Mather *et al.* (1955) and Scadding (1956a) believe there is often a direct aetiological relationship between tuberculosis and sarcoidosis. Those who support the tuberculous aetiology would regard sarcoidosis as an example of tuberculous infection in which there is a high resistance and immunity, but in which immunological response has been associated with marked granulomatous formation (Robb-Smith, 1956). None the less, this combination in the same patient is not often found (Cowdell, 1954). In sarcoidosis the patient appears to have an enhanced capacity to destroy tubercle bacilli in the tissues, which accounts for the inability to identify them in sarcoid follicles. This cannot apply to acid-fast bacilli as a whole, as B.C.G. organisms remain alive at vaccination sites for as long a period in patients with sarcoidosis as in normal susceptible controls (Rostenberg *et al.*, 1953; Forgacs *et al.*, 1957).

It is possible that sarcoidosis and B.C.G. vaccination are coincidental (Törnell, 1954; James, 1958). The incidence of sarcoidosis as compared with tuberculosis is greater in vaccinated than in unvaccinated groups of patients, and the discrepancy is too great to be accidental (Fried and Genz, 1958). The incidence of post-B.C.G. sarcoidosis is higher than the normal morbidity rate for sarcoidosis in Switzerland (Birkhäuser, 1957). It is unlikely that the B.C.G. vaccination precipitates sarcoidosis in view of the long time interval between vaccination and the onset of sarcoidosis in our own and other writers' cases, although in leprosy there can be an interval of up to 20 years between contact and the development of granulomatous formation (Muir, 1948). Löfgren (1953) thinks vaccination may provoke sarcoidosis in patients when the disease is latent. It may well be that without B.C.G. vaccination these cases would normally have developed tuberculosis and that the vaccination protects and modifies the case to one of sarcoidosis. In this country more cases may appear as more school-leavers are vaccinated and followed up for several years. In children under 15 years of age only 113 cases of sarcoidosis had been recorded in a world survey of the literature (McGovern and Merritt, 1956).

Summary

A histologically proved case of sarcoidosis occurred in a girl given B.C.G. vaccination seven years previously. She recovered spontaneously, and the tuberculin sensitivity, which became negative during her illness, reverted to positive. The literature on the occurrence of sarcoidosis in B.C.G. vaccinated cases is reviewed. It is suggested that had she not been vaccinated she might have developed tuberculosis instead of sarcoidosis. The time interval was too long for vaccination to be regarded as the cause of the sarcoidosis.

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CONTROLLED HYPOTHERMIA IN INFANTS AND CHILDREN

BY

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The use of hypothermia now occupies a definite though restricted place in medicine. When we know more concerning oxygen transfer to the body cells, and its utilization by them during hypothermia, many of the present restrictions governing the use of lowered body temperatures may be removed, and the indications for its use may be extended considerably.

In cardiac surgery in children, when hypothermia is utilized, various technical requirements are desirable, the essential elements of which are:

1. A central body temperature which can be maintained accurately at any desired level, usually 30° C. This is estimated by the temperature recorded in the lower third of the oesophagus. Cooper and Kenyon have shown this to be a fairly accurate assessment of the central blood stream temperature during surface cooling, and we have also found that this temperature corresponds very closely to the temperature of the cerebral cortex.
2. A reasonable rate of fall in body temperature. This should be rapid enough to avoid the necessity for any extension of the normal operating-time.
3. Means whereby the body temperature may conveniently be raised or lowered while surgery is in progress.
4. Restoration of the body temperature to normal, as soon as possible after the completion of the operation, with minimal handling of the patient.
5. Accurate control of the rate of change of body temperature and facilities to stabilize it rapidly at any desired level, thus preventing any "overswing."

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6. The avoidance of additional major surgery solely for the purpose of producing cooling.

The use of blood-stream "extracorporeal" cooling as utilized by Delorme (1952), Ross (1954), and Lucas (1956) fulfils most of these requirements, but it has various technical, mechanical, and physiological disadvantages, which are discussed later.

Present methods of surface cooling, with or without the use of long-acting drugs (Bigelow *et al.*, 1950; Swan *et al.*, 1953; Lewis and Taufic, 1953; Dundee *et al.*, 1953; Bailey *et al.*, 1954; Ripstein *et al.*, 1954), do not fulfil these requirements. It is difficult to control the rate of cooling, and it is impossible to assess or to control the duration and degree of "overswing." There is also very little in the way of cooling or rewarming that can be done whilst the surgeon is at work.

The use of intragastric cooling (Khalil, 1957) is slow and not a practical proposition in association with surgery.

FIG. 1.—The patient is shown on the operating table with "polythene"-covered rubber blankets tied in close contact with the body. In the background is the "hypothermia machine," and on its top left-hand corner is the electrical thermometer.

The method presented here of inducing hypothermia and rewarming is by body-surface action. The skin of the patient is in close contact with rubber blankets containing a continuous capillary through which iced, hot, or tepid water is pumped and recirculated. The machine used to supply and pump the water is shown in Fig. 1.

Equipment

Hypothermia Machine.*—This contains three copper tanks, one of which contains 6 gallons (27.3 litres) of hot water thermostatically controlled at 40–42° C.; another contains 5 gallons (22.7 litres) of water at a temperature of 25–28° C.; and the final tank has 2½–3 gallons (11.4–13.6 litres) of water at 2–3° C. Outflow and inflow connexions for five blankets are housed below a central control panel, which regulates the rate of flow through each blanket, also the contents of the blankets, hot, tepid, or ice-cold water. Automatic valves ensure non-mixing between tanks when the water circulating in the blankets is changed from one tank to another. Hence it is possible to circulate water from any tank through any blanket at whatever rate is required. The temperature gradient between the outflow and inflow connexions on the machine when circulating iced water

at the usual flow rate is less than 1.5° C. The total amount of ice cubes used averages about 40 lb. (18 kg.) over a period of three to four hours, which is the average time taken on such cases. The machine is portable and readily moved to a satisfactory position in the operating theatre. The length of tubing from the machine to the blankets will determine its distance from the patient; about 6 feet (1.8 metres) has been found a convenient distance. All connexions are of a simple bayonet self-sealing type.

Blankets.†—These are made of rubber and contain a continuous capillary enabling water to be circulated throughout their entirety; this assures an even distribution of temperature all over the blanket. Three blankets measuring 18 by 40 in. (46 by 101 cm.), 12 by 32 in. (30 by 81 cm.), and 8 by 32 in. (20 by 81 cm.) have been found adequate for all cases, from small babies to children 13 years of age.

Temperature Recorder.—It is essential to have available facilities for accurately and quickly recording the body temperature, preferably in more than one situation. The recording apparatus should be situated conveniently close to the hypothermia machine, and well away from the patient so that no inconvenience will be caused to the surgeons or anaesthetists during the operation. The electric universal thermometer, type T.E. 3, manufactured by Elektrolaboratoriet, Copenhagen, has been found admirably suited to our requirements. Rectal and lower oesophageal leads are regularly employed, and a periodic check of the pharyngeal temperature may be made by the anaesthetist, using a mercury thermometer. In addition a needle applicator, with a thermojunction situated at the needle tip, has been used experimentally to measure the temperature in the cerebral cortex and the aorta during cooling, both of which closely correspond to the temperature in the lower third of the oesophagus.

Methods

The anaesthetized unclothed patient is placed on the operating table on a large rubber blanket. All leads are then connected—for example, rectal and oesophageal for temperature recording, intra-arterial "polythene" tubing for continuous blood pressure, subcutaneous needles for E.C.G. and the diathermy plate. It is considered essential to monitor the heart's action continuously, using a cathode-ray oscilloscope, whenever hypothermia is employed—in fact, this safeguard is used routinely for all cardiac surgical procedures in our unit. In all "open heart" procedures a continuous record of the intra-arterial blood pressure is also regarded as desirable.

The child is placed in position, supine or lateral, depending on the nature of the operation. A blanket is placed on top of the patient, covering the abdomen and legs, and a narrow blanket is placed between the legs and thighs. The blankets are then tied together, overlapping where necessary, but obtaining maximum contact with the skin. The only exposed parts of the body are the head, neck, arms, and that part of the thorax where the surgeon is to operate (Fig. 1).

A long piece of rubber tubing, ½ in. (1.3 cm.) external diameter, is then coiled around the neck, fitting snugly but not too tightly, and making as many coils as possible in order to obtain maximum skin contact; this is usually

*Manufactured by Ebsray Pumps Pty. Ltd., Sydney.

†Manufactured by Dunlop Rubber, Australia, Ltd., Sydney.

three to four coils (Fig. 2). This tubing makes the fourth connexion with the machine, leaving one spare connexion.

Water at 2–4° C. is circulated through all the blankets and the neck coil. The rectal and oesophageal temperatures are recorded at regular intervals in graph

FIG. 2.—The neck coil is shown in position. The chest is exposed for bilateral thoracotomy.

form, and so long as no alterations are made to the rate of flow through the blankets or the temperature of the water contained therein, it is found that there is a linear rate of fall in the body temperature. The exact time can be predicted at which the body will cool to any desired temperature. As the body temperature falls and approaches the required level it is possible to circulate tepid or hot water through any or all of the circuits simply by turning the control knob, or any blanket can have its circulation stopped independently of the others. This allows great flexibility and ideal control.

As soon as the blankets have been connected and the patient has been positioned, the surgeon can scrub up and proceed with the operation; then, while the operation proceeds, the temperature is being lowered to the required degree, and when this point is reached it may be stabilized and held there. When desired, rewarming can be initiated by circulating hot water through the blankets, and by the time the operation is completed the temperature of the patient is invariably raised sufficiently to allow safe transport from the theatre. The child is then taken to a recovery ward together with the temperature-recording apparatus and placed in an oxygen tent. The temperature is regularly recorded at 10-minute intervals and active steps are taken to prevent any rise above 37° C.

Fifty patients have been subjected to this procedure, their ages ranging from 3½ months to 12 years. These cases have included the following conditions: atrial septal defect, pulmonary stenosis, aortic stenosis, aneurysm of the pulmonary artery, transposition of the great vessels, very severe tetralogy of Fallot, coarctation of the aorta, an unusual case of mitral stenosis in a girl of

7 years (this will be the subject of a special case report), and one case of persistent ductus arteriosus in a 6-months-old baby in severe heart failure. Recently all cases of coarctation of the aorta have been operated on under hypothermia because it is believed that the danger of a spinal artery thrombosis is lessened, and the slower heart rate greatly relaxes the aorta and makes it safer and easier to handle during its repair. In addition we have been impressed with the post-operative course of these patients, who require smaller and less frequent doses of analgesic and sedative drugs in the immediate post-operative period. They are obviously much less distressed by the procedure than similar cases operated on at normal temperatures. The decision to utilize hypothermia in the repair of coarctation of the aorta in children was made following the occurrence of paraplegia, fortunately incomplete, after the otherwise uncomplicated resection of a coarctation in a boy of 8 years in whom it was necessary temporarily to occlude an aberrant right subclavian artery arising just above the site of the coarctation.

Results

The method of hypothermia and rewarming described above has produced most gratifying results in all cases. An adequate rate of cooling was invariably maintained, a typical case being shown in Fig. 3. Rapid rates of cooling are not advised (Lucas, 1958), as it is considered that an excessive gradient between peripheral and central-blood-stream temperatures heightens the incidence of ventricular fibrillation (Lucas, 1955).

The use of a coil of rubber tubing around the neck, bringing the circulating water into close proximity with the large vessels in the neck, accentuates the rate of fall in temperature; the resulting change in gradient is illustrated in Fig. 4. The average rate of fall in temperature in the six cases before using neck cooling was 4.5° C. an hour, and after neck cooling was introduced the average fall in temperature was 5.5° C.

FIG. 3.—Showing the method by which the body temperature was reduced and restabilized at the lower temperature. A. Water circulation stopped. Iced water left in blankets. B. Hot water circulated for five minutes. C. Surgeon requested temperature to be lowered to 31° C. Iced-water circulation restarted. D. Water circulation stopped. Iced water left in blankets. E. Hot water circulated. F. Water circulation stopped. Hot water left in blankets and patient's temperature allowed to drift slowly upwards. Active rewarming begun as indicated by circulating hot water again.

an hour. In some of these latter cases it was necessary to exclude some of the circuits because the rate of cooling was unnecessarily rapid.

Infants and small children cooled at a more rapid rate than larger children owing to their greater surface area in proportion to their weight.

Other factors influenced the rate of cooling, such as a large shunt in the circulation or a coarctation with a

FIG. 4.—Illustrating the value of the neck coil in accelerating cooling. Blanket cooling only was used for the first 45 minutes, following which it was supplemented with the neck coil. The marked increase in the rate of cooling can be seen. Rewarming is also facilitated in a similar manner. Blanket cooling, 2.2°C. per hour; blanket plus neck cooling 5.25°C. per hour in this instance.

poor blood supply to the lower half of the body, or an obese patient with a poor peripheral circulation. Such factors will retard the rate of cooling not only by this method but also by blood-stream (extra-corporeal) methods. Even so, by the time the surgeon was ready to occlude the circulation the patient was always stabilized at the required temperature.

An appreciable variation has been found between body

temperatures recorded at different sites, and this variation was often increased during cooling and rewarming of the body.

We consider it important that the body temperature recorded should approximate that of the cerebral cortex at the same moment. It was found that the temperature in the lower third of the oesophagus was always within 0.2°C. of the cerebral cortex temperature, both during cooling and rewarming and also while the temperature was stabilized. The pharyngeal or rectal temperatures were not nearly so satisfactory in this regard. The rectal temperature as shown in Fig. 3 reflected variations in cooling or rewarming very slowly.

In this case of coarctation of the aorta a temperature of 32°C. was asked for, but after opening the chest and inspecting the coarcted segment it was felt that the right subclavian artery might be aberrant and become involved in the clamps; hence it was decided to undertake the anastomosis at a temperature of 31°C. A close inspection of Fig. 3 will show the ease with which the body temperature was further reduced and restabilized at the lower temperature. Alterations in temperature were clearly shown in the oesophageal record, which we believe accurately reflects the central-blood-stream temperature, yet the rectal temperature recorded none of these changes; however, on close inspection it shows a slight change in the rate of fall in temperature some 10 to 15 minutes after this had already been demonstrated in the oesophageal lead. Also it will be seen how the rectal temperature gave a false impression of overswing, as the difference between rectal and oesophageal temperatures at the onset of rewarming was some 2°C. This crossing over of the rectal and oesophageal temperatures during cooling always occurred: they recrossed back to their original dispositions during rewarming. During stabilization the

oesophageal temperature slowly rose for some 40 minutes while the rectal temperature was falling; however, it must be remembered that during this time no active steps were made to rewarm the patient, as the aim was to stabilize his oesophageal temperature at about 31°C. The average time taken to turn a patient's temperature from one of cooling to rewarming, or to stabilize it, was usually less than nine minutes.

From a comparison of the blood stream, cerebral cortex, and oesophageal temperature readings we believe that the recording of temperatures in the lower third of the oesophagus is reliable, and much more accurate than rectal or pharyngeal temperatures, and should be used in all cases of hypothermia. Delorme (1956) made a plea for conformity in taking the body temperature and suggested a mid-oesophageal recording.

Rewarming presented no difficulties, but temporary setbacks may occur if large amounts of cold blood are urgently transfused. All blood is now warmed to 35°C. prior to transfusion, and this problem has been eliminated. It is possible to rewarm the patient when the only effective circulation is cardiac massage. This was done on one occasion, and as the temperature rose the ventricular fibrillation present spontaneously reverted to sinus rhythm and the patient made an uneventful recovery.

No cardiac irregularities have occurred in this series that could possibly be attributed to the use of hypothermia.

The patients were rewarmed to at least 33°C. before removing the blankets, and were then taken from the operating theatre to a warmed bed. At this stage the rectal temperature, being within a degree of the oesophageal, was used to monitor the patient's temperature for the next 24 hours.

It was not necessary to rewarm patients actively over 33°C. , as they always continued to rewarm at a steady rate without the aid of the blankets. Graphs were made of the temperature by the nursing staff, together with pulse and respiratory rates when in the recovery ward, and, if the temperature was not levelling off at or below 37°C. , active measures were carried out, such as removal of all coverings, tepid sponging, reducing the temperature in the oxygen tent, or even placing ice-packs around the patient in order to achieve a normal stable body temperature.

It is important that the nursing staff should be familiar with these facts and thoroughly conversant with the procedure necessary to prevent hyperpyrexia developing.

Discussion

The body temperature of children undergoing cardiac surgery has been controlled with great satisfaction and safety since using this method of surface cooling with the machine circulating water through special rubber blankets.

Previously we had been accustomed to immersing children in a cold-water bath, drying them on removal, and placing them on an electric blanket that could be warmed. However, we were never satisfied, chiefly because we did not have adequate control. It was impossible to forecast the amount of overswing: the smaller the child the more difficult this became, and rewarming was difficult as the electric blanket was not adequate to perform this task. Further, the practice of

immersing a child with altered haemodynamics in a hot bath immediately after a long and sometimes difficult thoracotomy is not wise. There was also the question of delay and mess in the theatre prior to operation, extra handling of the patient, and extra movement of the attendants, such factors being apt to increase the risks of infection, prolong the duration of anaesthesia, and disturb the normal theatre routine.

The use of extracorporeal blood-stream cooling (Ross, 1954, 1956; Brock, 1956) must be restricted to patients undergoing bilateral or right thoracotomy. The blood is subject to the effects of pumping and also to very cold temperatures in the plastic tubing coil; further, this tubing passes into the actively contracting heart, where it may remain for several hours, including the time when the circulation is occluded and the surgeon is repairing cardiac defects. This must represent a certain hazard, and is a major surgical procedure in itself. Also it introduces the possibility of trauma to the heart or great vessels, and might possibly distract the surgeon or interfere with his movements. The tubing can, of course, be disconnected and then reinserted for rewarming purposes, but this means extra handling of an overworked and irritable myocardium. In addition, there must be some risk of haemolysis or thrombosis of the blood in the extracorporeal circuit.

There are also mechanical problems such as flaws in the tubing, kinking during the pumping, inadequate venous return, and so on, any one of which could be serious if it occurred. Rewarming must be initiated and reach a certain stage before the heart can be closed and the operation completed; this adds further to the delay, exposure, and handling of the heart.

In general it will be found that in our method the rate of cooling and rewarming is a little slower than the blood-stream cooling recommended and described by Ross (1954, 1956) and Brock (1956).

The advantages claimed for the method described are as follows: (1) There is no overall delay, since the operation can be started as soon as cooling has been initiated. (2) The procedure is extremely effective and controllable. Cooling and rewarming are achieved at a satisfactory rate, so that the desired temperature is reached by the time the surgeon requires it and adequate rewarming has been established by the time the operation has been completed. (3) No additional surgery is necessary to effect cooling, and it can be employed for any operative procedure for which it would seem to be indicated without necessarily opening the right chest or the pericardium. (4) It is not necessary to begin cooling prior to opening the chest, a decision for or against hypothermia being made after direct inspection of the lesion, if desired. (5) Rewarming is effective while the chest is open, and can be achieved whilst the circulation is maintained with cardiac massage, if necessary. (6) The procedure is simple, clean, and aesthetic, and there is minimal interference with the normal aseptic ritual in the operating theatre.

Our thanks are due to Dunlop Rubber, Australia, Ltd., for donating the special blankets used in this procedure, and in particular to Messrs. Waring and Sharpe of that firm for the time and trouble involved in developing a satisfactory set of blankets for our requirements.

We pay tribute to Mr. V. R. Ebsary, whose ingenuity and initiative were responsible for the development of the hypothermia equipment. This ingeniously contrived

machine has done all that has been required of it in every case in which it has been used. In addition, Mr. Ebsary has attended, in every case in which hypothermia has been employed, to operate the machine for us. Although the machine is simple to use, his skilful regulation of the body temperature has relieved the anaesthetic and surgical staff from any worries in this regard, and has allowed us to concentrate wholly on the medical aspects of the particular case.

Finally, we recognize the contribution of Mr. A. Harper, of the Commonwealth Scientific and Industrial Research Organization, who also gave willingly of his time and knowledge to advise us on certain technical aspects of heat transference, and who kindly attended the theatre for the first few cases to assist in the organization and supervision of this procedure.

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TEMPERATURE GRADIENTS DURING HYPOTHERMIA

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The most commonly used method of reducing the body temperature is by the surface cooling of an anaesthetized subject. A well-controlled method (Cohen and Hercus, 1959) has been used by us in all cases requiring hypothermia for cardiac surgery. Although much experimental work on various aspects of hypothermia has been done, we have been unable to find any record of studies having been made of the changes in temperature of the cerebral cortex in relation to temperature changes occurring simultaneously in other parts of the body. This investigation was undertaken in order to find out what part of the body will reflect most closely the changes in temperature occurring in the cerebral cortex during cooling, stabilization, and rewarming.

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