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## HYPOTHERMIA WITH AUTONOMIC BLOCK FOR THE POOR RISK PATIENT IN THORACIC SURGERY.

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Modern methods of surgery and anaesthesia together with drug therapy have, within comparatively recent times, extended the benefits of operation to countless numbers of patients with pulmonary disease who, not so very long ago, were considered outwith the realm of surgery. At the Thoracic Surgical Unit, Mearns Kirk Hospital, experience has taught us that there is a category of patient with pulmonary disease who, no matter the urgency and desirability of operation, is seldom able to withstand the necessary surgical intervention. Particularly is this the case in poor risk patients suffering from advanced pulmonary tuberculosis or from bronchial carcinoma with cachexia associated with abscess formation and retention pneumonia. The technique of hypothermia associated with blockade of the autonomic nervous system as described by Dundee *et al.* (1953) seemed to us worth a trial in such cases.

This article, which is in the nature of a preliminary report, is concerned with our experience in relation to five patients who, by previous standards, would have been considered desperate risks for major surgery. It is perhaps premature to draw conclusions at this early stage but the fact that a favourable result has been achieved in four of the five patients seems a justification of the method.

Maintenance of adequate tissue oxygenation, support of the cardiovascular system and modification of the body's reaction to surgical trauma are fundamental aims in modern surgery and anaesthesia. To this end anaesthetic drugs of low toxicity, muscle relaxants, controlled ventilation with high oxygen content, intravenous transfusion and vasoconstrictor drugs are used to protect the patient as far as possible from the traumatizing effects of major surgery. In spite of such methods and especially in the longer surgical procedures of two hours or more, it is found that the general condition may deteriorate and shock develop.

In thoracic surgery the open chest provides an added hazard. Manipulation of, and direct traction on, the heart, great vessels and trachea may be unavoidable and constitute additional shock-producing stimuli. With the aim of providing further protection various workers (Laborit, 1950; Laborit & Huguenard, 1951; Smith & Fairer, 1953) set out to obtain paralysis of the autonomic nervous system by employing the so-called 'lytic cocktail,' the main constituents of which are chlorpromazine (largactil), promethazine (phenergan) and pethidine. Another approach concerns the reduction of the oxygen requirements of the tissues rather than increasing the oxygen-carrying capacity of the circulating blood and this may be effected by the production of hypothermia. It has long been known that lowering the temperature of the body reduces metabolism and oxygen consumption. Dundee *et al.* (1953) combine both of the above methods and their technique has been the basis of our method in dealing with the cases described below.

#### METHOD OF HYPOTHERMIA PRODUCTION.

Premedication consists of pethidine 50-100 mg. coupled with promethazine, 50 mg. and is administered either orally or intramuscularly about four hours before the operation is due to commence. We have found that a more satisfactory sleep-producing effect is procured when the intramuscular route is used. One hour later a slow intravenous infusion of 5% glucose in water is commenced and is thereafter utilized as a vehicle for the administration of the 'cocktail' components. Originally a glucose-saline mixture was employed until it was found that the sodium content of this solution could produce dangerous fluid retention in the lungs of those seriously ill patients, most of whom were undergoing pneumonectomy.

Immediately the drip is functioning satisfactorily a 1 ml. test dose of 'cocktail' is injected into the tubing. The composition of the lytic compound is pethidine 100 mg. promethazine 50 mg. and chlorpromazine 50 mg., the latter drugs being made up in 2 ml. ampoules and the total mixture comprising 6 ml. Chlorpromazine is apt to irritate and it is therefore advisable to inject high up in the drip tubing and thus ensure adequate dilution before the vein is reached. Somnolence usually follows the test dose and the patient is then placed in the lateral position with the operation side dependant. This posturing is of paramount importance in those thoracic cases where copious sputum is the rule and the dangers of aspiration during deep narcosis are very real. In addition, a head-low position is maintained to avoid postural hypotension. Provided no undue reaction indicating sensitivity in the form of excessively deep narcosis and/or marked fall in blood pressure becomes apparent, further 1-2 ml. doses of the lytic compound are administered at intervals of from 10-15 minutes. The total dose may vary from 6-12 ml. Temperatures are most

conveniently recorded electrically by means of a thermistor which is inserted into the rectum and connected to a graduated scale. Where no such equipment is available a lotion thermometer, encased at each end by rubber tubing, makes a reasonably satisfactory substitute.

In the main our findings have corresponded with those of Dundee *et al.* (1953). A good reaction is indicated by deep narcosis which is characterized by slowing of the rate and increase in the depth of respiration. Colour improves where cyanosis has been a feature. As a general rule an initial rise followed by a fall in both heart rate and systolic blood pressure are observed. A drop in temperature may accompany the onset of narcosis but this is not usual in our experience. In the narcotic state which develops the patient appears to be deeply unconscious but will respond to strong stimuli.

At this stage, some 60-90 minutes after commencement of the 'cocktail' infusion, the reaction of the thermo-regulatory mechanism is tested by stripping the patient of all clothes and then covering him with a bed sheet which has been rinsed out in cold water. If shivering ensues, complete blockade of the thermal controls has not been achieved and further doses of 'cocktail' are indicated. In the absence of such response, icing is commenced. The ice, crushed and wrapped in gauze, is strategically applied over the main superficial arterial trunks in groins and axillae. The absence of shivering is once more the guide to extension of the icing process to the trunk and lower limbs. (Frostbite may result when the ice is applied directly to the skin.) It must be stressed that surface cooling with ice should not begin until adequate doses of the lytic components have been administered. During cooling close attention must be observed for evidence of shivering. Dundee (1954) contends that shivering is more easily prevented than controlled. Our experience tallies in respect of gross shivering which, short of the induction of anaesthesia and curarization, may be well nigh impossible to control. Slight shivering on the other hand has been readily abolished by small doses of thiopentone.

Once the temperature begins to fall it is apt to continue rapidly in its downward trend. If one aims at hypothermia in the region of 30°C (86°F) the cooling process is discontinued when the rectal temperature registers 34°C or 33°C (93.2°F or 91.4°F). At this point the patient is ready for transfer to the anaesthetic room. A further fall of from 1°C to 3°C may be expected during the induction of anaesthesia and after the chest is opened and this fall may continue into the early post-operative period.

#### ANAESTHESIA AND OPERATION.

Anaesthesia in all five cases was induced with thiopentone (average dose 0.3 g.) and maintained with nitrous oxide and oxygen (usually 2 litres of each). Apnoea was established with d-tubo-curarine chloride (average dose 25 mg.) and controlled ventilation with carbon dioxide

absorption was secured by means of the Blease Pulmoflator. Adequate spontaneous respiration was readily restored by neostigmin at the end of operation. We stress the importance of directing meticulous care towards the protection of all pressure points. Blood replacement was estimated not to exceed blood loss. Pulse rates and blood pressure levels tended to be lower than usual. Vaso-dilatation, as indicated by a relative increase in pulse pressure, was not a conspicuous feature. No observations were made in regard to bleeding and clotting times but the consensus of opinion was that haemorrhage tended to be reduced. The patients seemed to be afforded protection against shock-producing surgical stimuli but cardiac irregularities were by no means abolished during such manoeuvres as dissection of the main pulmonary vessels. In spite of the excellent drainage afforded by the 'face-down' position which was adopted in the four cases of pneumonectomy, mucopurulent secretions were so copious in Case 3 that temporary blockage of the airway occurred. In retrospect, a Thompson's blocker positioned in the left main bronchus would have been a decided advantage in this case.

#### POST-OPERATIVE COURSE.

As a precaution the routine procedure of nursing major thoracic cases in an oxygen tent was adhered to during the immediate post-operative period. We are not yet certain whether oxygen therapy at this stage may be dispensed with. Initially one blanket only is allowed and the surrounding temperature is kept low. Several hours pass before there is complete return to consciousness and amnesia extends to a very early stage of preoperative preparation. Case 4 was an exception in that he was able to recall details of the initial preparations for cooling—this and the subsequent uncontrollable shivering may be attributed to an inadequate build up of the lytic 'cocktail.' A normal temperature may not be regained until 72 hours or more have elapsed. Provided the temperature is showing signs of rising no attempt is made to hasten the rewarming process as we believe that a state of 'hibernation' helps the poor risk patient to make a better recovery from operation. In cases where the temperature shows no tendency to rise some method of rewarming is indicated and a brief application (20-30 minutes) of an electric blanket has proved satisfactory. Dundee (1954) believes that a state of cold narcosis may exist at low temperatures when restoration of temperature does not take place without assistance.

The postoperative discomfort which usually follows major thoracic surgery appears to be less in these cases and sedation has been readily achieved with a 50 mg. dose of pethidine. Wounds have healed well, bronchial closure has been satisfactory and no instance of bed sores has occurred. Transient pulmonary oedema complicated pneumonectomy in two patients (Cases 3 & 4), and these incidents underline the advisability of reducing intravenous fluids to the minimum.

## CASE SUMMARIES.

During the first three months of 1954 a total of five patients have undergone major thoracic procedures under the protective influence of controlled hypothermia. In each instance the patient's general condition gave rise to serious doubts as to his capacity to withstand an extensive intrathoracic operation. More detailed consideration of these cases will afford a more realistic impression of the gravity of the condition in each.

*Case 1.* A female aged 21 years laboured under the combined disabilities of a tetralogy of Fallot, pyelonephritis, and pulmonary tuberculosis. Marked cyanosis was accompanied by progressively increasing dyspnoea. The lung lesion, which consisted of scattered deposits of caseous disease throughout the right lung, showed considerable improvement following a ten month period of sanatorium bed rest combined with drug therapy. Although a doubtful risk for surgery it was considered that hypothermia, by reducing basal metabolism, tissue respiration and oxygen consumption would compensate for the additional depletion of respiratory function consequent upon the pulmonary tuberculosis. Accordingly pulmonary valvotomy was performed in the right lateral position on 8th January, 1954.

Hypothermia was induced without difficulty and was notable for the marked improvement which was observed in the patient's colour. In all 9 ml. of 'cocktail' were administered. Slight shivering, which occurred during the cooling process, was abolished following the induction of anaesthesia. The operation, which lasted 80 minutes proceeded uneventfully, the patient's colour remaining excellent throughout. The temperature fell to 30.8°C (87.4°F), and was restored to preoperative levels by 24 hours. She had a smooth post-operative course and she has benefited from the operation.

*Case 2.* A male of 54 years had a proven epidermoid carcinoma of the right bronchus. This patient was in exceedingly poor general condition being markedly dyspnoeic even at rest and almost continuously febrile. Sputum was copious. Chest radiography showed a huge cancerous mass occupying most of the right upper lobe with obvious evidence of necrosis and central abscess formation. He was deemed possibly operable by bronchoscopic standards but his general condition ruled out all thought of operative intervention. After careful consideration the shock-cushioning effect of hypothermia with autonomic block was thought to offer a chance of successful tumour extirpation.

On 29th January, 1954, right pneumonectomy in the face-down position was successfully performed under hypothermia. A total of 8 ml. of 'cocktail' was administered. Shivering at one point was controlled with 2 ml. of 5% thiopentone. The operation, which took 2½ hours to complete, was technically difficult because of extension of tumour tissue up to the carina and along the pulmonary vessels. A portion of the left main bronchus was found to be involved and had to be resected. It was necessary to exert considerable traction on the heart during intra-pericardial ligation of the main pulmonary vessels. At this point cardiac irregularity, tachycardia and a fall in blood pressure to unrecordable levels became manifest. Following a rest of 10 minutes, regular cardiac action was restored and no further anxiety as to the patient's general condition was experienced.

On return to bed the temperature, which had fallen to 30.8°C (87.4°F) during operation, continued on its downward trend but steadied at 28°C (82.4°F) two hours later. Thereafter, with extra coverings, the patients gradually rewarmed and by 11 p.m. the same evening the temperature was 32.8°C (91.0°F). By this time he could be roused but was not coherent. The pulse was barely perceptible

and was irregularly irregular. The blood pressure was unrecordable. Without restoratives of any kind this patient improved progressively throughout the night and by next day he was rational and possessed of a regular, good quality pulse. His temperature took four days to return to normal levels and he left hospital apparently well three weeks after operation.

Although this man was able to regain a normal temperature unaided we now consider a temperature in the region of 28°C (82.4°F) in an adult to be dangerously near a state of cold narcosis. The rewarming process as already described should be assisted by a brief application of an electric blanket.

Ten weeks after operation Case 2 was readmitted in a very breathless and depleted condition. He was harassed by a broncho-stenotic cough which produced copious, frothy, purulent sputum. Three weeks after admission he died. At autopsy, a fungating, cauliflower-like regrowth of tumour tissue was discovered at the site of amputation of the right main bronchus. The carinal gland was grossly enlarged and had produced severe compression of the left main bronchus which was reduced to a mere slit. There were generalized bronchopneumonic changes throughout the left lung.

*Case 3.* A male aged 55 years was admitted to hospital in an emaciated, dyspnoeic and very ill condition on 21st December, 1953. Bronchial biopsy revealed the presence of an epidermoid carcinoma and X-ray showed a massive neoplasm of the left lower lobe. There was persistent intermittent pyrexia and he developed a cellulitis of the right forearm without any apparent predisposing cause. Grave doubts were entertained as to his capacity to withstand the rigors of pneumonectomy, although bronchoscopically he appeared to be a reasonable possibility for operation. On 12th February, 1954, hypothermia was embarked upon, 9 ml. of the lytic 'cocktail' being administered. Slight shivering was controlled by 0.1 g. thiopentone. Left pneumonectomy was performed in the face-down position taking 1½ hours to complete, during which time the rectal temperature remained steady around 29°C (84.2°F). During the course of the operation anxiety was caused by a poor heart action which took the form of a slow fibrillation. This may have been related to the low temperature or to the vigorous endobronchial suction which was necessary to clear the airway partially obstructed by copious mucopurulent secretion. Regular rhythm followed the injection of atropine gr. 1/100 and, at the completion of operation, the patient was looking well.

On return to the ward the temperature quite suddenly dropped further to 27.6°C (81.7°F). With the addition of further blankets and finally an electric blanket for 30 minutes heat was gradually regained. Throughout the next 24 hours the temperature remained below 34°C (93.2°F) and only by the evening of 16th February had it attained the height of 37°C (98.6°F).

On the third postoperative day this man developed cough with frothy sputum and other signs of pulmonary oedema. He responded rapidly to low sodium intake, ammonium chloride and intramuscular mersalyl. He was finally discharged to convalescence in the country five weeks after operation having made a satisfactory recovery.

*Case 4.* A male aged 26 years. At the time of admission to hospital this man had suffered from bilateral pulmonary tuberculosis for nine years. Progressive stenosis of his left main bronchus had ultimately reduced it to slit-like dimensions and had led to progressive destruction of his left lung. By reason of the stenosis he suffered from recurrent febrile attacks due to retention of grossly infected secretion in the lung. These incidents with temperatures of 103°F-104°F were becoming frequent and were producing a rapid decline in his general condition. All the known antibiotics had been tried and found useless. He was a toxic, thin, pale, lethargic youth

totally confined to bed and subject to attacks of paroxysmal tachycardia which brought him to the verge of syncope. A chest skiagram also revealed scattered fibro-calcified disease in the right upper lobe but no cavitation was demonstrable by tomography.

After preliminary transfusion with the packed cells of four pints of blood during the ten days prior to operation, left pleuro-pneumectomy with thoracoplasty was undertaken in the face-down position on 19th February, 1954. In spite of 10 ml. of 'cocktail' 0.25 g. thiopentone and 40 mg. of gallamine triethiodide, shivering occurred intermittently during the cooling process and was not finally controlled until anaesthesia proper was induced. The operation was performed without undue difficulty, the patient's condition giving no cause for anxiety at any time. The lowest temperature recorded was 29.6°C (85.3°F) and he required 36 hours for the restoration of normal temperature.

On the day following operation this man showed evidence of left ventricular imbalance with copious, frothy sputum and dyspnoea. This responded to oxygen, low sodium intake, ammonium chloride and mersalyl. It is possible that the above incident resulted from excessive transfusion. In addition to the blood preoperatively he had, what is for these patients an unusually large quantity of normal saline, namely, two pints. In estimating fluid replacement cognizance should be taken of the fact that sweating is reduced or absent in the hypothermic state.

This patient is now well and is convalescing in a sanatorium ward of the hospital.

*Case 5.* Female aged 24 years. This girl had suffered from pulmonary tuberculosis for a total of five years. The disease in her right lung had been treated by the induction of an artificial pneumothorax six months after diagnosis. Some eight months later an effusion appeared and this rapidly became purulent. By late 1951 she had evidence of a bronchopleural fistula with expectoration of tuberculous pleural space contents. She was finally admitted to a sanatorium ward of Mearns Kirk Hospital on 3rd August, 1953. Chest X-ray showed a totally collapsed right lung with a pyopneumothorax and gross pleural thickening. The left lung was clear. After a six month preparatory period she was finally subjected to right pleuro-pneumectomy with thoracoplasty under protective hypothermia on 26th March, 1954.

Cooling was not easily achieved in this patient despite the early induction of somnolence, 11 ml. of 'cocktail,' and the most extensive application of ice over a period of 75 minutes. Slight shivering was readily controlled with 0.15 g. thiopentone. At the time of induction of anaesthesia the temperature had fallen to 35.8°C (96.5°F) and, by the end of operation, registered 33.2°C (91.7°F). The pleuro-pneumectomy itself was technically extremely difficult and took two hours to complete. By reason of the prolonged suppuration the tissue layers were excessively indurated. The intimate fusion of lung to diaphragm necessitated resection of the 9th rib to allow of more direct access. To complete the mobilization the 7th and 8th ribs were severed posteriorly and displaced backwards to provide adequate exposure. In addition, the subsequent routine thoracoplasty entailed the resection of ribs 2-6.

Throughout the above shock-producing procedure this ill patient remained in good condition and, apart from a fall in blood pressure to 60 mm. of mercury systolic, gave no cause for anxiety. To all present the shock-cushioning effect of the lytic 'cocktail' was apparent.

Three hours after return to the ward the temperature had fallen to 32°C (89.6°F). With the addition of further blankets the temperature gradually rose and a total of 48 hours were required to reach normal temperature. Apart from transient difficulties with secretion at the end of the first week, this girl has made steady progress since operation.

## DISCUSSION.

In a thoracic surgical unit no problem exists when a patient in reasonably good general condition presents with a destroyed tuberculous lung. Pleuro-pneumonectomy with thoracoplasty in such cases has become a routine procedure and the beneficial results of operation are considered a justification of any risk that may be involved. This remains true even in the presence of disease in the contralateral lung, provided such disease is stable or has shown a favourable response to bed rest and drug therapy. An entirely different situation arises in assessing the patient who is seriously ill, emaciated, toxic, subject to prolonged bouts of fever and deriving no benefit from any form of preparatory treatment. Without surgery death is inevitable and may be imminent: with surgery there is hope provided the patient can withstand the rigors of a major surgical procedure. To deny operation where hope exists can be a distressing decision. Several cases of this nature have indeed made a satisfactory recovery following operation but the toll has been heavy. If hypothermia with autonomic block will lead to improved results in such cases, and there is reason for concluding that it may, then it seems reasonable to persevere with the method. The benefit to the community of rendering a highly infective patient non-infective is, of course, obvious.

The problem of the seriously ill case with cancer of the lung is in many respects similar although the ultimate gain to the patient may not be comparable. We consider that if operation is even remotely possible then thoracotomy should be undertaken. For some the only final advantage may be a less distressing death but for others the result has been decidedly more rewarding. Cases 2 and 3 by previous standards would have been considered quite unfit for surgery. We admit that Case 2 was inoperable by most standards and possibly pneumonectomy should not have been attempted but we adhere to our policy of tumour extirpation whenever possible, be it only palliative.

It is unlikely in our view that the hypothermic state will have an application in thoracic surgery generally but the category of case described above seems a reasonable indication for the method—at least first impressions are favourable. We have also induced hypothermia with autonomic block in two children suffering from Fallot's tetralogy and undergoing the Blalock type of operation. The reduction of oxygen consumption in these cases proved a decided advantage and both children have done well.

## CONCLUSIONS.

Only tentative conclusions may be drawn from such a small series of cases. They are:—

1. Hypothermia with autonomic block may be safely induced in a purely clinical centre and elaborate equipment is not essential.

2. It is possible to increase the operability rate for lung resection in certain desperately ill patients suffering from tuberculosis and bronchial carcinoma.
3. To ensure a satisfactory hypothermic state with surface cooling the following points are important :—
  - (i) Adequate time for preparation—four hours may be necessary.
  - (ii) Premedication in adequate dosage by the intramuscular route.
  - (iii) Induction of deep narcosis by the lytic compound before the application of ice.
  - (iv) Control of shivering as soon as it becomes apparent with further doses of the lytic drugs and/or thiopentone.
  - (v) Allow for a continuing drop in temperature during the induction of anaesthesia, when the chest is open and in the very early postoperative period.
  - (vi) Resistance to cooling may be encountered in toxaemic and pyrexial states presumably due to increased basal metabolism.
4. Blood and fluid replacement should not exceed loss and excess sodium should be avoided.
5. A postoperative state of 'hibernation' may be beneficial but some artificial means of restoring heat is necessary at low temperatures.

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