In 1956 Gordon Murray reported the use of fresh aortic valve homografts transplanted into the descending thoracic aorta for amelioration of the consequences of native aortic valve insufficiency. His initial operations preceded by 5 years the availability of the Starr-Edwards mechanical aortic valve prosthesis. Although this operation was only partially successful hemodynamically, the homograft valves had remarkable durability and performance. Four patients cited by Heimbecker had no calcification or gradient, with normal leaflet function for up to 13 years, and two patients continued to demonstrate excellent valve function for up to 20 years. Kerwin’s subsequent reports support the contention that aortic leaflet homograft pliability and performance were well preserved in these early patients. These clinical trials were preceded by laboratory investigations, especially that of Lam and coworkers. Hemodynamic improvements were demonstrated in both stenotic and regurgitant aortic valve disease by the various early methods of reconstructing diseased aortic valves, and the results ultimately obtained with replacement utilizing the Starr-Edwards and other prostheses supported replacement treatment for ventricular outflow valvular disease, with excellent result continuing to be reported today with both mechanical and bioprosthetic valves.

Professor Gunning has cited an unsuccessful operation in 1961 by Drs. Bigelow and Heimbecker as the first clinical insertion of an aortic valve homograft in the orthotopic position, but the first operation with the patient surviving was by Ross, based on laboratory work reported in 1956 by Brewin. In 1962, the initial clinical use of aortic valve homografts was reported independently by Donald Ross of England and Sir Brian Barratt-Boyes of New Zealand. Duran and Gunning developed a technique in the laboratory for implanting the aortic valve homograft utilizing a single running suture line technique. Interestingly, the initial homograft valve transplants were performed utilizing freshly harvested valves minimally treated and inserted into the orthotopic position relatively quickly after harvest with no attempt at ABO Blood group matching. These initial valves had remarkable performance and durability and gave great impetus to the early workers pursuing this method of aortic valve replacement.

Limitation of donor availability led to preservation attempts to increase storage time and to establish homograft valve “banks.” Storage techniques included freeze-drying and antibiotic sterilization with prolonged refrigeration at 4°C. Concerns about transmission of infection led to aggressive sterilization techniques, including multiple antibiotic incubation, irradiation, and glutaraldehyde pretreatment. Unfortunately, although they increased the availability, these techniques resulted in shortened functional survival of homograft valves and caused significant disenchantment with the technique during the 1960s and early 1970s.

It is the purpose of this chapter to examine in detail the earlier experiences with valve
homografts and to elucidate valuable lessons pertinent to valve transplantation today.

**Early Homograft Work**

In 1952 Lam and his associates demonstrated that it was technically possible to transplant canine aortic valve homografts into the descending aorta of a recipient animal; however, if the cusps were not “used” and were constantly in the open position, they deteriorated. If aortic insufficiency was induced in the recipient dog, thereby “forcing” the transplanted valve to function, valve integrity was greatly enhanced. This fascinating study has relevance today and was the basis on which Murray and others developed the technique for clinical use.

The studies of Heimbecker and colleagues demonstrated that treatment with gamma irradiation or β-propiolactone markedly diminished the durability of transplanted homograft valves. The use of radiation was confirmed by others as having deleterious effects and has been completely abandoned.

Flash freezing was one of the harsher preservation methods tested, but it resulted in poor clinical results and laboratory evidence of damage to the elastic properties of the native valves. Other groups found great difficulties in the durability of frozen irradiated aortic valve homografts and advised against their use because of the increased failure rates beginning around the fifth to sixth postoperative year.

Patient valve survival was in the 50% range at 7 years, which was equivalent to contemporaneous series of xenograft and mechanical prosthetic replacements performed during the mid-1970s. Apart from patient survival, durability of valves prepared with the harsher methods was markedly inferior to mechanical valve replacements.

**Fresh Wet-Store Homograft Valves**

During the late 1970s attention turned to the use of fresh aortic allografts in which cadaveric valves were harvested with variable ischemic times and then antibiotic-sterilized and stored at 4°C in nutrient media. Although donor cellular viability was probably not preserved, these gentler techniques improved valve and patient survival. The contrast between the use of exceedingly fresh valve tissue for transplant and the use of harsh chemical sterilization or storage techniques was stark, and thus the larger experience has been gained with the relatively gentler methods of storage: antibiotic-sterilized, “fresh wet-stored” valves.

A number of series have been reported that demonstrated good medium-term (7–10 years) results with the wet-storage technique. Ross’ group from the National Heart Hospital (London) in 1980 reported on 615 valves followed for up to 15 years, including 145 freeze-dried homografts, and 179 pulmonary autografts. The study clearly demonstrated the superiority of the autografts and fresh homografts; there were excellent clinical results with up to 90% of patients free of valve-related death at 10 years. Others have also reported good results with the pulmonary autograft transplant to the aortic position.

The Stanford series of 114 patients receiving fresh aortic homografts between March 1967 and March 1971 revealed ten operative deaths (8.8%); six deaths during the first year (5.8%) and then a mortality rate of 1.5% per year. Of the late deaths, only six were due to valve dysfunction, whereas 12 were due to other cardiac causes. A total of 3.2% of patients per year required re-replacement for regurgitation (n = 20), and only one valve developed calcific stenosis. Of 53 patients followed for 5 years or more, 47 had minimal or no disability. In 1986 the Stanford group reexamined 83 patients of this original series such that 773 patient-years of follow-up were available with a maximum to 19 years. For this subgroup the calculated actuarial estimate of freedom from all modes of valve failure was 83 ± 4% at 5 years, 62 ± 6% at 10 years, and 43 ± 7% at 15 years; 92 ± 3% of patients were free from endocarditis at 8 years after operation. Freedom from reoperation was 88 ± 4% at 5 years, 67 ± 6% at 10 years, and 45 ± 7% at 15 years. Interestingly, 94 ± 3% of patients were free of valve-related deaths.