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Homograft Replacement of the Human Mitral Valve

A Preliminary Report

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THE long-term fate of the homograft heart valve has been a matter of great controversy. The early work of Lam[1] has suggested that the aortic valve homograft does not continue to function when placed in the thoracic aorta of the dog. At the same time, he recognized that such studies were very difficult because it was so essential to create some degree of aortic insufficiency in the experimental animal before the donor valve would be stimulated to function and so preserve its gross architecture. Dr. Gordon Murray[2] of Toronto reported experimental studies of homologous aortic valve transplants in the treatment of aortic and mitral insufficiency. He subsequently operated upon four patients in which the homograft aortic valve was placed in the thoracic aorta for the correction of severe aortic regurgitation. There has been clinical improvement in all of these patients, with diminution in heart size and a greatly improved exercise tolerance. Precise physiological studies were performed on several patients, one of whom is six and a half years postoperative. Direct pressure studies and dye dilution curves performed by the Braunwald method[14] show that these valves are still functioning very well.[3] At the same time Willman and Hanlon[13] reported deterioration of the transplanted aortic valve in dogs. This usually developed some three months after the dog's mitral valve had been replaced by an aortic valve homograft.

It is well known that the plastic prosthesis is not as satisfactory in the mitral valve area as in the aortic valve area.[4-9] Starr[10] seems to have avoided the thrombus problem quite successfully by the use of a silicone rubber ball valve which is surrounded by a stainless steel cage, the latter being sutured in place by an adjacent Teflon cloth "fixation ring". Even here thrombus formation and embolism can be a problem unless the patients are managed on long-term anticoagulants. The autologous pulmonary valve has been successfully used in animals to replace the dog's mitral valve.[11] Good function has apparently continued for as long as a year.

Experimental Studies

A. *Tricuspid Valve Replacement*

Experimental studies on tricuspid and mitral valve replacement have continued since 1959. Mongrel dogs were placed upon extracorporeal circulation by means of a right thoracotomy. The tricuspid valve was exposed through a right atriotomy and the three tricuspid leaflets were carefully excised. A fresh, sterile aortic homograft valve had been previously prepared and trimmed to shape, with careful excision of all extraneous tissue. This valve had been taken under sterile technique from a recently sacrificed dog.

The donor valve was carefully sutured in place so that the donor valve ring was approximated to the dog's tricuspid valve ring by a simple running suture. The apices of the three commissures of the donor valve were then sutured to the interior of the right ventricular chamber by means of mattress sutures which were brought out through the right ventricular wall (Fig. 1a). In later experiments a small Teflon ring was incorporated into the suture line of the donor valve annulus. This gave mechanical support to the donor tissue and also facilitated the insertion of the flimsy donor valve.

B. *Mitral Valve Replacement*

In another group of experiments, dogs were placed upon cardiac bypass through a left thoracotomy incision. A single large atrial catheter was placed in the right atrial appendage, after which siphon drainage diverted all the venous flow from the heart and produced a beautiful, bloodless

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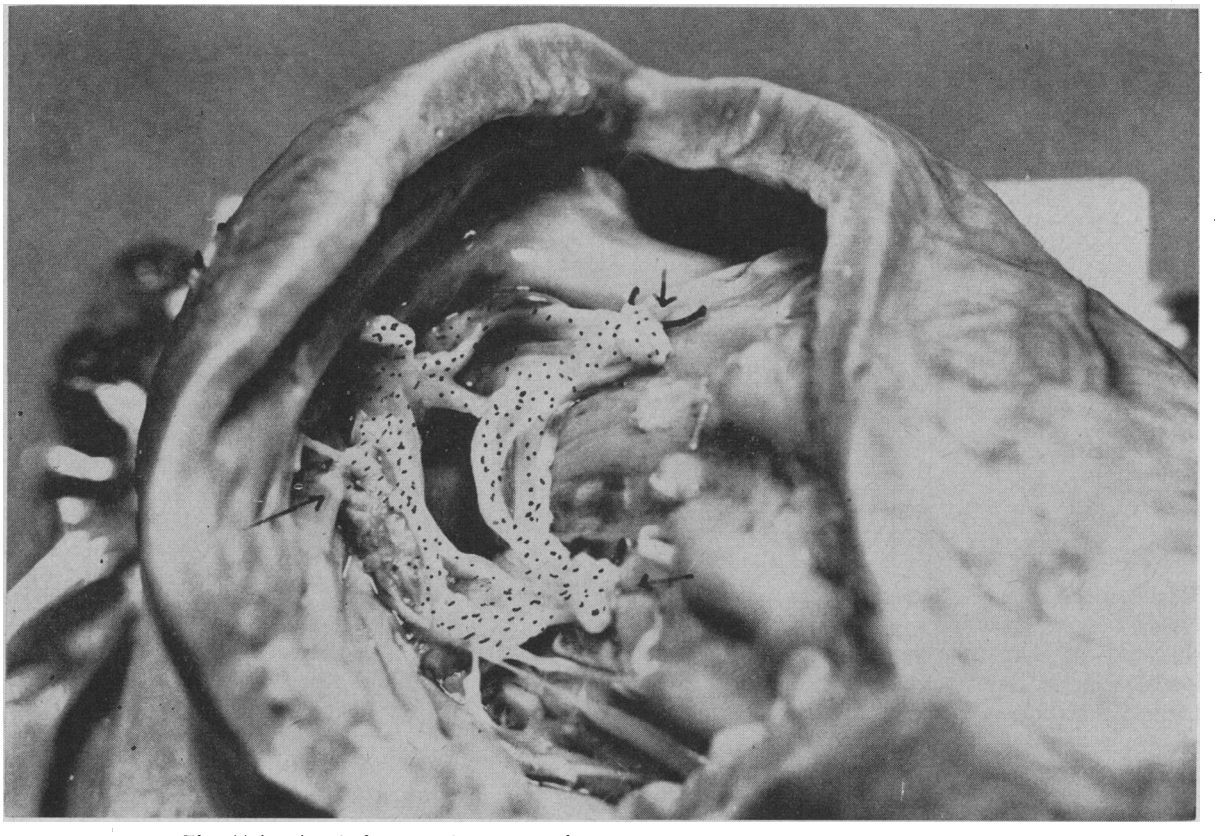

Fig. 1(a).—Aortic homograft valve replacement of the tricuspid valve. Dog No. 18: Donor valve (stippled) is observed from below, occupying the tricuspid valve ring. Three donor commissures are respectively sutured to the right ventricular wall by mattress sutures (arrows). Death occurred four days postoperatively owing to pulmonary complications. The gross appearance of the cusps is quite normal.

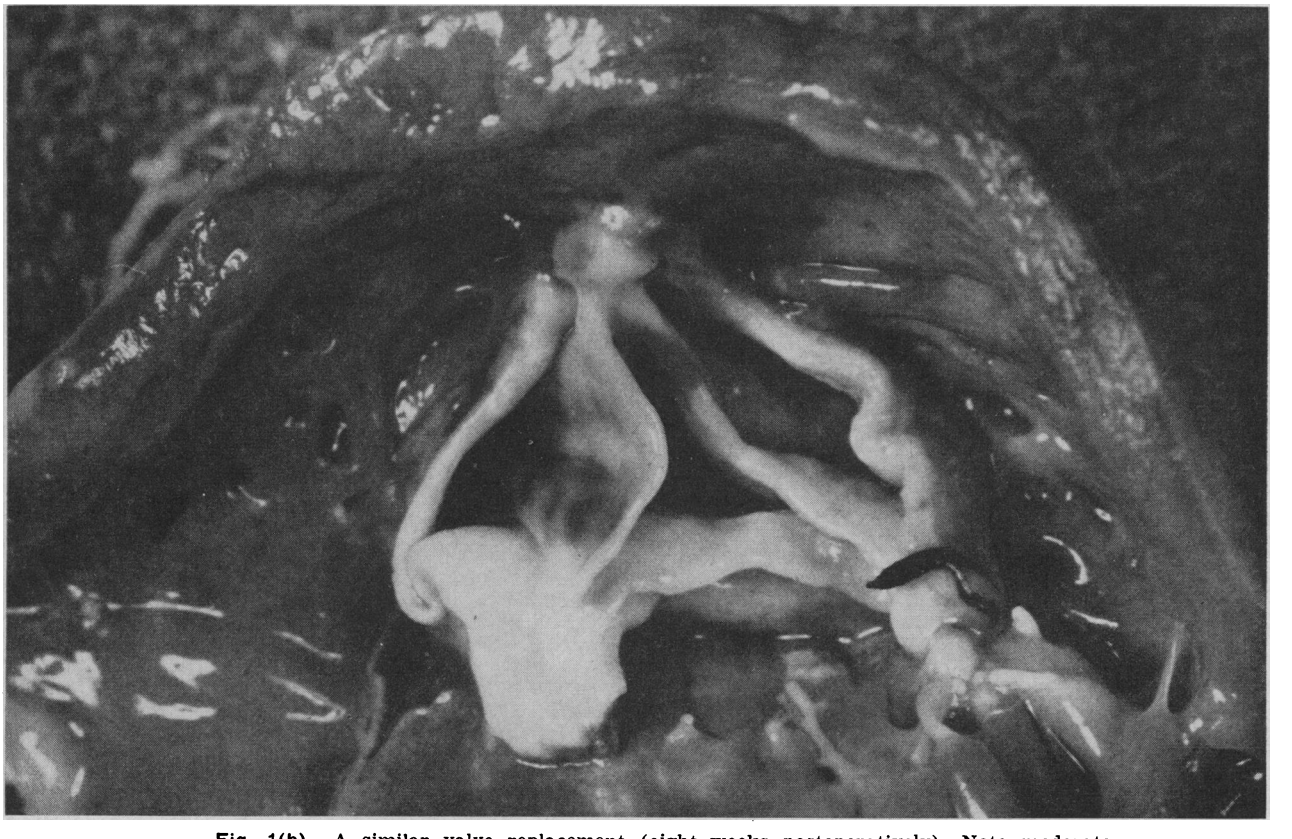

Fig. 1(b).—A similar valve replacement (eight weeks postoperatively). Note moderate cusp edema which did not interfere with cusp mobility. The junction between host and recipient tissues is not discernible.

operative field. These animals were then operated upon through a left atriotomy which gave an excellent exposure of the mitral valve. The two mitral leaflets were carefully excised along with their chordae tendineae, whereupon the aortic valve homograft was carefully sutured in place as before. A running continuous suture attached the donor valve ring to the mitral annulus. Three apical mattress sutures were passed from the apices of the donor valve commissures through the left ventricular wall and were then tied (Fig. 1a).

RESULTS

A. *Tricuspid Valve Replacement*

Replacement was carried out in 34 dogs, many of which died postoperatively of atelectasis, anesthesia difficulties, poor surgical technique or hemorrhage. Others died during the first month from distemper or atelectasis. Most authors would agree that a lengthy cardiac bypass carries a higher operative mortality in the dog than in the human.

Seven dogs survived and remained well for several months, but subsequently were sacrificed, or died of distemper or cardiac failure. Some stenosis was often present in the donor valve. One dog is well and free of murmurs one and a half years after operation, which was performed in August 1960.

Donor valve thrombosis occurred in only one experiment, although in two other instances thrombus formed on the atriotomy suture line extended partially into the donor tissue.

Catheterization studies in a few animals have shown normal valve function four months postoperatively (Fig. 2).

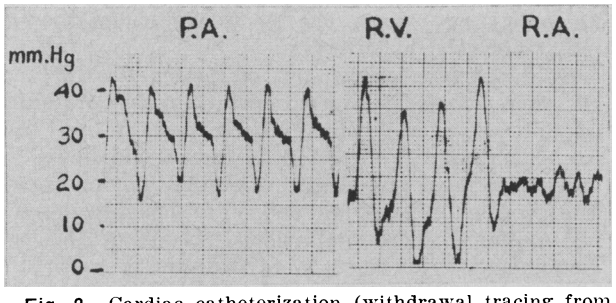

Fig. 2.—Cardiac catheterization (withdrawal tracing from pulmonary artery through the transplanted valve) four months after replacement of the tricuspid valve by an aortic homograft valve. All pressures show normal dynamics with no evidence of stenosis or insufficiency.

Acceptance of the donor valve was good but somewhat variable. Some had cusp edema at eight weeks (Fig. 1b). It was remarkable to see no zone of junction between donor and host tissue.

B. *Mitral Valve Replacement*

Mitral valve replacement was carried out in 14 dogs. Minor surgical errors were much more serious on this side of the heart where pressure differences were much greater. Even minor valvular insufficiency at the end of the procedure resulted in rapid death.

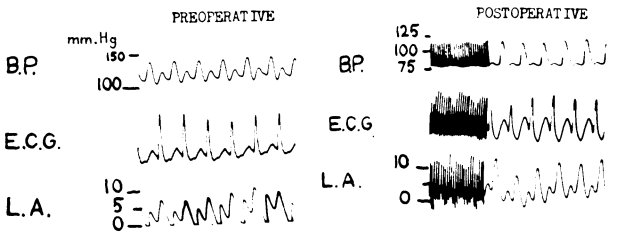

Fig. 3.—Total mitral valve replacement by a homologous aortic valve transplant. An excellent anatomical position resulted, so that valve function was normal. Note normal blood pressure, normal electrocardiogram, and normal left atrial pressure postoperatively.

Only four dogs survived beyond 24 hours. These succumbed, by the third day, from atelectasis, hemorrhage and late tearing of sutures.

Surgically produced stenosis was the cause of death in two dogs.

On the other hand, a patient whose heart has slowly adjusted to a long period of mitral valve disease would undoubtedly tolerate some residual stenosis or insufficiency much better.

A perfect operation resulted in perfectly normal dynamics in the left atrium (Fig. 3).

CLINICAL APPLICATION

The reports of Dr. Gordon Murray were very encouraging. The homologous aortic valve could continue to function in the thoracic aorta for as long as six and a half years. At the same time, our own laboratory studies showed that the homologous aortic valve could function within the heart for as long as a year and a half. The normal human aortic cusp is less vascular than that of the dog,[15] suggesting that it may be even more suitable as a homologous transplant. Excellent valve performance could be obtained, provided the surgical technique was careful and precise in order to keep the cusps in good anatomical position.

Thrombosis and embolism was rarely a problem in this series of dogs, which are probably more susceptible to left atrial thrombus and fibrin deposition than is the human being.[7]

CASE REPORT

A 35-year-old salesman had been first seen in 1951 with the onset of shortness of breath on exertion, palpitations, hemoptysis and fatigue. There was no history of rheumatic fever. Mitral commissurotomy was performed by a finger fracture in 1952. There was a minimal amount of calcium along the free margins of the valve cusps at that time. Satisfactory relief of symptoms continued for five years, after which symptoms returned.

In 1958 he was considered to have developed restenosis. A mitral commissurotomy was performed through the right chest at that time because of the previous operation through his left chest. The valve had become much more heavily calcified and showed a small amount of insufficiency as well. Both cusps were somewhat rigid, but a good opening was obtained by splitting through the calcified commissures out to the valve ring. There was good symptomatic improve-

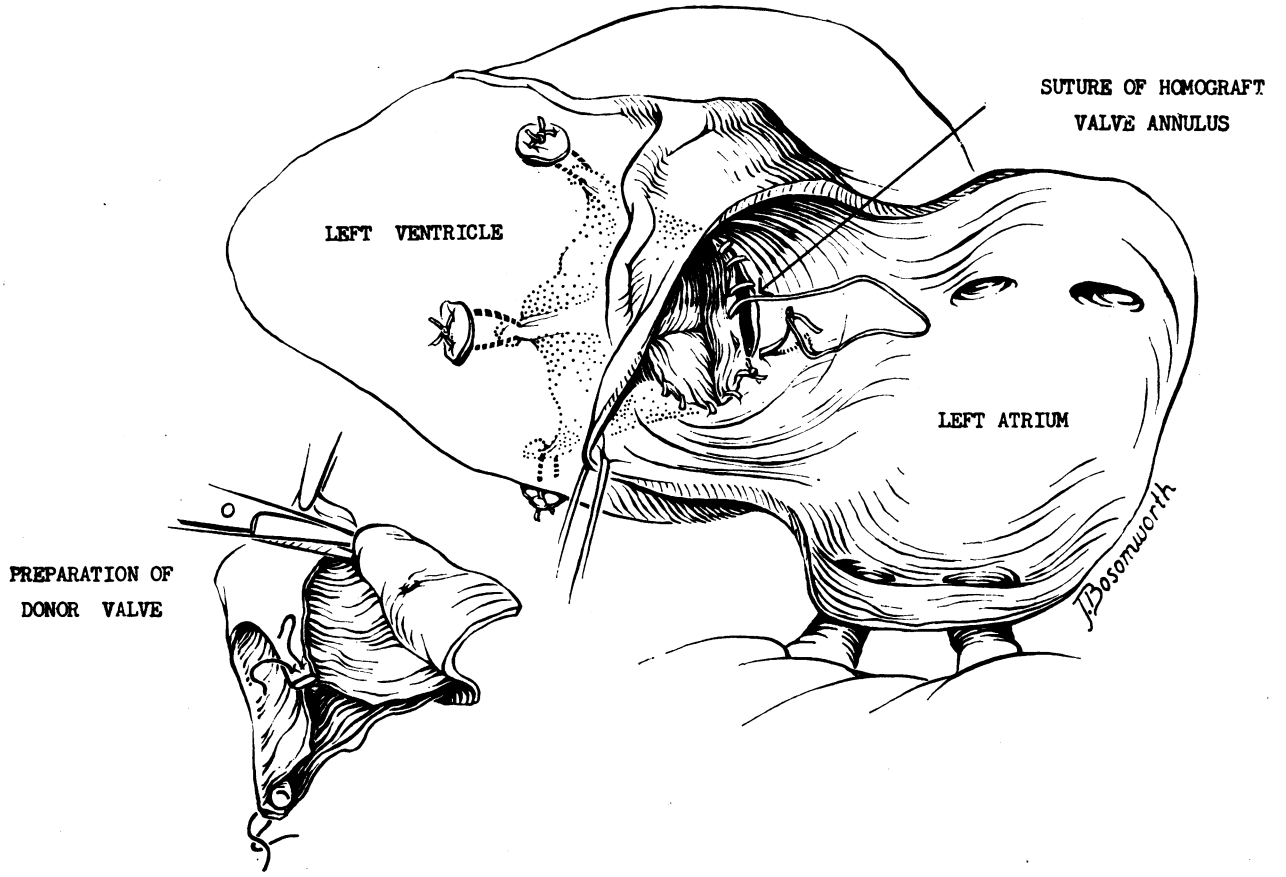

Fig. 4.—Aortic homograft valve replacement of the mitral valve, Patient D.P., March 23, 1962. The chest has been opened through a generous left thoracotomy. Cardiac by-pass was obtained by a right ventricular cannula and siphon drainage to the pump. Arterial return was provided through a left femoral artery cannula. A generous left atriotomy provided a beautiful exposure of the diseased valve. The homograft aortic valve was carefully trimmed of all excess tissue before insertion (see lower left). The donor valve annulus was then carefully sutured to the patient's mitral annulus. The donor commissures were individually sutured to the interior of the left ventricle by means of three mattress sutures which were brought through the ventricular wall and tied over Teflon buttons on the outside of the heart. It is probably of importance to the left ventricle to preserve as many chordae tendineae as possible, for they act as guy wires, and so assist left ventricular function.

ment following this procedure, although it was feared that cusp fibrosis and rigidity would mitigate the effectiveness of the operation.

Two years later there was again a return of symptoms with shortness of breath on exertion, severe fatigue and two or three episodes of hemoptysis. For the few weeks preceding his present admission he had had several attacks of paroxysmal nocturnal dyspnea and quite marked right heart failure in spite of good medical therapy.

Upon admission to hospital he was given vigorous medical therapy which included digoxin, chlorothiazide and mercaptomerin, with considerable improvement in his general condition. On examination he was found to be small and thin. There was jugular venous distension to the angle of the jaw. Basal rales were present in both sides of the chest. The blood pressure was 130/80 mm. Hg, and the heart was fibrillating at 72 per minute. The apex beat was in the sixth left interspace, well outside the mid-clavicular line. A Grade III mitral diastolic murmur was audible. There was no opening snap. A Grade I systolic murmur was also present. The liver was enlarged three fingerbreadths below the costal margin and was slightly tender. There was no swelling of the ankles.

A chest radiograph showed pronounced cardiac enlargement. The right ventricle, pulmonary conus and left atrium were large. Gross calcification was seen in the mitral valve area. The electrocardiogram showed right ventricular hypertrophy.

Operation was carried out on March 23, 1962. A left thoracotomy was performed through the fourth left interspace, the patient's chest being in the true lateral position. The pelvis was kept at about 45° in order to facilitate cannulation of the left femoral artery. The previous thoracotomy and mitral commissurotomy had produced dense adhesions throughout the left pleural cavity, but these were dissected free without too much difficulty. The pulmonary artery pressure was palpated to be about 90 mm. at this time. The left atrial pressure was difficult to palpate because of a stony hard mass of calcium embedded in the left wall of the left atrium. The left atrial appendage had been removed at previous thoracotomy and commissurotomy.

Cardiac bypass was instituted (at 30° C.) at 3600 c.c./minute by means of a right-angled steel cannula placed in the right ventricular outflow tract. A No. 2 purse-string suture was used to maintain a dry field at this site. Perfusion was continued for almost an hour and three-quarters, and a good dry field was obtained. There was no arrhythmia of the heart during this entire period. On opening the left atrium an excellent view of the mitral valve was obtained.

Babcock clamps were placed along the anterior margin of the incision in order to bring the valve into better view. Heavy scissors had to be used because

of the dense calcification of the left atrial wall. No fresh clot was found. The valve was stenosed to the size of about one finger, and the cusp margins were very rigid and contained a lot of calcium. The valve ring and the body of the aortic cusp were free of calcium and fibrosis. The mitral dilator split the valve under direct vision and produced obvious incompetence at this time.

We then proceeded to remove cusp tissue both anteriorly and posteriorly in order to create an orifice capable of allowing the insertion of two fingers. Chordae tendineae were preserved where possible, but two or three had to be excised. A large amount of calcium was removed by means of a subaortic resector as well as by right-angle scissors. Finally a good orifice was obtained which readily admitted two fingers. The homograft aortic valve was then brought into position. The apical mattress sutures of the donor valve were passed through the left ventricular wall by means of large needles (Fig. 4). One suture was placed at 12 o'clock, one at 9 o'clock and one at 6 o'clock. Pledgets were placed over the sutures, but the sutures were not tied until later. A circumferential running suture was then inserted from the aortic valve ring to the mitral valve cusp and ring. A small plastic catheter piece was placed through the donor valve orifice at this time to keep the valve incompetent and thus prevent the danger of air embolism. When the circumferential suture had been finished, the other sutures were tied down over the pledgets and at the same time the finger within palpated this area to make certain that the mattress sutures were under the right tension and in good position. Large plaques of calcium then had to be stripped from the atrial wall in order to allow suture of the atriotomy incision. The surface left by this removal did not seem unduly rough or prone to thrombus formation.

Bypass was then gradually discontinued and the heart took over very nicely. The patient was oligemic initially, and it was only after his blood volume was totally replaced that we obtained a systemic pressure of 90-100 mm. Hg. It was somewhat disturbing to see that the pulmonary artery pressure was still quite high. The left atrium felt quite soft on palpation, although the pressure was obviously somewhat elevated. Pressure studies were then performed, at which time the systemic pressure was around 100 mm. Hg. The pulmonary artery pressure reading was 90 mm. Hg, and at the same time a left atrial pressure recorded peaks to about 40 mm. Hg with a mean pressure of around 20 mm. Hg. The heart continued to take over well, and no thrill was palpable in the mitral valve area. Moreover, the left atrial pressure seemed to subside somewhat with the passage of time.

The patient's early postoperative course was surprisingly smooth. Because of the severe pulmonary hypertension and because of his two previous thoracotomies, it was found that an elective tracheotomy followed by positive pressure ventilation was a very worth-while adjunct in this case. No significant cardiac murmurs could be heard. He has since developed hepatitis and a small empyema. He continues free of cardiac murmurs.

SUMMARY

The homograft cardiac valve has long been the subject of considerable study and of even more controversy. Animal experiments have resulted in conflicting reports, some of which indicated that the valve function was short-lived, lasting only a matter of weeks. Other reports have shown excellent function for as long as six and a half years when transplants have been placed in the thoracic aorta of the human.

Our laboratory studies have shown that the aortic homograft valve will replace the tricuspid or mitral valve very effectively. Excellent function has been observed for as long as one and a half years.

The first reported open-heart replacement of the diseased human mitral valve by an aortic valve homograft has been described. The immediate postoperative result is very encouraging.

ADDENDUM

The patient died a month after operation, of chest infection and electrolyte imbalance. Autopsy showed the donor cusps to be completely normal, in good position and functioning well.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

A marked decrease in the number of cases of scarlet fever in Toronto during the month of March is shown as compared with 1911. In March last year there were four hundred and forty-one cases, this year there have been one hundred and sixty-three. Twelve typhoid cases were reported during March this year, while fifty-eight occurred during the same month in 1911. Only two cases of measles have been reported during March this year, as compared with eighty-seven during the same month last year. No cases of tuberculosis have been reported this year, but seventy-two were reported in March last year. On the other hand, diphtheria shows a considerable increase, one hundred and fifty-seven cases being reported this year as compared with one hundred and one during the same months last year.—*Canad. Med. Ass. J.*, 2: 444, 1912.