Hypothermia in Surgery

Analysis of 100 Clinical Cases*

HENRY SWAN, M.D., ROBERT W. VIRTUE, M.D., S. GILBERT BLOUNT, JR., M. D., AND LORENCE T. KIRCHER, JR., M.D.

Denver, Colorado

From the Departments of Surgery and Medicine, University of Colorado School of Medicine, Denver, Colorado

I. INTRODUCTION

TWO YEARS AGO, at the 1953 meeting of this society,[2] our group presented some physiologic observations on experimentally induced general hypothermia in dogs, and a few biochemcial observations on three clinical patients. Since that time at the University of Colorado, we have continued our experimental and clinical interest in the surgical application of hypothermia, and have slowly explored some of the potentials of this technic. Many other laboratories both in this country and abroad have also investigated various aspects of the problem. For a reasonably complete review of the rapidly growing literature in this regard, reference is made to a recent monograph by one of us (R. W. V.).[5] The present report is concerned with an analysis of our experience with the first 100 patients whom we have subjected to this deliberate physiologic adventure, with particular reference to its dangers and limitations, as well as to its potential and actual usefulness in the attainment of operative objectives.

As experimental interest has become widespread, seemingly contradictory physiologic data have been presented and, therefore, terminology is important in this regard. We define general hypothermia as being the physical state of an homothermic individual in whom the body temperature is below the normal range for that individual. For man, therefore, with a normal range of 36° C. to 37.5° C. rectal temperature, any persistent temperature below 36° we would accept as representing a state of hypothermia. Obviously, the range of hypothermia is great.

It would be agreeable to think that uniform and consistent physiologic states accompany specific decrements in temperature, and indeed, both in our thinking and in that of other workers, this tacit assumption has been made. However, as our experience, both clinical and experimental, has increased, we have come to realize that the physiologic variations from normal which accompany acute hypothermia are subject to influence by a multitude of variables other than the body temperature. Respiratory rate and the type of induced respiratory cycle, for example, have significant effect upon electrolyte and water distribution, and upon cardiac irritability and myocardial competence. Anesthetic agents and depth of anesthesia appear to affect myocardial tolerance to cold, oxygen consumption, the metabolic pattern of response to hypothermia, and the sympathetic–parasympathetic balance as it affects cardiac function. In addition, preconditioning to environmental cold is apparently of great importance in such fundamental matters as myocardial metabolism and irritability, general glucose metabolism, and nerve conduction, to mention only a few. Clinically, the pre-existing state of the

* Presented before the American Surgical Association, Philadelphia, Pa., April 27, 1955.

This study aided in part by grant-in-aid from the United States Public Health Service (H-1559 (C)), and in part by grant-in-aid from The American Heart Association.

heart, whether normal, hypertrophied, or "strained," is of great importance in that organ's response to hypothermia, or hypothermia plus hypoxia, and various types of diseased hearts tolerate such insults with widely varying lethal threshholds. Finally, age and pre-existing chronic hypoxia are other obvious critical parameters.

Under these conditions it has become increasingly clear that general hypothermia is complex, that a wide variety of physiologic states may exist at lowered body temperatures just as they may at normal or increased temperatures, depending on other variables. A dog at 25° C., anesthetized in winter with ether and artificially respired to a state of alkalosis is an entirely different animal than a summer dog under Pentothal at the same temperature in acidosis. Physiologic conflict, therefore, is to be expected until the parameters can be defined, evaluated, and eventually understood.

Since hypothermia appears to us to have serious inherent risks, and if pursued far enough inevitably results in death, the major aim of experimental effort should be directed toward increasing our understanding of the relationship between the variables and the cardiac, circulatory, cerebral, hematologic and metabolic tolerance to hypothermia, so that deliberate control of such variables may be employed to increase the safety of the technic, and thus expand its clinical utility. We believe that a small beginning in this direction has been achieved. The present report describes our current thinking and practices in the effort to influence risk by the control of variables; how much remains to be elucidated we are sure will be painfully evident.

II. INDICATIONS

The prime indication for the use of hypothermia in this series has been the desire to perform an operation in a bloodless field during temporary occlusion of the blood supply to or through the organ. Hypothermia was used as an agent to prolong the time-tolerance to ischemia, and thus allow safe operating periods. That a low body temperature achieves this aim by its reduction in tissue metabolic rates has been clearly shown by many investigators, and needs no elaboration here. All of the open intracardiac procedures, and about half of the non-cardiac operations (cerebral and aortic), were performed during hypothermia for this reason.

The open intracardiac technic for heart surgery has been emphasized in our studies as being fundamentally sound. It is important in all surgery that the operator see clearly what he is doing; surgery of the heart is no exception. "Finger vision" is capable of a limited success, and bears the same relationship to real vision in surgery that it does in life—one can read braille with moderate facility, but the chromatic values of the Mona Lisa escape one, and to shoot the winging mallard or to fly an airplane is impossible. That the blind but educated finger is capable of accomplishing much within the heart is to be freely admitted, and much admired; that it should be considered as the best method in the long run is absurd. Risk is the deciding factor. The open procedures must not only accomplish what the closed ones cannot but must be capable of execution at mortality and morbidity risks at least equivalent to those of indirect methods.

Our exploration of hypothermia has been undertaken largely in an effort to achieve some progress toward this goal, and selection of patients for open heart procedures has been largely limited to congenital diseases for which pre-existing operative technics had proven to yield poor results (pulmonary valvular stenosis),[3] or those in which standardized methods had not been developed (septal defects). That open technics of a high degree of effectiveness and of a safety comparable to or superior to closed ones are possible by means of hypothermia we believe has been demonstrated.

A second indication has been to attempt to improve the operative risk in patients with

congenital or acquired heart disease by achieving either better oxygenation of the patient (as in cyanotic cardiopathies), or slowing of the heart rate in severe tachycardia (as in "atypical" *patent ductus*). In some instances we have been most pleased with the apparent effectiveness of hypothermia for this purpose. A deeply cyanotic child with a pulse rate of 150 to 175 may achieve an almost normal color with a pulse rate of 100 at 30° C. His tolerance to the cardiovascular stress of operation appears to be obviously improved. On the other hand, adult patients with valvular lesions affecting the left side of the heart appear to tolerate hypothermia less well; they seem, particularly if there is left ventricular hypertrophy or strain, to be unduly susceptible to ventricular fibrillation. Our experience with this group is very small as yet, and we have only very preliminary impressions. However, it may develop that for some cardiac patients hypothermia improves the operative risk, for others it does not. Most of the closed cardiac procedures in this series were cooled for this purpose, though some were cooled in order to be prepared to establish temporary circulatory arrest if it seemed desirable, a need which in these instances did not develop.

A third indication was to explore hypothermia as a method of achieving hypotensive anesthesia in an effort to diminish operative blood loss, without actual circulatory occlusion. A few patients with large visceral neoplasms were operated for this reason. However, the results were disappointing in that although operative hemorrhage was diminished, later ooze from unidentified vessels resulted in a total blood loss essentially undiminished.

The matter of arterial blood pressure during hypothermia is of great interest. Experimentally, of course, one finds a progressive fall in mean pressure with a narrowing of pulse pressure as the animal is cooled to 25° C. Clinically, a common experience has been the complete disappearance of the blood pressure as obtained by sphygmomanometer as the body temperature falls. Typically a blood pressure obtained at 37° C. as 120/80, becomes 100/75 at 33° C., and 90/? at 30° C. Then, abruptly, it cannot be heard. However, as determined by direct arterial recording, even when the temperature has fallen to 26° C., the arterial pressure is still about 80/70. It can occasionally be guessed at by palpation, but it is totally lost to auscultation, even though the mean pressure is above 70. This phenomenon offers grave difficulties in the proper evaluation of the circulatory status of the patient. In addition, as will be elaborated below, it is quite possible to close a wound which appears dry, only to have serious postoperative hemorrhage when the patient is re-warmed and the blood pressure again rises. For hypotensive anesthesia, effective control of blood pressure and particularly the ability to rapidly restore normal levels before wound closure is essential. We no longer use this indication.

The fourth and final indication used in this series was also an anesthetic one. Since hypothermia of sufficient degree is itself a potent anesthetic agent, it appeared to us possible that it might be less toxic to the individual than pharmacological agents, particularly under certain conditions. In patients who were facing very prolonged and extensive procedures or in whom there was hepato-cellular damage, cold might be less damaging than drugs. Examples in this category were patients undergoing portacaval shunts for cirrhosis. In some of these patients, the ounce of ether used during induction and cooling was the total amount used during the six to eight hour procedure. The agent was of course entirely exhaled during the early part of the operation, and from a pharmacological point of view, they were considered to have had a very brief anesthesia. The postoperative course of many of these patients was so free of any apparent effects of their anesthesia that we are continuing to explore the merits of this indication for hypothermia.

III. SAFETY MEASURES

1. *Respiratory Control.* On the basis of early experimental experience, we became convinced that hypoxia and hypercapnia were undesirable, and in addition, that deliberately induced hypocapnia (respiratory alkalosis) played a valuable role in reducing the incidence of ventricular fibrillation.[2] We subsequently have presented evidence to show that ventilation appears to affect the myocardial metabolism of potassium,[1] namely, that during hypoventilation, the myocardium is storing potassium, whereas during hyperventilation, the myocardium is in potassium balance. Whether or not the potassium ion is critical in this situation, the effect of adequate ventilation is so convincing to us that we subject all of our patients to deliberate hyperventilation throughout the cooling, operative, and warming period. If circulatory occlusion is planned, a pH of right auricle blood (determined at the patient's body temperature) is obtained, and a pH greater than 7.5 is considered desirable before circulatory arrest is established. This is one reason why we consider hypothermic anesthesia a two man job; one must constantly devote full and undivided attention to the maintenance of successful ventilation; to his associate go all the other multiple activities associated with modern anesthesia.

2. *Sympathetic-Parasympathetic Balance.* On the basis of laboratory evidence, we have recently[1] suggested that at least one of the factors underlying the myocardial irritability of hypothermia might be a disturbance in the balance between the sympathetic and parasympathetic impulses affecting the heart. The observations suggested that cold depressed vagus function to a greater extent than it did sympathetic function. Experimentally, it was found that acetylcholine, neostigmine (anti-cholinesterase) and stimulation of the cut vagus nerve all served to inhibit ventricular fibrillation during hypothermia. Recently some corroboration of this concept has emerged in the renewed interest in this country of a method first suggested in France, namely, procaine block of the area of the sino-auricular node. Pharmacologic or operative sympathetic blockade has also been suggested. We have recently used neostigmine in doses of 0.6 to 1.6 ml. of a 1–4000 solution injected into the root of the clamped aorta after inflow occlusion (a method we have designated as coronary perfusion) routinely as the first step in all open heart procedures. It is our impression that the incidence of ventricular fibrillation has been diminished by this procedure (see below).

If doses larger than this amount are used, the rate of the heart may be materially lowered. Indeed, with larger doses, on two occasions the heart failed to resume a strong beat for some time, and resuscitative measures were required. On one occasion we delayed too long in restoring an effective cardiac beat, asphyxia occurred, and eventually fibrillation supervened with a fatal outcome. Since neostigmine exerts a potassium-like effect upon the myocardium, calcium is an antagonist. We now do not hesitate to use this ion in small doses at once if prostigmine appears to have unduly depressed the heart beat following restoration of circulation. In the large human heart of congenital disease, however, the doses mentioned appear to be helpful in reducing irritability, although usually the heart rate is not materially lowered.

Similar reasoning regarding parasympathetic paralysis has led us to refrain from using atropine as a preoperative agent. It might be wise to employ some form of sympathetic blockade in conjunction with neostigmine.

3. *Coronary Air Embolism.* The avoidance of coronary air embolism has been one of the serious problems of open heart technics, and in our hands has been a major limiting factor in the application of hypothermia to intracardiac lesions. The moment of prime danger is that associated with the restoration of the integrity of the heart cavities. While they are open to the air, neither fluid nor

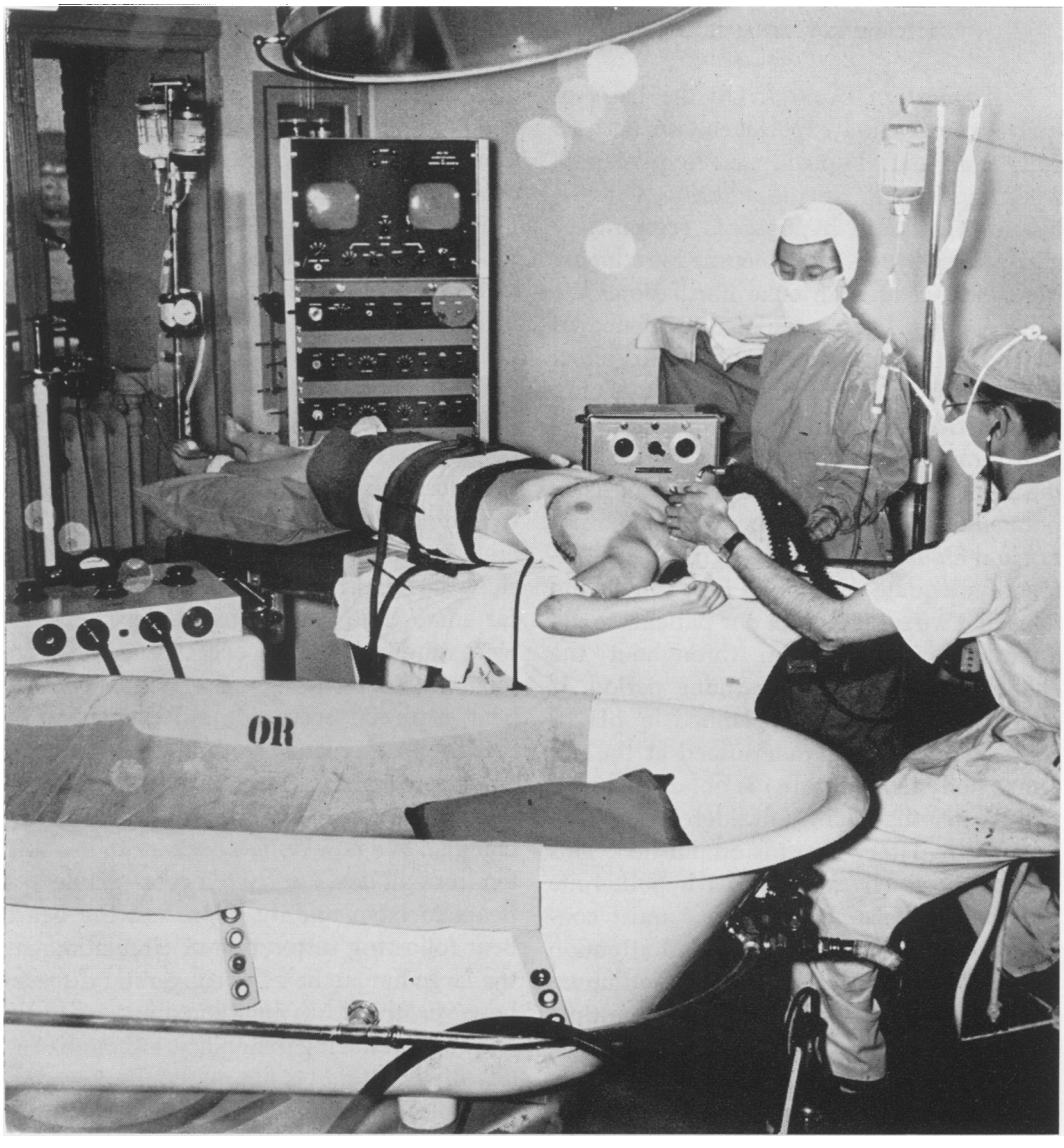

FIG. 1. The operating room equipment includes the tub, a rectal thermometer, a diathermy unit, a multi-channel electronic recording device, the defibrillator, a direct writing EEG, and a standard anesthesia machine. At least two intravenous plastic cannulae are in place. The patient is in the operating position immediately after wound closure.

gas is moved by muscle contraction. Immediately following closure of the cardiotomy, however, the first beat will be effective, and if any air is trapped in the left side of the heart, it will almost surely find its way into the coronaries. The crux, then, is to trap no air. To achieve this we devised the following technic, which has uniformly been used in all patients.[4] First, the incision in the chest is always a transverse sternal splitting incision, usually in the fourth interspace on both sides. This allows for a free exposure of all chambers of the heart, excellent for cardiac resuscitation, and also (particularly important in the present regard) for permitting a right heart cardiotomy or pulmonary artery

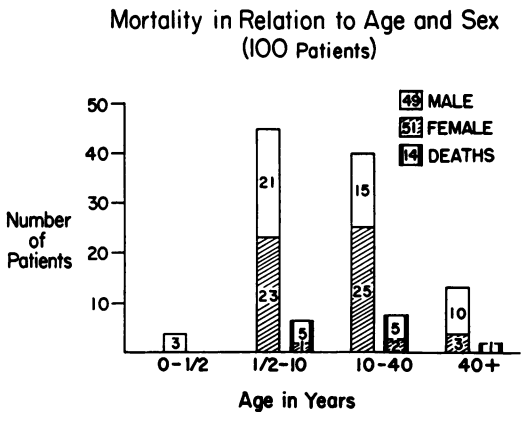

FIG. 2.

incision *to be positioned at the uppermost portion of the heart.* Lateral or vertical tilting of the table is used to assure achievement of the objective. Second, after inflow occlusion has been induced and the neostigmine perfusion of the myocardium completed but before the cardiotomy is opened, a non-crushing clamp is placed across the base of the aorta and pulmonary artery, both to arrest outflow and to occlude the ostia of the coronary arteries. This assures that no flow into the coronaries will occur until the moment the operator elects to remove this clamp. The heart is opened, residual blood sucked out, and the desired operation performed. If a septal defect is present, the heart is filled with Ringer's solution before the last suture is tightened. This maneuver removes the air from the left chambers. With the edges of the auricular incision held up, the heart and chest cavity are again flooded with Ringer's solution, and when all air seems to have been expelled, a non-crush-clamp or ventricular stay sutures close the cardiotomy. Inflow occlusion and outflow occlusion are now instantaneously released, and blood flow is allowed to resume.

This routine has been effective in our hands to the extent that coronary air embolism has occurred only twice in this series. Careful observation of the visible coronaries is always made following return of circulation to identify the presence of bubbles. On the two occasions when it did occur, the complication was immediately recognized, and the following maneuvers employed successfully. The heart was manually compressed vigorously three or four times to expel any further air into the aorta. A non-crushing clamp was applied to ascending aorta. Manual compression was now again begun, attempting to create a coronary hypertension sufficiently strong to push the air bubbles onto the venous side of the circulation. If the visible bubbles did not progress at once, they were gently massaged along with the tip of the finger. After all air was out of the arterial system and the heart muscle appeared pink, the clamp on the aorta was removed. This entire maneuver did not take more than two minutes. In one patient, the air was eliminated rapidly and the heart appeared to suffer no ill effect; in the other, ventricular fibrillation occurred just as the air was expelled, but the rhythm was immediately restored without difficulty by electric shock.

The importance of the special location of the cardiotomy in relation to the cardiac chambers in this technic is obvious. Unless it is uppermost, the air will not escape, and will thus be trapped. We have not yet been able to devise an approach and a position for the patient which will place a left cardiotomy in an equivalent fashion.

We have recognized no postoperative manifestations which would suggest that air embolization of any other organ had occurred.

4. *Cardiac Resuscitation.* More will be said below concerning ventricular fibrillation during hypothermia in patients with hypertrophied or strained hearts, but here we thought it worthwhile merely to record our methods in combatting cardiac arrest.

Ventricular standstill was treated by manual cardiac compression. This alone has always been effective in restoring cardiac rhythm. Seven patients in this series under-

went cardiac standstill during some phase of the operation; all seven were resuscitated without use of pharmacological agents.

Ventricular fibrillation has been combatted as follows. Manual cardiac compression is initiated, and is continued until the myocardium is pink and of good tone. Electric defibrillation with metal electrodes delivering 170 volts and about 2.5 amperes for 0.1 or 0.05 seconds placed at the apex and over the base of the heart is next tried. Two or three shocks are given in fast succession. This maneuver alone has usually been successful. If it is not 3 to 5 ml. of K Cl solution (1 mEq./ml.) is injected by coronary perfusion. This has chemically defibrillated the heart on occasion. If not, electric shock is repeated after manual compression has dispelled myocardial cyanosis. If, after repeated failure with these methods, the heart becomes flabby with very fine fibrillations, adrenalin chloride, 1 ml. of 1:10,000 solution, has been injected into the left auricle. On one occasion this appeared instrumental in improving the tone of the muscle, coarsening the fibrillation, and thus setting the stage for subsequent successful electric defibrillation.

Meanwhile, every effort to warm the patient as rapidly as possible is instituted. Since resuscitation is being undertaken with the chest wound open and the patient draped, certain limitations on surface cooling technics are obviously imposed. In about the first third of this series, the patient was lying on a rubber mattress through which could be circulated warm water. In addition, warm saline solution in copious amounts was circulated through the pleural cavities. It was found, however, that this method was extremely inefficient, and warming occurred at rates of about 1° C. for each 30 to 45 minutes. One patient, who entered fibrillation at a rectal temperature of 24.5° C., could not be permanently converted until the temperature reached 28° C. two hours and 20 minutes later. Circulation, of course, was maintained during this period by manual compression. This patient is still alive and well.

Because of the inefficiency of this method, we recently have been using a standard diathermy unit with the coil wrapped around the pelvis.

This has resulted in much more rapid warming, at rates not materially different from those obtained by immersion in water at 45° C. The size of the patient appears to be pertinent in this regard, as one might expect. Great care must be taken to avoid superficial burns, however. The skin must be absolutely dry, the coil is very evenly spaced, and is separated from the body by a felt pad. Current is applied intermittently, two minutes on and one minute off. In spite of these precautions we have had a few minor skin burns, chiefly over the sacrum. Occasionally, for reasons not apparent, the diathermy has also proved inefficient.

In our opinion, the ability to warm the patient rapidly while manual cardiac compression is in progress is a critical facet of the application of hypothermia. The development of an adequate instrumentorium for this purpose is a great current need. In our hands at least, this problem is far from solved. It is possible that extra-corporeal technics would be of real advantage in this regard.

5. *Medications.* No preoperative drugs to affect cardiac action were used except that digitalis was given to patients in frank failure. Quinidine was not employed prophylactically. Glucose intravenously was run slowly throughout the cooling, operative and warming periods. Preoperative penicillin was routinely administered.

IV. TECHNIC OF HYPOTHERMIA

The preparation of patients for hypothermic anesthesia is carried out in much the same fashion as it would be for anesthesia at normal temperatures. The use of morphine, demerol, or barbiturates is routinely

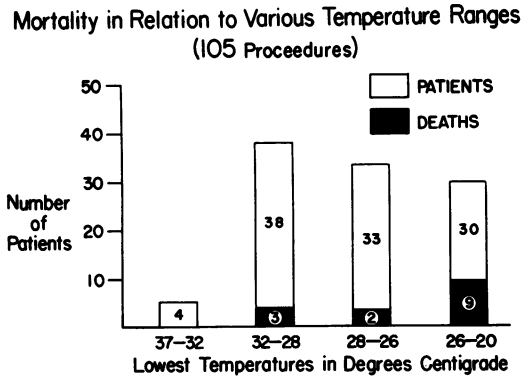

FIG. 3.

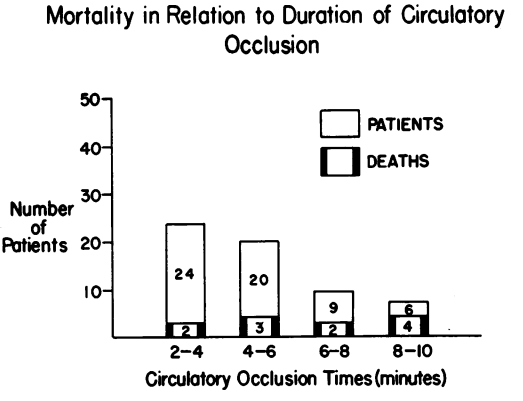

FIG. 4.

practiced. Scopolamine is preferred to atropine because smaller quantities of belladonna drug during premedication are desirable. The patient is brought to the operating room and anesthetized as he ordinarily would be for any surgical procedure. Ether has been the preferred anesthetic agent. Provision for intravenous fluids must be made quite adequate. This is done in the arm because such severe vasoconstriction frequently follows cooling a patient's limbs that blood will not flow through a long leg vein. Electrocardiograph leads are attached, being sure that no constriction of limbs is possible. Needle electrodes in the skin are more satisfactory than the use of electrode paste for the leads. A rectal thermometer with a four foot lead wire is inserted.

A surgeon is scrubbed, prepared to do an immediate thoracotomy, before cooling is begun. When a patient is in second plane, third stage anesthesia he is put into a tub of cold water. The head is kept out of the water and the hands may be taped to the sides of the tub to keep them above water. If any shivering ensues, curare is given. The anesthesia may be slightly deepened at this point. Relaxation is necessary because a patient who shivers will tend to maintain his temperature and be difficult to cool. When it is seen that the temperature has begun to drop, ice is added to the cold water. The anesthetic agent can be turned off at this point, and when the patient's temperature has dropped to approximately 31 degrees Centigrade, the ether can usually be washed out. Hyperventilation is carried on from the time the endotracheal tube is inserted until circulation is occluded during the operative procedure.

The patient is removed from the ice water before the desired operating temperature has been reached. It has been found that the lowering of temperature continues after the patient is removed from the ice water. The drop after removal is approximately two-thirds that observed during the time of immersion. For example: if a patient's temperature drops six degrees while he is immersed, it continues to drop about four degrees further after his removal. This figure of two-thirds varies considerably with individuals, and cannot be definitely relied upon. Cooling of an adult usually requires about 45 minutes. When the patient is removed from the tub, he is very thoroughly dried. His lower abdominal area is then wrapped closely with an inch of felt, which is taped in place. The felt is surrounded with one and one-half turns of a diathermy coil. The turns are kept at constant distance from each other by insulated separators. The area to be warmed by

TABLE I. *Operative Procedures During Hypothermia.*
(100 patients, 105 procedures)

	Patients	Deaths
I. Intra-cardiac Direct Vision with Circulatory Arrest	59	12
II. Closed Cardiac Procedures without Circulatory Arrest	21	7
III. Non-cardiac Procedures	20	3

diathermy is kept off the table so the patient will not rest his weight on the diathermy coils. This avoids burns from the combination of heat and pressure. If the patient's temperature should then tend to drop to a dangerously low level, the diathermy can be turned on to offset such a trend.

Blood is started when the incision is made, and the policy has been to replace blood as it is lost. It might well be remembered, however, that there is a diminution of circulating plasma volume during hypothermia, and that the giving of more blood because of this factor may be necessary.

TABLE II. *Temperatures at which Blood Pressure Was no Longer Obtainable by Auscultation.*

Temperature (C.)	Patients
37–35	36
35–33	17
33–31	14
31–29	10
29–20	8
Not taken	12
Never lost to auscultation	8

About half the patients show auricular fibrillation when they reach 29 degrees. This is not deemed serious unless the electrocardiogram also shows a current of injury. Approximately five minutes before occlusion of circulation, further curare is given intravenously to prevent contraction of the diaphragm at the time blood is again allowed to flow. A determination of blood pH is usually made shortly before occlusion, and it is desirable that the pH be at least as high as 7.5 to be sure that there is no excess of carbon dioxide in the blood. During the time of occlusion, the anesthetic machine is disconnected from the tracheal tube to be sure that no lung motion will interfere with the surgical procedure. The surgeon occludes inflow of circulation, allows a few seconds for the heart and lungs to empty partially, then occludes outflow circulation and injects neostigmine at the base of the aorta so that it will perfuse the coronary arteries. After an additional 15 seconds, the surgical manipulation is carried out.

TABLE III. *The Relationship of Body Weight to Rapidity of Warming.*
(degrees C per minute)

	0–50 Pounds	50–150 Pounds	Over 150 Pounds
Diathermy	.10	.052	.041
Water at 45° C	.09	.07	.04

At the end of occlusion, the patient is again ventilated with oxygen, and any accumulated carbon dioxide is, of course, eliminated. The patient may receive only oxygen until the end of the procedure. If further anesthetic agent is needed it usually consists of 50–50 nitrous oxide-oxygen.

It is desirable that the patient have an adequate blood flow and blood pressure before closure of the chest, so that there will be no unseen latent bleeding. Diathermy is therefore turned on intermittently as soon as the surgical manipulation of the heart has been completed. It is necessary that diathermy be used intermittently to avoid burns near the diathermy coils. This enables the patient to have an auscultable blood pressure before the chest is closed. When the surgical manipulation has been finished, the patient may or may not be immersed in a tub of warm water to warm him further. The usual temperature of waking is about 34 degrees Centigrade. The criterion for removal of the endotracheal tube is adequate spontaneous ventilation. The next hour or two is an extremely critical period because of the difficulty of knowing just how much blood replacement should be made. A few

cases of severe shock have ensued at this time. More recently blood volume studies have been made before operation so that blood volume studies after operation can give some information as to what the circulatory status may be. Even though blood volume may be adequate, the patient appears quite pale at this time, probably due to peripheral vasoconstriction.

V. CLINICAL EXPERIENCE

The gross tabulation of our over-all experience in open heart surgery is seen in Table VI. The patients selected for the various procedures were chosen roughly on the basis of the following criteria. For pulmonary valvular or isolated infundibular stenosis, the patients all had clinical evidence of tight stenosis, right cardiac hypertrophy, and either symptoms or a right ventricle pressure above 90 mm. Hg systolic. The operation performed was direct vision valvuloplasty or infundibular resection. In atrial septal defect, no patient was turned down, no matter how large the heart or how severe the symptoms, provided that catheterization data indicated a significant shunt of blood from left to right. We have not operated on patients with a right to left shunt except those with pulmonary valvular stenosis (Trilogy). The operation performed was direct vision suture closure of the septal defect *via* the right auricle. All of the patients with interventricular septal defect (save one who was explored with a different diagnosis) had large hearts, with large, proven shunts. Two were approached through the ventricle, two through the right auricle, and direct suture closure attempted.

TABLE IV. *Waking Temperatures.*

Temperature (C.)	Patients
30–32	10
32–34	21
34–36	23
36–38	19

In the multiple defect group, the patients with Tetralogy were believed to be in need of operation on the same basis that they would have been selected for a shunt-type of procedure. The operation performed was direct vision attack on the right outflow obstruction. Attempt to close the ventricular septal defect was not made. Patients with the Trilogy were selected who had marked pulmonary stenosis and limitation of exercise tolerance.

TABLE V. *Temperature of Extubation.*

Temperature (C.)	Patients
Below 30	2
30–32	17
32–34	41
34–36	31

TABLE VI. *Intra-Cardiac, Direct Vision Procedures with Circulatory Arrest.*

I. *Pure (Single) Defects*

Disease	Patients	Total Cure	Partial Cure	Died
Pulmonary Valvular Stenosis	12	11	1	0
Pulmonary Infundibular Stenosis	2	1	1	0
Auricular Septal Defect (Secundum)	22	19	2	1
Auricular Septal Defect (Primum)	3	–	1	2
Ventricular Septal Defect	5	–	1	4
	44	31	6	7

II. *Combined (Multiple) Defects*

Tetralogy of Fallot				
A. Valvular Stenosis	4	–	4	0
B. Infundibular Stenosis	6	–	4	2
Auricular Septal Defect with				
A. Pulmonary Stenosis (Trilogy)	4	1	1	2
B. Ventricular Septal Defect	1	–	–	1
	15	1	9	5

The closed cardiac procedures were performed during hypothermia either because of intense cyanosis, or because of very rapid heart rates with large hearts, or because it was thought possible that circulatory arrest might be needed.

The indications for selection of the noncardiac procedures have already been men-

TABLE VII. *Closed Cardiac Procedures.*

Disease	Patients	Improved or Cured	Unimproved	Died
Patent Ductus Arteriosus	4	4	–	0
Tricuspid Atresia	3	–	1	2
Tetralogy	2	2	–	0
Pulmonary Valvular Stenosis	2	1	1	0
Aortic Regurgitation	2	–	–	2
Aberrant Pulmonary Veins	2	1	–	1
Aorto-pulmonary Window	1	1	–	0
Aortic Stenosis	1	–	1	0
Auricular Septal Defect, Primum	1	–	1	0
Single Ventricle	1	–	–	1
Idiopathic Pulmonary Hypertension	1	–	–	1
Mitral Stenosis (re-operation)	1	–	1	0
	21	9	5	7

tioned. The patients with cirrhosis had pulmonary hypertension and hepato-cellular dysfunction. Those with aneurysm were to have resection of thoracic or abdominal lesions. The cerebral lesions were either aneurysms of the internal carotid or hemangioma. In these, temporary occlusion of all blood flow to the head was performed intermittently by means of tapes around the vertebral and carotid arteries. The procedure was extremely satisfactory. The patients with visceral cancer required massive extirpative procedures.

VI. DISCUSSION

A. *Complications.* Complications which have occurred in this group of patients are listed in Table IX. Of these, several are apparently specifically related to hypothermia, or at least to our technic of cooling and warming. For example, skin burns have occurred both when the warm water mattress was used, and following diathermy. It is presumed that in spite of our best precautions, when rapid on-the-table warming is desired this complication will occasionally ensue. The burns have been mostly of second degree and small in size, although on two occasions, hospital morbidity was increased because of them, and in one, the burn may have been the site of entry for a fatal staphylococcic septicemia.

Thrombophlebitis of mild degree in two patients, and thrombo-embolism in two others, does not appear to be an undue incidence considering the type of operations performed, including so many vascular and cardiac incisions. In one of the patients with fatal thrombosis, a 32-year-old lady three days following suture repair of her atrial septal defect, the lesion appeared to be either multiple embolism, or progressive thrombosis of the pulmonary arterial tree. Autopsy showed no intracardiac thrombosis over the suture lines in the right auricle or the auricular septum. It is possible, of course, that the lesion could have been embolism from some systemic vein. In the other patient, seven days following repair of a huge atrial septal defect, multiple emboli to the lungs occurred. Autopsy revealed a small thrombus on the left side of the atrial septal repair. However, the patient had in addition a ventricular septal defect, so reversed paradoxical embolism of the lungs was presumed to have occurred. These two deaths were listed as possibly related to the hypothermia, although the connection seems slight indeed.

No significant wound complications occurred (three minor stitch infections), and there was no delay in wound healing.

Gastro-intestinal dysfunction seemed to us to be more prominent following hypothermia than following thoracotomies in the warm patient. The bilateral nature of the incisions, the dissection of the mediastinum, and possible disturbance of vagus function may also be factors. In any event, gastric dilatation occurred in two or three patients, so that awareness of the possibility has led us to use the naso-gastric tube freely in these patients for two or three days following operation, and to be slow in advancing the oral intake.

Pulmonary complications appear to loom large in the table. However, in the entire series no pulmonary or thoracic complication (except hemothorax) was considered to have been important in the death of any

patient. Occasionally a collection of exudate or air required tapping. Atelectasis or splotchy consolidation occurred in 13, in spite of vigorous prophylactic measures instituted immediately after operation. In view of the fact that the operations involved slightly over 150 thoracotomies (because of the bilateral exposure in so many patients), it has been hard for us to interpret these data as indicating any definite influence of hypothermia on the incidence of pulmonary or thoracic postoperative complications.

TABLE IX. *Non-Fatal Complications.*

Burns During Warming	8	Pulmonary	24
Water Mattress	2	Fluid	8
Diathermy	6	Pneumothorax	3
		Atelectasis	8
Thrombophlebitis Other than at Site of Cutdown	2	Pneumonia	5
		Neurologic Sequelae	12
Wound Infection	3	Peripheral Neuropathy	12
Superficial Abscess	3	Central Nervous System	0
Delayed Wound Healing	0	Anuria	1
Ileus	18	Subcutaneous Fat Necrosis	1

TABLE VIII. *Non-Cardiac Procedures.*

Disease	Patients	Improved	Unimproved	Died
Cirrhosis of Liver	5	3	1	1
Aortic Aneurysm	5	5	–	0
Cerebral Vascular Lesion	5	4	–	1
Extensive Abdominal Carcinoma	3	1	2	0
Fibro-thorax with Scoliosis	1	–	–	1
Exploratory Thoracotomy	1	–	1	0
	20	13	4	3

Of real interest, and very disturbing, has been the occurrence in 12 patients of postoperative evidence of peripheral nerve dysfunction of varying degrees of severity. An asymmetrical pattern involving the extremities of both sensory and motor dysfunction has been observed. In some instances, the syndrome has appeared to fit a definite pattern, such as peroneal or lower brachial plexus palsy; in others, however, it has been bizarre. Tingling has been a very common manifestation. It has been our impression that at least some of these neuropathies were probably due to the prolonged pressure of the rubber straps encircling the extremities to hold the electrodes of the electrocardiograph, or to other pressure phenomena. We are currently using needle electrodes in the hope of avoiding this complication. It may be that the hypothermic nerve is prone to pressure injury; this possibility is being currently studied by our neurologic service. Fortunately, all of these patients have recovered complete or almost complete function during the first few postoperative weeks.

One instance of multiple subcutaneous fat necrosis and one prolonged episode of profound oliguria due to hypovolemic shock also occurred.

As regards morbidity, of 47 patients with cardiac operations performed at Colorado General Hospital, four had prolonged hospital stays because of mild heart failure or burns (32, 33, 33 and 75 days). The average postoperative hospitalization of the remaining 43 was 10.7 days.

B. *Deaths.* In the initial clinical trial of a new and complicated technic, even though every effort has been made to reduce hazard by means of many experiments in the laboratory, lessons remain to be learned through sad experience. Even in more proven fields, how often is our sense of inadequate understanding of the multiple variables! So has it been in our exploration of a new physiologic modality simultaneously with development of new surgical technics applied to various types of patients, including those in advanced stages of cardiac disability. That the failures may be most instructive, they must be carefully analyzed and their components defined. Our interpretation of these failures is the concern of this section of the report.

In Table X is presented the mortality for the series broken down roughly into etiologic categories. The deaths which clearly

TABLE X. *Deaths.*

I. Probably or possibly related to hypothermia		14
A. *Probably*		
1. Ventricular fibrillation unconverted	5	
2. Ventricular fibrillation converted, but followed by failure or hemorrhage	5	
3. Ventricular standstill converted, but followed by failure	1	
B. *Possibly*		
1. Thrombo-embolism	2	
2. Heart failure	1	
II. Unrelated to hypothermia		8
	Total—	22

appeared to have no relationship to the episode of hypothermia are withdrawn as being essentially uninstructive in our current study. Typical of this type of death were a five-week-old, intensely cyanotic child, who died ten days following exploration of his idiopathic pulmonary hypertension; an eight-year-old cirrhotic in liver failure, who died of liver failure 18 days following exploration; an 18-year-old boy with profound kypho-scoliosis and marginal pulmonary function, who died 28 days later of a tragic nursing accident in the care of his tracheotomy, which drowned the patient; and a 48-year-old man who died 23 days following ligation of a cerebral aneurysm of a complication of his original brain hemorrhage. Eleven of the deaths seemed clearly related to the episode of operation during hypothermia, and three possibly so.

From our earliest experimental efforts in the laboratory, we were convinced that within the temperature range of 20° to 30° C. in the dog, the myocardium itself was the most vulnerable organ, and responded altogether too frequently by the fatal arrhythmia, ventricular fibrillation. A standard preparation was an animal at 25° C. who had a thoracotomy and then 15 minutes of circulatory arrest. Surviving animals were entirely free of evidence of brain, liver, kidney, or intestinal injury; the deaths were cardiac. As mentioned above, clinical trial was not begun until we felt that reasonable control of this phenomenon had been experimentally achieved. However, the data in Table X clearly shows that in the human, as in the dog, disturbance of myocardial function still remains the major, in fact almost the only, cause of death when patients with diseased hearts are subjected to cardiac surgery during hypothermia. We are convinced, therefore, that the road to safer utilization of this method lies in the direction of better understanding and control of myocardial loads, myocardial metabolism, and myocardial responses to trauma. Our laboratory, as well as those of many others, must continue to seek this trail.

In the attempt to discover any evident relationships between certain obvious clinical variables and the deaths associated with hypothermia, the data were compiled as shown in Figures 2, 3 and 4.

The figures are not felt to have statistical significance, but some matters of interest appear to emerge.

The age of the patient appears to have little if any bearing on his tolerance to hypothermia. One frequently hears the statement that the young of a species tolerate cooling better than adults. This is based on experimental data derived from the use of very young or neonatal animals. We have not been impressed with any great safety factor in the younger individuals in this series. It may be true that the premature or neonatal term infant might tolerate a greater degree of hypothermia more safely than a 60-year-old, but from our point of view, as one looks at fatal myocardial irritability statistics, an infant becomes an adult as far as hypothermia is concerned at about six months or a year of age.

What does the reader think of the factor of sex as expressed in Figure 2? Although the patients as a whole mirror almost exactly the national population in this regard (51 females to 49 males), yet of the 14 deaths, only three were females. The types of operation performed were about evenly divided between the sexes.

The mortality rates, when related to the levels of the lowest temperature (Fig. 3) and to various durations of circulatory occlusion (Fig. 4), fall, we think, into an expected pattern, and probably simply reflect the selection of patients for the various groups. For the more complex operations, as, for example, inter-ventricular septal defect which we felt were likely to require the longest operating time, the patients were cooled to deeper levels in the hope that the protection against hypoxia of circulatory arrest would be greater. One might logically expect a higher risk in these patients. However, we feel that this data suggests that increasing the degree of hypothermia has not, as presently employed in our hands, increased the safety of longer occlusion times. Whether the difficulty of the procedure and the severity of the disease of the heart are critical components of this picture or not, the fact remains that temperatures lower than 26° C., and occlusion times longer than eight minutes, are associated with sharply rising risk rates.

The importance of cardiac arrhythmia in hypothermia for cardiac surgery is emphasized again, as we recall that the total number of such arrhythmias which occurred in this series was by no means limited to those who died. Analysis of the problem from this point of departure reveals the following:

Twenty-two patients in this series underwent some form of cardiac arrest, an incidence of one in five; nine of these patients are now alive.

Seven patients experienced cardiac standstill. Two of these occurred during induction or cooling, two after removal from the tub but before cardiac manipulation, and three after return of arrested circulation. The risk of standstill, therefore, seems to be fairly well spread throughout the cooling and operative periods. All of these seven patients were easily resuscitated by immediate thoracotomy (if needed) and manual cardiac compression; all but one are now alive, and all but one underwent their definitive operation and are improved or cured. The one death occurred 20 hours postoperatively, of heart failure. This type of cardiac arrest, therefore, can be managed successfully, and standstill occurring during the thoracotomy is not considered a contraindication to proceeding with the operation, provided that the beat of the heart returns to a strong efficient level. The importance of having one member of the surgical team scrubbed and in readiness throughout the induction and cooling periods is apparent.

Fifteen patients underwent ventricular fibrillation. Five occurred during the thoracotomy, three during the cardiac surgery, and seven immediately after release of the circulatory occlusion. The asphyxiated, manipulated, cold abnormal heart, therefore, is particularly prone to enter ventricular fibrillation at the time when attempt is being made to restore circulation. Of these patients, five resisted all efforts to restore a rhythmic heart beat, while ten were resuscitated, using manual compression, electric shock, neostigmine, and potassium chloride as appeared indicated. Two-thirds of the patients with this complication, therefore, were effectively resuscitated. However, the long term survivors number only three, while seven, who were successfully resuscitated, died during their postoperative course. Two of these were considered victims of their underlying unrelieved cardiac abnormality; four died of a complication of postoperative hemorrhage, while one died of heart failure. These last five patients, then, represent real therapeutic failures, and comprise the potentially preventable deaths in the series.

The four deaths resulting from postoperative hemorrhage are particularly distressing. They were due, we believe to three fundamental difficulties: (1) failure to secure good hemostasis at the time the chest was closed; (2) failure to be able to recognize shock in the post-hypothermic patient; and (3) delay in re-operation to control the hemorrhage.

It is our custom, when the heart action is satisfactory, to warm the patient with diathermy until the blood pressure is obtainable at a level of 90 mm. Hg systolic, or more, before the thoracotomy wound is closed. In this fashion, we have hoped, vessels which did not bleed during the hypotension of hypothermia but which would bleed with return to normotension would reveal themselves. This has been a satisfactory safeguard in most instances, and we think it a good principle to delay wound closure until significant hypotension has disappeared. However, in these patients with ventricular fibrillation and continuing irritability of the heart, we had the great urge to warm the patient as soon as possible, and thus improve the quality of the heart beat and reduce its irritability. The chests were closed rapidly, therefore, in order to place the patient in the tub of warm water. This course of action, we believe now, was probably ill-advised; it would have been better to have delayed wound closure indefinitely until the blood pressure reached a reasonable range, using the method of diathermy to achieve this end.

Even assuming the hemorrhage occurs, why could we not recognize it? We must confess that to date the clear-cut differentiation between heart failure and shock in the immediate post-hypothermic patient is one we cannot make. For a period of about four to eight hours following hypothermia, all patients appear pallid and slightly dusky, even if their pulse, blood pressure and respiratory exchange are quite normal. They are lethargic; they do not sweat. This, we think, is some form of aftermath of the cooling experience; it may even be peculiar to the surface technic of cooling. We have always been impressed with the cherry redness of the skin which is submerged in the ice water during cooling; we have occasionally noticed that the muscles will ooze red while the skin and subcutaneous tissues ooze blue during wound closure. All patients following hypothermia then have a most alarming appearance, even though they are doing quite well. The important point is that inspection, even including a search for venous distention, fails to yield reliable information on the state of the circulation.

In the post-hypothermic post-ventricular fibrillation patient whose blood pressure has persistently remained at subnormal levels, or perhaps has risen and then falls off again, and whose pulse has increased in rate until it is clearly above normal, something is amiss. Is it hypovolemic shock? Is it due to inadequate blood replacement during operation? We attempt in all instances to measure blood loss by gravimetric means during the procedure, and apply an additive correction factor of 40 per cent for blood replacement which has worked well in presumably comparable thoracic procedures in warm patients in our clinic. This pragmatic method has resulted in low postoperative blood volume determinations in the cooled patients, and we have felt that in the desire to avoid straining the heart by over-enthusiastic blood replacement, we have often erred on the side of inadequacy in our volume of transfusion. Is it due to continuing postoperative hemorrhage? One might think that the answer would be clear from observation of drainage from the large bilateral chest tubes which are always placed in the posterior axillary line. However, in two of the four instances, the blood apparently clotted sufficiently rapidly to fail to emerge through the tubes in a volume adequate to suggest the true nature of events. The bleeding decreased in amount as the blood pressure fell, and the patient remained in a state of hypovolemic shock for an hour or two, or even longer, before real effort at blood replacement was undertaken. In two of these patients postoperative cardiac arrest occurred, the chest was entered, and we were amazed and mortified to find large amounts of clotted blood in the pleural spaces, quite adequate to explain the disaster; in the other two, blood replacement was vigorous but continued too long before re-exploration in

the hope that clotting and cessation of the bleeding would occur.

The opposite mistake is equally possible. In the face of a rising pulse, falling blood pressure, and in the absence of visible venous distention, the assumption was made in a two-year-old child, four hours after operation that blood replacement had been inadequate. This boy promptly died after 50 ml. of blood was pumped in, and immediate inspection of the heart revealed it to be a flabby, distended sac, *i.e.*, acute failure with dilatation. This was a doubly bitter defeat since the inter-ventricular defect was subsequently found to have been completely closed.

From this experience, we have decided that by and large, blood replacement should equal loss in patients with congenital heart lesions involving shunts productive of expanded preoperative blood volume; that the chest incision should not be closed until the blood pressure has achieved reasonable levels whether or not the heart has fibrillated; and that re-exploration should be done promptly if excessive postoperative loss is recognized, rather than attempt continued transfusion in the hope that intra-vascular clotting will solve the problem. Had this program been followed, we believe that these four hemorrhagic deaths would have been prevented; we intend to adopt it from here on.

We do not know whether the bleeding in these patients was due to an aberration in clotting mechanism caused by cold. Studies of the blood failed to reveal any abnormality, including heparinemia or fibrinolysin. Although a hemorrhagic state has been mentioned as a possible sequella to hypothermia, we have been unable to document this in the few patients we have studied. However, we have not explored this as diligently as we should.

As this clinical series was in progress, laboratory effort was constantly directed toward further understanding of methods to lower the incidence of ventricular fibrillation. The work on the agent neostigmine reached a point in early 1954, where it seemed reasonable to give it clinical trial. Our experience with this agent in open heart surgery may be summarized as follows: In a group of 30 patients who did not receive prophylactic coronary perfusion of neostigmine, nine had ventricular fibrillation; of 29 patients who did have it, three fibrillated. This comparison, however, is not entirely valid, since in a few instances ventricular fibrillation occurred before the stage of circulatory occlusion was reached. The 29, therefore, are a select group in the sense that they had undergone cooling and a duration of operation up to the point of the definitive stage of the procedure without fibrillating; several of those falling in the group of 30 first mentioned were not so fortunate; they fibrillated early in their course, and thus never had a chance to have "prophylactic" coronary perfusion.

Our clinical impression, however, is that coronary perfusion of neostigmine probably reduces the hazard of post-occlusion fibrillation, and we intend to continue to evaluate its value.

The problem of ventricular fibrillation has been particularly stressed since, in our opinion, control of this complication would materially lower the risk of cardiac surgery under hypothermia. We think it important to emphasize strongly that *the presence of a diseased heart appears to be a critical ingredient in the incidence of this complication.* In the group of 20 patients who had presumably normal hearts and in whom hypothermia was induced for non-cardiac procedures, there was not a single episode of ventricular fibrillation, and no patient died of causes related to hypothermia. A cardiac operation on a diseased, cold heart apparently is the combination which produces this phenomenon. In the patient with a normal heart, hypothermia, conducted as described herein, appears to carry a very low risk.

C. *Evaluation.* It appears to us at the present time that hypothermia offers a safe

method of achieving certain distinct benefits in the solution of a variety of surgical problems.

First, as a technic for achieving direct vision intracardiac operations, within certain limitations, it is highly effective and quite safe. These limitations at the present time are: (1) congenital lesions which can be approached from the right side of the heart, and (2) which can be repaired in less than eight minutes. These operations can and should be done at a level of hypothermia not to exceed 26° C. as the lowest body (rectal) temperature. As examples of our experience with patients in this category, reference is made again to Table VI.

A word of explanation in regard to this chart is in order here. Since the volume of patients seen in our clinic is not large compared to many other centers, we have felt it important to evaluate our postoperative results by objective studies as completely as possible. All the cardiac patients in this entire series who were subjected to open heart procedures have had cardiac catheterization both before and after operation. In Table VI, therefore, the column "Total Cure" means that the cardiovascular system on the basis of objective evidence has returned to a status that would fall within the generally accepted limits of normal; the column "Partial Cure" means that the status is improved over the preoperative situation but the result has not achieved a status which might be described as normal. Of course, it goes without saying that the objective of open heart surgery in congenital lesions is cure. Palliation only, or mere subjective improvement, is a poor compromise.

Referring to the table then, we note three lesions which fill these requirements; namely, isolated pulmonary valvular stenosis, isolated pulmonary infundibular stenosis, and pure inter-atrial septal defect of the secundum type. We have operated on 36 patients with these diseases, with one death, a mortality rate of 2.8 per cent. Thirty-one of these patients can be considered to be cured, while five are improved. We believe these results are as good as, or better than, any achieved by closed or blind procedures, and the mortality rate is equivalent. In our clinic, therefore, we believe the operation of choice for these lesions is open repair under direct vision.

The same procedures can be applied to the combination of pulmonary stenosis with a septal defect, as in the tetralogy and the trilogy of Fallot. In the former, however, the risk of too complete a relief of stenosis is a real threat, and we are currently not recommending this operation pending standardization of a curative operation (including closure of the ventricular septal defect), whether it involves hypothermia or other methods. In the Trilogy we have sought to achieve cure by attacking, first, the pulmonary stenosis, then the septal defect. Although we have had total success in one patient, using two stages, and expect success in another when the second stage is attempted, nonetheless, we currently believe it would be better to attempt closure of the atrial septal defect first, and intend to treat our next patient in this fashion.

Patients with interventricular septal defects or atrial septal lesions of the primum type, however, presented technical problems which forced us to exceed the safety limits, particularly as regards the occlusion times. These lesions are too complicated to be carefully and completely repaired within the time limit which has proven to be relatively safe. At least, this has been true in our hands (H. S.). Blind procedures have been reported as equally inadequate. The safe cure of these lesions, therefore, we feel must await the refinement of perfusion technics, or the knowledge necessary to safely apply much deeper hypothermia than we are now using.

Exploration of the application of the open approach to other heart lesions must be undertaken slowly as means to forestall coronary air embolism in left heart approaches are developed.

The use of hypothermia as an anesthetic adjunct in the management of patients with cyanotic heart disease, or in those patients who have rapid bounding pulses, has proven desirable. This indication is difficult to analyze objectively, and mortality data are meaningless except in very large numbers. However, our clinical impression at the present time is that operation is tolerated by these individuals better, and the risk is less when cooling is employed. There is one maneuver, however, which appears dangerous to employ during hypothermia, namely, cross-clamping of the aorta in patients with enlarged or strained left ventricles. In two patients, intractable ventricular fibrillation occurred after the aorta was clamped for the insertion of a plastic valve in the treatment of aortic regurgitation. It may well prove to be the case that patients with left heart hypertrophy or strain tolerate hypothermia less well than when the cardiac lesion subjects the right heart to strain.

For protection of the viability of body areas or specific organs during temporary total ischemia, hypothermia is quite effective. The potentialities of this indication, particularly for surgery of the brain, great vessels, and extensive ablative operations for cancer, appear to us to be worthy of extensive exploration.

VII. SUMMARY

1. Experience with 100 patients undergoing 105 operative procedures during general hypothermia is presented and discussed. Of these, 59 had direct vision intracardiac procedures, 21 had closed cardiac operations, while 20 had operations unrelated to heart disease. The total mortality was 22, the hypothermic-operative mortality, 14.

2. For achieving direct vision intracardiac operation, the technic is both effective and safe in congenital lesions which can be repaired through a right heart approach, with occlusion times of eight minutes or less at body temperatures not lower than 26° C. The mortality rises sharply when these limits are exceeded. Extension of the technic to acquired lesions, or to those requiring left heart approaches, has not been explored. At the present time, we consider it the method of choice in the treatment of isolated valvular or infundibular pulmonary stenosis and of inter-atrial septal defect.

3. As a technic for reduction of operative risk in patients with congenital heart disease characterized by deep cyanosis or by hypertrophied overactive hearts, our impression is favorable. It may be less well tolerated, or even non-beneficial in the presence of left heart strain.

4. As a technic to allow temporary regional or organ ischemia to achieve a bloodless field, the method is both effective and quite safe.

5. In the human, acute hypothermia above 26° C. *per se*, appears to carry a very low risk provided many detailed precautions are observed.

6. The prime cause of mortality is ventricular fibrillation and its sequellae. The risk of this complication exists primarily in patients with diseased hearts who undergo cardiac manipulation, and it rises progressively as more complicated, extensive, and prolonged operations on these hearts are attempted.

7. General hypothermia appears to be of sufficient safety and value to warrant further clinical evaluation and continued use.

BIBLIOGRAPHY

[1] Montgomery, A. V., A. E. Prevedel and H. Swan: Prostigmine Inhibition of Ventricular Fibrillation in the Hypothermic Dog. Circulation, **10**: 721, 1954.

[2] Swan, H., I. Zeavin, J. H. Holmes and A. V. Montgomery: Cessation of Circulation in General Hypothermia. I. Physiologic Changes and Their Control. Ann. Surg., **138**, 360, 1953.

[3] Swan, H., H. C. Cleveland, H. Mueller and S. G. Blount, Jr.: Pulmonic Valvular Stenosis. J. Thorac. Surg., **28**: 504, 1954.

[4] Swan, H., and I. Zeavin: Cessation of Circulation in General Hypothermia. III. Technics of Intracardiac Surgery Under Direct Vision. Ann. Surg., 139: 385, 1954.

[5] Virtue, R. W.: Hypothermic Anesthesia (Monograph). Chas. C Thomas, Springfield, Illinois. In Press.

DISCUSSION.—DR. HENRY WILLIAM SCOTT, JR., Nashville, Tennessee: I would like to congratulate Dr. Swan on the most stimulating review of his very extensive experience with hypothermia. On the basis of our own much less extensive experience I would like to endorse his views as to the value of hypothermia as an adjunct to the surgery of various types of congenital heart disease.

Operations on poor risk, cyanotic infants with tetralogy, with tricuspid atresia, and with valvular pulmonic stenosis, can be done more safely under hypothermia, in my opinion.

Aside from facilitating the direct suture of arterial defects, which Dr. Lewis is going to tell us about in a moment, I believe that one of the most significant applications of hypothermia at the present time is, as Dr. Swan has pointed out, its application to the direct visual repair of valvular pulmonic stenosis.

I had a short movie which I hoped to show, demonstrating Dr. Swan's technic in the direct transpulmonary arterial repair of a valvular stenosis, but unfortunately my "Metro-Goldwyn-Mayer" associate, Dr. Rollin Daniel, who was to bring the movie, has not yet arrived.

This procedure is a very fine approach to the problem of valvular pulmonic stenosis, and offers a good deal that the blind approach by the transventricular method does not offer. The valvular obstruction can be completely relieved in each instance by the direct visual method, while this has not been consistently accomplished by the older technic.

DR. HENRY SWAN II, Denver, Colorado: I would like to thank Dr. Scott for his comments. With your permission, I would like to document one point that we made.

(Slide) This is a list showing that the blood pressure obtained by the usual method disappeared in hypothermia as we have applied it. I show this merely to point out the great variability. We do not understand this phenomenon at all. At these various temperature levels it was no longer possible to hear by auscultatory methods a blood pressure recording. Nonetheless, the pulse was still palpable, and if measured intra-arterially there was a significant pulse pressure.

(Slide) One point which is of real interest is the neurologic sequellae which we have had. We have had no brain sequellae at all, but we have had a peripheral neuropathy appear in 12 patients, and we believe this is possibly due to increased susceptibility of the cold nerve to pressure, because these patients have electrocardiographic electrodes on their arms with an encircling rubber band. Currently we are using needles to avoid that pressure.

Thank you very much.