10F) guiding catheters with lumen diameters up to 3 mm (0.120 inch) are still used occasionally for certain procedures such as directional or extraction atherectomy. The standard guiding
Use of deep-guiding catheter engagement to facilitate coronary intervention. Complex lesion in the right coronary artery including aneurysm and diffuse distal disease. Left Amplatz guiding catheter (AL-1) is deeply engaged to provide optimal support for stent placement. After stent placement, the vessel is widely patent, but replacement of the Amplatz catheter with a conventional right Judkins catheter (JR4) shows how effective the Amplatz has been in straightening out a severe upward bend (shepherd’s hook) in the proximal right coronary artery. Although progressive improvements in device profile and trackability have made such deep engagement less necessary, the technique is still of great value in selected cases.

Deep seating of the guiding catheter needs to be done with great care and with coaxial advancement of the guiding catheter over a balloon catheter, to avoid injuring the proximal coronary artery. Catheter length is 100 cm, but shorter (90 cm) guides are available to allow more distal passage of devices with limited working lengths during procedures on distal lesions in saphenous vein or internal mammary grafts (see later discussion). Much of the technology developed for interventional guiding catheters (e.g., thin walls, soft tips) has now been fed back into the design of diagnostic catheters to allow safer coronary engagement and brisk contrast injections through 6F (and even 5 or 4F) catheters.

To function adequately, the guiding catheter must be able to selectively engage the ostium. This requires the selection of an appropriate catheter shape and the ability to manipulate the catheter under fluoroscopic guidance (see Chapter 11). Engagement of the desired vessel, however, must not interfere with arterial inflow. Although this is routinely possible in the left coronary artery, damping of the guiding catheter in the right coronary artery ostium was once a common and vexing problem before the introduction of guiding catheters equipped with side-holes that allow ongoing perfusion despite wedged engagement. However, because the guiding catheter must deliver small boluses of contrast medium into the involved vessel (as needed to visualize vascular side branches and the target lesion for angioplasty), contrast flow out of such side-holes may increase the total contrast load used during a procedure. A second important function of the guiding catheter is to provide adequate support for advancement of the dilatation catheter across the target stenosis. This support derives from the intrinsic stiffness of the guiding catheter material, a catheter shape that buttresses it against the opposite aortic wall, and/or deep engagement of the guiding catheter into the coronary ostium (Fig. 23.3). Deep engagement was routinely required in the mid-1980s, when poor balloon catheter performance demanded a large measure of support if the balloon was to be forced across a severe stenosis. Unfortunately, deep engagement of the guiding catheter was also a well recognized cause of complication (i.e., ostial dissection). Although deep-guiding catheter engagement is still required on occasion (particularly with smaller, 6F guiding catheters), guiding catheter–induced dissection has become far less frequent with the incorporation of an atraumatic bumper on the tip of most guiding catheters and deep engagement of the guiding catheter only by its coaxial advancement over the balloon catheter. When a deeply engaged guiding catheter is used to push a dilatation balloon or other device across the lesion, the operator cannot forget to then withdraw the guiding catheter back to a more neutral position (just within the vessel ostium) to avoid its migration into an even deeper position as the device is withdrawn. In this sense, the ability to actively use the guiding catheter constitutes one of the important skills required for effective management of the overall angioplasty equipment system.

FIG. 23.3.

Use of deep-guiding catheter engagement to facilitate coronary intervention. Left: Complex lesion in the right coronary artery including aneurysm (dark arrow) and diffuse distal disease (open curved arrow). Center: Left Amplatz guiding catheter (AL-1) is deeply engaged to provide optimal support for stent placement. Right: After stent placement, the vessel is widely patent, but replacement of the Amplatz catheter with a conventional right Judkins catheter (JR4) shows how effective the Amplatz has been in straightening out a severe upward bend (shepherd’s hook) in the proximal right coronary artery. Although progressive improvements in device profile and trackability have made such deep engagement less necessary, the technique is still of great value in selected cases. Deep seating of the guiding catheter needs to be done with great care and with coaxial advancement of the guiding catheter over a balloon catheter, to avoid injuring the proximal coronary artery.

Guidewires

The original dilatation catheter designed by Gruentzig had a short segment of guidewire (spring coil) attached to its tip to help it follow the vessel lumen and avoid subintimal passage as the catheter was passed to and across the stenosis (Fig. 23.2). Because the shape and orientation of this leading wire could not be modified once the catheter had been introduced, it provided the operator relatively little control over whether the catheter followed the desired path or was diverted into a side branch proximal to the lesion. In contrast, the movable guidewire system designed by Simpson in the early 1980s contained a standard 0.018-inch Teflon-coated wire that extended and moved freely through the central lumen of the dilatation catheter (8). If this guidewire selected the desired vessel, it could continue to be advanced until it crossed the target lesion. If the guidewire instead selected a more proximal side branch, the balloon catheter could be advanced into the main vessel to a point just before the side branch to hold that place as the wire was withdrawn and reshaped in an effort to choose the desired path beyond. By a series of such iterative advancements of wire and dilatation catheter, many lesions could be crossed with the guidewire and then with the
dilatation catheter. The first “steerable” guidewires were introduced in 1983, and guidewire technology has continued to improve with the evolution of a wide range of wire sizes (down to 0.009-inch), tip stiffness, shaft support, and lubricious coating.

In contrast to crude early guidewires, modern guidewires are designed to combine tip softness, trackability around curves, radiographic visibility, and precise torque control, which allow the guidewire to be steered past vascular side branches and through tortuous or stenotic segments. With these refinements, crossing a subtotal lesion with the guidewire has become a task that takes seconds rather than minutes to hours, helping to open up the more distal portions of the coronary circulation to a variety of interventional devices. The basic guidewire consists of a solid core (stainless steel or the superelastic alloy known as nitinol) that is ground to a progressive taper in its distal portion. This taper helps retain torque control when the wire is steered around the series of bends located in the guiding catheter and proximal coronary anatomy and allows the stiffer proximal portions of the wire to follow the soft tip into side branches. This core is covered by a spring coil, which is usually Teflon-coated stainless steel on the body of the wire and platinum on the distal 3 to 25 cm (for greater radiographic visibility). A family of plastic-covered guidewires with a hydrophilic coating is available to aid in crossing vessels with extreme tortuosity or total occlusion, but the spring-coil design is still dominant. At the tip of the guidewire, the coil is welded to the tapered core, either directly or through an intermediary shaping ribbon that allows the operator to kink or bend the tip of the wire to a shape that is appropriate for navigating the vessel features it must pass-such as larger-diameter bends for selecting left anterior descending (LAD) versus circumflex artery, smaller kinks or bends for selecting diagonal versus LAD. If greater probing force is required (e.g., for crossing a chronic total occlusion), stiffer tip designs (intermediate or “standard” rather than floppy) are available. When more shaft support is needed to help advance a stiff device (e.g., a stent) around a bend, extra support wires are available with a thicker and stiffer inner core. To allow exchange of one device for another, double-length (300-cm) exchange wires are widely available. I use these exchange-length wires as my initial wire in most cases, because they help retain access to the distal vessel as a series of devices (balloons, rotational atherectomy burrs, stents) is employed, without the risk of subintimal passage of the second guidewire as it crosses the partially dilated segment (9). A similar strategy can be followed with shorter (175 cm) guidewires if “rapid-exchange” balloon catheters and stent delivery systems are used (see later discussion). These advanced features are now obtainable in guidewires whose diameters range from 0.010 to 0.018 inch (0.25 to 0.5 mm) in 0.002-inch increments. The largest-diameter guidewire that is compatible with the lumen of the particular device (usually 0.014 inch in current practice) is employed, to minimize any potential mismatch between the wire and the tapered tip of the balloon catheter that might impede smooth passage. Although the movable guidewire concept (implemented in the current spectrum of highly sophisticated steerable guidewires) has simplified, shortened, and improved the success rate of coronary angioplasty, it is still important to heed the advice of Dotter and Judkins (1) that “the guidewire is passed across the atheromatous block more by the application of judgment than of force.”

**Dilatation Catheters**

The dilatation catheters for coronary angioplasty have undergone radical evolution since 1977. As described previously, the original Gruentzig catheters were designed with a short segment of guidewire permanently affixed to the catheter tip to decrease the risk of subintimal passage during advancement down the coronary tree. The shaft of this catheter had two lumens—one for inflation and deflation of the balloon and one for distal pressure measurement and/or contrast injection. This reflected the reliance on monitoring of transstenotic (i.e., aortic root to distal coronary) pressure gradients as a way of assessing lesion severity, given the difficulty in performing adequate contrast injections through small-lumen guiding catheters around the large (4.3F, or 1.3 mm) shafts of early balloon catheters. In contrast, virtually all dilatation catheters since 1982 have used an independently movable and/or steerable guidewire extending the entire length of the dilatation catheter, as described by Simpson and coworkers (Fig. 23.2). The central lumen of such dilatation catheters must have a sufficient caliber to allow free movement of the guidewire, but it is generally no longer used for either pressure measurement or contrast injection. The concept of using transstenotic pressure gradients to evaluate the significance and completeness of correction of coronary stenoses, however, has undergone renewed interest with the advent of solid-state pressure measurement guidewires (see Fractional Flow Reserve in Chapter 18).

An important feature of the dilatation catheter is the diameter of the smallest opening through which the deflated balloon can be passed (its “profile”). Compared with the 0.060-inch (1.5-mm) profile of the original Gruentzig design, current over-the-wire dilatation catheters have profiles of 0.032 in (0.8 mm) or less. Specially designed...
“fixed-wire” devices, which consist of a balloon mounted directly on a steerable wire core, were developed and used widely in the late 1980s to provide deflated profiles as small as 0.020 in (0.5 mm). Ongoing refinements in balloon technology, however, have allowed competitive performance from over-the-wire systems, thereby restricting the use of such fixed-wire devices to special situations (e.g., dilating side branches through the struts of a stent placed in the parent vessel). To preserve the best balloon profile, a “negative” or “aspiration” preparation (rather than a “positive” preparation, in which the balloon is first aspirated and then inflated with contrast material) is generally preferred, maximizing the probability that the balloon will cross a severe lesion. Although the primary and secondary (i.e., after an initial inflation) balloon profiles are important aspects of performance, the ability of the balloon to bend so as to advance easily through tortuous vascular segments (trackability) and the presence of sufficient shaft stiffness (pushability) to force it through the stenosis are also important. Delivery of the balloon is also aided by the incorporation of a friction-resistant coating (silicone or a hydrophilic coating such as polyethylene oxide) to improve surface lubricity. Other specialized properties of balloon catheters include whether the catheter travels over the wire along its full length or just in its tip (rapid-exchange or monorail style) to allow quick removal and reinsertion of a catheter over a short (i.e., 175-cm) guidewire. So-called “perfusion balloon” catheters also have been designed with either a series of side-holes in the shaft proximal and distal to the balloon segment or a spiral channel within the balloon to allow ongoing antegrade blood flow and thereby mitigate myocardial ischemia during prolonged balloon inflations (Fig. 23.4). Although prolonged inflations do help control elastic recoil and stabilize some dissections, they do not improve long-term results (freedom from restenosis). In the era when stents are used for recoil and dissection, the use of perfusion balloons has become rare.

FIG. 23.4.

Use of a perfusion balloon catheter. **Top:** The inflated perfusion balloon (arrow) is shown in the left anterior descending artery (LAD) and can be recognized by the presence of the non-contrast-filled (white) perfusion lumen running through the center of the balloon. **Bottom:** Injection through the guiding catheter (left curved arrow) shows direct opacification of the circumflex (straight arrow) as well as contrast flow into the distal LAD: this flow enters through proximal side-holes, passes through the perfusion lumen within the balloon, and flows out into the distal vessel (right curved arrow). The 40- to 60-mL/min flow to the distal vessel through the perfusion lumen helps mitigate myocardial ischemia during prolonged balloon inflations, but use of such high-profile devices has become less common since the advent of more effective ways (i.e., stents) to stabilize coronary dissections.

Other than these factors that influence the ability to deliver the balloon catheter across the target lesion, the most important characteristic of the dilatation catheter is its ability to inflate to a precisely defined diameter despite application of pressures that average 10 atm (150 psi). This was not possible with early balloons manufactured from polyvinyl chloride, whose compliance led to balloon oversizing and rupture at pressures as low as 6 atm. More suitable performance can be readily achieved today with balloons manufactured from polyethylene, polyethylene teraphalate (PET), polyolofin (POC, SciMed), or nylon, with a wall thickness as low as 0.0003 to 0.0005 inch. More compliant balloon materials such as polyolofin tend to reach their rated (nominal) diameter at 6 atm (90 psi) and then grow by up to 20% above their nominal size (e.g., a 3.0-mm balloon growing to 3.5 mm) at 10 atm. Semicompliant balloon materials such as polyethylene or nylon grow by less than 10% over this pressure range, whereas truly noncompliant balloon materials such as PET can retain their defined diameter up to 20 atm (300 psi) to allow dilatation of calcific stenoses or full expansion of coronary stents (Fig. 23.5).

FIG. 23.5.

Successful dilatation of a rigid calcific lesion. This rigid lesion (top, arrow) in the middle left anterior descending coronary artery of a patient who had undergone coronary artery bypass surgery (note surgical clips) resisted dilatation at 300 psi (20 atm) but yielded to an inflation pressure of 330 psi (22 atm) (middle two photographs), with an excellent angiographic result (bottom). Such pressures are obtainable only with special high-pressure balloon construction, because most standard angioplasty balloons have rated rupture pressures of only 180 psi (12 atm). In current practice, such lesions would more likely be treated by rotational atherectomy (see Chapter 24).

Balloon compliance characteristics must be kept in mind especially whenever a compliant or semicompliant balloon is
inflated pressures above 6 to 8 atm (90 to 120 psi), to avoid overstating the adjacent normal vessel. Because the noncompliant balloon materials preclude growth in normal segments upstream and downstream of a rigid lesion, they may be desirable whenever high pressures are needed, and they may also help to treat resistant lesions by concentrating dilating force on the stenosis itself (rather than in balloon growth and dilatation of the adjacent vessel). Regardless of which balloon type is used, staying within the prescribed range of inflation pressures is also important to prevent balloon rupture. This pressure range is specified in terms of the rated burst pressure (i.e., an inflation pressure at which the probability of balloon rupture is less than 0.1%). Taking any balloon catheter above its rated burst pressure increases the risk of balloon rupture, with the potential for air embolization (if the balloon was incompletely purged), local dissection, or difficulty in removing the balloon from an incompletely dilated lesion (11). This risk grows the further above rated burst pressure that the balloon is inflated, until it reaches 50% risk of rupture when the average burst pressure is reached. With the availability of effective therapies for calcified or fibrotic lesions (e.g., rotational atherectomy [see Chapter 24]), it is usually unnecessary to take any balloon catheter to pressures more than 1 to 2 atm above the rated burst pressure except in rare circumstances such as stent postdilatation in a calcified or fibrotic lesion that has not been adequately predilated or pretreated with rotational atherectomy.

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Dilatation catheters that meet these design specifications are currently available from a variety of manufacturers with inflated diameters of 1.5 to 4.0 mm, in 0.5-mm increments, to match the size of the coronary artery in which the stenosis is located. Larger balloons (i.e., 4.5, 5.0, and 6.0 mm) are occasionally needed for treatment of large right coronary arteries or saphenous vein grafts. These once had to be obtained as special orders of the bulkier balloons used for peripheral vascular intervention, but large-size coronary balloons are now available in most coronary balloon lines. Quarter-sized balloons (e.g., 2.25, 2.75, and 3.25 mm) are also available, but that degree of precision probably exceeds the operator’s ability to gauge vessel size, and stocking “quarter-sizes” tends unfavorably to increase the size of a laboratory’s balloon inventory. The usual length of the inflatable balloon segment is 20 mm, but most balloons can be obtained with inflated segment lengths that are shorter, such as a 10- or 15-mm length for a high-pressure dilation completely within a 15-mm stent, or longer, such as 30 or 40 mm for dilation of a diffusely diseased segment (12), (13). Most lesions can be dilated effectively with balloon catheters from any of the several manufacturers, but the fact that there are still subtle differences in performance characteristics that can make the difference between success and failure makes it necessary for each interventional laboratory to stock a variety of balloon types. Although competition has brought the average balloon price down substantially (from its high of almost $700 to less than $300), continued pressure on catheterization laboratory budgets has raised the possibility of resterilization and reuse. At least one recent trial of this concept, however, showed an increase in procedure time and device failures for resterilized product (14).

PROCEDURE

In that catheters are introduced under local anesthesia, a coronary angioplasty procedure bears a superficial resemblance to diagnostic cardiac catheterization. However, because angioplasty involves superselective cannulation of diseased coronary arteries with guidewires and balloon catheters, temporary occlusion of antegrade coronary arterial flow, and an attempt to manipulate the offending atherosclerotic lesion by balloon inflation, the procedure is a great deal more complicated and entails roughly 10 times the risk (i.e., 1% vs. 0.1%) associated with diagnostic catheterization (15). These risks should be discussed in detail with the patient and family before the procedure. The potential use of new devices and any alteration in management related thereto (e.g., need for additional antiplatelet therapy including oral agents or intravenous platelet IIb/IIIa integrin receptor blockers) should also be discussed, along with the probability that a repeat intervention may be necessary if restenosis of the dilated segment occurs. Special problems, such as the risk of “no reflow” during vein graft intervention or loss of involved side branches,
should be described, if relevant. These small but very real risks of major complications highlight why angioplasty should be attempted only by experienced personnel in a setting where full cardiac surgical and anesthetic support is available (16).

Although patients were once admitted the night before elective angioplasty, current cost-driven protocols delay admission until the morning of the procedure. Details of the patient evaluation, informed consent, and preprocedure laboratory work usually have been completed in a separate outpatient visit or are compressed into a very brief encounter immediately before the procedure. This is particularly true for patients who come to catheter-based intervention at the conclusion of what began as a diagnostic catheterization (“ad hoc angioplasty” or “catheterization with angioplasty standby”). The patient should have been prepared by prescription of oral intake after midnight on the evening before the procedure, and pretreatment with a calcium channel blocker (to prevent vessel spasm at the treatment site) and aspirin 325 mg/day to diminish platelet deposition on the disrupted endothelium (17). Other antiplatelet agents, including low-molecular-weight dextran and dipyridamole 200 mg/day, were once administered in conjunction with angioplasty but have now been abandoned due to lack of demonstrated efficacy, potential allergic or volume-overload side effects with dextran, and the availability of more potent antiplatelet agents. The increasing use of stents and the importance of oral platelet adenosine diphosphate–receptor antagonists (ticlopidine and clopidogrel) (18), as well as the important benefit of intravenous platelet IIb/IIIa integrin receptor blockers in preventing periprocedural infarction and emergency revascularization for vessel closure (19) (Table 23.1), has made either or both classes of agents commonplace additions to aspirin therapy. Controlled trials have yet to show that any type of antiplatelet therapy consistently decreases the incidence of subsequent restenosis. Because aspirin reduces late cardiac mortality in patients with coronary disease, it is generally continued indefinitely after the procedure. In the aspirin-allergic patient, use of these alternative antiplatelet agents (sometimes with the addition of oral sulfipyrazone) is mandatory.

Angioplasty may be done by the brachial approach, although more than 90% of current procedures are done from the femoral approach. Although most catheter-based interventions can be performed safely without right-sided heart catheterization, I still prefer to place a right heart catheter to allow potentially valuable measurement of baseline and intraprocedure filling pressures in patients with abnormal baseline left ventricular function or who are undergoing treatment of major vascular territories. The venous sheath also allows rapid initiation of ventricular pacing, although experience shows that placement of a prophylactic pacemaker is seldom needed in patients undergoing coronary angioplasty (20). After placement of the arterial sheath, intravenous heparin (70 units/kg, or 7,000 to 10,000 units) is administered. Because there is wide patient-to-patient variability in heparin binding and activity, the activated clotting time (ACT) should be measured, and additional heparin should be administered as needed to prolong the ACT to 275 to 300 seconds before any angioplasty devices are introduced and to maintain it at this level throughout the case. Lower levels of ACT (less than 250 seconds) are associated with a marked increase in the incidence of occlusive complications (21), although ACTs in the 275-second range are acceptable when adjunctive IIb/IIIa receptor blockade is used. Higher ACTs (greater than 300 to 350 seconds) tend to increase the risk of bleeding. In setting the target ACT, it is important to understand which machine is being used, because measurement with the Hemochron system (International Technidyne, Edison, NJ) tends to give values 30 to 50 seconds higher than those measured by the rival HemoTech machine (Medtronic Hemodynamics, Minneapolis, MN). Preliminary testing suggests that other direct thrombin inhibitors (e.g., low-molecular-weight heparin, hirudin, bivalirudin [Hirulog], argatroban) may find increasing use during angioplasty, based on more predictable dose-response characteristics than heparin and potentially greater efficacy against clot-bound thrombin (22–25). They may also be useful in patients with the heparin-induced thrombocytopenia or thrombosis syndrome (see Chapter 3).

Baseline angiograms are then obtained of one or both coronary arteries, using either standard diagnostic catheters or the angioplasty guiding catheter. When the guiding catheter is used for baseline angiography, it must be manipulated carefully, because its large diameter and nontapered tip increase the risk of ostial injury. Coronary injections should be repeated after the administration of 200 mg of intracoronary nitroglycerin to demonstrate that spasm is not a significant component of the target stenosis and to minimize the occurrence of coronary spasm during the subsequent angioplasty. My colleagues and I have seen cases where the intended target of a catheter-based intervention resolved with intracoronary nitroglycerin, and an unnecessary intervention was avoided! Baseline angiography also serves to evaluate any changes in angiographic appearance (interval development of total occlusion, thrombus formation) that have occurred since the diagnostic catheterization and to permit the selection of those angiographic views that allow optimal visualization of the stenoses and their surrounding branch vessels.
The appropriate guiding catheter is connected to the pressure manifold (see Chapter 11) by way of an extension tube and a rotating hemostatic valve (Tuohy-Borst valve) and positioned in the coronary ostium. The hemostatic valve contains an adjustable O ring that allows introduction and free movement of the angioplasty balloon while maintaining a sufficient seal around the balloon shaft to permit pressure measurement and contrast injection. The angioplasty guidewire is then steered across the target lesion, guided by puffs of contrast material through the guiding catheter, in a projection that shows the desired path free of foreshortening or overlapping side branches. Some operators advance the guidewire through a dilatation catheter that has been placed into the guiding catheter through the hemostatic valve so that it lies just inside the distal tip of the guiding catheter. Others (myself included) prefer a bare-wire technique, in which an exchange-length guidewire is placed into the hemostatic valve through a needle-like guidewire introducer. This permits free movement of the wire during advancement through the guiding catheter and down the involved coronary vessel, while preserving excellent contrast injections absent an obstructing balloon catheter. Once the position of the wire tip in the distal vasculature has been confirmed by contrast angiography, the introducer is removed from the hemostatic valve, and the desired angioplasty balloon or other device is selected.

Experience has shown that the best and safest angioplasty results are obtained with a balloon whose diameter closely approximates that of the presumably nondiseased “reference segment” adjacent to the site being treated (balloon/artery ratio, 0.9:1.1) (26,27). A slightly larger balloon (1.1 to 1.2 the reference lumen) may be used if an intravascular ultrasound study (see Chapter 19) shows that the outer vessel diameter in the reference segment (external elastic membrane diameter) is significantly larger than the reference lumen. On the other hand, a slightly smaller initial balloon may be chosen if it is difficult to estimate the correct reference size in a diffusely diseased or rapidly tapering vessel, or if great difficulty is anticipated in crossing the lesion. The selected balloon is prepared by flushing the central (guidewire) lumen with heparinized saline and filling the balloon inflation lumen with a dilute radiographic contrast material (Renografin-60, or Renografin-76 diluted to half strength). When balloon rupture was more frequent, contrast filling was accomplished by a “positive” preparation, in which the balloon was inflated with contrast material and then aspirated to remove any air. With more robust balloon materials, however, it is now more common to perform only a “negative” preparation, in which a contrast-filled syringe is used to pull air from the balloon lumen and then to let the balloon aspirate a small amount of contrast material when vacuum on the syringe is released. This method of preparing the balloon catheter avoids inflation of the balloon before it is across the target lesion and therefore helps to maintain the lowest possible deflated profile for crossing a severe stenosis. The prepared and flushed balloon catheter is then loaded onto the free end of the guidewire. The tip of this balloon is brought down to the O-ring, which is loosened to permit passage of the balloon into the guiding catheter, down the proximal vessel, and across the lesion.

Once the dilatation catheter has been positioned within the target stenosis, the balloon is inflated progressively using a screw-powered, handheld inflation device equipped with a pressure dial. At low pressure (i.e., 2 to 4 atm, or 30 to 60 psi), the balloon typically has an “hourglass” appearance due to its central restriction by the coronary stenosis being treated. In soft lesions, this restriction, or waist, may expand as pressure is gradually increased, allowing the balloon to assume its full cylindrical shape. In more rigid lesions, the restriction may remain prominent until the balloon expands abruptly at a “stenosis yield pressure” that may be anywhere between 4 and 10 atm (60 to 150 psi) (28). Some operators increase pressure rapidly until all balloon deformity resolves, in the hope that pushing rigid lesions to higher pressure will produce further balloon expansion, but this increases the risk of dissection when a fibrotic or calcified plaque yields suddenly. With the availability of effective tools for dealing with such fibrotic or calcific plaques (i.e., the Rotablator; see Chapter 24), one must then consider whether it is preferable to treat a plaque that resists expansion at 10 atm by rotablation, rather than pushing to the pressures (15 to 20 atm, or 225 to 300 psi; Fig. 23.5) that may be required for full dilation. Calcified or fibrotic rigid stenoses resist expansion at conventional pressures, but elastic (usually eccentric) stenoses are also problematic. These lesions allow full balloon expansion at low pressures but then tend to recoil promptly once the balloon is inflated. This type of lesion was once treated by repeated inflations or cautious use of oversized balloons, but they are now treated routinely by stenting (with or without prior debulking by directional atherectomy). The “cutting balloon,” its surface modified by the application of three to four microscopic blades that protrude slightly above the balloon surface when inflated, has also been used for fibrotic or elastic lesions (29).

Despite the more than 20-year history of balloon angioplasty, there is still little objective science behind the speed and maximal pressure used to inflate a dilatation balloon. The classic approach is to go deliberately (over 10 to 15 seconds) to a pressure that resolves the balloon waist, and then maintain that pressure for 1 minute. On the other hand, some operators prefer a slower speed of inflation and are prepared to tolerate mild persistent balloon...
deformities that have failed to resolve at moderate (6 to 8 atm) pressure (30) (Fig. 23.6), although the evidence for improved outcome is still inconclusive (31). In addition to this operator-to-operator variability in inflation speed, there is wide variation in the duration of inflation. Early data from Kaltenbach et al. (32) suggested that inflations of 1 minute might offer more benefit than the 30-second inflations used in the early 1980s. Even longer (15-minute) inflations with a perfusion balloon may produce slightly better acute results, with no difference in long-term patency (10).

FIG. 23.6. Demonstration of low-pressure balloon inflation (2 atm, or 30 psi) Left, top: Long calcified lesion in the middle left anterior descending coronary artery (small arrows). Left, center: Rotablator burr (1.75 mm, arrow) being advanced across the lesion. Left, bottom: Result after application of Rotablator shows residual stenosis despite improvement in lumen (long arrow). Right, top: Low-pressure inflation of a 2.5 × 30 mm balloon shows full expansion of the balloon at either end of the lesion but tubular mild constriction throughout the lesion (arrows). Right, bottom: Despite absence of full balloon inflation, a postdilation angiogram shows excellent luminal patency without dissection (open arrow). Although higher inflation pressure might have produced further lumen enlargement, it would probably have caused prominent local dissection, resulting in the need for stent implantation despite the unfavorable small caliber and long length of the target lesion.

Whatever inflation strategy is selected, the response of each lesion to balloon dilatation must then be assessed individually so that the dilatation protocol can be tailored to achieve the best possible result. The most common way to assess lesion response to balloon dilatation is repeat angiography performed through the guiding catheter. By leaving the exchange-length guidewire in place during such angiography, access to the distal vessel and the ability to perform additional intervention (e.g., repeat balloon inflation, stent placement) are maintained. Complete normalization of the vessel lumen would be the ideal end result of coronary angioplasty. Given the mechanism of angioplasty (see later discussion), the more typical result of a successful angioplasty is a 30% residual diameter stenosis (i.e., a 1.9-mm lumen in a 3-mm vessel) with some degree of intimal disruption (reflected as localized hazziness, filling defect, or dissection). The operator must decide whether this result is adequate or whether further treatment is needed. Some additional benefit frequently can be obtained by repeated or more prolonged balloon inflation, (i.e., 3 to 5 minutes rather than the usual 1 minute), which may require use of a perfusion balloon to attenuate associated myocardial ischemia. A larger balloon may provide greater lumen enlargement. This possibility can be explored by exploiting any compliance in the initial balloon (e.g., inflating it to higher pressure, such as 10 rather than 6 atm) or by using the next-larger balloon size. In doing so, however, one must weigh any potential benefits against the clear risk of using an oversized balloon: Although dilatation with a larger balloon may improve luminal caliber, it also may increase the risk of producing a large dissection leading to abrupt vessel closure (26). This creates a clear dilemma, however, because “better is frequently the enemy of good”: Striving for “perfect” luminal enlargement with balloon angioplasty not uncommonly led to conversion of a patient with a fair result to one who had to go to immediately to the operating room for treatment of a dissection caused by “one more balloon inflation.”

In the stent era, of course, much less emphasis is placed on pushing the results of balloon angioplasty to the maximum. Most lesions that can be stented are stented. Even if stenting is not planned, the mere availability of stenting to treat balloon-induced dissection has helped improve the results of balloon angioplasty by allowing the operator to push for the best result, knowing that stenting is always available to fine-tune the angioplasty results if there is persistent stenosis of more than 20% or to repair a balloon-induced dissection. It remains uncertain what percentage of patients must be stented for such a “provisional” stent strategy to have its results approach those of preemptive stenting (see also Chapter 25). In trials evaluating provisional stenting, upwards of 40% of balloon angioplasty patients received stents before short and long-term results were as good as those in patients who underwent preemptive stenting (see Chapter 25). But even stenting in the approximately 15% of patients with the worst angioplasty outcomes has substantially improved the results of balloon angioplasty (both acute success and complications, as well as long-term freedom from clinical and angiographic restenosis) in the “control” arm of trials comparing new devices to balloon angioplasty performed after the 1994 introduction of widespread stenting in the United States. In the current view, the best position for stand-alone balloon angioplasty is in lesions that are poorly suited to stenting—vessels smaller than 2.5 mm, with lesions longer than 30 mm, particularly in patients with diabetes mellitus.

Given the importance of achieving the best acute angiographic result and the uncertainty about the adequacy of the acute result as assessed angiographically, a number of other techniques have been employed to grade the quality of an
angioplasty result. In the initial years of PTCA, operators relied heavily on the transstenotic gradient as an index of dilatation adequacy, seeking a postdilatation pressure difference of less than 15 mm Hg between the aortic pressure (measured through the guiding catheter) and the distal coronary artery pressure (measured through the tip of the dilatation catheter). In practice, measurement of the gradient is complicated by the presence of the dilatation catheter within the stenosis and the small size of the dilatation catheter lumen; these factors, together with the switch to low-profile over-the-wire dilatation catheters, led to abandonment of the gradient measurement by 1988 (33). There has been some recent reawakened interest based on the availability of newer, solid-state pressure-measuring guidewires that can be used to assess the transstenotic gradient at baseline flow and during maximal hyperemia (34).

The fractional flow reserve (FFR) is defined as the ratio of distal coronary pressure to aortic pressure during adenosine-induced hyperemia (see Chapter 18), with a goal FFR greater than 0.95 after a successful angioplasty. The same type of physiologic assessment can be done using Doppler flow-measuring guidewires to assess diastolic/systolic flow ratios or coronary flow reserve (CFR) as an index of baseline lesion significance and a confirmation of adequate dilation. Alternatively, intravascular ultrasound (IVUS; see Chapter 19) can more accurately measure lumen diameter and cross-sectional area after dilation. IVUS has been helpful in procedures (such as directional atherectomy or stenting) where additional dilation is likely to provide further improvement in luminal caliber. It has provided important mechanistic insights into balloon angioplasty but is not used in more than 10% to 15% of routine clinical cases because of the added procedural time and expense. In most laboratories, the postdilation angiogram remains the “gold standard” for determining whether an adequate result has been obtained. If the intent is to perform stand-alone balloon angioplasty and the angiogram shows that a technically appropriate attempt at conventional dilatation has produced a poor result (residual stenosis greater than 50%, prominent dissection, frank abrupt closure), secondary use of a new device such as a stent is indicated.

Once adequate dilatation is deemed to have been achieved, it is common to withdraw the balloon catheter completely from the guiding catheter. The exchange-length guidewire is then left across the dilated segment for several minutes, while the treated vessel is observed over several minutes for angiographic deterioration. Injections through the guiding catheter with the balloon removed provide excellent angiographic visualization, while the indwelling guidewire provides easy access to the dilated segment to permit readvancement of the balloon if needed. With more predictable interventions such as stenting, however, a single set of postprocedure angiograms in orthogonal views is usually sufficient to document a suitable result in the treated lesion and the absence of dissections or branch occlusions in the adjacent portions of the vessel. Once stability of the dilated segment has been established, the guidewire is withdrawn, and other significant lesions are dilated similarly or the patient is transferred to a recovery area.

**POSTPROCEDURE MANAGEMENT**

Although the heparin administered during PTCA was once reversed to allow immediate removal of the femoral sheaths, it later became routine to leave the sheaths in place overnight with continued heparin infusion, perfusion of the sheath lumen (Intra-flow II, 30 mL/hr), and monitoring for distal limb ischemia. This practice allowed prompt vascular reaccess should delayed abrupt closure occur (35). In current interventional practice, however, such delayed abrupt closure occurs so infrequently (well less than 1%) that most laboratories now remove the sheaths later the same day, as soon as the heparin effect wears off. There is no evidence that prolonged postprocedure heparin infusion improves outcome (36), and there are compelling data that same-day ACT-guided sheath removal has lowered the incidence of femoral complications and facilitated next-morning discharge. The current standard is thus to give no further heparin after an uncomplicated procedure that has had a good angiographic result, and then to perform same-day sheath removal once the ACT has fallen below 160 seconds. When angioplasty is performed with 7F or 8F sheaths, control of the arterial puncture site during sheath removal can be achieved with the same manual compression techniques used for diagnostic catheterizations. With larger sheaths (or more intense anticoagulation protocols), however, prolonged compression (more than 30 minutes) may be required; this is better performed with the use of a mechanical aid, such as Femo-stop (USCI) or Compressar (Instromedix, San Diego, CA). The other alternative is to perform immediate sheath removal in the setting of full heparinization by using one of the several arterial puncture sealing devices now available (see Chapter 4).

After sheath removal, the patient typically remains at bedrest for 18 to 24 hours and then ambulates before discharge. On discharge, patients are usually given a calcium channel blocker for 6 weeks (longer if required for another
indication such as hypertension) and aspirin (325 mg/day) indefinitely. Patients who received a stent are also given additional antiplatelet therapy (ticlopidine or clopidogrel) for 2 to 4 weeks. With a good angiographic result in the treated lesions, marked relief of ischemic symptoms should be expected unless other significant disease has been left behind. In the patient with multivessel disease (see later discussion), it may be particularly helpful to evaluate the postangioplasty physiologic state by a maximal exercise test in the first few weeks after discharge. Earlier (i.e., predischarge) exercise testing was once performed on a routine basis but has now been largely abandoned due to the potential for groin rebleeding, delay of discharge, or the small risk of precipitating thrombotic closure of the dilatation site. Patients may return to full activity within 72 hours, by which time the groin puncture site should have healed sufficiently to allow even brisk physical activity.

Patients should expect to have no anginal symptoms early after discharge. Ongoing anginal symptoms suggest persistent untreated disease or a poor result at the treatment site. On the other hand, initial symptomatic relief followed by recurrence of symptoms after 2 to 6 months suggests restenosis of the dilated segment. Recurrence of symptoms 1 or more years after successful angioplasty suggests progression of disease at another site. Along with education regarding these possibilities and their proposed management (repeat exercise testing and catheterization, with the possibility of more catheter intervention or bypass surgery), the acute angioplasty admission should be viewed as an opportunity to educate the patient and family about changes in lifestyle or drug therapy (to control hypertension or lipid abnormalities), and to reduce the risk for the progression of atherosclerotic disease (37).

MECHANISM OF PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY

According to the original explanation proposed by Dotter and Judkins (1) and by Gruentzig et al. (3), the enlargement of the vessel lumen after angioplasty was ascribed to compression of the atheromatous plaque-akin to footprints in the snow. In fact, true plaque compression accounts for the minority of the observed improvement (38). Extrusion of liquid components from the plaque does permit some compression of soft plaques but contributes minimally to improvement in more fibrotic lesions, even when balloon inflation is prolonged to 1 minute. Absent significant reduction in plaque volume, most luminal improvement after PTCA seems to result from plaque redistribution-more like footprints in wet sand. Some of this takes place by longitudinal displacement of plaque upstream and downstream from the lesion. Most improvement in the lumen, however, results from controlled overstretching of the entire vessel segment by the PTCA balloon. This stretching leads to fracture of the intimal plaque, partial disruption of the media and adventitia, with consequent enlargement of both the lumen and the overall outer diameter of the vessel (38) (Fig. 23.7). Although use of a full-sized balloon (balloon/artery ratio of 1:1) should theoretically eliminate all narrowing at the treatment site, the overstretched vessel wall invariably exhibits elastic recoil (39), (40) after balloon deflation, as well as some degree of local vasospasm (41). These processes typically leave the stretched vessel with a 30% residual stenosis (i.e., a 2-mm lumen in a 3-mm vessel that has been dilated with a 3-mm balloon). Newer devices such as stenting or directional atherectomy are able to provide lower (0% to 10% rather than 30%) postprocedural residual stenosis, by reducing or even eliminating this elastic recoil and vascular tone.

FIG. 23.7.

Proposed mechanism of angioplasty. A: Deflated balloon positioned across stenosis. B: Inflation of the balloon catheter within the stenotic segment causes cracking of the intimal plaque, stretching of the media and adventitia, and expansion of the outer diameter of the vessel. C: After balloon deflation, there is partial elastic recoil of the vessel wall, leaving a residual stenosis of 30% and local plaque disruption that would be evident as “haziness” of the lumen contours on angiography. (From Willerson JT, ed. Treatment of heart diseases. New York: Gower Medical, 1992.)

In addition to wrestling with tendencies of the deeper vessel wall to exhibit elastic recoil, the operator also must contend with the problems produced by localized trauma to more superficial plaque components. This trauma is apparent as an almost universal haziness of the lumen margin in the post-PTCA angiogram, reflecting superficial plaque injury (42). Greater degrees of disruption are reflected by intimal filling defects (Fig. 23.8), contrast caps outside the vessel lumen, or spiral dissections that may interfere with antegrade blood flow (Fig. 23.9). This local
disruption has been seen on IVUS, on angioscopy, and on histologic examination of postmortem angioplasty specimens, and its extent correlates with the risk of an occlusive complication (43) (see Abrupt Closure). Given the amount of “angioblasty” that takes place, it is remarkable that dislodgment and distal embolization of plaque fragments seemed to be infrequent in both experimental studies (44) and most early angioplasty procedures. Disruption of the plaque, however, may clearly lead to embolization of atherosclerotic debris in patients undergoing dilatation of a saphenous vein bypass graft and in those with large thrombi adherent to the lesion (45). In these patient, distal embolization of large (more than 1 mm) plaque elements is usually manifested as an abrupt “cutoff” of flow in the embolized distal vessel. In contrast, microembolization of plaque debris or adherent thrombus may be more common than suspected (46) and may contribute to postprocedure chest pain and enzyme elevation. In 2% to 5% of angioplasties (particularly of vein grafts or platelet-rich thrombi in patients with recent myocardial infarction [MI]) there may be a dramatic reduction in antegrade flow with manifestations of severe ischemia (chest pain, ST-segment elevation). This may be caused by release of vasoactive agents (including serotonin, which may cause intense arteriolar vasospasm of the distal microvasculature) or by liberation of a very large number of microemboli that physically plug the distal microcirculation. It is important to distinguish this “no-reflow” phenomenon from more proximal causes of flow restriction (dissection, spasm, proximal thrombosis), because the no-reflow phenomenon can usually be quickly reversed by administration of low doses of intracoronary calcium channel blockers (e.g., 100 g of verapamil or 500 g of diltiazem) into the distal vessel (47),(48). Others have reported reversal with distal injections of other vasodilators such as adenosine or nitroprusside, but the syndrome is usually not responsive to nitrates. When drug therapy is not effective at restoring normal flow, the patient with no reflow will almost certainly go on to sustain a substantial MI, and consideration should be given to intraaortic balloon counterpulsation support. In patients with vein graft disease, alternative approaches (distal occlusion aspiration devices or debris filters) are being investigated to prevent this problem before it occurs (see Chapter 24).

FIG. 23.8. Normal healing of percutaneous transluminal coronary angioplasty (PTCA)–related coronary dissection. Compared with the baseline angiogram (A), the immediate post-PTCA angiogram (B) shows enlargement of the left anterior descending coronary artery lumen with two small filling defects typical of an uncomplicated coronary dissection. C: Follow-up angiogram 3 months later shows preservation of luminal caliber with complete healing of the localized dissection. (From Baim DS. Percutaneous transluminal coronary angioplasty. In: Braunwald E, ed. Harrison's principles of internal medicine: update VI. New York: McGraw-Hill, 1985.).

FIG. 23.9. Coronary dissection leading to abrupt reclosure. The appearance of a right coronary artery stenosis before (A) and immediately after (B) coronary angioplasty, with an evident localized dissection. Within 15 minutes after removal of the dilatation catheter, the patient experienced chest pain associated with inferior ST-segment elevation and angiographic evidence of progressive dissection with impeded antegrade flow (C). Standard management in 1980 (when this case was done) consisted of emergency bypass surgery, which was accomplished without complication. Current practice would be to attempt to recross the lesion and “tack down” the dissection by repeat balloon inflation or, more likely, to place a stent. (From Baim DS. Percutaneous transluminal angioplasty: analysis of unsuccessful procedures as a guide toward improved results. Cardiovasc Intervent Radiol 1982;5:186.)

Although it is a theoretical possibility with sufficient local stretching trauma, frank vessel rupture has turned out to be a rare consequence during conventional balloon angioplasty, barring the use of significantly oversized balloons (49). Such vessel perforation is more common (approximately 1% incidence) when new atherectomy devices such as directional atherectomy, rotational atherectomy, or laser angioplasty are used (50) (see Chapter 24).

ACUTE RESULTS OF ANGIOPLASTY

Early published data on coronary angioplasty success derive mostly from the 3,000-patient NHLBI Angioplasty Registry, which collected all procedures performed between 1977 and September of 1981 (51). Although case selection in the registry focused on “ideal” PTCA candidates—those with proximal, discrete, concentric, subtotal, noncalcified stenoses of a single vessel—the primary success rate of 63% would be considered disappointing by current standards. The main explanations for this low rate were failure to cross the lesion with the dilatation system (29% of cases) and failure to dilate the lesion adequately once having crossed it (12% of cases). These failures resulted from two factors: the relative lack of experience of operators contributing cases to the registry (the “learning curve”) and the use of original Gruentzig fixed-wire dilatation catheters, which had limited maneuverability, a comparatively high deflated balloon profile, and a low peak inflation pressure.
Despite the inclusion of patients with more difficult coronary anatomy, progressive improvement in equipment (with widespread availability of steerable guidewires since 1983) has pallowed progressive improvement in the primary success rate of coronary angioplasty (5). The second PTCA registry enrolled patients at 14 centers between 1985 and 1986 (52), with a success rate of 90%. Moreover, analysis of complications in the 1985–1986 registry (53) shows a concomitant reduction in the incidence of emergency bypass surgery (from 5.8% to 3.5%) and a reduction in the mortality rate for patients with single-vessel disease (SVD) (from 0.85% to 0.2%), although overall procedural mortality remained close to 1% because of the inclusion of greater numbers of patients with multivessel disease. In the late 1980s and early 1990s, success was obtained in roughly 85% of patients undergoing balloon angioplasty, with major complications occurring in roughly 6% of patients and including death in 1.5%, Q-wave MI in 1.5%, and emergency surgery in 3%. These outcomes have improved further with the introduction of new devices (late 1990s), with acute procedural success rising to more than 95% and major adverse cardiac events falling to roughly 3% (death, 1%; emergency surgery, 0.7%; and Q-wave or large non–Q wave MI, 1.3%).

Anatomic improvement after an angiographically successful PTCA correlates with elimination of anginal symptoms and improved function on atrial pacing or conventional exercise testing (54),(55). Studies using thermodilution, videodensitometry, and Doppler flow measurement have shown restoration of coronary flow reserve after successful coronary angioplasty, although full normalization may take a matter of weeks to return (see Chapter 18).

**COMPICATIONS**

As a specialized form of cardiac catheterization, coronary angioplasty is attended by the usual risks related to invasive cardiac procedures (see Chapter 3). In contrast to diagnostic procedures, the larger-caliber guiding catheter used for angioplasty is more likely to result in damage to the proximal coronary artery and to cause local bleeding complications at the catheter introduction site. Selective advancement of guidewires and dilatation catheters into diseased coronary arteries may lead to vessel injury if they are manipulated too aggressively. The most common complications of coronary angioplasty, however, relate directly to local injury at the dilatation site caused as part of the angioplasty process (56), as described in the section concerning mechanisms (see earlier discussion).

**Coronary Artery Dissection**

Although plaque dissection may be caused by overly vigorous attempts to pass the guidewire through a tortuous stenotic lumen, most dissections are the result of the “controlled injury” induced intentionally by inflation of the dilatation catheter (37),(38). In fact, localized dissections can be found routinely in animal or cadaveric models of angioplasty and are evident angiographically in approximately one half of patients immediately after angioplasty (42). When these dissections are small and nonprogressive and do not interfere with antegrade flow in the distal vessel, they have no clinical consequence other than transient mild pleuritic chest discomfort. Follow-up angiography as soon as 6 weeks after the angioplasty procedure usually demonstrates complete healing of the dissected segment (Fig. 23.8), although localized formation of aneurysm at the site of dissection has occasionally been described (57),(58).

**Abrupt Closure**

Although small dissections may be well tolerated, large progressive dissections may interfere with antegrade flow and lead to total occlusion of the dilated segment (a phenomenon known as abrupt closure; Fig. 23.9). With the use of balloon angioplasty alone (before the advent of new devices), abrupt closure occurred in approximately 5% of patients as the result of compression of the true lumen by the dissection flap (43), with superimposed thrombus formation, platelet adhesion, or vessel spasm. In one study (59), postangioplasty dissections were evident angiographically in 40% of dilated lesions, with spiral (type D) dissections (51) in 3.5% of patients. The presence of a type D dissection increased the risk of frank or “threatened” abrupt closure (residual stenosis greater than 50%, with reduced antegrade flow) from a baseline of 6.1% to 28%. This finding supports the earlier findings of Ellis et al. (60), showing a five-fold increase in abrupt closure with postprocedure dissection and stressing the relative importance of the postprocedure result (as opposed to preprocedure clinical or angiographic variables; Table 23.1) on the risk of abrupt closure.
Most abrupt closures after stand-alone balloon angioplasty developed within minutes after the final balloon inflation, so that it was desirable to observe the patient for 10 minutes before leaving the catheterization laboratory. Abrupt closure could also occur up to several hours later (in 0.5% to 1% of cases), particularly as the heparin anticoagulation wore off. Under those circumstances, it was heralded by severe chest pain and clear electrocardiographic changes (usually ST-segment elevation) similar to those observed during prolonged balloon inflation. Before 1985, most patients who experienced abrupt closure of a major epicardial coronary artery went directly to emergency surgery, in an effort to minimize the consequent amount of myocardial damage. The rate of emergency surgery was 5% to 6%, but even with emergency surgery within 90 minutes after the onset of vessel occlusion, up to 50% of patients sustained a Q-wave MI (61). The development of “perfusion” catheters-infusion catheters or angioplasty balloons with multiple sideholes along their distal shaft to allow 40 to 60 mL/min of blood to enter proximal to the site of occlusion, flow through the central lumen, and reexit into the lumen distal to the point of occlusion-allowed patients to go to the operating room in a nonischemic state (Fig. 23.4), reducing the incidence of transmural infarction during emergency surgery to approximately 10% (62). Once it was realized that many abrupt closures can be reversed by simply readvancing the balloon dilatation catheter across the lesion to “tack up” the dissection via repeated balloon inflation (35) (Fig. 23.10), the emergency surgery rate fell in half, to roughly 3%. Prolonged balloon inflations-up to 20 minutes, using an autoperfusion balloon (63) to limit ongoing ischemia-further improved the ability to reverse abrupt closure.

FIG. 23.10.

Reversal of abrupt closure by repeat balloon inflation. Eccentric stenosis in the mid-right coronary artery (left, arrow) dilates (center) with production of a large dissection (curved arrow), focal dye stain (open arrow), and retarded distal flow. Repeat inflations with a 0.5-mm-larger balloon catheter, using inflation durations of up to 5 minutes, “tacked up” the dissection to provide a stable luminal appearance (right, arrow). Approximately 50% of abrupt closure events can be reversed in this manner, with up to 90% reversal by use of a coronary stent.

Since 1993, the availability of coronary stents has increased the certainty of reversing abrupt closure to almost 90% (64). This success has made it routine to stent any patient with a large postprocedure dissection, as a preemptive treatment for “threatened” abrupt closure even when flow compromise is not apparent. With elective stenting of more than 80% of interventional procedures, this problem has been largely eliminated, and emergency surgery rates have fallen below 0.5%. Because emergency surgery is still required in some cases, the recommendation is still in place to perform elective coronary angioplasty only in settings where the resources for prompt emergency bypass surgery are available (16).

Beyond the mechanical issues of residual stenosis and local dissection, it is now clear that platelet-rich clots contribute significantly to the abrupt closure process. The presence of thrombus, reflected as a globular filling defect, increases the risk of abrupt closure from 7.2% to 27.8% (59). The role of thrombus in abrupt closure is further supported by an increased risk of abrupt closure in patients with a subtherapeutic ACT value (20) and by the reduction of ischemic end points seen in patients treated with a bolus plus infusion of various platelet IIb/IIIa integrin blockers (Table 23.2) (17). Although platelets may adhere to damaged vessel walls through other receptors, it is the activation of the 50,000 to 80,000 glycoprotein IIb/IIIa receptors on each platelet's surface that allows them to bind avidly to fibrinogen to cause platelet aggregation and thrombosis. Vessels with moderate local dissection but preserved antegrade flow are more likely to stay patent in the presence of agents that reduce the affinity of the activated IIb/IIIa receptor for fibrinogen, thereby reducing the incidence of emergency surgery or unplanned (bailout) stent placement. These agents also appear to reduce the incidence of peri procedural MI, particularly the incidence of creatine kinase (CK) elevations (non-Q wave MIs) that are seen in 10% to 30% of patients undergoing coronary intervention (65). Until it is clear that prophylactic use of such agents improves hard end points such as mortality or emergency surgery, however, the expense and increased bleeding risks associated with the use of these agents has constrained their use in most laboratories to the 30% to 40% of patients who have high-risk lesion morphologies or a suboptimal mechanical result after mechanical intervention.

In certain subgroups-those with extensive prior or ongoing myocardial damage, multivessel disease, a large myocardial territory perfused by the target stenosis, or prior coronary bypass surgery-the consequences of abrupt closure may be more severe. Before the widespread availability of stenting, these patients had a procedure-related
mortality rate several times higher than the 0.3% to 0.6% rate seen with elective coronary angioplasty (66). This required the most vigilant surgical standby and immediate availability of hemodynamic support devices, including intraaortic balloon counterpulsation and, potentially, percutaneous cardiopulmonary support (CPS) via 18F femoral arterial and venous cannulas (67),(68) (see Chapter 21). More recently, however, the high degree of reliability of stent intervention has meant that such patients do well with nothing more than prophylactic intraaortic balloon counterpulsation.

Other Complications

A number of other complications have been described as the result of coronary angioplasty. Q-wave MI occurs in approximately 1% of patients (53), often as a result of abrupt closure or “snowplow” loss of a major side branch originating within or in close proximity to the lesion being treated. If creatine kinase MB (CK-MB) isoenzyme levels are measured routinely, however, 10% to 30% of patients show some elevation after apparently uncomplicated procedures (65), usually as the result of distal microembolization or loss of smaller side branches. The importance of these “infarctlets” is still the subject of some debate. Certainly larger non–Q wave infarctions—those with absolute CK-MB levels greater than 5 times the upper limit of normal or those associated with new ST-T wave abnormalities—probably have the same import as a periprocedural Q-wave infarction. Overnight electrocardiographic monitoring is prudent, and discharge should be delayed for 24 to 48 hours to ensure clinical stability. The debate, however, centers on smaller elevations of CK-MB, between 1 and 5 times normal. These events do not significantly impair ventricular function or increase the 1-year mortality rate, and in our laboratory we do not generally classify such enzymatic abnormalities as significant infarctions or delay the timing of planned discharge (69). On the other hand, a number of large studies have demonstrated that patients with CK-MB elevations 1 to 5 times greater than normal have an increased incidence of adverse events (variably identified as death, repeat MI, repeat revascularization) at 3 to 5 years. Were this a cause-and-effect relationship, one would expect those randomized device trials in which one study arm had greater CK elevation (e.g., directional atherectomy) to show higher mortality, which has not been the case (70). One would also expect that drug interventions that decrease the frequency of CK-MB elevation (e.g., IIb/IIIa platelet receptor blockers) would significantly lower mortality, but this has been seen only for post hoc selected subgroups. In a pooled analysis of more than 12,000 interventional patients enrolled in randomized trials of IIb/IIIa receptor blockers versus placebo, the odds ratio for mortality at 6 months was 0.90 (95% confidence interval, 0.70 to 1.16; \( p = .41 \)) (17). If the relationship is not cause-and-effect, the other possibility is that both the CK elevations and the variety of late events are related to a common factor (a confounder), such as the diffuseness of atherosclerotic disease. By analogy to the example of the association of carrying matches and lung cancer (through the confounder of cigarette smoking), devices or drugs that decrease the incidence of CK elevation would not change the underlying disease process or its late manifestations (any more than banning matches would eliminate smoking-related lung cancer). Until and unless a cause-and-effect relationship is demonstrated (i.e., through an across-the-board reduction in late mortality by periprocedural IIb/IIIa blocker administration), the practice in my laboratory is to use these agents only for the approximately 30–40% of patients who have certain high-risk lesions or lesions in which the best attempt at mechanical revascularization still fails to provide an angiographically perfect result.

Other than embolization of plaque constituents, embolization of large thrombi that are adherent to the stenosis may occur and should be taken into account during angioplasty of patients with unstable angina or acute MI (see earlier discussion). This may include overnight intracoronary infusion of a thrombolytic agent or use of one of the new mechanical thrombectomy devices (see Chapter 24). Embolization of smaller thrombus or plaque particulates, which can cause slowed antegrade perfusion and transmural ischemia in the absence of proximal vessel compromise or distal cutoffs, known as the “no reflow” phenomenon (45). It is most common (2% to 8%) in patients who undergo treatment of a lesion responsible for recent MI or treatment of a saphenous vein graft. The mechanism may include embolization of platelet-rich thrombi that release vasoconstrictive substances (e.g., serotonin) which can cause intense vasospasm of the distal microcirculation, or release of atherosclerotic plaque debris (particularly during vein graft intervention) that can “sludge” the distal vessels (46).

Occlusion of branch vessels originating from within the stenotic segment occurs in 14% of vessels at risk during angioplasty of the main vessel, according to what has been called the “snowplow effect” (71) (Fig. 23.11). If the branch vessel is small, this event usually has no significant clinical sequelae and should not discourage attempted angioplasty. On the other hand, if a large branch vessel originates from within the stenosed segment, simultaneous dilatation of the main vessel and the involved branch with two separate dilatation systems (the “kissing balloon”
The "snowplow" effect. Dilatation of mid-right coronary artery stenosis resulted in occlusion of a diseased right ventricular branch that originated from within the stenotic segment. There were no clinical sequelae. Approximately 14% of involved branches suffer a similar fate. (From Baim DS. Percutaneous transluminal angioplasty. In: Braunwald E, ed. New York: McGraw-Hill, 1985.)

Bifurcation atherectomy. Bifurcation stenosis involving the circumflex and the large obtuse marginal branch. Directional atherectomy of circumflex has provided a large smooth lumen, with ongoing stenosis of the origin of the marginal branch. After atherectomy of the marginal branch, excellent patency of both the main vessel and the involved side branch have been secured.

Position of the directional atherectomy catheter during cuts in the circumflex. Position of atherectomy catheter during cuts in the marginal branch. Atherectomy of the main branch and involved side branch, followed by kissing balloon dilatation, remains an effective way to approach such lesions (see reference 74), although several stent-based approaches are being developed (see Chapter 25).

Bifurcation atherectomy. Left, top: Bifurcation stenosis involving the circumflex (arrow) and the large obtuse marginal branch. Left, center: Directional atherectomy of circumflex has provided a large smooth lumen (curved arrow), with ongoing stenosis of the origin of the marginal branch (small arrow). Left, bottom: After atherectomy of the marginal branch, excellent patency of both the main vessel and the involved side branch have been secured. Right, top: Position of the directional atherectomy catheter during cuts in the circumflex. Right, bottom: Position of atherectomy catheter during cuts in the marginal branch. Atherectomy of the main branch and involved side branch, followed by kissing balloon dilatation, remains an effective way to approach such lesions (see reference 74), although several stent-based approaches are being developed (see Chapter 25).

Perforation of the coronary artery with a stiff guidewire occurs rarely and does not necessarily have dire consequences, unless a device is passed over the wire or the wire perforation takes place in a patient receiving a platelet IIb/IIIa receptor blocker. Frank rupture of the coronary artery resulting from use of too large a dilatation balloon or use of an atherectomy device (see Chapter 24) can cause vessel perforation that leads to rapid tamponade and hemodynamic collapse (49),(50). Tamponade also may result from perforation of the right atrium or right ventricle during placement of temporary pacemaker electrode catheters, particularly in angioplasty patients who are receiving antiplatelet therapy in addition to full heparinization. This potential complication and the infrequency (less than 1%) of severe bradycardiac complications support our recommendation against prophylactic pacing during coronary angioplasty (19). Ventricular fibrillation occurs in approximately 1% of angioplasty procedures (53), usually as the result of prolonged ischemia during balloon advancement or inflation. In addition to causing electrical instability, ischemia during balloon inflation may cause marked electrocardiographic changes, (75) abnormalities in regional left ventricular systolic and diastolic function (76),(77), and regional myocardial lactate production.
Although angioplasty guidewires and catheters are extremely reliable devices, failures can occur when any device is subjected to severe operating stresses, as when a guidewire is rotated repeatedly in a single direction while its tip is held fixed in a total occlusion or when a balloon catheter is inflated past its operating pressure range in an attempt to dilate a resistant stenosis. In a small percentage of cases, this may lead to detachment of a part of the wire or dilatation catheter, with a fragment remaining in the coronary artery (78). In the stent era, this also includes dislodgment of a bare-mounted stent from its delivery balloon. To avoid the need for surgical removal, the angioplasty operator should be familiar with the techniques of catheter retrieval (79). Finally, the operator must be careful to limit the amount of contrast material administered (usually to 3 or at most 4 mL/kg) to avoid renal toxicity, particularly during complex or multivessel procedures.

THE HEALING RESPONSE TO CORONARY ANGIOPLASTY: RESTENOSIS

After successful balloon angioplasty, the body attempts to repair the damage caused by the procedure-related mechanical injury. Within minutes, a carpet of platelets and fibrin is deposited. Within hours to days, inflammatory cells begin to infiltrate the site, cytokines are released, and vascular smooth muscle cells begin to migrate from the media toward the lumen. These smooth muscle cells and fibroblasts convert from their normal phenotype to a synthetic phenotype and remain in this form as they undergo hypertrophy, proliferate, and begin to secrete extensive extracellular matrix. The luminal surface is simultaneously colonized by endothelial cells that slowly regain their normal barrier function and secretory functions in making tissue plasminogen activator (tPA) and endothelial-derived relaxation factor. Along with this proliferative neointimal response, there may be further elastic recoil and fibrotic contraction of the vessel wall during this period. Different arteries and interventions appear to result in different degrees of proliferation and vessel contraction—for example, stents renarrow exclusively by neointimal hyperplasia, whereas most other devices also undergo a significant amount of late narrowing due to contraction (unfavorable remodeling) of the entire vessel wall (80). There are also significant patient-to-patient variations in the late healing response after coronary intervention, reflected in variables amounts of “late loss” in lumen diameter between the completion of the intervention and the time when the repair process stabilizes (roughly 6 months) (Fig. 23.14). Follow-up angiography shows continued maintenance of lumen diameter at the treated site beyond 6 to 9 months (81).

FIG. 23.14.

Mechanisms of restenosis: cross-section of a restenotic lesion in the left anterior descending coronary artery 5 months after initial coronary angioplasty shows the original atherosclerotic plaque (AS), the crack in the medial layer induced by the original procedure (star), and the proliferation of fibrocellular tissues (FC) that constitutes the restenotic lesion. (From Serruys PW, et al. Assessment of percutaneous transluminal coronary angioplasty by quantitative coronary angiography: diameter versus videodensitometric area measurements. Am J Cardiol 1984;54:482.

If the healing response is excessive, however, most or all of the gain in lumen diameter produced by the initial intervention may be lost to the healing process. This causes the return of a severe stenosis and ischemic symptoms—a phenomenon known as restenosis of the dilated segment (82) (Fig. 23.15). Throughout the 1980s, restenosis was considered to be a dichotomous outcome (i.e., it either did or did not develop). A large number of competing dichotomous restenosis definitions (e.g., loss of half the gain, late loss more than 0.72 mm) were developed, adding to the general confusion about restenosis rates. Although a great deal was learned about restenosis from the study of conventional angioplasty patients (e.g., its time course, histology, various clinical factors correlating with an increased incidence of restenosis) (83), data derived from stent and atherectomy procedures have led to new paradigms for evaluating restenosis (84). It is now considered more useful to consider restenosis as a continuous variable. A cumulative distribution curve may be used to show the ranked population distribution of the late result, expressed either in terms of late lumen diameter or late percent diameter stenosis, for the whole treated population (Fig. 23.16). On the diameter stenosis curve, the percentage of the population with a late diameter stenosis of more than 50% (analogous to the original dichotomous Emory definition) serves as a useful benchmark for comparing the angiographic “restenosis rates” between different populations or treatment groups.

The view of restenosis as a continuous process that takes place to some degree in every treated segment favors displaying the late result (here, percent stenosis at follow-up) for the whole treated population. For patients treated by balloon angioplasty, directional atherectomy, or stenting, the y-axis shows the percentage of patients who have a stenosis greater than the value on the x-axis. The ability of stenting and atherectomy to lower restenosis is shown by a shift of their “cumulative distribution function” curves to the left. If a dichotomous definition of restenosis is applied, the intersection of each curve with a late diameter stenosis of 50% (vertical line) corresponds to a dichotomous restenosis rate of 43% for angioplasty, 31% for atherectomy, and 26% for stenting. (From Kuntz RE, et al. Novel approach to the analysis of restenosis. 1992;19:1493.)

Further understanding is gained by comparing the acute gain in lumen produced by the intervention to the late loss in lumen diameter that results from the healing process. Every treated lesion undergoes some degree of late loss, but this process usually negates only part (roughly half) of the acute gain, so that a long-term net gain in lumen diameter (and alleviation of ischemia) results. Another important finding is the tendency toward a linear relationship between late loss in lumen diameter (caused by the proliferative and fibrotic reaction of the artery during the healing phase) and the acute gain in lumen diameter caused by the intervention. The slope of this relationship (the loss index) is roughly 0.5 for most interventions, corresponding to the payment of a late loss “tax” equal to about half of the acute gain. Larger lumen diameters immediately after intervention translate into larger lumen diameters at 6-month angiographic restudy (the “bigger is better” dictum). To date, all new mechanical devices (e.g., stents, directional atherectomy) that have lowered the restenosis rate compared with balloon angioplasty have done so by providing a larger acute lumen diameter (more acute gain). Once minimal lumen diameter is included in the statistical model, the particular device used (stent or atherectomy versus PTCA) is no longer an important determinant of restenosis (Fig. 23.17).

The strongest determinants of the probability of restenosis (using a definition of late diameter stenosis greater than 50%) are a large postprocedure lumen diameter and a low residual percent stenosis. Once these variables are taken into account, it no longer matters which device was used—it is the result and not the device that matters. Balloon angioplasty (triangles) resulted in a 2- to 2.3-mm lumen with a 40% restenosis rate, whereas stenting produces a 2.9- to 3.2-mm lumen with a 20% restenosis rate (slightly worse results with stenting in the STRESS study are shown, as well). Directional atherectomy (squares) had an angioplasty-like result in CAVEAT but a more stent-like result in BOAT and OARS (see Chapters 24 and 25). (Modified from Kuntz RE, et al. A generalized model of restenosis following conventional balloon angioplasty, stenting, and directional atherectomy. J Am Coll Cardiol 1993;21:15.)

The importance of postprocedure geometry to the late result does not, however, mean that other biologic variables are unimportant. A number of biologic factors (e.g., diabetes, LAD lesion location, prior restenosis, the presence of previously activated smooth muscle cells) have been shown to increase the loss index to as high as 0.70 (84), a level at which even perfect (0% residual stenosis) acute results are associated with a large late loss, a small net gain, and a high restenosis rate in vessels smaller than 4 mm. From this perspective, a drug or other treatment that could decrease the loss index “tax” rate would be dramatically effective in reducing restenosis. Efforts to reduce the restenosis rate by manipulating procedure-related variables such as duration of conventional balloon inflation (10) have been largely unrewarding unless, like stenting, they produce markedly more favorable acute results (i.e., a larger posttreatment...
LONG-TERM RESULTS OF ANGIOPLASTY

Although the preceding discussion of restenosis emphasizes mechanistic and quantitative angiographic analyses of late outcome (with an emphasis on the status of the treated site), the long-term clinical benefit of coronary angioplasty as a strategy for treating patients with coronary artery disease derives from its ability to prevent subsequent ischemic events. The traditional measure of this ability has been the freedom of angioplasty patients from any subsequent events. The search for such treatments is vital, however, since finding an agent that would decrease the loss index even slightly (e.g., from 50% to 35%), would have a major impact on angiographic restenosis rate. Because the complex healing response involves so many mechanisms (smooth muscle cell proliferation, matrix synthesis, recoil, and fibrotic vessel contraction), and because it appears to be driven by a variety of agonists (e.g., platelet-derived growth factor, thrombin), agents (such as antisense DNA to the protooncogene c-myc) that selectively inhibit a final common pathway (smooth muscle cell division) may be of benefit (85). In conventional angioplasty, where late vessel contraction (in addition to the neointimal proliferation response) plays an important role, drugs such as probucol, which seem to favorably affect late remodeling, may be of value (86). On the possibility that antirestenosis drugs might have to be delivered locally or in high concentration or prolonged duration to the treatment site, a number of local drug delivery systems and sustained-delivery vehicles are being investigated (87). The other promising approach is local radiation therapy (brachytherapy). Studies with both ( - and (-radiation (88,89,89a) suggest that a dose of roughly 1,400 to 1,800 rad (cGy) delivered to the treatment site by a catheter system retards the local proliferative response and may be a promising primary or secondary treatment for restenosis, particularly the purely proliferative restenosis that takes place within stents.

Recurrent angina caused by progressive disease in a nondilated segment. Left coronary artery in right anterior oblique projection before (A) and after (B) successful dilatation of the middle left anterior descending (LAD) coronary artery. Despite the presence of a moderate lesion in the circumflex marginal branch, this patient had an entirely normal exercise tolerance test until the recurrence of symptoms 1 year later. C and D: Preserved patency of the LAD but interval progression of the circumflex stenosis, which was then dilated successfully to restore an asymptomatic status. (From Baim DS. Percutaneous transluminal coronary angioplasty: analysis of unsuccessful procedures as a guide toward improved results. Cardiovase Intervent Radiol 1982;5:186.)
patients (a 31% restenosis rate), 36 of whom had associated symptoms. Only 4 additional patients who had a patent angioplasty site at 6 months developed restenosis later during follow-up (a 3% later restenosis rate), although 25 patients (18%) went on to develop significant narrowing at other nondilated sites during follow-up. At 10 years, patients with single-vessel versus multivessel disease at the time of initial PTCA had substantially better clinical outcomes, with a lower actuarial incidence of MI (9% vs. 29%); MI or bypass surgery (26% vs. 48%); and MI, bypass surgery, or repeat PTCA (37% vs. 44%). They also had better symptomatic status, with freedom from angina in 79% versus 67%, respectively.

These long-term data from this “index” angioplasty series are mirrored in more recent studies (except for a much higher initial procedural success rate). Because most of the late events relating to the treatment site occur in the first 6 to 8 months, it is appropriate to concentrate on a shorter follow-up period (i.e., 1 year). A follow-up report on 838 patients with SVD in the 1985–1986 Registry (92) showed mortality in 1.6%, MI in 1.9%, repeat angioplasty in 18.1%, and bypass surgery in 6.2% within the first year after hospital discharge. In more recent studies, in which balloon angioplasty has included stenting of the worst acute results (see earlier discussion of provisional stenting), the incidence of repeat revascularization within the first year in patients with single-vessel intervention has fallen further, with a TLR rate (by either catheter intervention or bypass surgery) of only 17%, and similarly-defined 1-year TLR rates in some stent trials as low as 12%.

The repeat revascularization rates for patients with multivessel disease are clearly higher (see later discussion). In the 1985–1986 Registry, patients with multivessel disease had a higher in-hospital mortality rate than those with single-vessel disease (1.7% vs. 0.2%); adverse events within the first year after hospital discharge were only slightly more common (mortality in 2.8%, MI in 3.4%), but patients with multivessel disease had an increased need for repeat revascularization. This has been borne out in the randomized trials (e.g., Bypass Angioplasty Revascularization Investigation [BARI]) comparing angioplasty with bypass surgery for patients with multivessel coronary artery disease, where up to 35% of angioplasty patients (but only 5% of surgery patients) required a repeat revascularization within the first year after treatment (92). Newer studies, in which patients with multivessel disease are treated with stenting (rather than with conventional balloon angioplasty alone, as in the studies performed in the late 1980s), have a reduced (approximately 20%) late need for repeat revascularization.

Until a practical and completely effective means of preventing restenosis is established, patients who develop recurrent symptoms in the months after a successful angioplasty should be presumed to have a problem with restenosis. They should be scheduled for repeat coronary angiography, with the anticipation that, should the presence of restenosis of the dilated segment be confirmed, a repeat intervention (Fig. 23.15) will be performed during the same procedure. When repeat balloon angioplasty was the only such procedure available, it was noted that the acute success and safety rates of a repeat angioplasty for restenosis were somewhat higher than those of first angioplasties, but that at least 30% of such patients would go on to develop a second restenosis (93). At particularly high risk (94) were men with long lesions or associated disease progression at other sites who presented with recurrent stenosis within 5 months after the first dilatation. Subsequent restenoses were treated by third, fourth, or even fifth dilatations, although the restenosis rate approached 50% as the number of repeat dilatations increased (95). Many patients with recurrent restenosis ultimately chose the alternative of surgical revascularization. In the new device era, most such patients will have undergone stent placement for these lesions at some point in their treatment history. Although this may decrease the incidence of subsequent restenosis, when it does occur the special considerations relating to the treatment of in-stent restenosis apply (see Chapters 24 and 25). With recent studies suggesting that local radiation (brachytherapy) is the key to controlling in-stent restenosis, however, this long-standing limitation of angioplasty may be largely controlled.

Several other causes of recurrent symptoms after apparently successful coronary angioplasty should be considered. The first is coronary artery spasm, which may be exacerbated within the first 6 weeks after the procedure (96). Many groups use calcium channel blockers during this period, particularly given the suggestion that uncontrolled spasm may increase the chance of organic restenosis (97). A second cause of recurrent symptoms after successful angioplasty is persistence of disease in undilated segments. Whereas cardiac surgeons routinely bypass all significant stenoses at the time of surgery, most angioplasty operators confine their efforts to the severe (greater than 70%) stenoses (98), leaving behind more moderate lesions that are unlikely to cause persistent symptoms. The rationale for this approach is that dilatation of these milder lesions requires additional time and administration of contrast medium, exposes the patient to additional hazards of abrupt vessel closure, and may initiate progressive restenosis leading to a more severe lesion than was present initially (99). On the other hand, failure to dilate significant and clinically
relevant lesions in patients with multivessel disease may cause persistent symptoms leading to subsequent need for revascularization (Fig. 23.18). When symptoms recur more than 6 months after successful dilatation, disease progression is the most likely explanation (100). Whether symptom recurrence is triggered by restenosis or lesion progression, repeat catheter-based intervention is usually effective in long-term nonoperative management (101). Late stenosis at the left or right coronary ostium (presumably the result of guiding catheter–induced injury) also has been reported as a rare cause of late symptom recurrence (102) and is readily apparent on angiographic restudy.

**CURRENT INDICATIONS**

With the improvements in equipment and technique that have been described, coronary angioplasty has grown progressively through the 1980s and 1990s (Fig. 23.1). By 1990, more than 400,000 angioplasty procedures were performed annually, represent almost half all revascularizations (angioplasty plus bypass) performed in the United States each year (5). By the end of the 1990s, the number of percutaneous catheter-based revascularizations (including both conventional balloon angioplasty and the ever-growing family of newer devices) had grown to more than 500,000. The fact that there has been no demonstrable fall in the use of bypass surgery during this period suggests that the use of angioplasty has moved beyond the narrow group of patients who would have undergone bypass surgery (as had been suggested in the original NHLBI registry guidelines) to the point where it is now also seen as an alternative to medical therapy in selected patients.

These trends toward greater reliance on catheter-based intervention are also evident in the record of individual programs. Since the mid-1980s, about one third of all patients coming through our diagnostic laboratory have been treated by coronary angioplasty. Data from Emory between 1981 and 1988 (103) show a similar pattern. The percentage of diagnostic catheterization patients going on to coronary angioplasty increased from 4.3% to 30.3%, while the percentage undergoing bypass surgery decreased only from 44.0% to 28.5%. Therefore, almost as much of the growth in angioplasty procedures over that period was explained by contraction of the fraction of patients treated medically (from 51.7% to 41.2%) as by the shift from surgery to angioplasty. In a survey of practice extending from 1989 to 1997 at the 17 U.S. sites that participated in the BARI trials (see Multivessel Coronary Artery Disease), the percentage of all revascularizations that were catheter based (versus surgical) increased from 52.2% to 62% by 1997, with a corresponding growth of new devices from 11.6% to 67% of all catheter-based procedures (104).

Because the person who is responsible for case selection is often the person who will perform the angioplasty, it is critically important that operators have a full understanding of the indications and outcomes so that only suitable patients are treated. The issues that need to be addressed include (a) how compelling is the clinical justification for revascularization, (b) do the “culprit” lesions have anatomic features that suggest reasonable level of safety and probability of successful dilatation, (c) what combination of conventional balloon angioplasty and newer interventional devices would offer the best short- and long-term outcomes, and (d) does angioplasty compare favorably (or at least equally) with the other therapeutic options such as bypass surgery or continued medical therapy. This evaluation process involves integration of complex clinical, angiographic, pathophysiologic, and technical knowledge to decide whether a particular patient is a “candidate” for angioplasty and therefore constitutes an important component of angioplasty operator training (see earlier discussion).

With the rapid growth of coronary angioplasty, several cardiology organizations have prepared position statements that attempt to outline its “correct” utilization (16), (105) (Table 23.3). These statements are useful compilations that outline some well accepted indications and contraindications for coronary angioplasty, but they each consign situations in which decisions are difficult and individualized to a “possibly indicated” category. In an effort to review some aspects of these evolving or controversial indications, the following discussion of various anatomic clinical applications of coronary angioplasty is offered.

**Single-Vessel Coronary Disease**

When the NHLBI registry was formed in 1979, patients were selected in the context of the abilities of then-current angioplasty equipment and the considerable risk of the new therapeutic modality. To be candidates for coronary angioplasty, a patient was required to have medically refractory angina, objective evidence of myocardial ischemia, and single-vessel coronary disease (51), with a lesion that was proximal, discrete, subtotal, concentric, and
Angioplasty of a totally occluded left anterior descending (LAD) coronary artery, shown before and after angioplasty. The proximal (PROX) and distal (DIST) LAD presence. This patient had normal anterior wall motion because of the presence of right-to-left collaterals capable of maintaining a distal occluded LAD pressure of almost 50 mm Hg, but not capable of meeting flow requirements during exertion. (From Dervan JP, Baim DS, Cherniles J, et al. Transluminal angioplasty of occluded coronary arteries: use of a movable guidewire system. 1983;68:776.)

However the clinical and anatomic circumstances have changed, patients with a single lesion needing treatment still account for the majority of angioplasty procedures. In the Emory data from 1988, 318 (46%) of 692 patients with SVD were treated by angioplasty, compared with 159 (30.1%) of 528 patients with double-vessel disease and 43 (10.6%) of 405 patients with triple-vessel disease (103). In those patients with SVD, the intent of angioplasty is not to improve life expectancy (which is already excellent with medical therapy), although Duke databank analysis does suggest a slightly higher 5-year survival rate with angioplasty (95%, vs. 93% with CABG and 94% with medical therapy) (108). Rather, the primary intent in the patient with angina due to SVD is to improve quality of life by alleviating angina. The Veterans Administration (VA) Angioplasty Compared to Medical Therapy (ACME) trial (109) suggested that even conventional balloon angioplasty is better able to achieve this goal than is ongoing medical therapy. Despite a PTCA success rate of only 80%, 64% of PTCA patients (compared with 46% of medically treated patients) were free of angina at 6 months, with the PTCA patients showing a greater increase (2.1 minutes) in exercise time off antianginal medication (compared with a 0.5-minute increase in the medical patients receiving antiangial drugs). The price paid for this symptomatic improvement was a small risk of acute complications (2% emergency bypass, 1% Q-wave MI) and a 23% need for a repeat procedure (PTCA in 16%, bypass surgery in 7%) in the cohort assigned to PTCA. In contrast, 9% of the group assigned to medical therapy had late angioplasty for refractory symptoms. At 6 months, there was one death in the medical group and none in the angioplasty group. Follow-up to 3 years showed ongoing symptomatic benefit in the angioplasty group. Based on these data, not all patients with stable angina resulting from SVD need to undergo angioplasty, particularly if they are reasonably content with their quality of life on medical therapy. Most patients, however, seek better exercise tolerance or relief from medication side effects, if angioplasty for an anatomically suitable single-vessel lesion can be offered at a low risk. This would appear to be an even more compelling option since the possibility of stent placement has further reduced the short-term risk of failure or complication, as well as the long-term risk of restenosis. In the setting of unstable angina or acute MI, the use of angioplasty to treat SVD becomes even more reasonable (see later discussion).

**FIG. 23.19.**

Angioplasty of a totally occluded left anterior descending (LAD) coronary artery, shown before (A) and after (B) angioplasty. C: The proximal (PROX) and distal (DIST) LAD presence. This patient had normal anterior wall motion because of the presence of right-to-left collaterals capable of maintaining a distal occluded LAD pressure of almost 50 mm Hg, but not capable of meeting flow requirements during exertion. (From Dervan JP, Baim DS, Cherniles J, et al. Transluminal angioplasty of occluded coronary arteries: use of a movable guidewire system. Circulation 1983;68:776.)

**Total Coronary Occlusion**

Although total occlusion was initially a contraindication to attempting angioplasty, it has been clear since the early to mid-1980s that many chronic total occlusions can be dilated successfully. The main reason to attempt such a procedure is if the distal myocardium receives collaterals that are adequate to maintain viability but inadequate to meet the increased demand of exercise (Fig. 23.19). The main challenge in angioplasty of a total occlusion is the need to pass a guidewire through the area of occlusion and into the vessel lumen beyond. This is best done by crossing through the path of least resistance (i.e., the “latent” true lumen), without causing vascular dissection or perforation in the attempt. The traditional approach is to use a series of guidewires (progressing from soft- to stiff-
tipped) to gently probe the stump of the occlusion until the latent vascular channel is entered. The wire is then rotated and advanced millimeter by millimeter through the total occlusion until it emerges into the distal coronary artery beyond. Even in experienced hands, this approach has a primary success rate in cases of chronic total occlusion of only 60% to 70% (110), mostly because of inability to advance the guidewire across the occlusion. The presence of one or more chronic total occlusions is one of the most common reasons for sending a patient to bypass surgery rather than attempting angioplasty. Until alternative approaches (such as drug- or laser-induced angiogenesis to enhance collateral inflow or more effective mechanical devices) are developed, the biggest factors in approaching total occlusions successfully will be careful case selection and operator expertise.

The success rate may be higher for chronic occlusions that have a tapered or funnel-like entry suggesting the presence of a small (0.010-inch) residual lumen (111). The presence of bridging (vasa vasora) collaterals across the area of total occlusion has been thought to be a negative predictor of success, but with careful technique (staying within the lumen rather than exiting into the vasa) success and safety comparable to that seen without such collaterals can be achieved (112). This is facilitated by aiming deliberately toward the continuation of the vessel, which can be aided by performing separate contrast injections into the contralateral (collateral-supplying) coronary artery to opacify the target vessel beyond the area of total occlusion, and by visualizing the anatomy with biplane fluoroscopy or frequent alternation of the single-plane projection. The success of crossing such lesions has improved with the introduction of stiffer and lubricious coated guidewires (Choice-PT, SciMed; Shinobi, Cordis Corporation, Miami, FL) (113) and ball-tip wires (Magnus, Sci Med) (114). A variety of other approaches have been evaluated, including low-speed rotational angioplasty (115), ultrasound vibrational angioplasty (116), and the excimer laser guidewire (117). None of these more aggressive techniques has significantly increased the ability to cross the chronic total occlusion, and they tend to increase the incidence of vessel perforation or extensive local dissection. Still newer techniques (including forward-looking imaging) are under development. If a device can be found that safely improves crossing success for these difficult lesions, it will greatly increase the number of patients who can be served by coronary angioplasty.

Once the guidewire has been passed into the distal vessel, treatment of the total occlusion proceeds as does any other catheter-based intervention. If crossing the lesion has been difficult or has required the use of aggressive guidewire manipulation, it is appropriate to confirm that the distal wire position is in fact intraluminal before advancing or inflating larger devices by performance of a distal injection through an infusion catheter (e.g., Ultrafuse-X, Boston Scientific, Natick, MA). This injection also evaluates the distal anatomy for additional areas of disease. Once these issues are clear, the lesion can be crossed with a balloon catheter and dilated in the usual manner. Perhaps because of competitive flow by way of distal collaterals, plaque bulk, or other lesional characteristics, successfully dilated total occlusions appear to have a higher (40% to 50%) restenosis rate than do subtotal stenoses (110). Several randomized trials have shown that long-term patency can be improved by the use of coronary stents, which further improve the acute lumen caliber, with a restenosis rate of 32% after stenting compared with 74% with balloon angioplasty alone (118).

Multivessel Coronary Artery Disease

With the improved success rate in single-vessel coronary angioplasty, extension of the technique to patients with multivessel disease seemed natural. Selected patients with severe stenosis of two or even all three coronary arteries began to be considered for true multivessel angioplasty in the late 1980s. But most patients with multivessel disease who received angioplasty actually underwent single-vessel dilatation, with the hope that correction of the most severe “culprit” lesions would control ischemic symptoms even though milder lesions in other vessels remained untreated (98). Although it is possible to attempt angioplasty on these milder residual lesions, experience showed that these dilatations carried a significant risk of acute vessel occlusion and their treatment could initiate the restenosis process, resulting in the formation of a severe stenosis within a matter of months (99). On the other hand, leaving significant lesions untreated increased the chance of a late repeat procedure (angioplasty or bypass surgery). In one analysis (119), performing incomplete revascularization (leaving behind stenoses greater than 50% in vessels greater than 1.5 mm in diameter) more than doubled the chance of a late event and increased the risk of 5-year events by 50% even after adjustment for other variables such as left ventricular function, angina class, and territory at risk. This is an important consideration, because fewer than half of the patients undergoing angioplasty in the setting of multivessel disease meet these strict criteria for complete revascularization (92),(120). Furthermore, angioplasty in multivessel disease is more demanding technically than single- vessel angioplasty and carries a higher risk of complications should vessel occlusion occur (52),(53).
Reanalysis of the medicine versus surgery trials from the 1970s only strengthened the conclusion that bypass surgery offers a clear benefit over medical therapy in patients with multivessel disease (121). It was therefore important to determine how well angioplasty as an initial strategy would compare with bypass surgery. Registries such as the Duke database suggested that surgery would have a survival benefit over angioplasty in patients with triple-vessel disease or double-vessel disease involving severe stenosis of the proximal LAD (108). To gain a clearer picture, several randomized trials of angioplasty versus surgery in multivessel disease were performed in the late 1980s. Several of the trials have been summarized in a metaanalysis by Pocock (122), and two are discussed here in some detail.

Both the Emory EAST trial (123) and BARI (92) showed that fewer than 15% of screened patients with multivessel disease could even be considered suitable for angioplasty—chief exclusions being one or more chronic occlusions, left main coronary artery disease, or a left ventricular ejection fraction of less than 25%. About 60% of the randomized group had double-vessel disease and 40% had triple-vessel disease. In EAST, angioplasty (compared with surgery) provided somewhat less complete initial revascularization (73% vs. 99%), a slightly lower incidence of major in-hospital complications (death, 1%; MI, 3% vs. 10%; stroke, 0.5% vs. 1.5%), and a lower initial hospital cost. Over the next 3 years, although patients treated by initial angioplasty had a similar total mortality rate (7.1% vs. 6.2%), they were much more likely to undergo an additional revascularization procedure (repeat angioplasty, 41% vs. 13%; bypass surgery, 22% vs. 1%) to treat angina due to restenosis of the dilated segment or a territory not revascularized during the initial procedure. Although this eroded much of the initial hospital savings, it did not increase the incidence of late irreversible events (i.e., death, MI). In the randomized portion of the BARI trial of 1,829 patients (92), all lesions were successfully dilated in only 57% of patients (an average 1.9 of 3.5 significant lesions per patient); in comparison, there was complete surgical revascularization in 91% of patients (3.1 coronaries bypassed). Despite a slightly lower incidence of in-hospital death or Q-wave MI (3.0% vs. 5.8%) and a similar 5-year survival rate (86.3% vs. 89.3%), patients treated with initial angioplasty were more likely to undergo a repeat revascularization (54%, including 31% with subsequent CABG) than patients undergoing initial bypass (8%). Of concern in BARI, patients with diabetes fared significantly worse with angioplasty than with surgery, with 5-year all-cause mortality rates of 34.5% and 19.4%, respectively (95% confidence interval for difference, 1.4% to 28.9%). This may reflect the more diffuse nature of coronary disease and the higher incidence of restenosis in diabetics (see Restenosis). The difference between surgery and angioplasty was much less pronounced in the BARI Registry (5-year mortality rate, 14.4% vs. 14.9% for surgery) (124). With the freedom of the registry, operators generally performed angioplasty on diabetic patients who had more localized angiographic disease. For example, the incidence of triple-vessel disease in registry was 35% for angioplasty and 60% for bypass; in the randomized BARI cohort, these figures were 43% and 45%, respectively. This complex issue needs to be addressed further in the 7 and 10-year follow-up of BARI (124a) and the planned BARI-II trial, but it is reasonable to continue to offer catheter-based revascularization to those diabetics who have reasonably discrete lesions while referring patients with more diffuse disease to bypass surgery (125).

Based on these data, fewer than 20% of patients with multivessel disease are likely to be judged as good candidates for coronary angioplasty, compared with more than half of those with SVD (103,123,124). These selected patients can be offered initial angioplasty without increasing their risk of subsequent death or MI, but they must be prepared to accept a four-fold (e.g., 54% vs. 13%) increased need for a subsequent revascularization procedure, including a 22% chance that they will ultimately need bypass surgery anyway. Otherwise, bypass surgery should remain the standard approach to patients with diffuse multivessel coronary artery disease, in whom it provides a more durable benefit than angioplasty, particularly in patients with underlying diabetes. The durability of the result may be improved, however, through the use of other non-balloon technologies such as coronary stenting. Preliminary data suggest that patients treated by multivessel stent placement have a lower and acceptable incidence of late revascularization, with repeat angioplasty rates of 25% to 30% and a low incidence of late bypass surgery (less than 5%) in anatomically suitable patients (126),(127).

Trials comparing surgery versus stenting are in progress to reexamine the question in the context on the modern new device era, but even these trials do not include newer modalities such as minimally invasive bypass of the LAD combined with catheter-based treatments of the circumflex and right coronary artery (128), or the inclusion of catheter-based treatments of significant left main coronary artery stenosis. Balloon angioplasty of left main lesions not “protected” by a patent graft to the LAD or circumflex was previously demonstrated to have a poor long-term outlook. Experience in the stent era indicates good acute results in elective left main procedures, but still a high (10% or more) mortality rate in the first year, probably reflecting restenosis (129). As the predictability and durability of
catheter-based intervention continue to improve, it is likely that its indications will encompass more patients with left main or multivessel disease.

**Bypass Grafts**

Bypass surgery provides excellent early symptomatic benefit, but 40% of saphenous vein conduits become occluded and many more develop severe narrowing within 10 years after surgery (130). Although only 2% of such patients require angioplasty or repeat bypass surgery within the first 5 years, 31% require a repeat revascularization by year 12 (including 20% reoperation and 15% PTCA) (131). Internal mammary conduits have a better long-term track record (132), but some of these grafts develop early significant stenosis at the distal anastomosis. Finally, patients with previous bypass surgery frequently develop new or progressive disease beyond a graft insertion site or in a nongrafted vessel over time. By these various mechanisms, it is common for the patient who has undergone a previous bypass operation to develop recurrent angina. Although this can be managed by repeat bypass surgery, repeat surgery is a higher-risk procedure in a patient population that is older and sicker than those undergoing initial bypass. With the progressive growth of coronary angioplasty, many such patients can be managed by catheter-based intervention on the diseased graft or a stenotic native vessel, and angioplasty of postoperative patients accounts for approximately 20% of current volume. Although angioplasty has a lower in-hospital mortality rate than reoperation (1.2% vs. 6.8%), late mortality is similar and angioplasty carries a higher incidence of repeat interventions, including a 24% 5-year risk of requiring reoperation (133).

When attempting angioplasty in a patient with previous bypass surgery, the operator should keep in mind that the extensive mediastinal fibrosis and risk of injuring functional anterior grafts would prolong the time required for emergency surgery should a complication of angioplasty occur. Although vein-graft stenoses that occur within the first year after surgery are caused most commonly by intimal hyperplasia and respond quite well to balloon dilatation, late vein-graft stenoses (average, 8 years after surgery) are caused more commonly by diffuse atherosclerosis that has a distinct tendency to fragment and/or embolize into the distal coronary bed during dilatation (134),(135) (Fig. 23.20). In a 1993 report of their experience with angioplasty for bypass grafts, de Feyter et al. (135) found a primary success rate of 88%, with complications including death (1%), MI (4%), emergency bypass (2%), and distal embolization (3%). Although these acute results may be acceptable, they also found that dilated graft lesions had a high restenosis rate (42% overall), and the rate was even higher in the midportion and body of the graft (58% and 52%, respectively). Other factors associated with increased risks of a poor acute result included grafts older than 3 to 4 years, multiple lesions or diffuse disease, small graft diameter, and the presence of intragraft thrombus, each of which increased the restenosis rate to almost 80%. In addition to plaque friability, older grafts frequently contain thrombus, which may embolize during attempted angioplasty. Grafts with large thrombotic filling defects were often pretreated by intracoronary infusion of a thrombolytic agent (136), such as urokinase 50,000 to 100,000 IU/hour or recombinant tissue plasminogen activator (r-tPA) 20 mg over 20 minutes, to dissolve clot and allow the underlying stenosis to be dilated (Fig. 23.21). More recently, such grafts have been approached with extraction atherectomy (TEC) or rheolytic thrombectomy (Possis AngioJet, Minneapolis, MN) to remove thrombi before definitive mechanical intervention (see Chapter 24). A similar approach can be used on grafts that are more chronically occluded, but poor long-term patency gives such procedures only marginal utility (137).

**FIG. 23.20.**

Saphenous vein graft intervention. **Left:** Eccentric stenosis in the midportion of an 8-year-old saphenous vein graft to the left anterior descending coronary artery. **Center:** After conventional balloon angioplasty, there is marked disruption of the plaque and elastic recoil, leaving a 70% residual stenosis. **Right:** After placement of a single Palmaz-Schatz stent, there is a smooth lumen with no residual stenosis. These excellent acute results, plus the favorable late restenosis rate, make stenting the treatment of choice for the focally diseased saphenous vein graft.

**FIG. 23.21.**

Thrombus-laden graft. **Top left:** Recently occluded saphenous vein graft in a patient with unstable angina shows long, lobulated filling defect consistent with thrombus. **Bottom left:** A drug infusion catheter (Tracker, Target...
Therapeutics) with 6 cm of side-holes between the gold markers (small arrows) has been placed across the thrombotic segment. **Top right:** After overnight infusion of urokinase (50,000 IU/hour), there has been marked cleanup of the thrombus, revealing the underlying focal stenosis in the distal third of the graft. **Bottom right:** Placement of a single Palmaz-Schatz coronary stent normalizes this area of focal disease. Recent trials with the rheolytic thrombectomy catheter have shown mechanical thrombectomy to be superior to prolonged infusion of a thrombolytic agent (see Chapter 24).

As with other lesion types, the availability of new devices has improved the results of vein graft treatment. Directional atherectomy has been used successfully, but the randomized CAVeAT-II trial failed to show significant benefit in long-term outcome (see Chapter 24). On the other hand, stenting has consistently shown superior short- and long-term results (Fig. 23.20). Early registries from both my institution (138) and the Washington Hospital Center (139) in the early 1990s used Palmaz-Schat coronary and biliary stents in a population whose mean graft age exceeded 8 years and achieved a 98% acute success, almost 0% residual stenosis, acute complications in less than 2%, and an angiographic restenosis rate in the 17% to 25% range. Although quite small (approximately 200 patients total) the randomized SApheous VEin graft Disease (SAVED) trial confirmed these benefits over conventional balloon angioplasty (140) and made stenting the preferred therapy for treatment of the diseased vein graft. With the introduction of second-generation stent designs starting in 1997, more flexible stent designs are now available, including the self-expanding Wallstent (see Chapter 25). But even effective local treatments like stents are unable to prevent late failures at other (nonstented) portions of the same or other vein grafts, contributing substantially to the need for repeat procedures in follow-up after successful vein graft intervention (141).

Despite the successes of stenting, the problem of distal embolism has continued to plague treatment of these older vein grafts (45–47). Even without angiographically evident filling defects, these diffusely diseased older grafts may contain sufficient debris to increase their risk of developing frank “no reflow” syndrome. This syndrome involves marked diminution in antegrade flow with profound myocardial ischemia, even though the proximal vessel is free of stenosis or dissection and there are no “cutoffs” in the distal vessel. When this condition represents distal microvascular spasm caused by the release of serotonin from platelet-rich thrombi, it can be reversed quickly by distal injection of a calcium channel blocker (see Chapter 3). In vein grafts, however, many such episodes are refractory to vasodilators and go on to cause large MIs and a substantial (20%) inhospital mortality. Recent work with a distal occlusion/aspiration device (GuardWire, PercuSurge, Sunnyvale, CA) (142) has demonstrated that the cause of “no reflow” in vein grafts is embolization of atherosclerotic debris (e.g., cholesterol clefts, foam cells), for which the best therapy is likely to be use of distal protective devices (including occlusion devices and filters). The advent of stents with impermeable coverings may also help control this distal embolization problem.

**FIG. 23.22.**

LIMA angioplasty. This 58-year-old man developed recurrent angina 5 months after bypass surgery that had involved grafting of the left internal mammary artery (IMA) to the left anterior descending (LAD) coronary artery (whose proximal segments had exhibited early restenosis after two rotational atherectomy procedures). **Left:** In the left lateral projection, severe stenosis (curved arrow) is seen at the distal anastomosis, where the IMA meets the LAD. **Center:** Inflation of a 3,0 mm over-the-wire angioplasty balloon at 70 psi. **Right:** Posttreatment angiography shows 20% residual stenosis. This site and timing (as well as the favorable response to conventional balloon angioplasty) are typical for postoperative problems with the IMA graft.

Unlike saphenous veins, **internal mammary artery grafts** are generally resistant to disease, with a 10-year patency rate of better than 90% (132). Still, some patients develop recurrent angina early (within 6 months) after bypass surgery due to stenosis of the internal mammary–native artery anastomosis. These lesions can be dilated effectively with the use of low-profile, trackable dilatation catheters (143), with a moderate (approximately 20%) restenosis rate (Fig. 23.22). Second-generation stents may easily track through internal mammary grafts to treat these distal anastomotic lesions. When evaluating patients with recurrent ischemia in the distribution of an internal mammary graft, it is also important to investigate the possibility of subclavian or brachiocephalic stenosis proximal to the internal mammary origin, which can now be treated by angioplasty or stent placement (144). Limited data regarding angioplasty of gastroepiploic artery grafts suggest similar results of angioplasty in these arterial conduits (145). Although they are technically also a “graft,” the response of the diffuse lesions characteristic of cardiac homografts (accelerated allograft vasculopathy) to coronary angioplasty have not been well characterized (146).
Stable Angina

The initial group of patients who were candidates for coronary angioplasty were patients with stable but medically refractory angina pectoris and suitable coronary anatomy. Occasionally patients with milder symptoms and ideal anatomy are candidates if they have favorable coronary anatomy and objective evidence of ischemia, and are willing to accept the small risk that angioplasty will lead to emergency bypass surgery and the 20% risk that they will need repeat intervention for the treatment of restenosis. This approach was borne out for patients with SVD in the VA ACME trial, which showed better freedom from angina and better exercise tolerance in patients randomly assigned to angioplasty treatment, at the expense of more repeat procedures for restenosis. However, patients with mild symptoms should be aware that the ACME trial failed to demonstrate any improvement in the already excellent rates of survival or freedom from infarction seen with medical therapy in a stable angina population with SVD. Of course, the ACME trial was performed before the widespread use of stenting, which has substantially improved the success, safety, and durability of catheter-based intervention, so that similar studies would have to be redone to provide relevant data for today's practice. The findings of the recent Asymptomatic Cardiac Ischemia Pilot study (ACIP) involving 558 patients with ambulatory electrocardiographic evidence of ischemia in the absence of significant symptoms suggest that even these patients may benefit from catheter-based revascularization.

One group worthy of separate mention is elderly patients with severe stable or unstable angina. Unlike bypass surgery (which carries a higher risk and a longer recovery period in the elderly), angioplasty has almost as favorable an outlook in this group as it does in younger patients. Although such patients tend to have more challenging anatomy (multiple, diffuse, or calcified lesions), they frequently can be offered palliation by angioplasty as an alternative to bypass surgery. Patients older than 65 years of age now constitute more than 35% of the 1988 Emory angioplasty population; 39% of the current patients at Beth Israel are 65 to 79 years of age, and 8% are age 80 or older.

Unstable Angina

Patients with unstable angina (including angina at rest, post-MI angina, accelerating angina, and new-onset angina) have accounted for the majority of interventions in most institutions. Early reports are available from the ThoraxCenter, and the 1985–1986 NHLBI PTCA registry. In the Registry, 857 patients had unstable angina, 79% of whom had rest angina. The majority of patients with new-onset angina had SVD, largely severe focal stenosis of the LAD coronary artery. Angioplasty was attempted on a mean of 1.6 lesions per patient, with success in 85% and major complications including death (1.4%), nonfatal MI (2.7%), and emergency surgery (4.3%). Complications were greatest in the subgroup of 219 patients with acute coronary insufficiency (rest pain for more than 30 minutes without diagnostic enzyme elevation).

This approach to the patient with unstable angina was evaluated further in the Thrombolysis in Myocardial Infarction (TIMI) IIIB trial, which examined the role of r-tPA as well as management strategy in 1,473 patients with unstable angina or non–Q-wave MI. In the early invasive strategy, patients underwent diagnostic catheterization at a mean of 1.5 days, which led to revascularization in 61% (38% by PTCA and 25% by bypass surgery). PTCA in this group of patients had a favorable outcome (success, 93%; death, 0.4%; nonfatal MI, 2.9%; emergency bypass, 0.7%). Of the patients assigned to a conservative (noncatheterization) strategy, 60% required catheterization primarily for failure of initial therapy, with revascularization in 49% of the patients assigned to this strategy (26% by PTCA and 24% by CABG) within 6 weeks after enrollment. Although there was no difference in the composite end point (death, MI, or positive exercise test) at 6 weeks, patients in the conservative arm required more repeat hospitalizations, more hospital days, and more medications to achieve this end. At 1-year follow-up, the patients receiving early invasive treatment showed a nonsignificant trend toward less death or MI (10.8% vs. 12.2%; p = NS), with fewer repeat hospitalizations (26 vs. 35%; p = .038), and only slightly higher cumulative revascularization rates (64% vs. 58%) with equal bypass rates (30%) at 1 year. The authors concluded that early catheterization after 18 to 48 hours of anti-ischemic therapy can be carried out safely, clarifies the therapeutic options, and allows prompt delivery of revascularization when appropriate.

The benefits of early catheterization and revascularization for patients with unstable angina were less clear in the 920 patient, VA-based VANQWISH trial, but this trial has been criticized for the relatively low use of...
revascularization in both arms (44% invasive, 33% conservative), the 11% surgical mortality in the invasive arm, and differentially high mortality in nonrevascularized patients (9% in the invasive arm, 5% in the conservative arm). In contrast, the recent Scandinavian trial, Fast Revascularization during Instability in Coronary artery disease (FRISC-II) showed clear benefits, in terms of mortality, readmission, and cost, for the strategy of brief initial medical stabilization (with anticoagulants as well as newer antiplatelet agents including Ilb/IIIa blockers), followed by cardiac catheterization and (if anatomically suitable) catheter-based revascularization including the use of coronary stents (153). Of the 2,457 patients, 91% of those treated invasively had an intervention within 10 days after hospital admission, and the invasive arm showed a 21% relative reduction in the 6-month composite of death or MI (9.5% vs. 12.0%), with an even greater reduction among males (9.1% vs. 13.9%), who also had a significantly reduced mortality rate (1.5% vs. 3.2%). Most U.S. centers now follow a similar strategy, with initial medical stabilization followed by a diagnostic catheterization performed with “angioplasty standby” so that suitable lesions can be treated by balloon dilatation or other catheter-based therapies during the same procedure.

Acute Myocardial Infarction

The treatment of acute MI has undergone a major revolution over the past 15 years, with the recognition that intracoronary thrombosis is the final mechanism of vessel occlusion and the understanding that prompt reestablishment of vessel patency offers significant clinical benefit (154). Current “front-loaded” or “double-bolus” regimens using potent thrombolytic agents (e.g., r-tPA) can open almost 75% of infarct vessels within 90 minutes after intravenous administration. A purely pharmacologic approach to the management of MI has not proved completely satisfactory, however, because approximately 15% of vessels fail to open in response to thrombolytic therapy, only half of the open vessels have normal (TIMI grade 3) flow, and at least 10% of vessels opened by thrombolysis either reocclude or cause recurrent angina during hospitalization due to the persistence of an underlying high-grade atherosclerotic stenosis (155). Although newer combinations of thrombolytics with platelet Ilb/IIIa receptor blockers may achieve higher rates of initial patency (156), they do so with an increase in bleeding complications.

These shortcomings of thrombolysis prompted several large clinical trials in the late 1980s to explore the optimal strategy of combining thrombolysis with mechanical revascularization using balloon angioplasty (if possible) or bypass surgery. These trials demonstrated that immediate catheterization and angioplasty carry an increased risk and offer no additional benefit in terms of survival or recovery of left ventricular function (157). In fact, the TIMI IIB trial reported that even routine delayed catheterization (18 to 48 hours after thrombolysis) offered no additional benefit over a conservative strategy in which catheterization and angioplasty were reserved for patients with recurrent spontaneous or exercise-provoked ischemia (158).

On the other hand, some operators reported excellent results using primary angioplasty instead of thrombolysis to open occluded vessels in the early hours of infarction (159) (Fig. 23.23). In the early 1990s, the Primary Angioplasty in Myocardial Infarction (PAMI) (160), the Zwolle (161) trials, and a metaanalysis of the four principal trials (total of 2,606 patients) (162) established that prompt primary angioplasty offered better acute patency, fewer reinfarctions, better mortality (3% to 4% vs. 6% to 7%), and fewer strokes than a strategy based on primary administration of a thrombolytic agent. Of course, these studies enrolled only thrombolytic-eligible patients, excluding elderly patients, patients with central nervous system disease, those with cardiogenic shock, and those who had ongoing ST-segment elevation after thrombolytic administration, who have an even higher mortality rate (15% to 20%) with medical therapy and would only be treatable only by acute angioplasty. While excluded patients have a higher mortality rate with primary angioplasty than do thrombolytic-eligible patients, there is strong evidence that acute revascularization does reduce the mortality in such patients with cardiogenic shock. In an analysis from the GUSTO I trial, patients with acute cardiogenic shock who underwent revascularization within the first 30 days (predominantly by angioplasty) had a significantly better 1-year mortality rate than those who did not (37% vs. 70%) (163). Similarly, there is evidence that patients with failed thrombolysis have an acute angioplasty success rate of 88% and a mortality rate of 8.6% after successful rescue PTCA that is similar to the 5.2% mortality rate for successful thrombolysis in GUSTO I (164).

FIG. 23.23.
Primary angioplasty for acute myocardial infarction (MI). A primary angioplasty procedure (left, top) shows baseline total occlusion of the proximal left anterior descending coronary artery (arrow) 2 hours into acute anterior MI with cardiogenic shock. Primary angioplasty (left, center) is shown with placement of a perfusion balloon across the area of occlusion. After angioplasty (left, bottom), there is no residual stenosis (arrow) and brisk antegrade flow. Despite a peak creatine kinase values approaching 2,000, this patient's hemodynamic status recovered promptly, with normal wall motion on gated nuclear ventriculography 6 weeks later. Below: Metaanalysis of more than 2,600 patients from studies comparing primary angioplasty with thrombolytic therapy shows significant reduction in mortality (from roughly 6% to 4%) with primary angioplasty. CABG, coronary artery bypass graft surgery; PTCA, percutaneous transluminal coronary angioplasty. (From Weaver WD, Simes J, Betriu A, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. JAMA 1997;278:2093, with permission.)

Based on those studies, our institution began in 1994 to offer primary angioplasty as our around-the-clock frontline therapy for acute MI. This requires a team of experienced angioplasty operators and catheterization personnel who can be in the cardiac catheterization laboratory within 30 minutes, so that a patient can be brought to the laboratory within 60 minutes and have the infarct-related artery open within 90 minutes after emergency room presentation (165). Results of primary angioplasty have improved further with the use of stenting and IIb/IIIa blockers during the procedure. Some studies have even suggested that community hospitals that do not themselves have cardiac surgery or elective angioplasty programs but are staffed by active interventional cardiologists can also deliver primary angioplasty effectively, although this activity is not included in the most recent (1999) revision of the ACC/AHA guidelines for management of acute MI (166). As thrombolytic regimens (and associated antithrombin and antiplatelet drugs) improve, it is likely that the role of mechanical versus pharmacologic thrombolysis will need to be reexamined, but at present we believe that primary angioplasty (where it is available) constitutes the best revascularization strategy for the patient with acute MI.

FINANCIAL AND REGULATORY CONSIDERATIONS

Because coronary angioplasty is performed in a cardiac catheterization laboratory under local anesthesia, it is attended by substantially lower in-hospital costs than coronary bypass surgery (167). On the other hand, this cost benefit is partially eroded by the greater need for repeat procedures to treat restenosis within the first year. The net cost savings therefore depend on the extent to which an intervention improves acute outcome and late freedom from restenosis, as well as its cost. In patients with SVD, stenting has proved to be a cost-effective or even cost-saving technology, whereas in patients with extensive multivessel disease catheter-based revascularization may be a more costly approach than bypass surgery. In general, however, catheter-based revascularization strategies offer less patient morbidity, faster return to work, and equivalent mortality benefit and symptom relief (barring the restenosis) and are therefore preferred when anatomically possible. Because the decision frequently is being made by the same operator (i.e., the cardiologist who performs the diagnostic catheterization, makes the decision about treatment, and then performs the coronary angioplasty), the large expense associated with catheter revascularization has increasingly made angioplasty a target for scrutiny in the managed-care environment (168).

In addition to issues about the appropriateness of angioplasty procedures and markedly different utilization rates across the country (169), there is also a major question about whether every hospital should offer bypass surgery or angioplasty. In fact, only about 1,500 of the nation's 7,000 hospitals do so, but there is continued pressure on those that do not to open such programs (170). Data from California (171) and a nationwide study of 217,836 Medicare beneficiaries who underwent coronary angioplasty (172) clearly show excess mortality and emergency surgery rates in hospitals that perform fewer than 200 angioplasty procedures per year.

These same issues concern the training and continued caseload for angioplasty operators (173). Early in the development of coronary angioplasty, physicians active in diagnostic catheterization learned to perform angioplasty by attending live demonstration courses and watching or assisting on a small number of procedures (i.e., 10 to 20) under the guidance of a knowledgeable operator. Given the ever-increasing complexity of the procedure, however, virtually all new angioplasty operators since the mid-1980s have received formal training consisting of a third (or third and fourth) year of interventional fellowship beyond completion of their training in diagnostic coronary angiography. During the interventional fellowship, a trainee should perform a minimum of 250 procedures (173a). There is evidence that operators who maintain an annual interventional caseload of fewer than 75 procedures have a
higher rate of risk-adjusted complications than higher-volume operators, not just for all patients, but also for low-complexity (AHA/ACC A or B1) lesions (174), and even for stenting (175). To further standardize interventional training in 1999, the Accreditation Council for Graduate Medical Education (ACGME) began certifying interventional fellowship programs, and the Board of Internal Medicine began offering an examination- and caseload-based Certificate of Additional Qualification in Interventional Cardiology (176). These changes will almost certainly put pressure on the more than 7,000 “angioplasty operators” in the United States, most of whom perform less than half of the recommended annual caseload of 75 interventions. As catheter-based interventions continue to evolve toward progressively more challenging clinical and anatomic situations, and as the development of new technologies for coronary intervention continues, increasing functional specialization will be required of “interventional” cardiologists. This action is in keeping with the recommendations of the 1993 ACP/ACC/AHA task force, which advised that “the proliferation of small-volume operators should be curtailed by appropriate institutional review” (16).

ROLE OF CONVENTIONAL ANGIOPLASTY IN THE NEW DEVICE ERA

Between its introduction in 1977 and 1990, conventional balloon angioplasty (POBA) was the only mechanical intervention available for percutaneous coronary revascularization. The choice of devices was very much like the situation described by Mark Twain: “To the man with a hammer, everything looks like a nail.” In contrast, the period from 1988 through 1994 saw unparalleled investigation of a wave of new stent and atherectomy devices (177). The first of the new devices (directional coronary atherectomy) was approved by the U.S. Food and Drug Administration (FDA) in 1990, followed by approval of two other atherectomy devices (rotational and extraction atherectomy), excimer lasers, and two balloon-expandable stents by 1994. Second generations of these devices have been developed, and even newer classes of devices (e.g., thrombectomy, distal protection, radiation) have continued to be introduced. Over only a few years, these new devices have progressively replaced POBA as the dominant stand-alone tool for coronary intervention.

To be chosen over balloon angioplasty, a new device must be expected to provide an advantage in terms of (a) the predictability of the acute result, (b) the quality of the acute result (less residual stenosis), (c) the ability to treat a lesion that would have been refractory to conventional angioplasty, or (d) the ability to reduce the incidence of subsequent restenosis. Moreover, such treatment must be provided in a cost-effective way (if it costs more, it also must provide a clinical benefit worth that extra cost [178]), and it must not unduly increase the complication rate. Although balloon angioplasty remains unmatched in its simplicity, anatomic versatility, and broad clinical applicability, the availability of new devices has made balloon angioplasty more of an adjunctive treatment (for predilation to aid in device passage or postdilation to improve the new device–created result) than a stand-alone treatment. Coronary stents have become heir apparent to balloon angioplasty and are currently being used in more than 80% of catheter-based interventions (see Chapter 25). The atherectomy technologies (directional and rotational atherectomy) are still beneficial for debulking certain lesion types (ostial, calcified, bifurcation lesions), as definitive treatment or to improve the results of subsequent stent placement. These same debulking treatments are also effective in treating in-stent restenosis, particularly when combined with local radiation therapy to inhibit regrowth of the proliferative neointima (see Chapter 24).

FIG. 23.24.
MI or creatine kinase more than 5 times normal), or emergency surgery—from 3.7% to 1.5%. By 1999, intravenous blockers of platelet glycoprotein IIb/IIIa receptor were used in approximately 30–40% of patients in whom a perfect mechanical result could not be achieved by catheter-based techniques.

Although there is still some uncertainty about which new device is best for which lesion, I believe that “lesion-specific new device therapy” is here to stay. In our practice, as shown in Fig. 23.24, the percentage of interventional procedures in which a new device was used has risen from roughly 50% in 1994 to more than 80% in 1998. During this time, there has been a progressive fall (from 5% to 1.5%) in the incidence of major adverse clinical events, including virtual elimination of emergency bypass surgery (less than 0.2%) and a stable mortality rate of 0.6% in non–acute-infarction patients, despite the treatment of an older, sicker patient population with more complex lesion anatomy. Although much of the research focus in interventional cardiology has shifted to understanding the mechanism, technique, and optimal indications for these new devices, I believe that balloon angioplasty will continue to play a crucial role as an adjunct to new device therapies. Whatever new modalities are introduced—be they forms of angiogenesis (179), (180), laser direct myocardial revascularization (181), or nonsurgical septal reduction for hypertrophic obstructive cardio-myopathy (182)—the skills, knowledge, and judgment derived from balloon angioplasty will continue to form the foundation on which broader interventional skills are built in coming years.