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Hypothermia, U. of Colo. Experience

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VISUAL INTRACARDIAC SURGERY IN A SERIES OF ONE HUNDRED ELEVEN PATIENTS

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• *The use of general hypothermia in order to permit cardiac surgery to be performed on the open heart with a dry field under direct vision has intrinsic, unknown risks. These have been analyzed in 111 patients, the largest group being 58 patients with atrial septal defects. Of 19 fatalities, 8 were due to cardiac failure, 4 to thrombosis, 4 to hemorrhage, and 3 to other causes. The hazards both of the cardiac arrhythmias and of the disturbances of clotting can be greatly reduced by not exceeding a limit of eight minutes of circulatory occlusion, by not using this technique for procedures that cannot be readily accomplished within this time limit, and by keeping the temperature within the range from 29 to 32 C (84.2 to 89.2 F). Within these limitations, pulmonary valvular and infundibular stenosis, atrial septal defect, and aortic stenosis can be readily repaired at low risk. The risk is justified by the sometimes dramatic improvement seen after operation in patients with otherwise hopeless conditions.*

This report is concerned with an analysis of our clinical experience with one method (hypothermia) for achieving the major goal of cardiac surgery; namely, open heart, dry field, and direct vision. Deep is our conviction that from the surgical point of view increasing experience will enable most if not all current and future operative procedures within the heart to be accomplished with deliberation under these conditions. By one technique or another, the risk to the patient will be as low or lower and with better results than current blind manipulations guided only by the sense of feel. Surely the accuracy that vision gives to technique, together with the versatility it allows in coping with unexpected variants of the defect, will effect results that are superior from all standpoints. This is already true of valvular and infundibular pulmonary stenosis, atrial septal defect, and ventricular septal defect. We believe it will eventually be true of all intracardiac procedures.

In the exploration of any new technique, however, though the successes be gratifying, the way is strewn with occasional bitter defeats that seem doubly difficult to accept as one realizes that increasing knowledge and experience will probably prove that many such failures would later be preventable. Yet, thus it is with all clinical exploration of new horizons, and one seeks strength in the conviction that in each patient the diagnosis was as certain as possible, the need for surgery was definite and urgent, and the background of experiment was as broad as possible. Not all the questions, however, can be completely solved in the laboratory; in the end, clinical trial must be made and the vital human problems faced.

The operations performed in this series of patients were all done during general hypothermia. The methodology of our management of hypothermia has been described in previous publications,[1] and will not be elaborated here. Moreover, the actual operative techniques have also been described,[2] so these will not be further discussed. We are primarily concerned here with the results of the procedures. When one is utilizing a new modality such as hypothermia, with its intrinsic but unknown risks, and then superimposes in addition a new technical method, such as open suture closure of atrial septal defect, open pulmonary or aortic valvuloplasty, or suture closure of ventricular septal defect, one may have difficulty in assessing the reasons for success or failure in a single patient. We have attempted to evaluate our results in spite of the complexity of the variables.

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Scope of Technique

The variety of cardiac defects for which the value of open operation was explored is illustrated in table 1, and the over-all results are also tabulated. From the beginning it was realized that certain complicated congenital lesions, such as transposition of the great vessels, single ventricle, and Ebstein's anomaly, were beyond the probable scope of the technique of hypothermia. Our experimental evidence suggested that 15 minutes of circulatory occlusion was an absolute limit at the temperature levels we were employing and that probably 10 minutes was a more reasonable limit to apply clinically. As our experience has increased, we have lowered this limit to eight minutes. In general, then, only those procedures that can be readily accomplished in eight minutes of intracardiac manipulation appear to be suitable for open operation during the hypothermia of present-day use. Because we limit our occlusion time, we have also been tending, in recent cases, to use somewhat higher body temperatures than the scope of this technique. Atrial septal defect and valvular pulmonary stenosis occur as single lesions and in an interesting variety of combinations. Table 2 illustrates the various combinations of defects that involved the atrial septum, and table 3 the combinations involving pulmonary stenosis. There is, of course, considerable overlap of patients in the two tables.

On the basis of this experience with our first 111 patients, we currently hold tentative opinions on the indications for specific operative procedures in isolated valvular pulmonary stenosis, isolated infundibular pulmonary stenosis, atrial septal defect secundum, trilogy of Fallot (a valvular pulmonary stenosis and an intact ventricular septum with right ventricular hypertrophy but with a right-to-left shunt through a defect in the atrial septum), tetralogy of Fallot, and aortic valvular and subvalvular stenosis.

There are no rigid indications for operative intervention in patients with valvular pulmonary stenosis and intact ventricular septum. In each patient the particular problem must be evaluated. In general, we feel that operative intervention is definitely indicated whenever the systolic pressure within the right ventricle is 100 mm. Hg or over. However, certain circumstances might lead to operative intervention in patients with right ventricular systolic pressures of less than 100 mm. Hg. Thus, with definite radiological and electrocardiographic evidence of right ventricular hypertrophy, operation would be considered even though the right ventricular systolic pressure was but 70 or 80 mm. Hg. Since the indications for operation center upon the results of the physiological studies and are not dependent upon the symptoms in the patient, we feel that cardiac catheterization should be performed in every patient in whom this diagnosis is suspected, not merely to verify the clinical impression, but also for evaluation of the significance of the lesion.

TABLE 1.—*Results in 111 Patients of Open Heart Surgery During Hypothermia*

Disease	Patients, No.	Recatheterized	Objective Cure	Improved	Unimproved	Dead	Too Recent to Evaluate
Atrial septal defect (secundum)	45	27	26	9	0	7	3
Atrial septal defect (primum)	1	1	0	1	0	0	0
Hiatus atrioventricularis communis*	3	0	0	0	1	2	0
Atrial septal defect and pulmonary stenosis (trilogy), cyanotic	8	3	0	4	0	2	2
Atrial septal defect and pulmonary stenosis, acyanotic	1	0	1	0	0	0	0
Ventricular septal defect	5	0	0	1	0	4	0
Tetralogy: infundibular stenosis	10	4	0	7	0	3	0
Tetralogy: valvular stenosis	7	4	0	7	0	0	0
Pulmonary stenosis, valvular	25	17	15	7	0	0	3
Pulmonary stenosis, infundibular	2	2	1	1	0	0	0
Aortic stenosis	3	0	0	1	0	0	2
Anomalous pulmonary veins	1	0	0	0	0	1	0
Total	111	58	43	38	1	19	10

* Defect including lower portion of atrial septum and upper part of interventricular septum, with abnormalities of atrioventricular valves.

we did previously in order to minimize the inherent risks of hypothermia itself, namely, cardiac arrhythmias and disturbances of the clotting mechanism. The current range of body temperature levels utilized is between 29 and 32 C (84.2 and 89.6 F).

Early in our experience it became evident that certain lesions were eminently suitable for repair within the limits of the technique, specifically, valvular pulmonary stenosis, infundibular pulmonary stenosis (both with intact ventricular septum), secundum type atrial septal defects, and, lately, aortic valvular stenosis. (Secundum type defects are central or posterior superior, with a rim of septal tissue situated inferiorly on the atrioventricular ridge; primum type defects are located inferiorly so that the inferior border of the defect is formed by the atrioventricular ridge. In addition, anomalies of the atrioventricular valves frequently occur.) On the other hand, a short clinical trial with ventricular septal defect proved this to be a lesion of such complexity and variety that its careful repair would inevitably require more time than allowable within the safe limits of hypothermia. This operation was, therefore, abandoned as being beyond

Present Clinical Trial

At the present time, open transarterial pulmonary valvuloplasty has been performed on 25 patients and, of this number, 17 have been recatheterized. There have been no deaths in this group of patients. The

postoperative physiological studies reveal that 15 of these 17 patients have achieved a cure, which we have arbitrarily defined as a postoperative residual systolic pressure gradient between the right ventricle and the pulmonary artery of 20 mm. Hg or less. In the 17 patients recatheterized, a systolic pressure gradient of less than 10 mm. Hg was noted in 9 patients and less than 20 mm. Hg in 6 patients. In the remaining two patients there were gradients of 26 and 28 mm. Hg. Diastolic pulmonary artery pressures have remained normal, and significant pulmonary regurgitation has not occurred in any patient. Although this series is still relatively small, it is our conviction that this current operative approach is a both safe and eminently effective one and is superior to the blind transventricular approach.

Infundibular pulmonary stenosis with an intact ventricular septum is a relatively rare congenital lesion. However, in this series such lesions have been evaluated in two patients, and resection of the infundibular stenosis performed. It is often difficult to be certain from the physiological studies as to whether the ventricular septum is intact, for oftentimes, although no shunt in either direction is definitely established, postmortem examination may reveal the presence of a small defect in the ventricular septum. However, when the stenosis is established as being in the infundibular area, there is no physiological evidence of either a left-to-right or right-to-left shunt at the ventricular level, and the right ventricle is hypertrophied with an elevated pressure, then surgery is definitely indicated. Since there is no defect in the ventricular septum, the surgeon can remove the area of infundibular stenosis completely without concern for the abrupt development of a significant left-to-right shunt after the removal of the infundibular stenosis.

The two patients in this series considered to have had this anomaly have both had excellent results, and one is considered cured. Thus, in one patient the systolic pressure gradient between the right ventricle and pulmonary artery was completely abolished, and the postoperative studies revealed no evidence of a shunt in either direction. The remaining patient, completely asymptomatic, had a postoperative pressure gradient of 27 mm. Hg. Again, the currently suggested approach to this lesion is considered to be both safe and effective.

The indications for surgery in the patient with trilogy of Fallot are in general similar to those for valvular pulmonary stenosis with intact septums. Patients falling into this group usually, although by no means invariably, have a higher systolic pressure within the right ventricle, and, thus, almost always the indications for surgery are clear-cut. Early in our experience we had hoped that, with the regression of the right ventricular hypertrophy after valvuloplasty and the change in the pressure-volume relationship of this ventricle, the right atrial pressure would fall, the right-to-left shunt would be abolished, and possibly the foramen ovale might close, should that have been the defect in the septum. The follow-up course on some of these patients has not been sufficiently long as yet to prove or disprove this hypothesis. However, it would appear that in some of these patients the defect in the atrial septum will remain open and that a second operation for closure of the defect may be necessary, whether it be a dilated foramen ovale or a true atrial septal defect.

We have operated upon nine patients who fall into this category, with two deaths. One patient, 7 months of age, who had been very cyanotic, with a peripheral arterial saturation of 49%, died suddenly 14 hours after surgery. The operation and immediate postoperative course until time of death were uneventful. The other mortality was in a 19-year-old boy with a preoperative right ventricular systolic pressure of 175 mm. Hg and who was very cyanotic, with a peripheral arterial oxygen saturation of 74%. The valvular pulmonary stenosis was relieved without event; however, it was then decided to close the defect in the atrial septum, which was found by palpation to be of great size. The patient developed ventricular fibrillation before the atrium

TABLE 2.—*Results of Surgery in Patients with Atrial Septal Defects*

Disease	Patients, No.	Operations, No.	Proved Total Cure	Improved	Unimproved	Dead	Too Recent to Evaluate
Atrial septal defect (secundum)	45	46	26	9	0	7	3
Atrial septal defect (primum)	1	1	0	1	0	0	0
Hiatus atrioventricularis communis	3	3	0	0	1	2	0
Atrial septal defect and pulmonary stenosis	9	10	1	4	0	2	2
Total	58	60	27	14	1	11	5

TABLE 3.—*Results of Surgery in All Patients with Pulmonary Stenosis*

Disease	Patients, No.	Operations, No.	Total Cure	Improved	Unimproved	Dead	Too Recent to Evaluate
Valvular stenosis	25	25	15	7	0	0	3
Infundibular stenosis	2	2	1	1	0	0	0
Trilogy	9	10	1	4	0	2	2
Tetralogy, infundibular	10	10	0	7	0	3	0
Tetralogy, valvular	7	7	0	7	0	0	0
Total	53	54	17	26	0	5	5

could be opened, and, although a normal sinus rhythm was finally established, the patient died six hours later. One patient on whom both pulmonary valvuloplasty and repair of atrial septal defect were done is now cured. The remaining four patients have all been greatly improved from the clinical viewpoint. Three have been catheterized postoperatively, one with complete obliteration of the preoperative right ventricle–pulmonary artery systolic pressure gradient. The remaining two had marked hypertrophy of the right ventricle and residual gradients of 33 and 31 mm. Hg.

The indications for resection of infundibular stenosis in the patient with a tetralogy of Fallot are less clear. However, in general, our experience has been that these patients are very significantly improved, and the improvement is certainly of an order equal to the anastomotic procedures of Blalock or Potts. However, the extent of the removal of the infundibular stenosis must be carefully judged, for, should the stenosed area be completely removed in the face of a large ventricular septal defect, dire consequences may result. With such

TABLE 4.—*Total Deaths in 111 Patients by Disease and Cause*

Disease	Hemorrhage	Postoperative Thrombosis	Cardiac Failure		Other
Atrial septal defect	1	4	2		
Hiatus atrioventricularis communis			2		
Trilogy	1			1	(Sudden death at 12 hr., cause undetermined)
Ventricular septal defect			4		
Tetralogy	1			2	(Transfusion anuria, death at 3 wk. of sepsis) (Postoperative aneurysm of right ventricle, died at attempted repair 3 mo. later)
Anomalous pulmonary veins	1				
Total	4	4	8	3	

complete relief of obstruction to outflow from the right ventricle, a large left-to-right shunt may be suddenly established, with resulting dilatation of the heart with myocardial failure or aneurysmal dilatation of the thin-walled infundibular chamber.[3] Thus, it is not considered wise to remove completely the stenosed area in these patients. Our results have in general been good with this procedure. The pulmonary artery pressure rises, and the pulmonary blood flow increases greatly. However, the right ventricular systolic pressure usually remains of the same order of magnitude as preoperatively. In general, then, removal of infundibular stenosis in the presence of a ventricular septal defect calls for partial excision. Total excision may result in great cardiac enlargement and congestive failure.

In 17 patients an open direct operative approach has been aimed at the pulmonary obstruction. Seven have had valvular obstruction and 10 infundibular. There have been no deaths in the first group and three in the second group. All patients have had marked improvement from the clinical standpoint, the cyanosis has disappeared or lessened to a striking degree, and their tolerance of exercise has been dramatically increased.

The patient with an atrial septal defect of the secundum type represents, in general, an ideal candidate for closure by direct vision during hypothermia. Although our criteria for operative intervention are still in the formative stage and will doubtless be altered as experience dictates, at the present time closure of a secundum type defect is being advised in all patients with a pulmonary index 2.5 times or more the systemic and in whom the total pulmonary vascular resistance is less than 350 dynes/seconds/cm.[5] Once again, there is no set figure for flow or resistance that can be considered as a rigid limit, and the over-all clinical evaluation of the patient remains of the utmost importance. However, it has been our experience that, in those patients with a pulmonary vascular resistance above 350 dynes, the risk of the operation has been great and the postoperative course has been complicated. Certainly, whenever possible, closure of the atrial septal defect should be urged and performed on children between the ages of 3 and 12 years, since, during this age period, the risk of the operation is least and the gain to be expected from operation is greatest. At the present time, 45 patients with atrial septal defects of the secundum type have been operated on, with 38 survivors. At surgery it was found that four of this number had, in addition, anomalous pulmonary venous connections to the right auricle or superior vena cava. In the last three of these patients, the defect was closed in such a way that drainage from these veins was into the left atrium at the completion of the closure.

Twenty-seven patients have been recatheterized following surgery, and it is considered that 26 have been cured, since complete obliteration of the previously existing shunt was demonstrated. In two patients there was a small residual left-to-right shunt. The first was the initial patient encountered with one pulmonary vein from the right lung entering the right atrium, and no attempt was made to alter the site of drainage when the atrial defect was closed. The remaining patient had a huge defect (7 cm. by 5 cm.), and, at that time, closure was being effected by interrupted sutures. It is assumed that a small opening between sutures has persisted. Clinically, however, this patient has experienced a very dramatic improvement. Currently, a continuous suture is used. This experience leads us to the conclusion that closure of atrial septal defect of the secundum type by this method is reasonably safe and is a curative procedure.

Our experience with a direct vision transaortic approach to aortic valvular stenosis is still limited. We believe that, even under conditions of direct vision, in the older age group when the aortic valve is markedly calcified and deformed, operative intervention offers relatively little except in rare instances. Ideal candidates are the young patients with congenital aortic valvular or subaortic stenosis or the patients below 40 years of age with acquired rheumatic disease but without evidence of calcification of the valve. To date, the

open operation has been performed in three patients, one with rheumatic stenosis of the aortic valve and the remaining two with congenital aortic disease, valvular in one and subaortic in the other. There have been no deaths, and the operative and postoperative course has been uneventful. It is felt that the accuracy of the visual procedure will help prevent the production of aortic regurgitation, a lethal complication of the blind technique.

Cause of Deaths

An analysis of the cause of death in this series is illuminating and in a sense encouraging, since it seems likely that current techniques will afford considerable safeguard against at least two of the major causative factors. Table 4 records the deaths by cause. The cause of death was most frequently cardiac in nature—in four patients irreversible arrhythmia and in four others failure of the heart to tolerate the combined insult of a major operation and the attending manipulation, the hypoxia of circulatory arrest, and at times the additional trauma of resuscitation. These particular complications will be largely avoided by using our current temperature levels, since almost all fatal arrhythmias occurred below 28 C (82.4 F) or in connection with prolonged occlusion times.

The probable tolerance of the heart for surgery can largely be predicted. Therefore, the selection of patients for operation can greatly modify the over-all outcome in this regard. However, except in the face of circumstances that place the patient in a category that must be accepted as inoperable (for example, marked elevation of the total pulmonary vascular resistance or intractable cardiac failure), we will continue to offer operation to the desperately ill, even though it is realized by all concerned that there is a very significant operative risk involved. The risk without surgery in these patients, however, must be considered to be 100%.

The other major fatal complication was a disturbance in the clotting mechanism, either tendency to bleed excessively during surgery or intravascular thrombosis occurring in the postoperative period. These are both, in all probability, risks inherent to any operation during hypothermia. As regards the bleeding tendency, operation, hypothermia, and multiple blood transfusions are the ingredients, and each may play specific roles. A bleeding tendency (coagulation defect) in cyanotic cardiac patients undergoing surgery at normal temperature has been recognized.[4] Experimental alteration in the concentration of the formed elements of the blood and in the clotting mechanism during hypothermia has been widely noted.[5] The influence of multiple transfusions of stored blood on the bleeding diathesis is also well documented. Again however, current practice offers much hope that the incidence of this complication can be reduced. No patient whose body temperature was above 28.5 C (83.3 F) manifested this tendency to bleed excessively (coagulation defect). We believe the limitation of the degree of hypothermia to the 29 to 32 C (84.2 to 89.6 F) range, together with the use of fresh blood rather than stored bank blood, will essentially eliminate this problem.

Thrombosis

As regards thrombosis, the nature of the malformation itself may play a definite role, since it has occurred only in patients with atrial septal defects. In two patients with large shunts and massive enlargement of the pulmonary vascular bed, pulmonary venous thrombosis occurred, once on the fourth day and once on the eighth. We believe that the sudden reduction in the rate of pulmonary blood flow that occurs at the time of closure of the defect in these patients may set the stage for this complication. Currently, therefore, we are heparinizing postoperatively all adults with this disease. The other two episodes, one thrombosis of a cerebral artery on the second postoperative day and the other thrombosis of both jugular veins on the night of surgery, remain unexplained, although avoidance of any constriction in the neck during anesthesia is currently being emphasized. In general, it is believed that, by staying within our current limitations of the technique, one may expect a marked reduction in the occurrence of both cardiac arrhythmias and the disturbances of clotting mechanism.

Summary

In 111 patients who underwent open heart, dry field visual surgery during hypothermia, a large variety of congenital defects was repaired. We have come to believe that the optimal temperature level is the range of 29 to 32 C (84.2 to 89.6 F) and that avoidance of lower temperatures will largely eliminate two of the major complications, namely, cardiac arrhythmias and disturbances in the clotting mechanism. At this temperature, we believe that six minutes of circulatory occlusion is safe and eight should not be exceeded. Within these limitations, pulmonary valvular and infundibular stenosis, atrial septal defect, and aortic stenosis can be readily repaired at low risk. The eminently satisfactory results of open operation in these diseases make an eloquent plea for a broader adoption of open heart techniques.

Addendum

Since the time of this study, 19 additional patients have undergone operation without loss of life. Thus, at a temperature range of 30 to 32 C (86 to 89.6 F), there has been only one death in the last 30 patients undergoing open operation for pulmonary valvular stenosis, aortic valvular stenosis, or atrial septal defect. As currently employed, open operation during hypothermia for these conditions should present a risk of less than 5%.

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References

1. Swan, H.; Zeavin, I.; Holmes, J. H., and Montgomery, V.: Cessation of Circulation in General Hypothermia: I. Physiologic Changes and Their Control, Ann. Surg. **138**: 360-376 (Sept.) 1953. Swan, H.; Zeavin, I.; Blount, S. G., Jr., and Virtue, R. W.: Surgery by Direct Vision in Open Heart During Hypothermia, J. A. M. A. **153**: 1081-1085 (Nov. 21) 1953. Swan, H.; Virtue, R. W.; Blount, S. G., Jr., and Kircher, L. T., Jr.: Hypothermia in Surgery: Analysis of 100 Clinical Cases, Ann. Surg. **142**: 382-400 (Sept.) 1955.

2. Swan, H., and Zeavin, I.: Cessation of Circulation in General Hypothermia: III. Technics of Intracardiac Surgery Under Direct Vision, Ann. Surg. **139**: 385-396 (April) 1954. Swan, H., and Kortz, A. B.: Direct Vision Transaortic Approach to Aortic Valve During Hypothermia: Experimental Observations and Report of Successful Clinical Case, ibid., to be published.

3. McCord, M. D., and Blount, S. G., Jr.: Complications Following Infundibular Resection in Fallot's Tetralogy, Circulation **11**: 754-760 (May) 1955.

4. Bahnson, H. T., and Ziegler, R. F.: Consideration of Causes of Death Following Operation for Congenital Heart Diseases of Cyanotic Type, Surg. Gynec. & Obst. **90**: 60-76 (Jan.) 1950.

5. Crosby, C. H., and Overton, R. C., in reports read before Hypothermia Conference, Washington, D. C., Oct. 28, 1955. Helmsworth, J. A.; Stiles, W. J., and W. Elstun: Changes in Blood Cellular Elements in Dogs During Hypothermia, Surgery **38**: 843-846 (Nov.) 1955.