Implantation of homologous and heterologous aortic valves in prosthetic vascular tubes¹

An experimental study

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Freeze-dried dog and pig aortic valves sutured within tubes of woven Teflon and knitted Dacron have been inserted into the descending aorta of 56 dogs with aortic incompetence. All the valves placed inside woven Teflon were destroyed, with one exception, where six months after insertion the valve was competent and in good condition. Most of the valves in knitted Dacron remained in good condition for up to three months after surgery. The few bad results with knitted Dacron were related to infection or bad haemodynamic conditions. There was no observable difference in behaviour between the homologous and the heterologous valves during the short follow-up of these experiments.

Homologous and heterologous aortic valves have been used, with encouraging results, to replace the diseased aortic valve in patients. Although the technique for their insertion is becoming standardized, further technical improvements are still desirable. The insertion of a homologous or heterologous aortic valve in a prosthetic framework would theoretically have technical advantages. A prosthetic framework would, for instance, simplify the surgical insertion by providing a rigid ring. Geha (1967) and Weldon, Ameli, Morovati, and Shaker (1966) have reported experimental work using a metal frame covered with Dacron in the sub-coronary position in the calf and in the mitral area of the dog. Ionescu, Wooler, Smith, and Grimshaw (1967) and Carpentier (1967) have recently used a Teflon ring to insert heterologous aortic valves into the mitral area.

In this work we have studied the fate of homologous and heterologous aortic valves sutured inside tubes of Teflon or Dacron and inserted into the descending aorta of 56 dogs in whom aortic incompetence had been produced. We felt that the surgical simplicity of this method would yield useful knowledge about the combination of heart valves and prosthetic materials.

TECHNIQUE

The pig aortic valves were obtained unsterile from the slaughter-house within 12 hours after the animal was sacrificed, the hearts having been kept in a refrigerated chamber. The dog aortic valves were collected immediately after death in the research laboratories. All specimens were kept in sterile jars in Hanks' solution (Gross, Bill, and Peirce, 1949) in a commercial refrigerator for the final dissection. This period of storage never exceeded eight days, the majority being stored for only 24 hours. The aortic valves were then trimmed so that only a few millimetres of aortic wall remained above, and a small cuff of myocardium and mitral valve below, the insertion of the cusps. The valve was then sutured into a Teflon³ or Dacron⁴ vascular tube and the whole was sterilized by immersion in liquid ethylene oxide for 30 minutes and subsequently freeze dried and stored in a vacuum. At the time of the insertion the valves were reconstituted by immersion in warm saline for 20 minutes.

The dogs were anaesthetized with intravenous nembutal, and the trachea was intubated and ventilated with a Starling's respirator. A left thoracotomy through the fourth intercostal space was performed and a segment of descending thoracic aorta was dissected out. A left sub-clavian artery/left femoral artery bypass was used with a siliconized 4 mm. internal diameter Tygon tube. No heparin or trans-

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³Teflon-Usci Woven, Catalogue No. 3010

⁴Dacron-Usci Knitted, Catalogue No. 6015

fusion was used in any of the animals. Arterial pressure was recorded with polythene catheters introduced into the right brachial and right femoral arteries. The aorta was clamped and transected, and a small segment of about 1 cm. in length was excised. The clamps were applied for between 11 and 25 minutes. During this time the arterial pressure distal to the clamp averaged a mean of 40 mm. Hg. The prosthetic tube was then anastomosed end-to-end to the aorta with an anterior and posterior suture of 4/0 Mersilene. The aortic clamps were removed and the bypass was discontinued. The stump of the left sub-clavian artery was then used to introduce a metal hook which was directed retrogradely towards the non-coronary cusp of the dog's aortic valve, which was perforated and split on withdrawal to make it incompetent. The degree of aortic incompetence was recorded from the right brachial artery pulsation while the competence of the grafted valve was recorded from the femoral artery pulsation. The chest was closed in layers. The chest was drained with a catheter which was removed at the end of the procedure. All dogs received penicillin and streptomycin for one week after surgery.

RESULTS

Fifty-six dogs were operated upon. Teflon was used in 15 dogs. In 10 of these dogs a pig valve was inserted, and in the remaining five a dog valve was used. In 31 dogs a Dacron tube was used, with 20 pig and 11 dog valves.

The operative mortality was high; 19 died within 24 hours of surgery (33%). The main causes of death were aortic incompetence, which was responsible for 12 deaths, and haemorrhage, which was the cause of three deaths. One died from failure of the respirator, and in three cases the cause of death could not be established.

Fifteen dogs with a Teflon graft survived the operation (2 dog valves and 13 pig valves). All died or were sacrificed from a few days up to six months after surgery. The specimens from these dogs showed, at the end of six days, a normal valve, but from then onwards all but one specimen showed a destroyed aortic valve. Both the aortic wall and the valve cusps were torn and had partially disappeared. In one dog (with a pig valve), sacrificed three months after surgery, the base of the destroyed valve had become calcified. The exception was a dog sacrificed six months after operation. Arterial pressures taken above and below the grafted pig valve prior to sacrifice showed a perfectly competent valve. The specimen of this dog showed the Teflon graft and anastomoses covered with neointima which bridged the pig aortic valve anastomosis, and the three cusps were in perfect condition (Fig. 1).

FIG. 1. Specimen from a dog with a Teflon graft and a pig aortic valve six months after insertion.

Twenty-two dogs with Dacron grafts survived the operation (8 dogs valves and 14 pig valves). All, except three which have been kept for long-term studies, have died or been sacrificed at one, two or three monthly intervals (11 dogs). The valve cusps were thin and present in all but three specimens (sacrificed 41, 72, and 82 days post-operatively). In two of these, the aortic wall was destroyed and specks of calcium deposits were present. In the third animal, one cusp had separated from the aortic wall. Two of them had infected thoracotomy wounds, and the other was suffering from distemper as well.

In five cases, all between 33 and 64 days after surgery, one or more cusps, although thin and present, were stuck to the aortic wall, making the valve incompetent (Fig. 2). These bad results were

FIG. 2. Dacron graft and a pig aortic valve 64 days after implantation. Note that the valve cusps, although present, are adherent to the sinus aortic wall.

possibly related to mechanical factors, because in one dog the valve grafted was incompetent from the moment of insertion. In another, not enough aortic incompetence had been created, and in a third, good incompetence at the time of surgery had become compensated one month later.

The other 11 dogs had valves which were thin and competent (Fig. 3). No difference in behaviour could be detected between the homologous and heterologous valves in the short follow-up of these experiments. In fact the two longest survivors with perfect valves had received pig valves (6 months with Teflon and 3 months with Dacron).

HISTOLOGY

The earliest change seen in the aortic wall, myocardial cuff, and valve is a loss of nuclei from the cells. This nuclear loss tends to be complete in the myocardial and aortic tissue, but small pyknotic aggregates remain in the valve cusp cells. These are found near the base or in relation to surface thrombus. In this respect no difference between the dog and pig valves could be seen.

In the first few days there is an acute inflammatory reaction at the outer surface of the pros-

FIG. 3. *Dacron graft with a pig aortic valve three months after implantation.*

FIG. 4. *Dacron transplant at one month. Inflammatory infiltrate and fibrous cuff on outer aspect of Dacron (below). (H. & E. $\times 85$.)*

FIG. 5. *Dacron transplant at three months. Fibrous outer layer continuous via wedge-shaped connexions with inner layer on luminal surface (above). (H. & E. $\times 45$.)*

FIG. 6. *Teflon graft at six months. Fibrous layer inside (above) and outside (below) Teflon is present but there are fewer and smaller wedge-shaped bridges as compared to Figure 5. (H. & E. $\times 40$.)*

FIG. 7. Teflon transplant at six months. The valve is acellular with only patches of persistent nuclei. Valve base is fibrous and continuous with luminal layer. Note acellular areas representing remains of aortic cuff. (H. & E. $\times 40$.)

thetic tubes. This reaction penetrates the graft but does not involve the valve base tissues, seeming to end more or less abruptly at the outer layer of aortic tissue or myocardium. In the ensuing weeks this infiltrate assumes a more chronic form and is attended by a proliferation of fibroblasts and fibrous tissue (Fig. 4). Later, fibrous tissue grows through the interstices of the prosthesis to become continuous with a fibrous layer on the inside whose nuclei lie parallel to the wall (Fig. 5). At this stage there is also some fibrous replacement of the outer part of the cardiac muscle cuff but the aortic tissue appears to remain separate.

The inner fibrous layer extends usually to the base of the valve only, but when the sinus contains organizing thrombus, as sometimes occurs, then it becomes continuous with this tissue. Much of the thrombus seen on the valve surface and on the inside of the prosthetic tubes, however, is of recent origin and shows no evidence of organization. It probably forms preterminally as the circulation slows, or it may be formed and lysed as a continuous process during life.

The reaction to the Dacron is considerably more pronounced than to the Teflon, and the ultimate fibrous matting produced in the interstices

of the tubes is less dense in the Teflon (Fig. 6). After several months the valve appears largely unchanged from earlier appearances. It is more or less acellular with persisting patches of pyknotic nuclei (Fig. 7). Thrombus when present is usually fresh, but occasionally, as earlier, in the sinuses organizing thrombus is seen. Even at six months the aortic wall cuff can still be recognized and is quite acellular. Other valve base tissues appear to be incorporated in the surrounding fibrous reaction. In two cases tiny foci of calcification occurred both in the new fibrous cuff and in the aortic wall remains. In long survivors there is still no appreciable difference between dog and pig grafts. Essentially the changes seen correspond closely to those described by us in detail with freeze-dried homografts (Duran and Whitehead, 1966) and heterografted aortic valves (Duran, Gunning, and Whitehead, 1967).

DISCUSSION

It is known that a freeze-dried and therefore dead aortic valve remains acellular but will function for long periods of time, both in the human (Barratt-Boyes, 1965; Ross, 1967) and in the animal (Duran, Manley, and Gunning, 1965). We

have recently studied four dogs with freeze-dried homologous valves inserted into the descending aorta between two and two-and-a-half years after their implantation in the dog. In one dog the transplanted aortic wall had become enormously dilated and the cusps could not be identified, but in the other three the cusps were in perfect condition, although in one of them the aortic wall showed areas of calcification. It is therefore reasonable to emphasize the biological difference between a fresh or freeze-dried aortic wall and an aortic valve cusp. The latter does not seem to need any intrinsic vascularization which, as we have shown elsewhere, is not normally present (Duran and Gunning, 1968). This fact might explain the difference between the bad results observed with arterial grafts in peripheral vascular surgery and the good results to date with valve grafts. If a valve inserted within a Dacron tube is shown to become incorporated into the animal for a few months, it is reasonable to assume that it will remain functioning for long periods of time. A longer follow-up will be required to establish the eventual fate of this type of experiment.

The difference found in these experiments between valves placed inside tubes of woven Teflon and those placed in knitted Dacron shows the importance of the porosity of the prosthetic material, allowing for the penetration of small blood vessels and the strong fixation of the base of the valve cusps. (The calculated porosity of knitted Teflon or Dacron is about 10 times higher than their woven equivalents.)

The lack of difference between the fate of freeze-dried homologous and heterologous valves in this situation is encouraging when heterologous valves are being considered for use in the human. However, the question of the long-term behaviour of these transplants still remains unanswered.

The incompetence of the inserted valve present in five dogs was due to one or more cusps becoming attached to the aortic wall. The fact that unfavourable haemodynamic conditions were present in three dogs emphasizes the importance of purely mechanical factors in the eventual fate of these transplants.

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