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DELIBERATE CIRCULATORY ARREST

THE USE OF HALOTHANE AND HEPARIN FOR DIRECT-VISION INTRACARDIAC SURGERY

BY

ROBERT H. ORTON AND KENNETH N. MORRIS
From Alfred Hospital, Melbourne, Australia

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To-day intracardiac surgery is firmly established. Scarcely a week passes without some new procedure being described which involves deliberately preventing blood from passing through the chambers and valves of the heart. In some of these operations, when considerable time is required for their completion, a partial solution has been found in the employment of by-pass techniques. These methods demand extensive vascular surgery to connect the apparatus to the patient, and large volumes of blood must be added to the circulation because of the extracorporeal pumping and oxygenation. As the result, the hazards of by-pass techniques are not negligible.

Various attempts have been made to perform the shorter intracardiac operations without the use of an extracorporeal circulation. In general, the principle used has been to arrest the inflow of blood to the heart during the time necessary to complete the operation. This has involved the arrest of the cerebral circulation, and the limiting factor has been the survival time of the cerebral tissues in the absence of circulation.

CIRCULATORY ARREST AND CEREBRAL DAMAGE

It is difficult to obtain accurate information on how long the cerebral circulation can be arrested at normal body temperature without causing permanent cerebral damage. By many, the accepted upper limit is two minutes, though Bigelow, Lindsay, Harrison, Gordon, and Greenwood (1950) in their work on hypothermia accepted four minutes. Experimental animals are of little value in this regard. For example, we have found that in sheep it is possible to occlude the superior and inferior venae cavae for 10 minutes without evidence of gross cerebral damage. Wright (1946) has shown that, with nerve tissue of any one species, the product of the survival time and the resting oxygen consumption is constant. Stated in another way, this means that the lower the resting oxygen consumption of the tissue the longer it can be deprived of oxygen without causing irreversible damage.

Bigelow demonstrated in dogs that there is a linear relationship between body temperature and oxygen consumption so that it was possible to halve the oxygen uptake by lowering the temperature to 28° C. From this fact was evolved the technique of hypothermia for prolonging the safe period of circulatory arrest. It is usually accepted that the lowest temperature that can be reached without the risk of spontaneous ventricular fibrillation is 28° C., and many present-day workers prefer to maintain the temperature above 30° C. With this limitation, the longest permissible period of circulatory occlusion under hypothermia is eight minutes.*

It has generally been stated that the cause of cerebral damage in circulatory arrest is oxygen lack, but Crowell, Sharpe, Lam, Bright, and Read (1955) showed that a second mechanism was important in dogs. They demonstrated large numbers of small clots in the blood during circulatory arrest, and showed that if the animals were heparinized before ventricular fibrillation the period of safe arrest could be doubled. In a control series of dogs, when circulatory arrest was produced by ventricular fibrillation, the permanent survival rate was 23% after five minutes of fibrillation. In a second series, where the animals were heparinized before fibrillation was induced, the survival rate rose to 92% with only one death due to inhaled vomitus.

They postulate that, during circulatory arrest and as the result of asphyxia, the coagulation time falls and intravascular clotting occurs. After restoration of the circulation, minute clots are spread throughout the body to produce damage to cerebral and other tissues. If intravascular clotting is prevented by the prior

*This statement would not find general agreement.—EDITOR.

administration of heparin, this cause of cerebral damage can be eliminated and the period of safe circulatory occlusion considerably extended.

Though it is generally assumed that the protective action of hypothermia is due to the lowered oxygen consumption, it must be remembered that hypothermia also delays the clotting of blood. In view of Crowell's work, this factor cannot be neglected.

An important case has been reported by Theye, Patrick, and Kirklin (1957) from the Mayo Clinic. As the result of a technical error in their heart-lung machine, a patient was left for six minutes without a circulation. The fault was then detected, the detached arterial lead connected, and the operation concluded. This patient made an uneventful recovery. The patient had received a dose of heparin as part of the preparation for the attachment of the machine and this factor may have determined the survival of the cerebral tissues.

Read, Lillehei, and Varco (1956) repeated Crowell's work. They were able to obtain a 50% survival rate in dogs after 10 minutes of circulatory occlusion both with and without the use of heparin, and they considered that heparin had no protective value. An important feature of their work that appears to have been ignored is that the dogs received as premedication 4 mg. of morphine per kilogram of body weight. There is considerable evidence that morphine in such doses causes a profound depression of metabolism and this may account for the high survival rate which they obtained.

In the present state of our knowledge, two conditions must be fulfilled if the cerebral tissues are to survive after prolonged circulatory arrest. First, the metabolism of the tissues must be lowered, and, secondly, intravascular clotting must be prevented. Hypothermia lowers metabolism and prolongs clotting time, but its application is limited by the increased irritability of the heart as the temperature falls below 30° C.

Halothane and Metabolism

In the course of investigating the anaesthetic properties of halothane ("fluothane") (Orton, 1958), it became evident that this substance reduced the carbon dioxide production of the human body and it seemed probable that it reduced the oxygen uptake as well. The former finding has been confirmed by Devine, Hamilton, and Pittinger (1958) and the latter by Krantz, Park, Truitt, and Zing (1958) and by Severinghaus and Cullen (1958). Frantz has shown that in monkeys at a concentration of halothane 50% of that required to produce respiratory arrest, the oxygen uptake of the body was reduced by amounts varying from 32% to 74%. Severinghaus and Cullen have found a decrease of between 15% and 20% in the oxygen consumption of the human subject anaesthetized with 1.5% "fluothane." The discrepancy between these figures arises from the lower concentration of halothane used by Severinghaus and Cullen. Since it requires 4% administered for 20 to 30 minutes to produce respiratory arrest (Raventos, 1956), it is probable that Krantz employed at least 2.5% halothane in his experiments.

The implications of the lowered oxygen uptake by the body under deep halothane anaesthesia are by no means clear. It is usual to state that deep anaesthesia causes histotoxic anoxia, and this implies that the tissue cells are rendered incapable of utilizing oxygen. It has been considered by anaesthetists that this effect is damaging to the cerebral tissues, but, until the introduction of muscle relaxants into clinical anaesthesia, deep anaesthesia with ether and chloroform was used regularly with little or no evidence of injury to the brain.

It is recognized that overdosage with any anaesthetic agent will result in cardiac arrest. Under these circumstances it seems probable that the work of the heart exceeds the energy available to it and the heart stops beating from asphyxia. If, however, it were possible to lower the work of the heart concurrently with the oxygen consumption, then the heart should continue to function.

As a working hypothesis, it is suggested that halothane lowers oxygen uptake of the body by depression of metabolism and that this depression is shared by all tissues of the body including cerebral and cardiac. This reduced oxygen consumption is not necessarily deleterious and in the case of deliberate circulatory occlusion it is advantageous. The decreased cerebral activity allows longer occlusion without cerebral damage, whilst the diminished work of the heart avoids cardiac asphyxia during the period when no coronary blood flow is present.

Clinical Application

Fourteen patients have undergone direct-vision intracardiac operations that have been based upon the above theoretical considerations. Halothane is used to depress tissue metabolism and heparin is administered to prevent intravascular clotting

as we are unwilling to discount Crowell's work at present. We also use morphine in moderate doses and consider that it is partly responsible for the metabolic depression and protection of the cerebral tissues.

Technique.—Our present technique of anaesthesia is as follows:

Some days before operation the patient is tested for morphine sensitivity by the administration of morphine, 1/6 grain (10 mg.), to an adult patient or the equivalent dose to a child. The patient is observed over a period of two hours for vomiting or circulatory collapse.

One hour before anaesthesia morphine, 0.25 mg. per kilogram body weight, is administered by hypodermic injection. No atropine or hyoscine is used. On arrival in the operating theatre anaesthesia is induced with intravenous thiopentone and laryngeal intubation performed under succinylcholine. Anaesthesia is continued with nitrous oxide and oxygen in the ratio of three to one. Abolition of the cough reflex is maintained by the subsequent use of decamethonium. Controlled respiration is employed throughout.

After laryngeal intubation, E.C.G. and E.E.G. electrodes are applied and a continuous simultaneous recording maintained. An intravenous infusion is set up in an arm vein and a catheter is introduced into a femoral artery in order to monitor the blood pressure with a capacitance manometer.

Anaesthesia is maintained with nitrous oxide and oxygen until the thoracotomy has been performed and all the necessary pressure gradients have been determined.

Heparin, 2 mg. per kilogram of body weight, is given intravenously. Higher doses than this were used in some patients, but we now feel that this was unnecessary.

The administration of halothane is begun. The reason for withholding it until this time is that, because of the associated hypotension, it may not be possible to obtain valid pressure gradients across the cardiac valves in its presence.

The concentration of halothane is steadily increased over a period of 10 to 15 minutes, a continuous watch being kept on the E.E.G. and blood pressure. We have found it necessary to use a vaporizer capable of delivering concentrations of halothane as high as 5%. This has been possible with the British Oxygen Co. "fluothane" vaporizer attached to the Boyle machine, and with the halothane introduced into a closed circuit using 3 to 4 litres of total gas flow.

No attempt is made to use 100% oxygen, and in most cases 50% oxygen and 50% nitrous oxide have been used. It is considered that high oxygen concentration may increase tissue metabolism.

At present our object is to lower the systolic blood pressure, as recorded by intra-arterial catheter, to 50 mm. of mercury. At the same time we attempt to obtain an E.E.G. which shows minimum activity.

With nitrous oxide and oxygen anaesthesia, the E.E.G. shows a normal fast activity once the thiopentone effect has passed. As halothane is introduced, the activity decreases in frequency but increases in amplitude. As anaesthesia deepens, the frequency drops further and the amplitude falls until bursts of slow activity are followed by periods of one to two seconds in which no electrical activity is recorded. Finally, the tracing becomes a straight line. Initially we considered that this final state was due to the associated hypotension, but we have now seen cases in which cerebral activity was absent whilst the blood pressure remained above 70 mm. of mercury.

If the blood pressure falls so rapidly that it appears unlikely that we will be able to produce cerebral quiescence, we reduce the concentration of halothane and proceed with the administration more cautiously. We like, if possible, before occlusion to lower the blood pressure to 50 mm. and at the same time produce a flat E.E.G. tracing. This latter is not always possible, and, at present, we consider it undesirable to lower the pressure below 50 mm. in an attempt to obtain it. Difficulty with cardiac resuscitation has been encountered in dogs if the blood pressure has been lowered below this figure.

Bradycardia, contrary to expectations, has not been a prominent feature of deep halothane anaesthesia in these cases. As the work of the heart during the period of circulatory occlusion must be related to heart rate, we avoid all drugs that are likely to increase it. Thus, atropine and hyoscine are not used for premedication, and gallamine is considered an undesirable relaxant.

Usually the pulse rate has been about 80 beats per minute at the time of occlusion. This may slow slightly during circulatory arrest, but it has never caused any concern.

The period occupied in introducing halothane into the patient allows the surgeon to place slings around the venae cavae and to prepare the aorta, pulmonary artery, or atrium, as the case may be.

When the E.E.G. and blood pressure are satisfactory, the circulation is occluded and the intracardiac manipulation performed. During occlusion the lungs are ventilated quietly with nitrous oxide and oxygen so as to empty them and the anaesthetic machine of the high concentration of halothane.

When the operation has been completed, the slings on the venae cavae are loosened and the circulation restored. If the blood pressure returns immediately, halothane should be cautiously re-introduced, as in some cases vagal release occurs with a rapid rise in blood pressure and an intense tachycardia. Halothane will control both of these undesirable effects. If they are left uncontrolled, secondary cardiac failure may follow the period of hypertension and a catastrophic fall in blood pressure and ventricular fibrillation may ensue.

If, after the release of the venae cavae, the blood pressure does not immediately begin to rise, gentle cardiac massage is used. We do not hesitate to employ intracardiac adrenaline under these circum-

stances, and have seen nothing but benefit from it. During the period of occlusion the blood lost from the heart should be replaced rapidly. If this is not done, the blood volume will be low when the circulation is restored and difficulty will be experienced in restoring an adequate blood pressure.

When the circulation has been stabilized anaesthesia can be gradually lightened, but no attempt is made to raise the percentage of oxygen administered above 50 until the wound has been closed. Following restoration of the circulation, the E.E.G. returns to normal in a time that appears to be directly related to the time of occlusion. In all cases the E.E.G. has shown a return of fast activity by the end of the operation.

The patient is returned to bed and is usually fully conscious within two hours. A feature of the recovery is the absence of evidence of cerebral irritation.

When a vertical sternal split incision has been used little sedation is required in the post-operative period, but we do not hesitate to employ morphine if pain is present.

Case Reports

Case 1.—R. C. was a boy aged 2 years, weighing 14 kg., in whom a cardiac murmur was discovered at birth. He was fairly active and had never been cyanosed, but he became breathless with moderate exertion. His clinical, electrocardiographic, and radiological findings were consistent with a diagnosis of simple pulmonary stenosis. Cardiac catheterization showed that the right ventricular pressure was 150/0 mm. Hg. The catheter could be passed up to the level of the pulmonary valve, but it could not be made to enter the pulmonary artery.

Operation (February 20, 1958).—The heart was explored through a vertical midline sternum-splitting incision. The right ventricle was seen to be greatly hypertrophied. The pulmonary valve ring was 5 mm. in diameter; above this the pulmonary artery was greatly dilated. A strong systolic thrill in the pulmonary artery began immediately above the valve ring, but no valve cone could be palpated at this level.

A cannula was inserted into the right ventricle and passed up into the pulmonary artery. This showed that there was a single pressure change situated at the level of the valve ring. The gradient across the pulmonary valve was 150 mm. Hg.

Rubber slings were passed about the superior and inferior venae cavae, and 28 mg. of heparin was injected into the right atrium.

A portion of the pulmonary artery was excluded by a curved clamp placed along its edge. A longitudinal incision was made in this excluded portion and fine stay sutures were placed in the edges.

The vena caval rubbers were now tightened, and, after a few heart beats, the clamp was taken off the side of the pulmonary artery.

The pulmonary valve was seen to consist of a thickened plate with a 2 mm. central orifice. Three thickened fused commissures could be recognized, and scissors were used to cut two of these out to the valve ring. The resultant valve aperture was the maximum that could be obtained without splitting the valve ring.

The pulmonary artery was allowed to fill with blood and the side clamp was re-applied before loosening the vena caval rubbers. The total time of circulatory occlusion was 2 minutes 15 seconds. The pulmonary artery was repaired.

The pressures in the right ventricle and pulmonary artery were again measured and a gradient of 100 mm. Hg was shown to be present. It was felt that this gradient represented the restriction produced by the very small valve ring and that no further relief of the stenosis could be achieved.

Protamine sulphate, 56 mg., was injected slowly into the intravenous drip line. The pericardium was loosely approximated and the chest was closed.

The child had an uneventful convalescence and appears to have derived some benefit from the incomplete relief of the pulmonary stenosis.

Case 2.—M. Q., a boy aged 2 years and weighing 10 kg., had been cyanosed since birth, and his development had been slow. At 2 years of age he could not walk, he tired easily even when feeding, and had little power in his arms and legs. His clinical, electrocardiographic, and radiographic findings were consistent with the diagnosis of simple pulmonary stenosis with atrial septal defect.

Cardiac catheterization showed the right ventricular pressure to be 130/10 mm. Hg when the femoral artery pressure was 74/50 mm. Hg. The catheter could not be made to enter the pulmonary artery or the left atrium. Femoral artery oxygen saturation was 64%.

Operation (March 13, 1958).—The operative exposure was similar to that described for Case 1. The appearance of the pulmonary artery was identical with that in Case 1, i.e., a valve ring of about 4 mm. diameter, at which level a systolic thrill began but with no palpable valve cone. The main pulmonary artery was dilated.

Difficulty was experienced in passing a hollow probe into the right ventricle for pressure measurements. It was evident that the cavity of the right ventricle was very small. The probe was finally passed successfully and a gradient of 115 mm. Hg was demonstrated at the level of the valve ring.

A Satinsky type of clamp was used to exclude a portion of the wall of the right atrium and a curved clamp was used to exclude a portion of the wall of the pulmonary artery. These excluded portions were opened and stay sutures placed in the edges.

Before producing circulatory occlusion, 20 mg. of heparin was injected into the right atrium. When the pulmonary artery was opened the pulmonary valve was seen to be a thickened plate similar to that in Case 1, but, in this instance, there were only two fused commissures, which were cut out to the valve ring to produce the maximum aperture. The

pulmonary artery was filled with blood and its side clamp was re-applied. The side clamp on the right atrium was now removed and an atrial septal defect about 1.5 cm. in diameter, situated in the region of the fossa ovalis, was oversewn. The inferior vena caval rubber was loosened and, as the atrium filled with blood, the side clamp was re-applied. The superior vena caval rubber was then loosened. The total time of circulatory occlusion was 5 minutes 15 seconds. After the restoration of circulation the heart action was feeble and the blood pressure remained at about 30–40 mm. Hg for several minutes. Gentle cardiac massage and an injection of 1 ml. of 1 in 10,000 adrenaline into the left ventricle produced a satisfactory heart action, and the blood pressure quickly stabilized at about 100 mm. Hg.

The pressure gradient across the pulmonary valve was again measured and found to be 75 mm. Hg. In view of the fact that the maximum possible aperture had been produced in the pulmonary valve, this unsatisfactory figure had to be accepted. Protamine sulphate, 40 mg., was injected into the intravenous drip line.

By the time the skin incision had been closed the child was breathing spontaneously and reacting briskly to painful stimuli. Shortly after his return to bed he was awake and talking. He was apparently normal and well 18 hours after operation, when he suddenly died.

Necropsy confirmed that the right ventricle was thick-walled with a very small cavity. The endocardium showed fibro-elastosis with scar tissues extending into the underlying muscle. Careful histological examination of the brain did not reveal any abnormality.

It is felt that this child died because the underdeveloped right ventricle could not tolerate the closure of the atrial septal defect in the face of an incompletely relieved pulmonary stenosis. If such a patient is encountered again, the atrial septal defect will be left open.

CASE 3.—V. P., a boy aged 14 years and weighing 73 kg., who had been known to have a cardiac murmur since infancy, had become progressively short of breath on exertion and his walking distance was limited to 30 yards. The clinical, electrocardiographic, and radiographic features were consistent with a diagnosis of severe aortic stenosis.

Left ventricular puncture was carried out using the technique described by Brock (1956). This showed that the pressure in the left ventricle was 218/4 mm. Hg when the brachial artery pressure was 78/46 mm. Hg. A withdrawal tracing was obtained using a fine plastic cannula inserted through the puncture needle into the left ventricle and aorta. This demonstrated only one level of pressure change.

Operation (March 20, 1958).—The operative approach was similar to that described in Case 1. Pressures measured in the left ventricle and aorta showed a pressure gradient of 75 mm. Hg across the aortic valve. A tape in a Rummel tourniquet was used to control the aorta above the aortotomy during the period of circulatory occlusion.

The aortic valve was seen to be conical, with two fused commissures. The opening at the top of the cone was about 4 mm. in diameter. The two commissures were cut with scissors out to the valve ring. The inferior vena caval rubber was loosened, and, as blood filled the aorta, the aortic side clamp was re-applied at the same time as the Rummel tourniquet was loosened. The superior vena caval rubber was then loosened.

The period of circulatory occlusion was 2 minutes 10 seconds. When the blood pressure had stabilized at 110 mm. Hg, the gradient across the aortic valve was measured and shown to be 25 mm. Hg.

In this patient 146 mg. of heparin and 292 mg. of protamine sulphate were used.

The patient had an uneventful convalescence and is now well.

CASE 4.—J. J., an 11-year-old girl weighing 33 kg., had been known to have a cardiac murmur since infancy.

She was first seen by us in 1955, at which time the clinical, electrocardiographic, and radiographic features were consistent with the diagnosis of severe aortic stenosis with slight aortic incompetence. Over the next three years the electrocardiogram showed evidence of increasing left ventricular strain. In March, 1958, she complained of central chest pain, palpitations, and dyspnoea.

Left ventricular puncture was performed, and this demonstrated that the left ventricular pressure was 270/3–30 mm. Hg when the brachial artery pressure was 100/55 mm. Hg. A withdrawal record was obtained by passing a fine plastic catheter through the needle into the left ventricle and aorta. This showed that, as the catheter was pulled back into the ventricle, the diastolic pressure fell to left ventricular level before the systolic pressure rose to ventricular level. This indicated that the stenosis was probably of the subvalvar type.

Operation (April 10, 1958).—The operative technique was similar to that used in Case 3. When the aorta was opened the aortic valve was seen to be normal. Two thin pieces of malleable copper were bent to an appropriate shape and used to separate the valve leaflets. About 1 cm. below the aortic valve there was a fibrous septum with a central hole about 6 mm. in diameter. If a suitable side cutting punch had been available it would have been very easy to cut away that portion of the septum which was not related to the aortic leaflet of the mitral valve. Unfortunately, no such instrument was immediately available, so a radial cut was made through the septum on its most anterior aspect and then a Brock aortic valve dilator was used to stretch the septum. This resulted in a great enlargement of the orifice. The aorta was closed, the circulation re-established, and the operation completed as with the other patients.

The total time of circulatory occlusion was 3 minutes. Heparin, 66 mg., and 132 mg. of protamine sulphate were used in this operation.

Left ventricular puncture was repeated on May 6, 1958. This showed that the gradient across the subvalvar stenosis was 90 mm. Hg.

The child made an uneventful recovery and is now well.

CASE 5.—P. C., a youth aged 18 years and weighing 56 kg., had been known to have a cardiac murmur for many years. He had been active and well, but, over the past 12 months, his exercise tolerance had progressively diminished.

The clinical, electrocardiographic, and radiographic findings were consistent with the diagnosis of simple pulmonary stenosis. Cardiac catheterization showed that there was a gradient of 70 mm. Hg across the pulmonary valve.

Operation (April 17, 1958).—The operative technique was similar to that used in Case 1. The pulmonary artery was dilated and a well-formed valve cone could be palpated. A gradient of 60 mm. Hg across the pulmonary valve was demonstrated. When the pulmonary artery was opened the pulmonary valve was seen to be composed of three leaflets. One commissure was completely fused and the other two commissures were partly fused. The valve orifice was about 6 mm. in diameter.

All three commissures were cut out to the valve ring to produce an orifice through which a finger could be passed into the right ventricle.

After repair of the pulmonary artery and restoration of circulation, the gradient across the pulmonary valve was again measured and found to be 15 mm. Hg.

The total time of circulatory occlusion was 1 minute 35 seconds.

Heparin, 112 mg., and 224 mg. of protamine sulphate were used in this operation.

The patient made an uneventful recovery and is now well.

CASE 6.—B. Q., a girl aged 10 years weighing 23 kg., was found to have a cardiac lesion when she was examined before tooth extraction. After the extraction of her teeth she developed an illness that was probably subacute bacterial endocarditis, but this was never proven.

After treatment of this illness she was sent to Alfred Hospital, where it was found that clinical, electrocardiographic, and radiographic features were consistent with the diagnosis of atrial septal defect. At cardiac catheterization an atrial septal defect was demonstrated.

Operation (April 24, 1958).—The right pleural cavity was entered by an anterolateral incision below the sixth rib with division of the sternum transversely but without entering the left pleural cavity. It was later decided that an incision below the fifth rib would have given better access. The pericardium was opened and the large right atrium was explored with a finger through an opening in the tip of the atrial appendage. The finger was withdrawn and a clamp was placed to control the opening in the appendage and to exclude a portion of the wall of the atrium. The opening in the appendage was then continued into the excluded portion of atrial wall and stay sutures were placed in the cut edges. Rubber slings were passed around the superior and inferior venae cavae. Heparin, 46 mg., was injected into the right atrium.

The caval rubbers were tightened and, after a few heart beats, the clamp was taken off the atrial wall. The septal defect was seen to be situated in the region of the fossa ovalis. It was about 3.75 cm. in length with a number of fenestrations in the septum immediately below it. The defect and its associated fenestrations were closed with two continuous sutures. The atrium was filled with blood by loosening the inferior vena caval rubber and the atrial side clamp was re-applied. The total time of circulatory occlusion was 5 minutes.

After release of occlusion, the heart action became normal immediately and the blood pressure quickly rose to over 100 mm. Hg, at which time 92 mg. of protamine sulphate was injected into the intravenous drip line.

The patient had an uneventful convalescence and is now well.

CASE 7.—M. P., a boy aged 7 years and weighing 21 kg., was investigated because of dyspnoea on exertion and under-development. The clinical, electrocardiographic, and radiographic features were consistent with the diagnosis of atrial septal defect. This diagnosis was proven by cardiac catheterization.

The operative technique was identical with that used in Case 6. The atrial septal defect of the fossa ovalis type was about 4 cm. × 2 cm. with one small area of fenestration above it. The defect and fenestration were closed with two continuous sutures. The total time of circulatory occlusion was 5 minutes. When the circulatory occlusion was released, the heart action was feeble for a few beats, but, after a little gentle cardiac massage, it quickly became strong and normal.

Heparin, 42 mg., and 94 mg. of protamine sulphate were used in this operation.

The child made an uneventful recovery and is now well.

CASE 8.—A. C., a man aged 42 years and weighing 55 kg., complained of increasing dyspnoea for two and a half years. Six months before operation he had been treated for subacute bacterial endocarditis. The clinical, radiological, and electrocardiographic features were consistent with the diagnosis of severe, calcified aortic stenosis. A left ventricular puncture was carried out and this showed a gradient of 125 mm. Hg across the aortic valve.

Operation (May 8, 1958).—The operative exposure was by means of a vertical midline sternum-splitting incision. The left ventricle was greatly enlarged, and the ascending aorta was very dilated and contained a strong, coarse, systolic thrill. Rubber loops were placed around the superior and inferior venae cavae and the aorta was mobilized just below the origin of

the innominate artery. The gradient across the valve was measured and found to be 70 mm. of mercury. A small Beck aneurysm clamp was used to exclude a portion of the aortic wall. This excluded portion was opened and fine stay sutures placed in the cut edges. Heparin, 110 mg., was injected into the right atrium, and, after several heart beats, vena caval occlusion was produced. After a further few heart beats, a Crafoord clamp was applied to the aorta, just below the origin of the innominate artery and the side clamp on the aorta was removed. The aortic valve was seen to be heavily calcified with a slit-like orifice, which was enlarged by cutting one corner with scissors and then opening a Brock expanding dilator along the length of the resultant slit. This produced a bicuspid aortic opening extending across the full width of the aortic ring with fairly mobile edges. The inferior vena caval rubber was now loosened and blood allowed to escape freely from the aorta. The side clamp was then re-applied to the aorta at the same time as the Crafoord clamp was removed. The superior vena caval rubber was loosened and the aortic incision was repaired. When normal circulation had been re-established, the gradient across the aortic valve was again estimated and found to be 20 mm. of mercury.

The total time of circulatory occlusion was 2 minutes 17 seconds.

Heparin, 110 mg., and 220 mg. of protamine sulphate were used in this operation.

The patient made a good convalescence and is now well.

CASE 9.—R. M., a boy aged 11 years and weighing 25 kg., had been known to have a cardiac abnormality since birth. He tired easily and could not play games. The clinical, radiological, and electrocardiographic features were consistent with the diagnosis of simple pulmonary stenosis of moderate severity. Cardiac catheterization showed a gradient of 86 mm. Hg across the pulmonary valve.

Operation (June 19, 1958).—The operative technique was similar to that described in Case 1. A gradient of 56 mm. Hg was demonstrated across the pulmonary valve. The pulmonary valve possessed three partly fused commissures. Two of these commissures were opened out to the valve ring.

After repair of the pulmonary artery and restoration of circulation, the gradient across the pulmonary valve was again measured and found to be 14 mm. Hg.

The total time of circulatory occlusion was 1 minute 50 seconds.

Heparin, 150 mg., and 300 mg. of protamine sulphate were used in this operation.

The patient made an uneventful recovery and is now well.

CASE 10.—M. D., a girl aged 16 years and weighing 47 kg., had had a thoracotomy carried out 10 years previously because of a mistaken diagnosis of patent ductus arteriosus. The clinical, radiological, and electrocardiographic findings were consistent with the diagnosis of simple pulmonary stenosis of moderate severity. Cardiac catheterization showed that there was a gradient of 140 mm. Hg across the pulmonary valve.

Operation (July 3, 1958).—The operative technique was similar to that used in Case 1. A pressure gradient of 67 mm. Hg was demonstrated across the pulmonary valve, which possessed three fused commissures. Two commissures were cut out to the valve ring. After repair of the pulmonary artery and restoration of the circulation, the gradient across the pulmonary valve was again measured and found to be nil. While the protamine was being administered, the heart suddenly developed a tachycardia and the blood pressure fell to 50 mm. Hg. The tachycardia was abolished by the intravenous administration of prostigmin, 0.5 mg., and the blood pressure rose to normal levels.

Total time of circulatory occlusion was 1 minute 30 seconds.

Heparin, 235 mg., and 470 mg. of protamine sulphate were used in this operation.

The patient had a normal convalescence and is now well.

CASE 11.—P. R., a man aged 49 years and weighing 76 kg., had been forced to abandon work six months previously because of increasing dyspnoea and central chest pain on exertion.

The clinical, radiographic, and electrocardiographic findings were consistent with a diagnosis of aortic stenosis. Left ventricular puncture showed a gradient of 87 mm. Hg across the aortic valve.

Operation (July 4, 1958).—The operative technique was similar to that described in Case 8.

As the operation proceeded and before halothane had been administered, the blood pressure progressively fell to 40–50 mm. Hg, at which time the gradient across the aortic valve was measured and found to be 45 mm. Hg.

The aortic valve was seen to be heavily calcified with a slit-like orifice. This slit was elongated at each end with a scissors cut and then a Brock dilator was opened in the same line.

After repair of the aorta and restoration of the blood pressure to a normal level, the gradient across the valve was measured and found to be 21 mm. Hg.

The total time of circulatory occlusion was 2 minutes.

Heparin, 150 mg., and 300 mg. of protamine sulphate were used in this operation.

The patient had a normal convalescence and is now well.

CASE 12.—P. C., a man aged 52 years and weighing 75 kg., had been well until six months previously when he noticed increasing dyspnoea on exertion. The clinical, radiographic, and electrocardiographic findings were consistent with a diagnosis of simple pulmonary stenosis. Cardiac catheterization demonstrated a gradient of 100 mm. Hg across the pulmonary valve.

Operation (July 10, 1958).—The operative technique was similar to that described in Case 1. A gradient

of 83 mm. Hg was demonstrated across the pulmonary valve. The pulmonary valve had three fused commissures. Two of these were opened out to the valve ring.

After repair of the pulmonary artery and the restoration of normal circulation, the gradient across the pulmonary valve was shown to be 8 mm. Hg.

The total time of circulatory occlusion was 2 minutes 4 seconds.

Heparin, 150 mg., and 300 mg. of protamine sulphate were used in this operation.

The patient had a normal convalescence and is now well.

CASE 13.—R. W., a boy aged 14 years and weighing 50 kg., complained of diminished exercise tolerance, noticed mainly when playing with other children.

The clinical, radiographic, and electrocardiographic features were consistent with a diagnosis of aortic stenosis. Left ventricular puncture with a withdrawal tracing through the aortic valve were carried out and this showed a single sharp pressure change of 47 mm. Hg. This was interpreted as demonstrating valvar stenosis.

Operation (July 24, 1958).—The operative technique was similar to that described in Case 3.

When the heart was examined there was no post-stenotic dilatation of the aorta, although it was somewhat enlarged at about the origin of the innominate artery. A striking feature was the great enlargement and tortuosity of the coronary arteries.

When the incision was being made into the aorta, it was seen that the wall of this vessel was about twice its normal thickness. When the aorta was opened the aortic valve could not be seen, being obscured by a shelf-like obstruction in the aorta with a 4 mm. central orifice. This obstruction was incised in two places and stretched to produce a widely patent aorta. The aortic valve was then seen to be normal. There was no subaortic stenosis. The supravalvar obstruction was about 1 cm. above the valve ring. The valve leaflets could impinge on it in systole. The openings of the coronary arteries lay below the supravalvar stenosis.

The gradient across the supravalvar obstruction was measured before and after its relief and found to have been changed from 50 mm. Hg to 22 mm. Hg.

The total time of circulatory occlusion was 3 min. 45 sec.

Heparin, 100 mg., and 200 mg. of protamine sulphate were used in this operation.

The patient had a normal convalescence and is now well.

CASE 14.—A. C., a woman aged 56 and weighing 76 kg., in whom a cardiac murmur was discovered at the age of 8 years, during the past two years had suffered from progressive dyspnoea on effort. This had culminated in an attack of cardiac failure, which appeared during an acute respiratory illness. The clinical, electrocardiographic, and radiological findings were consistent with the diagnosis of aortic stenosis. Left ventricular puncture showed that there was a gradient of 112 mm. of mercury across the aortic valve.

Operation (August 7, 1958).—The operative technique was similar to that described for Case 8. The aortic valve was seen to be a calcified cone with only one commissure partly open. The valve opening was enlarged with scissors and then stretched with a Brock aortic valve dilator.

The gradient across the aortic valve measured during operation was found to be 111 mm. Hg before valvotomy and 30 mm. Hg after valvotomy.

Circulation was occluded for 2 min. 38 sec. Heparin, 150 mg., and 300 mg. of protamine sulphate were used in this operation.

The patient made a good recovery and is now well.

DISCUSSION

The first open operations upon the pulmonary valve were performed by Varco (1951), who used two minutes of circulatory occlusion without ancillary aids. He did not persist with this technique, but recently it has been revived by others (Lam, 1957; Björk, 1957). The use of hypothermia enabled Swan, Zeavin, and Blount (1953) to prolong the time of circulatory occlusion for this operation, thus making provision for the unusual or complicated case. It is felt that the use of halothane and heparin for this procedure is a simpler method of providing such a safeguard and to date its use has not been accompanied by any undesirable features, such as ventricular fibrillation.

Aortic valvotomy under direct vision was first achieved by Lewis, Shumway, Niazi, and Benjamin (1956) using hypothermia. The main disadvantage of this method is that the greatly hypertrophied left ventricular muscle is susceptible to ventricular fibrillation, and a number of patients have died from this cause. In 1956 Lillehei, DeWall, Gott, and Varco used the pump oxygenator to gain direct access to the aortic valve, and they described the techniques and problems associated with this method in 1958. The pump oxygenator extends the permissible time of exposure, but it necessitates the use of a complicated organization in order to obtain an exposure of the aortic valve, which, in most instances, need only be for about three minutes. Lillehei and others (1958) operated upon one patient suffering from aortic stenosis using five minutes of circulatory occlusion with standard anaesthetic methods and no pump oxygenator or hypothermia. The patient died after 36 hours with severe myocardial damage as a result of the temporary ischaemia.

Our experience with circulatory occlusion, using halothane and heparin for direct-vision aortic

valvotomy, is confined to six cases. This small series appears to show that there is no tendency to ventricular fibrillation; if anything, the cardiac irritability is decreased and the heart tolerates handling and disturbance by sucker points with apparent impunity.

One of the technical difficulties in transaortic exposure of the aortic valve is the placing of the side-excluding clamp on the aorta. This can be difficult and dangerous if there is much tension within the aorta. In the operations that have been described here, this step was facilitated by the hypotensive state produced by the deep "fluothane" anaesthesia. Similarly, when the aortotomies were being repaired, the aortic pressure was regulated at a low level. It was felt that this is a real safety factor in the operation.

Atrial septal defects were first successfully closed under direct vision by Lewis and Taufic (1953) using hypothermia and by Gibbon (1953) using the pump oxygenator. The pump oxygenator is the method of choice for any atrial septal defect in which there is evidence that it is not of the simple variety. The technique that has been described here, using halothane and heparin, appears to be satisfactory for the closure of uncomplicated atrial septal defects, and it has the advantage of being a straightforward surgical procedure without the attendant complexities of apparatus and personnel which are necessary for hypothermia or pump oxygenator work.

In this series of 14 cases there has been one death. It is felt that this death was not due to the use of halothane and heparin with circulatory occlusion, but to the imposition of an intolerable strain on an under-developed right ventricle by closing an atrial septal defect in the presence of an inadequately relieved pulmonary stenosis.

The experimental work on animals, which has formed the background for our hypothesis, has not been given in this paper. Investigations are continuing and will be the subject of a separate communication.

In regard to the use of heparin, we do not consider that the work of Crowell has been proven. We have had no harmful effects from its use, and consider that, at the present state of our knowledge, it is justifiable to continue to use it.

Sufficient evidence is available to say that both morphine (Moyer, Pontius, Morris, and Hirshberger, 1957; Haxholdt and Jensen, 1957) and halothane lower the metabolism of the body. It is reasonable to assume that the brain shares in this effect and, indeed, experimental evidence is available to confirm this statement (Moyer and others, 1957).

Whether or not lowered metabolism protects cerebral tissues from the effects of anoxia still must be determined. Our cases, apart from those of atrial septal defect, do not prove our hypothesis. Even these latter cases are borderline, the longest period of successful occlusion being five minutes.

We feel, however, that it is reasonable to report our results and to continue our investigations.

SUMMARY

A description is given of a technique by means of which 14 intracardiac operations were carried out under direct vision.

Morphine premedication and deep halothane anaesthesia were used to lower cerebral and cardiac metabolism. Heparin was administered to prevent intravascular clotting and cerebral embolism.

It is considered that, under these circumstances, periods of circulatory arrest of at least five minutes, and probably longer, can be achieved with safety.

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