vessels. Arteries leaving this pericapsular anastomosis enter numerous bony foramina at the base of the femoral neck and pierce small openings in the attachment of the joint capsule. All these arteries are accompanied by a rich plexus of veins, which play an important part in the intravascular thrombosis associated with avascular necrosis of the femoral head.

Ontogeny

During the growth period the circulus articuli vasculosus is situated on the periphery of the epiphysial plate of cartilage and sends branches deeply to the bony epiphysis as well as recurrent vessels to the actively growing metaphysial region (Fig. 6). The marked vascularity of this juxta-epiphysial area, compared with the adjacent diaphysial bone, is obvious in injected specimens (Fig. 7). Harris (1933) pointed out that these metaphysial vessels terminate in large tortuous loops as end-arteries—in contrast to the epiphysial vessels, which anastomose freely. The retinacula in the growing child are well developed, but they are shorter and more firmly attached to the periosteum of the neck than in the adult hip-joint.

Freshly injected specimens demonstrate that the greatest concentration of intra-osseous blood vessels is in the region of Babcock's triangle. This triangle appears in antero-posterior skiagrams as an area sparse in trabecular bone situated inferiorly to the femoral head. An equally obvious triangle, often obscured by the acetabular rim, is seen superiorly at the junction of head and neck (Fig. 8). In fact, the whole base of the head is surrounded by this triangular tunnel, which is utilized by blood vessels to supply and drain the head of the femur. The afferent arteries to this vascular circle can be seen entering the subcapital bony foramina (Fig. 2).

Conclusions

The head and neck of the femur derive their significant blood supply from the pericapsular anastomosis at the base of the neck. The vessels which pierce the capsular attachment are subject to severe trauma and compression in dislocations of the hip-joint and in basal fractures of the femoral neck. These factors, together with pressure from local haemorrhage, jeopardize the vascular channels of the head of the bone.

Basal fractures of the neck of the femur in childhood are frequently complicated by avascular necrosis of the head. The more firm attachment of the synovial membrane to the periosteum of the neck is suggested as an aetiological component for this complication. While the epiphysial plate of cartilage is present the head of the femur depends on the retinacular vessels for its nutrition, as the consensus of reliable opinion is that the vessels in the ligamentum teres are immaterial for the vitality of the head.

Babcock's triangle is a common site for the early manifestations of bony tuberculosis of the hip-joint in children. This very vascular growing region, which is subject to repeated minor traumata and has a slow rate of blood flow, offers a well-protected culture bed for any circulating tubercle bacilli.

In transvesical adduction fractures of the femoral neck the superior and anterior retinacular vessels are always torn, whereas the vessels in the pedunculated postero-inferior retinaculum often escape actual rupture in their continuity but are badly distorted. This alteration of alignment and lumen, which slows or obstructs the local circulation and may lead to eventual thrombosis and avascular necrosis, is a strong argument in favour of early and gentle reduction of this fracture as advocated by recent writers.

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HYPOTHERMIA WITH AUTONOMIC BLOCK IN MAN

BY

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The reduction of oxygen consumption that accompanies a fall in body temperature and the possibilities that induced hypothermia opens up in the field of cardiac surgery and for the poor-risk patient have been the topics of numerous recent publications (Bigelow, Callaghan, and Hopps, 1950; Bigelow, Lindsay, Harrison, Gordon, and Greenwood, 1950; Churchill-Davidson *et al.*, 1953; Annotation, *Brit. J. Anaesth.*, 1953; *Lancet*, 1953). So obvious are the advantages of a state of affairs wherein the cellular oxygen requirements are markedly reduced that they need not be further discussed.

In the past local hypothermia had been produced for a variety of purposes—for example, the relief of pain (Bell, 1812) and the treatment of carcinoma (Arnott, 1851)—but it was not until 1936 that Smith and Fay first induced generalized hypothermia as a treatment for neoplasm (Smith and Fay, 1939). These workers appreciated the necessity of abolishing the body's normal reactions to cold—namely, shivering and vasoconstriction—to facilitate the cooling, and for this purpose they used deep narcosis. The increase in oxygen consumption produced by shivering had already been noted by Voit in 1878, and it was not until 1916, when Krogh eliminated this reaction by curarization, that a fall in oxygen consumption could be demonstrated at lowered body temperatures (Martin, 1930).

In 1948 McQuiston pointed out the possibility of applying the principle to cardiac surgery in hypoxaemic children, and published details of 25 cases (McQuiston, 1949).

The term "artificial hibernation" was originally used by Simpson (Simpson and Herring, 1905) and later by Smith and Fay (1939) to describe the state of induced generalized hypothermia. The recent reintroduction of the term is due in the main to the French workers Laborit and Huguenard (1951). They first studied the potentiation of anaesthesia by promethazine ("phenergan") and diethazine ("diparcol") (Laborit, 1950), and postulated that these drugs produced a partial block of the autonomic nervous system, thus diminishing the body's unfavourable reactions

to surgical trauma (Goldblat, 1951). These workers believe that in certain circumstances death may result from overaction of the autonomic nervous system in an attempt to maintain constant the body's internal environment (Laborit and Huguenard, 1951). Following this reasoning, they attempt to produce a block as complete as possible of the neurovegetative system at all levels, and it is this state which they refer to as "artificial hibernation." To achieve this result the "lytic cocktail" was devised, consisting of the above-mentioned drugs, together with pethidine and chlorpromazine ("largactil"). This latter is known to be a profound depressor of autonomic activity (Courvoisier *et al.*, 1953). A mild degree of hypothermia (34–35° C.) is used to reinforce the autonomic block (Huguenard, 1953).

The technique which we describe is a combination of induced hypothermia and "artificial hibernation," wherein the lowered body temperature is obtained by surface cooling, the lytic cocktail being employed to eliminate the body's normal responses to cold. Our object differs from that of the French workers in that we are primarily concerned with obtaining a reduction in body metabolism, the autonomic block being used only to facilitate the production of hypothermia.

The studies of Kayser and Hiebel (1952) have shown how inaccurate is the term artificial hibernation as applied to man. For this reason we prefer to call the technique "induced hypothermia with autonomic block." This paper is a report of 26 cases in which this technique has been used for major surgery.

Techniques

Production of Autonomic Block and Cooling

With a few minor exceptions the technique followed was the same in all cases. Premedication consisting of pethidine, 100 mg., and promethazine was given intramuscularly three to four hours pre-operatively. An intravenous infusion of normal saline or 5% dextrose was set up about one hour later as a vehicle for administration of the lytic cocktail. The constituents of this were the same for all cases—namely, chlorpromazine 50 mg. (2 ml.), pethidine 100 mg. (2 ml.), and promethazine 50 mg. (2 ml.). Because of the irritant effect of chlorpromazine the injection was made into the drip tubing as far away from the needle as possible. The initial injection was generally 2 ml., followed by supplements of 0.5 to 1 ml. at intervals of 15 to 20 minutes. Modifications in this dosage are discussed later.

Those patients who were not asleep before the beginning of the infusion became unconscious after the first or second dose of the cocktail. With one exception this had occurred within 30 minutes of administration of the first dose. The rapidity of onset of unconsciousness and its depth were a guide to the time to begin surface cooling. On an average this was one and a half hours before operation (range one to three hours). Ice-bags were first placed on the groin, and, in the absence of a response to this, the body was completely covered with ice. Shivering was looked for closely, and its occurrence taken as an indication for a further dose of the cocktail. In all cases cooling was continued until the patient was taken to the theatre. The amount of ice used in the early cases was much less than in later ones; this was partly due to attempts to follow the French methods and partly to caution with a new technique.

During the period of preparation, observations were made of B.P., pulse, and respiration every 15 minutes. Rectal temperatures were taken with a thermocouple which had been previously checked against a mercury clinical thermometer. These were recorded together with frequent observations on the condition of the patient, as assessed by colour, degree of consciousness, presence or absence of shivering, and the drugs administered.

Anaesthesia

The principles of this did not vary from those we would have used for similar cases under normal circumstances. Abdominal and thoracic cases received a sleep dose of barbiturate (if necessary), a relaxant, and nitrous oxide and oxygen (usually 2 litres of each), respiration being controlled or aided throughout. Endotracheal intubation by the oral route was carried out in every case. Induction in non-abdominal cases was with thiopentone and suxamethonium, intubation following topical application of 2% amethocaine or lignocaine to the larynx. Maintenance was with nitrous oxide and oxygen, with or without trichlorethylene or pethidine. There was an enormous variation in dosage from that which would be expected in normal cases, and this is discussed later. Replacement of blood loss was carried out as for normal cases. During the operation observations were made as for the period of cooling.

Rewarming

No attempts were made to hasten this process. On return to bed the patients were covered with a single sheet, and the appearance of shivering was an indication for the application of further covering. It was explained to the nursing staff that for the first 12 hours or so after operation they were to consider their patients to be poikilothermic and to treat them as such, removing blankets should a hyperpyrexia occur. In addition to the routine observations of temperature, B.P., etc., details were noted of post-operative analgesics and sedatives as regards both dosage and time of administration. Note was made of when the patients responded to their name, and this was later compared with the time when they themselves thought they wakened.

Special Investigations

Oxygen uptake was determined at various times during the cooling, the operation, or the rewarming in 12 cases, all of which maintained their spontaneous respiration comparatively undepressed. This was determined by using a Benedict–Roth spirometer. Pre-operative readings were carried out before the pethidine and promethazine were given. Observations during operation were limited to those cases in which, because of the depth of unconsciousness produced by the lytic cocktail and hypothermia, it was possible to avoid the use of an inhalational anaesthetic agent. It was felt that the presence of a gas such as nitrous oxide would unduly complicate the interpretation of results. Towards the end of the series routine analysis of the urine was carried out before and for several days after operation.

Observations

Table I gives a list of operations performed and details of patients.

TABLE I.—*Details of Patients and Operations*

Case No.	Sex	Age	Operation	Duration Hr.	Min.
1	M	24	Portocaval anastomosis	4	40
2	M	33	Oesophago-jejunostomy	4	20
3	M	25	Devascularization of stomach and oesophagus	4	25
4	M	61	Total cystectomy	4	30
5	F	50	Pyelolithotomy	1	20
6	F	44	Partial gastrectomy	2	30
7	F	64	Radical mastectomy	2	0
8	M	60	Partial gastrectomy	2	20
9	F	24	Thyroidectomy	1	5
10	F	58	Splenectomy	2	5
11	M	55	Oesophago-jejunostomy	5	20
12	F	59	For intestinal obstruction		45
13	F	24	Exploration of femur	1	0
14	M	52	Colectomy	2	5
15	M	57	Devascularization of stomach and oesophagus	2	45
16	M	77	Bladder diverticulectomy	2	30
17	F	48	Mitral valvotomy		45
18	F	20	Thyroidectomy	1	0
19	F	60	Oesophago-gastrectomy	3	35
20	M	53	Laparotomy-colostomy		35
21	F	47	Oesophago-gastrectomy	4	10
22	M	53	Devascularization of oesophagus and gastrectomy	6	25
23	M	57	Splenectomy		35
24	F	73	Total cystectomy	4	0
25	F	60	Exploration of bile ducts	1	30
26	F	47	Total cystectomy	3	30

Respiratory System

Despite the fact that neither atropine nor hyoscine was given as premedication, no increase in secretions was noted during either cooling or operation in any case. The lytic cocktail invariably slowed the respiratory rate, but this was accompanied by a slight increase in tidal volume. At the temperatures which we reached before operation (36° to 27.4° C.) there were no instances of alarming decreases in respiratory rate, 8 to 10 a minute being the average when the patients were taken to the theatre. These changes were reversed during rewarming. Diminished sensitivity of the larynx, as might be expected from the doses of pethidine used, was very marked. Intubation was carried out in six cases at the end of the cooling, without any barbiturate, and in no instance was there a very pronounced reaction from the patient. This laryngeal insensibility was a disadvantage in one case.

Case 20.—The operation was laparotomy for intestinal obstruction. During cooling, moist sounds in the chest were heard and pulmonary oedema was diagnosed. On closer examination silent regurgitation of gastric contents was detected. Tracheal suction was carried out and the passage of an oesophageal tube revealed a full stomach.

Cardiovascular System

Average blood-pressure changes during the cooling and the operation are shown in Table II, and the suggested principal factors causing the pressure falls during operation in Table III. Hypotension of varying degrees occurred during establishment of the autonomic block in every case and during most of the operations. Pressure falls following the first 2 ml. of the cocktail varied enormously from patient to patient and were unpredictable. This led us to introduce a test dose of 1 ml. in poor-risk cases, subsequent doses depending on the B.P. response to the first injection. The fall in B.P. which followed administration of the lytic cocktail had a large postural element in each case, and could be reduced, but not abolished, by raising the foot of the bed (Fig. 1). The rise in pressure that was noted in one case during operation was attributed to the Trendelenburg position, which was used during the whole procedure.

TABLE II.—*Blood-pressure Changes During Cooling and Operation*

During cooling and autonomic block:	
Fall	26 cases
During operation:	
No change	5 „
Rise	1 case
Fall	20 cases
Actual readings:	
Average fall during cooling	45/30
„ pre-op. B.P.	110/80
„ during operation	80/55
„ fall	30/25
„ minimal B.P. during operation	60/30
„ maximal fall	50/50

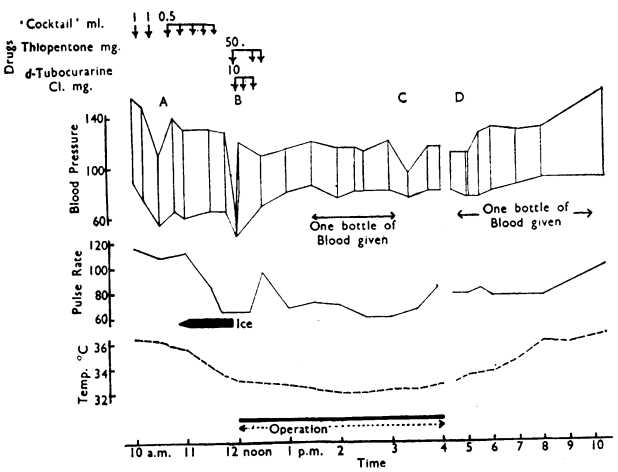

FIG. 1.—B.P., pulse, and temperature changes occurring before, during, and after operation in Case 24. Postural falls in pressure occurred as follows: A=after first dose of cocktail with patient sitting up; B=removal from bed to theatre; C=when head of table was raised. A and B were treated by the head-down position and C recovered spontaneously. D=patient back in bed.

From Table II it can be seen that pulse pressure is affected little during the operation, even at the lowest pressures. This might be expected because of vasodilatation due to chlorpromazine. A prominent feature throughout the series was the extreme sensitivity of the B.P. to haemorrhage. Quite significant falls occurred after even slight loss, the pulse remaining almost unchanged. This is due to loss of compensatory mechanisms.

TABLE III.—*Suggested Principal Factors Causing Fall of B.P. During Operation*

Posture	11	Hypothermia	2
Blood loss	5	Barbiturates	1

In the absence of shivering the pulse rate fell by 10 to 20 beats a minute during the establishment of the autonomic block and cooling. Shivering invariably raised the rate by 20 to 40 a minute. The changes were very variable during operation, but on the whole there was little variation from that produced by the cooling. The average rate during operation was 80 a minute, values ranging from 55 to 104.

Cardiac irregularities were detected in three cases during cooling. In two instances auricular extrasystoles appeared at the lower temperatures, but disappeared spontaneously during the rewarming. These irregularities were of less importance than the auricular and ventricular fibrillation occurring in the following two cases.

Case 21.—A marked fall in B.P. followed the test dose of cocktail. Cooling was easily achieved, the temperature dropping rapidly to 32° C. At this stage cardiac irregularities were detected. Following thoracotomy the temperature fell to 28° C. and the pulse was grossly irregular, remaining so throughout the operation. A post-operative E.C.G. confirmed the presence of auricular fibrillation. Recovery was slow, and 34 hours post-operatively, when the temperature had reached 32.5° C., normal sinus rhythm reappeared.

Case 17.—A woman aged 48 was admitted for mitral valvotomy. She had a grade 3+ condition of her valve and was frequently in failure. She was orthopnoeic, cyanosed, and had a greatly enlarged right ventricle with signs of basal congestion. She was considered an extremely grave risk by the physicians, but, in view of her complete invalidism and hopeless prognosis, exploration was thought to be justified. After 4 ml. of cocktail the temperature dropped to 32.5° C. Her condition was described as much improved and she had become pink in colour. Her B.P. had dropped from 110/60 to 80/50 and her pulse rate from 80 to 48. When her temperature had reached 31.8° C. ice-bags were applied, and an hour later the temperature was 30.7° C. but her B.P. suddenly became unrecordable. Her pulse rate was 60. Elevation of the foot of the bed restored the B.P. to 85 systolic. Unfortunately, there was a delay in beginning the operation owing to the previous case taking much longer than had been estimated, and her temperature was allowed to fall to 28.4° C. before she was taken to theatre. This was 4 hours 20 minutes after the initial dose of cocktail and three hours after the first application of ice. Her systolic B.P. was 95 and she had had 9 ml. of cocktail. Her pulse was satisfactory, and she was pink. On opening the chest her temperature fell nearly 3°, to 25.7° C., and her heart rate slowed to 50. The surgeon estimated her systolic pressure at 100 and her pulmonary arterial pressure at 60 mm. Hg. The heart seemed to have shrunk to less than its normal size and did not fill the pericardial sac. The ventricular beat seemed weak and rather ineffective. On dilatation of the valve ventricular fibrillation began and was arrested after five and a half minutes by application of an electrical defibrillator (110 V. in 0.1-second impulses). Normal beat was resumed, but fibrillation recurred during suture of the auricular appendage. All efforts to restore this heart failed.

In the majority of cases the B.P. and pulse returned to normal as the temperature rose. In a few patients, however, a secondary fall in B.P. occurred about one to two hours post-operatively This always responded to posture and small transfusions.

Temperature Changes

On the average a drop of 0.5° C. was obtained during the administration of the cocktail before the application of ice. During the period of cooling before operation a further average drop of 3.4° C. (1 to 10° C.) occurred. Fig. 2 shows temperatures existing during operation in 24 cases. Perhaps the most significant observation was the fall in temperature of about 2° C. occurring in all cases in which the chest was opened. This did not take place after abdominal section.

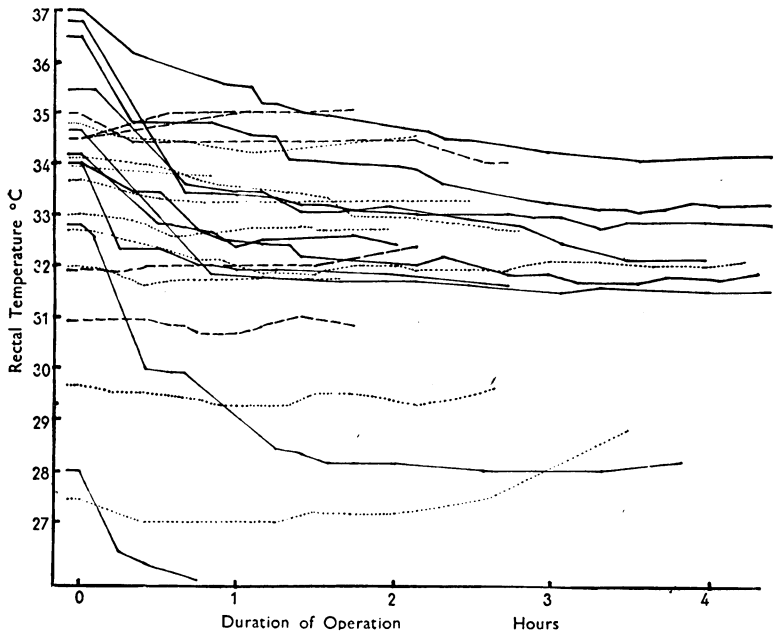

FIG. 2.—Temperatures recorded during operation. Continuous lines=thoracic and abdomino-thoracic cases. Dotted lines=abdominal cases. Broken lines=non-abdominal cases.

The majority of patients had regained their normal temperatures in about 10 hours after operation, though one case already reported (Case 21) remained subnormal for 48 hours.

Bleeding

This varied considerably from case to case, and apparently bore little relation to the existing B.P. In 14 cases there was a marked postural ischaemia; in four cases, despite suitable posturing, bleeding was much increased, while in the remaining eight the amount of bleeding appeared normal. One case of reactionary haemorrhage occurred. This took place 16 hours post-operatively and was of moderate severity.

Excessive bleeding in the absence of any rise in arterial B.P. may be attributable to a rise in venous pressure. This may be a factor at lowered temperatures, when, as has been shown by Bigelow, Lindsay, and Greenwood (1950), venous pressure is likely to rise.

Case 7.—This patient showed excessive bleeding during radical mastectomy; the degree of hypothermia was only moderate (34° C.), but may have been sufficient to exacerbate an already raised venous pressure due to a failing myocardium.

Apart from any consideration of the B.P., bleeding at low temperatures may be due to some interference either with the ability of vessels to retract or with the formation and contraction of blood clot. This may have applied to Case 22.

Case 22.—This man, undergoing splenectomy and transection of the stomach for portal hypertension, bled excessively throughout the operation, which, largely for this reason, lasted six and a half hours. During most of the time his B.P. ranged from 50 to 90 systolic and 40 to 65 diastolic. All efforts to arrest the oozing in the portal bed were unsuccessful, and when the patient was returned to bed his rectal temperature was 31.5° C. and blood was pouring out of his under-water drain almost as fast as it was transfused. Owing to the large replacement of blood, adequate amounts of calcium gluconate and vitamins C and K were added to the transfusions, but only when the temperature reached 32° C. did the haemorrhage stop. At this time he had received 19 pints (10.8 litres) of blood; the measured loss corresponded. Altogether during and following his operation this man received a total of 21 pints (11.9 litres) to compensate for his loss, and he died 48 hours later, apparently from a transfusion reaction. Necropsy was not performed. At operation the liver was about half the normal size and an advanced degree of cirrhosis was present. The pathologist expressed the opinion that it was remarkable how he had managed to carry on with so little liver tissue. There seemed little doubt that this man's prothrombin level was so low that the clotting of his blood even with slight degrees of hypothermia was seriously affected.

Anaesthesia

The total dosage of all drugs given in thoracic and abdominal cases is shown in Table IV. From this it is immediately apparent that there is a striking reduction in the amount of thiopentone used. If those cases with liver damage are excluded a similar, though less marked, reduction in the amount of D-tubocurarine chloride used is evident. In cases with liver damage comparatively large doses of D-tubocurarine chloride were required (Table V), showing that the observation of Dundee and Gray (1953) in this respect holds true in hypothermic patients. Reversal of the effects of the D-tubocurarine chloride by neostigmine at the end of operation was as in normal cases (Fig. 3). Where suxamethonium was used for intubation its duration of action was normal.

TABLE IV.—*Total Dosage of Anaesthetic Agents in 22 Abdominal and Thoracic Cases*

Thiopentone	No. of Cases	D-tubocurarine Chloride	No. of Cases*
Nil	7	Up to 20 mg.	6
Up to 100 mg.	7	20–30 mg.	5
100–200 mg.	4	30–40 mg.	4
250 mg.+	4	40 mg.+	1
Pethidine	**No. of Cases**	**Others**	**No. of Cases**
Nil	18	Nil	15
Up to 50 mg.	3	Lytic cocktail	5
50 mg.+	1	Chlorpromazine	2

* Excluding five cases with known liver damage. One case received gallamine triethiodide as relaxant.

TABLE V.—*Comparison of Amount of D-tubocurarine Chloride Required by Patients with Abnormal Liver Function, and Those in Whom There Was no Reason to Suspect Liver Damage*

Liver Function	No. of Cases	Average Duration of Operation (Minutes)	Average Dose of D-tubocurarine Chloride (mg.)
Normal	16	160 (35–320)	26 (5–48)
Abnormal	5	244 (145–385)	58 (50–75)

Post-operative Period

One formed the impression that the general condition of these cases was better than normal after operation. There was a reduction in the amounts of analgesics needed in the first two post-operative days, compared with normal requirements (Table VI). Seven subjects received no sedative or analgesic drug from the end of operation to their discharge from hospital. Although, on the average, patients responded to their names about three and a half hours after opera-

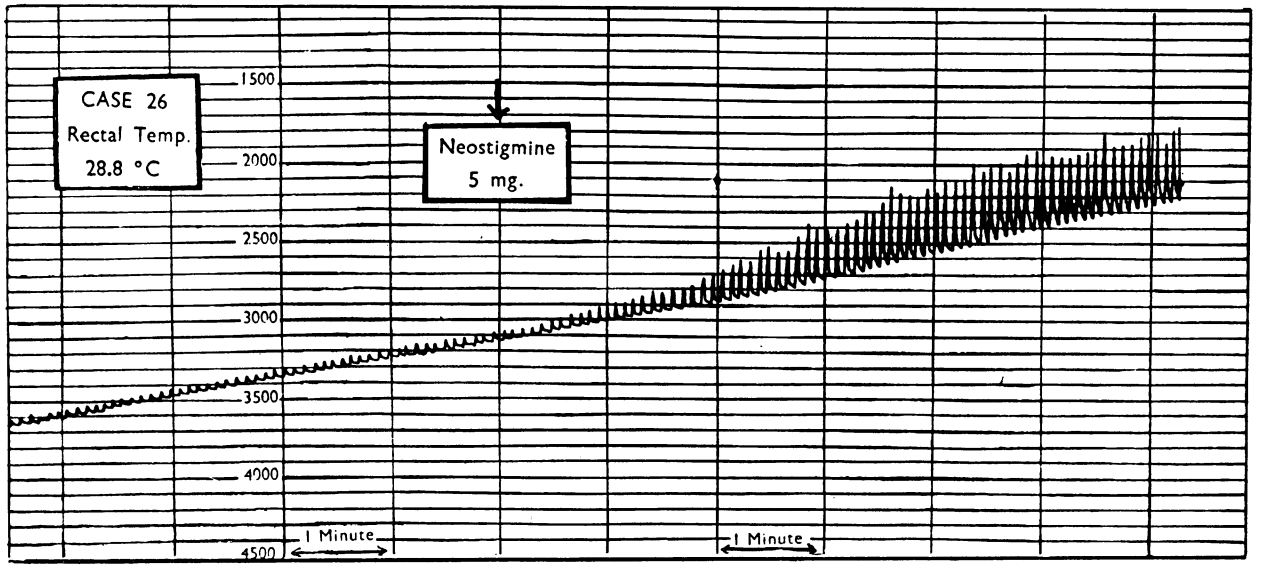

FIG. 3.—Spirometry tracing showing satisfactory reversal of gallamine triethiodide by neostigmine. The last dose of relaxant (40 mg.) had been given 30 minutes before the neostigmine.

tion, yet they themselves think that they did not waken for a further seven hours. This time is significant, as it coincides with the time of administration of the first dose of analgesic.

The complications occurring during this period are listed in Table VII. The three cases with respiratory trouble cleared up with orthodox treatment. The haematemesis which occurred in Case 24 was attributed to trauma during removal of the thermocouple from the oesophagus. It is worth mentioning that this was the only occasion on which rectal temperatures were not recorded, the reason being that excision of the rectum was contemplated in addition to removal of the bladder. Paralytic ileus, which eventually proved fatal in Case 4, was attributable to the surgical procedure, although one cannot dismiss the possibility that autonomic block played some part.

The only hyperpyrexia that was noted occurred in our first case, which is worthy of mention.

Case 1.—The patient was returned from the theatre with a temperature of 34° C. and instructions were given that readings should be taken every 15 minutes. Two hours later a nurse, who was not conversant with the thermocouple, took the oral temperature and found that it was not recordable by a clinical thermometer. She immediately covered the patient with a heat cradle, and by the time the next reading was due the temperature was 39° C. Once the source of heat was removed the temperature gradually returned to normal.

Nursing staff who have been trained to conserve body heat on all occasions find it difficult to get used to patients lying in bed after operation covered only by a sheet. When the lessons from this case were pointed out to them we had no more trouble.

TABLE VI.—*Post-operative Analgesics (22 Cases). All Analgesics Recorded as Equipotent Doses of Pethidine (10 mg. Morphine or 8 mg. Methadone Considered Equal to 100 mg. Pethidine)*

A. Average dosage and time of administration of first dose from end of operation, compared with average requirements of 27 unselected cases, having orthodox anaesthesia and undergoing similar operations

	First Dose		Total Dosage (mg.)	
	Time from End of Operation	mg.	First 24 Hrs.	Second 24 Hrs.
Hypothermia	10·5 hrs.	60	100	140
Orthodox anaesthesia..	3·25 „	130	340	250

B. Analysis of dosage in cases of hypothermia

	No. of Cases	
	First 24 Hours	Second 24 Hours
Pethidine:		
Nil	7	7
100 mg.	12	6
200 „	1	6
300+ „	3	4
Promethazine 50 mg. ..	3	1
Phenobarbitone 200 mg.	1	1

TABLE VII.—*Post-operative Complications (Excluding Ketosis, as This was not Looked for in Every Case)*

	No. of Cases
First 48 hours:	
Vomiting	3
Restlessness	3
Lobar collapse	2
Pneumonia	1
Continued haemorrhage	1
Reactionary „	1
Prolonged hypotension	1
Sudden B.P. fall	1
Paralytic ileus	1
Haematemesis	1
Hyperpyrexia	1
Later:	
Paralytic ileus	1
Pulmonary embolism	1

Deaths

Five deaths occurred in this series of cases (Table VIII). We feel that in two cases (Cases 17 and 22) hypothermia may have contributed to the outcome. One cannot dismiss the possibility that the technique played some part in Cases 4 and 24, although this seems unlikely, since the deaths occurred on the 16th and 13th post-operative days respectively. It is difficult to say what parts surgery and hypothermia played in the following case.

TABLE VIII.—*Cause of Death*

Case No.	Time Post-operatively	Cause
4	16 days	Paralytic ileus and peritonitis
16	24 hours	Peritonitis and cardiac failure
17	On table	Ventricular fibrillation followed by asystole
22	48 hours	? Transfusion reaction
24	13 days	Pulmonary embolus

Case 16.—This patient suffered from senile dementia with incipient cardiac failure. The instability of this cardiovascular system was shown by a marked B.P. fall following the first dose of cocktail. Hypotension persisted throughout the cooling and for most of the operation, during which the temperature fell to 31.6° C., at which the pulse became irregular. There was a moderate reactionary haemorrhage 16 hours after operation. Rewarming was slow, but the patient's condition gradually improved.

Death occurred suddenly 24 hours post-operatively, when the temperature had reached 34° C. Necropsy revealed peritonitis and appearances suggestive of left ventricular failure.

Difficulties Encountered During Production of Autonomic Block and Hypothermia

In 17 cases there was no shivering or difficulties of any kind. Since this is a new technique the difficulties we encountered in the remaining nine cases are discussed in detail. These are listed in Table IX. Inability to control shivering

TABLE IX.—*Difficulties During Cooling*

	No. of Cases
Shivering difficult to control	4
Difficulty in producing hypothermia	3
Cardiac irregularities	3
Regurgitation	1
Restlessness	1
Uncontrollable B.P. fall	1

was generally accompanied by a slow fall in temperature. Resistance to the production of autonomic block occurred in the following four cases.

Cases 9 and 18.—Whereas the average dose of cocktail was 7 ml., in the presence of thyrotoxicosis we administered 12 and 13 ml. respectively to these patients, supplemented by intramuscular pethidine and diethazine in No. 18, and with thiopentone in both. Once the initial difficulties were surmounted, satisfactory cooling occurred in both.

Case 13.—This patient was a morphine addict, and even after 10 ml. of the cocktail the autonomic block was incomplete, and the rectal temperature never fell below 35.5° C.

Case 23.—Although this patient weighed only 9 st. 7 lb. (60 kg.) and had a Hb of 41% he proved the most difficult case encountered to date. The administration of 12 ml. of the cocktail over 100 minutes produced no effect on the B.P., and intense shivering was occurring. During the next hour 50 mg. of pethidine and 150 mg. of diethazine were given intramuscularly, the same doses together with 50 mg. of chlorpromazine and 50 mg. of thiopentone being given intravenously. This did not abolish shivering and the temperature fell to only 35° C. Shivering was then controlled by curarization, but in spite of the intensive application of ice the temperature fell by only 1° C. in 50 minutes.

This subject had been receiving nightly doses of butobarbitone (400–600 mg.) and promethazine twice daily for a month. These may have led to a tolerance to the drugs administered, but cannot explain the resistance to cooling when shivering had been completely abolished.

Further difficulties are illustrated in the following cases.

Case 11.—In this instance there was considerable doubt about the activity of the chlorpromazine. Despite the elimination of obvious shivering, presumably accomplished by the pethidine (Dundee *et al.*, 1953), the fall in temperature was negligible. This view is substantiated by the appearance of vasoconstriction following the application of ice.

Case 2.—A peculiar feature here was the almost complete absence of the usual narcotic effects of the cocktail despite a satisfactory response in all other respects. This deficiency was remedied by the use of 25-mg. doses of thiopentone.

Special Investigations

Oxygen Intake.—Fig. 4 includes all the observations that were made on 12 subjects, values being expressed as a reduction from the normal and temperatures as falls from 37° C. As can be seen, it was possible to follow only half the patients throughout the whole procedure, but isolated observations on the remainder were in agreement with these. The overall picture of falls in oxygen intake with hypothermia agrees with the findings of Bigelow, Lindsay, Harrison, Gordon, and Greenwood (1950) and Dundee, Scott, and Mesham (1953) in dogs. A constant observation not shown in Fig. 4 was a drop of 8–10% in oxygen intake that occurred after the cocktail, before the application of ice and drop in body temperature.

Urine Analysis.—This was done in eight cases only. A slight reddish coloration was present for three to four days in three cases. There was no haematuria on spectroscopic examination, and the colour is probably due to the breakdown products of the phenthiazine derivatives, as two of these cases received promethazine as a sedative in the post-operative period.

The presence of ketone bodies could be detected in three cases after cooling and post-operatively, although clinically and biochemically there was no evidence of acidosis. In one case this persisted until the fifth post-operative day, but

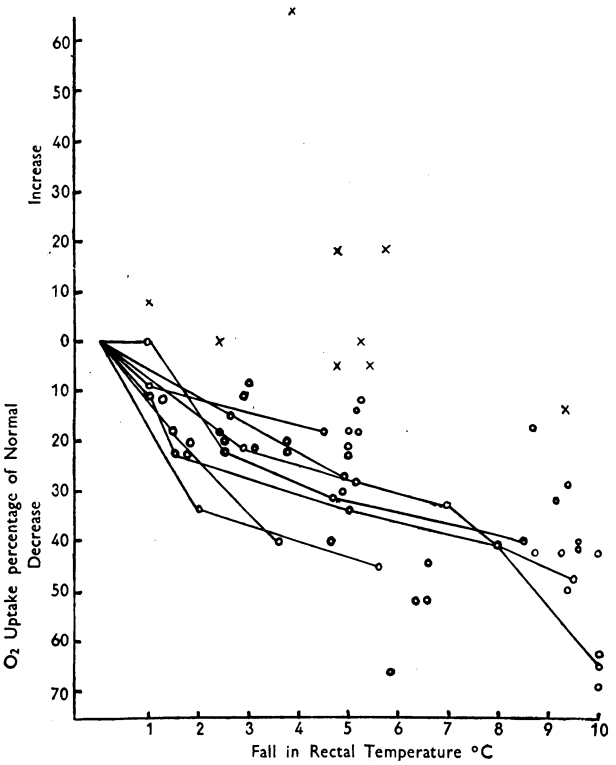

FIG. 4.—Relationship of oxygen intake (expressed as a percentage of normal) to fall in rectal temperature (expressed as variation from 37° C.). o——o = observations made in the absence of shivering. Those joined together are serial readings during cooling and operation. O indicates isolated observations at any period of the procedure. X = readings taken when the patient was shivering.

cleared up after 48 hours in the others. Glycosuria was detected in two cases; in both instances the patient had received dextrose intravenously when the temperature was 30–32° C. This cleared up when the temperature was raised. Depression of the glycogenic activity of the liver at low temperatures is a possible explanation of this phenomenon.

Discussion

This paper has been written with the purpose of drawing attention to some dangers of hypothermic techniques. All the patients in this series stood to benefit from the production of hypothermia. Some who were rejected for anaesthesia by orthodox techniques made a highly successful recovery. The high mortality occurred in the group of patients who were seriously ill and who were grave operative risks by any standards. It is considered that in this group the method gave the best chance of survival. Our purpose in observing this series has been to obtain a preliminary assessment of the method of producing hypothermia by external cooling combined with autonomic block. It is useful to know that reduction of temperature can be satisfactorily and easily produced in patients, without the necessity for an extracorporeal arteriovenous shunt (Delorme, 1952), a procedure which it seems to us carries its own risks. It is apparent from our experience that any degree of hypothermia can be obtained by this technique. It is a method, moreover, which avoids an undesirable depth of anaesthesia or prolonged periods of respiratory arrest due to curarization, which would otherwise be necessary to avoid shivering.

Our experience both in this series and in animal experiments has led us to two conclusions. First, that the danger

of serious cardiac irregularity at temperatures lower than 28° C. is real, and is particularly imminent if cardiac manipulation is required. Secondly, the difference in oxygen consumption between a patient at 28° C. and one at 25° C. is insufficient, in the present state of our knowledge, to warrant the extra risks involved by proceeding to lower temperatures.

The reduction in bleeding during hypothermia has not always been as marked as was expected. At low temperatures the prolongation of the clotting time and/or bleeding time has on occasion been a source of embarrassment. We are proceeding to investigate the effect of different prothrombin levels on the clotting time of blood at different temperatures. We feel that, before hypothermia is employed for cases of portal hypertension with liver cirrhosis, the clotting-time of the patient's plasma should be estimated at various temperatures so that the critical level may be ascertained.

It seems to us reasonable also that hypothermia might be an added risk in patients whose myocardium is damaged (see Cases 7, 17, and 21). Initial heart–lung experiments which we have performed in the dog have confirmed the findings of Knowlton and Starling (1912) that the myocardium is affected at lower temperatures, and suggest that the Starling response to stretching the myocardial fibres is less efficient. It is therefore questionable whether any degree of hypothermia—say below 30° C.—is justifiable in cases with a damaged myocardium until further work has been carried out to elucidate this problem.

A weakness in this technique has been the comparative lack of control of the patient's temperature. If the hypothermia becomes too intense, as when allowance has not been made for the 2–3° C. fall which always occurs on opening the chest, there is no adequate means of correcting the situation. This is no fault of the autonomic blockade, but is a technical problem, to which we are giving consideration.

The indications for hypothermia would seem to be:

1. When a degree of hypotension is required to control haemorrhage either for patients in whom large blood loss is expected, or in whom even a small blood loss will embarrass the work of the surgeon. We have never been convinced of the safety of hypotensive techniques in which the supply of blood carrying oxygen to the tissues is reduced without any effort being made to reduce to some extent the oxygen demands.

2. In patients with a severe degree of anaemia which cannot be corrected before operation. This series has included four cases of oesophageal varices in which there was a marked degree of anaemia and which responded to transfusion only by further haematemesis. The combination of anaemia with the hypotension which is so helpful to the surgeon in these cases is justifiable only if the oxygen demands of the patient are reduced by hypothermia. This is well illustrated by Case 3 (Fig. 5), when a patient whose Hb was only 50% was maintained for 4½ hours at a B.P. averaging 60/30 (minimum 35/25). His recovery was complete and uneventful.

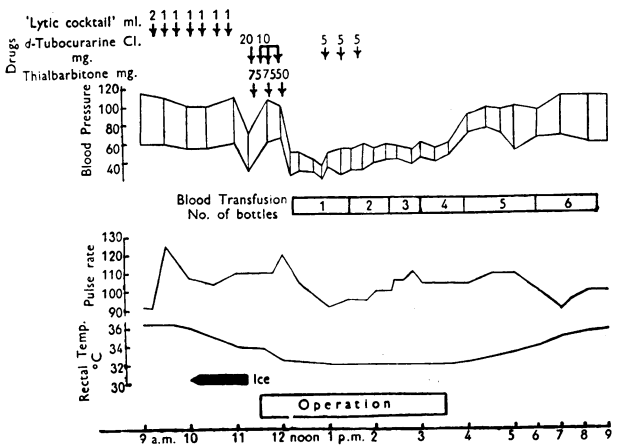

FIG. 5.—B.P., pulse rate, and temperature recordings in Case 3, showing the degree of hypotension that was present for most of the operation.

3. In operations on the heart and great vessels in which it may be necessary to cut off the cerebral circulation for a period of time. In this regard a startling observation was made in Case 17. For 17 minutes, at 25° C., after all possibility of cerebral circulation had ceased, this patient's respiratory centre continued to function, as evidenced by quite normal respiratory movements.

4. In thyrotoxicosis which cannot be controlled by medical treatment. One case in this series had been presented for operation on two previous occasions and returned to the ward because of an uncontrollable pulse rate of 160 a minute. Induction of hypothermia reduced this to 80 a minute, considerably improved the general condition of the patient, and enabled an operation to be performed, which was followed by an uneventful recovery.

5. Presumably in neurosurgery there will be indications for this technique, but up to the present we have had no experience with this application.

6. In certain therapeutic indications such as hyperpyrexia occurring in pituitary disorders or post-operatively in children, and in thyroid crises.

Summary

The history of the production of hypothermia in man is reviewed, and a method described for its production in man with the help of block of the autonomic nervous system.

The use of this technique in 26 cases undergoing operation is described.

Observations are recorded of the changes that occurred in the respiratory system, the cardiovascular system, and the body temperature, with the amount of bleeding.

Dosages of anaesthetic agents and post-operative analgesics are discussed, as are post-operative complications and deaths that occurred.

The troubles that we encountered during the production of the autonomic block and cooling have received special mention.

Our findings concerning the relationship of oxygen intake to temperature, and the presence of abnormal constituents in the urine following this technique are reported.

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