6 had a subsequent child, giving an average of half a child per couple. In 10 instances the couples were not reassured at all. They either thought even a small risk too great to run, or else said they did not believe what they were told. Only 2 of the 10 had a subsequent child. It should be added that a few couples were clearly anxious to find additional reasons to reinforce their reluctance to have further children, a reluctance based on reasons other than the genetic outlook.

It is, I am afraid, a measure of failure that we succeeded in fully convincing only half these couples that the risk was in fact very small and not unreasonably out of proportion to the risk run by any random couple any time they have a child. When the study is complete we may perhaps strengthen our letters to family doctors, mentioning that experience shows that some couples are not fully reassured and that further talks by him reinforcing the advice given might be a good plan.

Conclusion

It is interesting to note how clearly the attitude to the advice given is reflected in the action taken and in the number of subsequent children the couples did in fact have. It may be hoped that as time goes on and genetic prognosis becomes increasingly the concern of the specialist, and above all of the family doctor, in addition to the specialized clinic, we shall get better results. Those who have to recognize that the risk is bad will be helped to reconcile themselves to their bad luck, and helped too in the matter of adoption. Those for whom the outlook is good may increasingly be encouraged by repeated assurances that in fact they have little to worry about, and so a higher proportion of those who do indeed want further children will be given the confidence to go ahead.

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"All of them [on these advisory committees] serve in a voluntary capacity and it is therefore of the greatest importance to stress this voluntary element because it carries with it a very grave hazard. You can only maintain this voluntary structure of the National Health Service if there are people willing to come forward and carry the burden of this service. It is becoming more and more difficult to recruit from younger members of our communities those who are willing to undertake service on committees of this kind. That is not surprising. They have other responsibilities. Their time is otherwise occupied. But I warn you, and I warn you in the strongest terms which I can command, that unless voluntary service is continued we can look forward to the National Health Service being completely under the control (I do not want to use this word in a pejorative sense) of bureaucracy in which the human element, which we are all endeavouring to ensure shall permeate the spirit of our health services, will have disappeared. That is why I would stress the great importance of this voluntary endeavour within the Health Service in its administration, its planning and in the advice which it gives to the Minister on general and on specialist topics." (Lord Cohen of Birkenhead addressing the conference of the British Hospitals Contributory Schemes Association.)

CLINICAL USE OF HYPOTHERMIA COMBINED WITH CARDIO-PULMONARY BYPASS*

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In Perth during the past two years various modifications of techniques of cardio-pulmonary bypass have been tried to obtain more satisfactory conditions for carrying out open heart surgery. Previously, bypass at normal temperatures had been attempted in the animal laboratory, using a modified bubble oxygenator (DeWall *et al.*, 1956; Cooley *et al.*, 1958), with disappointing results. When Drew *et al.* (1959) described their technique of achieving profound hypothermia by means of a low-flow bi-ventricular bypass and using the patient's own lungs to oxygenate the blood, it was decided to develop this method.

However, this technique seemed unsuitable for certain types of clinical case (Simpson *et al.*, 1960), and to avoid the disadvantages of bi-ventricular bypass and yet retain the advantages of deep hypothermia animal experiments were carried out using deep hypothermia induced by means of a heat exchanger (Brown *et al.*, 1958) combined with a bubble oxygenator (Fig. 1). In

FIG. 1.—Diagram of the extracorporeal circulation using a bubble oxygenator and heat exchanger to induce profound hypothermia.

this technique cooling by means of a partial bypass was begun; then as cooling took place and the heart as a result began to fail the bypass automatically became complete. When the pharyngeal temperature reached 15° C. the circulation was discontinued while the intracardiac procedure was carried out.

Experimental cardiac surgery using profound hypothermia in this way was followed by a much higher survival rate than when bypass without hypothermia was employed. The occasional incidence of pulmonary

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oedema and the occurrence of left atrial pressures of up to 60 mm. Hg when the bypass was running and the heart was not beating effectively have led us to decompress the left atrium routinely by means of a small cannula leading to the venous reservoir of the machine.

Present Series

Altogether 14 patients, whose ages ranged from 4 to 32 years, were operated on using profound hypothermia induced in this way (Table I). In each case the definitive intracardiac surgery was carried out during a period of total circulatory arrest. The perfusion details of these cases are summarized in Table II. It will be seen that the bypass flow-rates varied from 28 to 104 ml./kg./min. The pharyngeal temperature at which the circulation was stopped varied between 14 and 18° C., and there was usually a further drop of 1 to 2°

TABLE I.—*Diagnoses in 14 Cases Operated On under Deep Hypothermia with Total Circulatory Arrest*

Case No.	Age	Pre-operative or Operative Diagnosis	Operation
1	32	Fallot's tetralogy; absent left pulmonary artery	Infundibulectomy
2	12	Infundibular stenosis; V.S.D.; A.S.D.; persistent ductus arteriosus	"
3	8	A.S.D.; anomalous pulmonary veins	Closure of A.S.D. Correction anomalous veins
4	13	A.S.D.	Closure of A.S.D.
5	25	"	" " "
6	7	"	" " "
7	13	"	" " "
8	12	Primun A.S.D.	" " "
9	23	A.S.D.	" " "
10	19	"	" " "
11	4	V.S.D.; corrected transposition	Teflon patch to V.S.D.
12	30	Severe mitral incompetence; some aortic incompetence	Plication mitral valve ring
13	11	Fallot's tetralogy	Complete correction
14	5	A.S.D.; anomalous pulmonary veins	Closure of A.S.D. Correction anomalous veins

TABLE II.—*Perfusion Data of 14 Cases Operated On under Deep Hypothermia with Total Circulatory Arrest*

Case No.	Weight (kg.)	Flow Rate (ml./kg./min.)	Pharyngeal Temperature (°C.)	Mediastinal Temperature (°C.)	Arrest Time (min.)
1	41	35	18	10	12
2	25	44	18	12	12
3	20	7	18	10	23
4	44	40	18	11	23
5	53	28	18	14	17
6	24	58	16	10	23
7	27	52	18	10	30
8	40	52	15	10	28
9	38	37	18	12	24
10	43	45	18	11	23
11	12.5	70	14	9	46
12	50	35	15	20	43
13	25	60	15	5	+10
14	13.5	104	16	13	44

during the period of occlusion. The lowest temperature measured in the pericardium was 5° C., but usually it was between 10 and 14° C. The longest period of complete circulatory arrest was 46 minutes and the shortest 12 minutes. All of these patients recovered consciousness rapidly after the termination of the anaesthetic, though five died subsequently.

Eight of the survivors had uncomplicated recoveries. The remaining patient developed a *Streptococcus viridans* endocarditis which responded satisfactorily to penicillin. About 48 hours post-operatively this patient also developed a partial asphasia, which gradually improved over the next two to three weeks and then disappeared. This episode may have been due to the technique, though we believe it to have been embolic.

Causes of the Deaths

The causes of the five deaths in the series are shown in Table III. It will be seen that all except one of these patients died because of the severity of their disease or because of the incomplete correction of the defect. The last of these deaths merits a more detailed report.

TABLE III.—*Causes of Death in Five Cases After Operation under Deep Hypothermia with Circulatory Arrest*

Case No.	Age	Pre-operative or Operative Diagnosis	Operation	Survival Time	Cause of Death
2	12	Infundibular stenosis; V.S.D.; A.S.D.; persistent ductus arteriosus	Infundibulectomy	36 hours	Haemorrhage; pulmonary oedema; sub-aortic stenosis
11	4	V.S.D.; corrected transposition	Closure V.S.D. with Teflon patch	12 "	Nodal rhythm; hypotension; patch tore out
12	30	Mitral incompetence; aortic incompetence	Mitral valve ring plication	6 weeks	Mitral incompetence; aortic incompetence; cardiac failure
13	11	Fallot's tetralogy	Complete correction	12 days	Pulmonary oedema; dehiscence of V.S.D. suture line
14	5	A.S.D.; anomalous veins	Closure of A.S.D.; diversion anomalous veins	7 weeks	Cerebral damage

A boy of 5 years had a small high atrial septal defect with anomalous drainage of all the blood from the right lung. During 36 minutes of circulatory arrest at 16° C. the lesion was corrected by enlarging the defect and suturing the septal flap to the right of the anomalous pulmonary veins. He recovered consciousness normally and was talking rationally a few hours post-operatively, and for the first 48 hours appeared to be making satisfactory progress. Thereafter he ran a high swinging temperature, became restless and unresponsive, began to have difficulty in swallowing, and developed purposeless movements of the arms and legs. He had obviously suffered severe cerebral damage, and his condition gradually worsened until his death in the seventh week after operation. Post-mortem examination showed evidence of tracheobronchitis and interstitial pneumonia, which were thought to be viral in origin, and of terminal left ventricular failure. There was no focal lesion of the brain, though some of the cells scattered throughout the brain stem, cerebellum, corpus striatum, and parietal cortex showed central chromatolysis, and a smaller number showed nuclear pyknosis.

We believe that this child died of cerebral damage which occurred at some stage during or immediately after his operation. As there was no post-operative hypotension, this damage was probably related to circulatory arrest during the operation, or to multiple small "cell emboli," or to air embolus, although similar damage has been reported using a bubble oxygenator without hypothermia or arrest (Ehrenhaft *et al.*, 1960).

Retinal Changes

During the operations on most of the clinical cases, and also during many of the animal experiments, the changes occurring in the retina and the retinal blood-vessels were studied, and in the clinical cases the retinae were examined in the post-operative period (Lamb, 1961). The changes observed may be summarized as follows.

At the onset of total circulatory arrest there is rapid and progressive collapse of the retinal vessels (Fig. 2). After about 15 minutes mottling of the retina and fragmentation of the blood column occur. (It is at about this time that we have noted sedimentation of the red

cells in the lines to the pump-oxygenator.) After about 20 to 25 minutes the changes in the retina are more advanced, the vessels are very attenuated or are invisible, and the whole retina is white. Within two to three seconds of restarting the bypass the retina appears normal. Three clinical cases, each having periods of circulatory arrest of more than 23 minutes, have had retinal transudates which became obvious by the fifth post-operative day, and slowly regressed over a period of weeks. One case, occluded for 31 minutes at 17° C., had three small symptomless retinal haemorrhages which also completely resolved.

On theoretical grounds it was thought that erythrocyte sedimentation could possibly lead to multiple small "cell emboli." It was also thought that the transudates and petechial haemorrhages were a manifestation of anoxia during the period of circulatory arrest, and that if they occurred in the retina they probably occurred in other organs. In animals none of these changes were observed during or after prolonged periods of deep hypothermia provided a circulation—even if only of 10 ml./kg./min.—was kept going, and this has since been found to be true of clinical cases also.

Oxygen Saturation

Another observation which was recorded in both clinical cases and experimental animals was that the venous blood returning to the machine after a period of circulatory arrest was always greatly desaturated, often as low as 30 to 40%, whereas just before the arrest it was usually over 90% saturated. The degree of desaturation depended on the duration of arrest and the temperature at which it took place. It was concluded that such a profound fall in oxygen saturation could only mean that severe tissue anoxia was occurring.

Sealy *et al.* (1960) showed that the oxygen consumption at 20° C. is 20 to 25% of normal and at 10° C. is probably about 10%. They suggested that the flow rate should be adjusted to keep the venous oxygen saturation above 70% so that tissue oxygen requirements may be met continuously. Björk (1960), after a series of animal experiments and clinical cases using a period of circulatory arrest at low temperatures, has suggested that brain damage may be caused by aggregated thrombocytes and white cells forming small emboli.

While still believing in the advantages of deep hypothermia as an adjunct to cardio-pulmonary bypass techniques, our case with the cerebral damage, our observations on the retinae, the irrational and deliberate induction of a period of total body anoxia when it could be avoided easily, and the observations

of Sealy *et al.* (1960) and Björk (1960), led us to alter our technique of applying deep hypothermia so as to avoid all but the very short periods of circulatory arrest that might be demanded by certain technical situations. Our present technique is to maintain relatively high flow rates in the shorter cases, or while greater degrees of hypothermia are being induced. When a low temperature is reached during the longer cases

FIG. 3.—Bypass apparatus, showing spinning disk oxygenator, heat exchanger, and mono pump.

the flow rate is reduced to the minimum required to keep the venous oxygen saturated above 70%. The temperature at which the aorta is cross-clamped and the cardiectomy performed depends on the expected duration of the intracardiac procedure.

Employing cardio-pulmonary bypass and hypothermia in this way, we have operated on six patients with one death. In the last four of these cases a spinning disk oxygenator and a Mono pump (Hall *et al.*, 1959) have replaced the bubble oxygenator and the sigmamotor pump (Fig. 3), but otherwise the circuit has remained the same. The details of these patients are summarized in Table IV.

Three (Cases B, C, and D) had atrial septal defects. The lowest pharyngeal temperature reached was 22° C. in one of them and 25 and 26° C. in the others. The flow rates (50, 60, and 90 ml./kg./min.) were not altered throughout the procedure. During the actual intracardiac surgery the heart was excluded from the circulation by cross-clamping the aorta and tightening the snares around the caval cannulae.

Two other patients (Cases A and E) had calcific aortic stenosis, and in both of them the piecemeal removal of calcium from the aortic valve was undertaken.

Case A.—A man aged 62 had been severely incapacitated by fainting attacks and crippling angina for four years, and also had evidence of an old myocardial infarct. Ventricular fibrillation occurred soon after the chest was opened and before either the heart or the external iliac artery was prepared for cannulation. Immediate cardiac massage after a hurriedly performed transventricular aortic valvotomy failed to

FIG. 2.—Photographs of a dog's retina. A, During high-flow cardio-pulmonary bypass. B, Just after complete circulatory arrest. C, After 20 minutes of complete circulatory arrest.

TABLE IV.—Details of Six Patients Undergoing Open Heart Surgery Using a Continuous-flow Hypothermic Bypass Technique

Case No.	Age	Weight (kg.)	Operation	Cooling and Rewarming Flow Rate (ml./kg./min.)	Cardiotomy Flow Rate (ml./kg./min.)	Pharyngeal Temp. (°C.)	Heart Temp. (°C.)	Result
A	62	65	Decalcification of aortic valve	22	22	17	—	Died
B	9	25	Closure of A.S.D.	50	50	22	—	Satisfactory
C	11	32.6	" "	60	60	25	—	"
D	7	18	" "	90	90	26	16	"
E	53	65	Decalcification of aortic valve	60	17	19	17	"
F	7	22.5	Complete correction Fallot's tetralogy	90	17-22	19	10	"

produce a palpable carotid pulse. The appropriate cannulations were made and the patient was placed on bypass after half an hour of probably ineffective cardiac massage. Though at this stage the prognosis was reckoned to be virtually hopeless, cooling was continued and the removal of calcium from the valve was proceeded with. Not unexpectedly, defibrillation could not be achieved after rewarming.

Case E.—A man aged 53 had suffered fainting attacks for 10 years and angina for five years. More recently he had a severe attack of left ventricular failure, and was completely bedridden for two months prior to operation. Hypothermia was induced to a pharyngeal temperature of 19° C., at which temperature the flow rate was reduced from 60 to 17 ml./kg./min., and the heart was excluded from the circulation. The removal of the calcium was begun, and during this procedure the valve cusps were holed in several places, and had to be repaired with a thin piece of compressed "ivalon." It was intended to perfuse the coronaries from time to time during the operation, but the coronary ostia were concealed by the last few plaques of calcium to be removed and were therefore not seen until just before closure of the aortotomy. Altogether the heart was completely without blood supply for 77 minutes at a temperature of 17° C., but it was defibrillated without difficulty when the pericardial temperature reached 30° C. on the rewarming run. His post-operative course was marred by a haemorrhage which eventually required decortication of the right lung, but since then he has made steady progress. Despite clinical evidence of aortic incompetence, he has had no angina since operation, his exercise tolerance has increased greatly, and he was back at work 10 weeks after his operation.

Case F.—A boy of 7 years underwent complete repair of Fallot's tetralogy. A flow rate of 90 ml./kg./min. was used until the pharyngeal temperature was 19° C. and the mediastinal temperature 10° C. At this stage the flow rate was reduced to 17 ml./kg./min., but because the venous oxygen saturation fell below 70% it was increased to 22 ml./kg./min. and kept at this rate for the 85 minutes of intra-cardiac surgery. During this time the coronary arteries were perfused for about 10 seconds approximately every 20 minutes by releasing the occluding clamp on the aorta. At no time was the bronchial flow a real hindrance; it was aspirated continuously, but, being only 750 ml. altogether, it was not found necessary to return it to the machine. This patient has made an uneventful recovery.

Conclusions

The use of hypothermia in combination with cardio-pulmonary bypass has been investigated and applied successfully to clinical cases.

A bypass is more manageable when used in combination with hypothermia because as cooling begins only a partial bypass is required. By the time the bypass becomes complete lower flow rates provide adequate oxygenation.

The reduction in oxygen requirements by hypothermia near 15° C. enables the heart safely to be excluded from an artificially supported circulation for longer periods than at normal temperatures.

Periods of complete circulatory arrest are soon accompanied by progressive changes in the retina and retinal blood-vessels. If similar changes occur in the brain and other organs it is conceivable that permanent damage could result.

If complete circulatory arrest is avoided except for the very short periods which might be demanded by certain technical problems—for example, abnormal anatomy, torrential bronchial flow—the use of a heat exchanger and an adequate pump-oxygenator as described above provides a simple technique for doing open heart surgery with a considerable margin of safety.

Our thanks are due to the staffs of the Instrument and Engineering Workshops, Anaesthetic Departments, and Cardiovascular Investigation Units of the Royal Perth Hospital and the Princess Margaret Hospital for Children for their invaluable assistance in this work. The original observations on the retinal changes were made by Mr. Adrian Lamb, to whom we are particularly indebted.

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"Our next visitor was Professor Ian Aird who, when he had finished being External Examiner in Surgery at Makerere, donned his other hat as a Visitor with a capital 'V' from the Royal College in London. This was a new institution, at our request and at the invitation of our University, and he studied our problems in East Africa at first hand, with special reference to postgraduate education in surgery. . . . To summarize, Professor Aird said that although his brief included only surgery he thought his findings could be applied to all the disciplines making up a medical man's education. In the text of the report he mentioned that the Medical School at Makerere would very soon reach its optimum and maximum planned annual intake of 60-80 students and he therefore recommended the urgent planning of a second full Medical School at Nairobi and suggested that all planning and appointments in Nairobi should be made with this object in view. Meanwhile King George VI Hospital should receive more attention from Makerere and should forge ahead with and enlarge its existing postgraduate education programmes. Makerere itself should increase its basic science facilities to cope with the Primary Fellowship type of training and should investigate the possibility of holding Primary Fellowship Examinations at Kampala. It would be reasonable to say that all these points have been accepted by our Association and we are pressing forward on these lines." (Introduction by retiring President, Mr. Gerald Nevill, Annual Conference of the Association of Surgeons, Kampala, June 28 to July 1, 1961, *East African Medical Journal*, November, 1961.)