Section of Anæsthetics

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[*April* 1, 1955]

DISCUSSION ON INDUCED HYPOTHERMIA

Dr. C. F. Scurr: Tissue anoxia due to circulatory arrest leads unless rapidly relieved to cellular death. The duration of anoxia necessary to kill cells varies: in the case of highly developed cells in the human brain a period of two to four minutes circulatory arrest leads inevitably under usual conditions to permanent cerebral damage. As a result, in cases of cardiac arrest the heart may be restarted by cardiac massage, but often because of delay, brain damage has occurred so that the patient never recovers consciousness. (In this connexion I am reminded that in one "cardiac-massage minded" centre across the water a framed notice hangs in the operating theatre which says in bold black letters, "As time flies, the neurone dies".)

If the body temperature be lowered cellular metabolism and oxygen demand are reduced, so that cells survive anoxia for longer periods. It has been shown in animal experiments that at a body temperature below 25° C., the circulation to the brain may be completely cut off for twenty minutes, and yet complete recovery may occur, there being no physiological or histological evidence of cerebral damage. It is of interest to note that at these low temperatures coronary occlusion was rapidly fatal, a reversal of the normal finding that the heart withstands anoxia better than the brain.

It follows from these observations that hypothermia might permit the performance of certain operations which would be impossible at normal temperatures owing to cellular death from anoxia.

Conditions in which a hypothermic technique might be valuable are:

(1) Intracardiac procedures requiring an open heart, with temporary occlusion of the venæ cavæ and *cessation of the circulation*—for example, repair of certain cardiac septal defects.

(2) Transposition of the great vessels—in which the operative treatment necessitates *circulatory occlusion.* The simple clamp and crossover operation has now been abandoned, however, owing to coronary artery anomalies.

(3) Operations for congenital cyanotic heart disease—although *circulatory arrest* is not as a rule *essential* in these cases, hypothermia reduces the oxygen demand and anæsthetic requirements: the safety margin may thereby be increased. The indication for hypothermia here is a relative one, the temperature need not be reduced to a very low level. Most of our series are in this group; I believe a number of cases employing a similar method have been operated on in d'Abreu's department at Birmingham (Inglis *et al.*, 1954).

(4) In intracranial procedures involving temporary arrest of the circulation to part of the brain. In this connexion it has been suggested that hypothermia might increase the margin of safety in induced hypotension for neurosurgical procedures.

(5) In certain abdominal and thoracic operations; for example, for aortic aneurysms, involving excision and replacement by graft or plastic tube. Under hypothermic conditions the kidneys and spinal cord can tolerate the period of circulatory arrest necessitated by the operation. Professor C. G. Rob has a very interesting series of such cases, the anæsthetic management of which has been described recently by Cheatle (at the Medical Society of London).

THE ADVANTAGES ACCRUING FROM THE HYPOTHERMIC STATE

(1) *Oxygen requirements are reduced.*—Provided shivering is prevented the oxygen consumption falls in a linear fashion with the reduction of body temperature. At 30° C. oxygen requirements are reduced to 55%, and at this level the B.P. is usually well maintained. At 20° C. oxygen consumption is approximately 15% of normal (Bigelow *et al.*, 1954). Lynn and others (1954) suggest that in dogs it would be approximately zero at 10° C.

(2) *Cardiac activity is reduced*—aerobic energy uptake and, to a greater degree, left ventricular work both decline (Edwards *et al.*, 1954).

(3) *Coagulation time is increased.—In vitro* at 20° C. it is approximately trebled (Macfarlane, 1948). Under hypothermic operation conditions there is a fall in the platelets which may seriously retard clotting and lead to post-operative hæmorrhage. To some extent these antithrombotic effects may be beneficial, as thrombosis is a well-known complication in certain types of cardiovascular surgery.

(4) *Anæsthetic requirements are reduced.*—It is reported that below 27° C. consciousness is lost, the hypothermia of itself inducing the anæsthetic state.

(5) *Harmful bacterial and enzyme activity is suspended.*

Dangers of the Method

(1) *The cold stress response* (Delorme, 1953) as manifested by endocrine activity and shivering; the latter gives rise to complexes which can be observed on the electrocardiographic record. At the start of cooling there is increased sympathetic action with associated release of adrenaline. Vasoconstriction results and tends to retard heat loss. There is increased production of ACTH and thyrotrophic hormone which tends to raise heat production.

The muscular activity involved in shivering leads to an increase in heat production and oxygen demand; this process can for a time prevent a fall in temperature in the initial stages of the cooling procedure. Shivering can and should be prevented by anæsthetics, by curarizing drugs and by chlorpromazine. This last agent is particularly effective in helping to lower body temperature, which it does by decreasing heat production in voluntary muscle, by producing vasodilatation and promoting heat loss, and possibly by an effect on the temperature-regulating centre. In addition to these effects chlorpromazine has a very wide spectrum of pharmacological activity, but it is not an essential agent in the hypothermic technique and has not, indeed, been used in the present series of cases.

(2) *Cold tissue injury.*—In methods involving surface cooling this can be prevented by avoiding extreme degrees of cold. It is unfortunate that infants may have a predilection for subcutaneous fat necrosis under these conditions because infant fat has a relatively higher melting point (Collins *et al.*, 1953).

(3) *Changes in the blood.*—(*a*) *Increased viscosity:* This occurs in the first place as a simple physical effect of cooling the blood, and secondly as a result of the hæmoconcentration which accompanies the induction of hypothermia. In cases of congenital cyanotic heart disease the blood is already very viscous (for example, the hæmoglobin may be 140%) and this effect is especially undesirable. Coupled with the vasoconstriction which accompanies cooling the increased blood viscosity leads to elevation in the peripheral circulatory resistance, so adding to the work of the heart.

(*b*) *A fall in the platelets:* This is especially marked in methods involving extracorporeal circulation of the blood. This effect may lead to serious post-operative hæmorrhage.

(*c*) *A fall in blood pH* (Fleming, 1954)*:* This is due to an increase in the amount of dissolved carbon dioxide (Cranston *et al.*, 1955). The solubility of carbon dioxide in blood increases as the temperature falls and this effect will tend to cause carbon dioxide retention. More important, however, is the fact that respiratory activity diminishes as the temperature falls. This fall in pH may be in part the cause of ventricular fibrillation, but it has possibly some slight compensatory advantage in promoting the dissociation of oxyhæmoglobin. This gaseous acidosis can be prevented completely by hyperventilation, which should therefore always be performed in these cases. Under conditions of hyperventilation the blood pressure (and so, presumably, coronary flow) is better maintained as the temperature falls, and experimentally survival to lower temperatures is possible before cardiac arrest occurs (Lynn *et al.*, 1954).

(*d*) The oxyhæmoglobin dissociation curve is shifted to the left: in other words, oxyhæmoglobin only dissociates at relatively lower partial pressures so that theoretically it is harder for the tissues to obtain oxygen; this is offset by reduced tissue oxygen demand and mitigated by any fall in pH. Experimentally the arteriovenous oxygen difference has been found to be within normal limits in cooled animals, and certain studies appear to show that the tissues can effectively utilize oxygen from the blood (Bigelow *et al.*, 1950*b*; Penrod, 1951).

(4) *The elimination of non-volatile anæsthetic agents* is greatly retarded; this is presumably due to the reduction in metabolism. As already noted, anæsthetic requirements are also reduced in the hypothermic state. Consciousness is lost at about 27° C., and respiratory arrest may occur at about 23°–25° C. Barbiturates and other respiratory depressants will predispose to respiratory arrest at relatively higher temperature levels. Because of these considerations drugs such as thiopentone and pethidine should be used in minute doses and post-operative sedatives should be given in reduced dosage. The metabolism of glucose is also retarded during hypothermia; Wynn (1954) has reported a blood sugar level of over 1,000 mg. per 100 ml. during hypothermic anæsthesia. For this reason a glucose solution should not be used for the intravenous drip.

(5) *The cardiovascular system.*—As the body temperature falls the heart-rate, cardiac output and blood pressure all decrease. For example, in dogs at 20° C. the cardiac output may be only 15% of normal (Bigelow *et al.*, 1950*a*). In proportion the blood pressure falls less than the other two factors. The mean arterial pressure is the product of the cardiac

output and the peripheral resistance, and although the cardiac output falls with the temperature, the peripheral resistance is increased, as already noted. As a result the reduction in blood pressure may be only slight until 30° C. or less, but it may then fall sharply as the temperature is reduced towards 25° C.

After an initial acceleration when cooling begins the heart-rate decreases in a regular and linear fashion as the temperature is reduced; at temperatures below 25° C. in man ventricular fibrillation may occur abruptly. The pulse shows a linear fall in rate, which is *not abolished* by vagal paralysis and is therefore presumed to be due to a direct effect upon the pacemaker (Burton and Edholm, 1955).

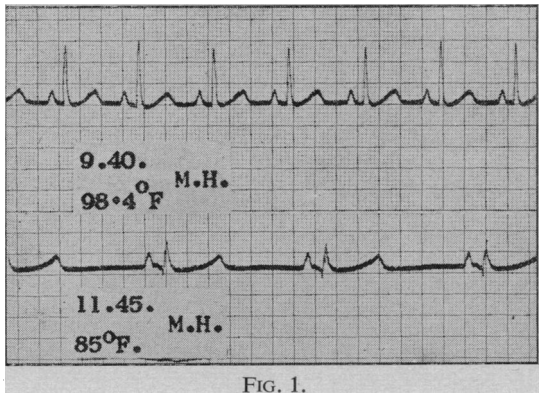

FIG. 1.

A bradycardia of 30 per minute is commonly encountered during operations under hypothermic conditions. At normal temperatures such slowing would be produced at the expense of an increase almost entirely in the diastolic phase. Under hypothermia the systolic phase is increased, in other words, the process of cardiac contraction is slow.

The electrocardiographic tracings shown in Fig. 1 (M. H.) demonstrate these changes: rate above is 100; rate below after cooling is 40.

As the temperature falls to critical levels cardiac irregularities may occur. Therefore electrocardiographic control is essential throughout these procedures. Cardiac irritability appears to be increased, and direct surgical stimuli may thus initiate ventricular fibrillation (Lynn *et al.*, 1954; Swan, 1954).

As further cooling takes place spontaneous ventricular fibrillation or cardiac standstill occurs and is the cause of death in progressive hypothermia. Dogs appear more prone to develop this condition than human beings. There is a great species variation in the temperature level at which this complication is encountered; in rats it may not happen until 12° C. (*Lancet*, 1954) but in adult man it is likely to occur around 25° C. Fortunately infants and young children are more resistant than adults in this respect, and it is in these young patients that the method at present finds its greatest applications. In those with acquired heart disease (for example, previous rheumatic disease) the liability to ventricular fibrillation is said to be increased and the method is probably contra-indicated in such patients (Bailey *et al.*, 1954).

The exact cause of ventricular fibrillation associated with hypothermia is imperfectly understood. Lange *et al.* (1949) blamed anoxia and reported amelioration with high oxygen tension. Some workers suggest that the fall in pH is responsible (Fleming, 1954) and it has been reported that hyperventilation has a protective effect (Lynn *et al.*, 1954; Fleming, 1954; Swan *et al.*, 1953*a*). On the other hand, there have been reports that a sudden fall in an abnormally high blood carbon dioxide can be a fibrillatory stimulus in the dog (Swan *et al.*, 1953*a*; Miller *et al.*, 1952). Ionic changes may be implicated but the evidence is contradictory—Sealy *et al.* (1954) suggested that post-hypercapnic ventricular fibrillation is due to increased serum potassium; improvement resulted from giving sodium and glucose. By contrast, Swan (Swan *et al.*, 1953*b*; Zeavin *et al.*, 1954) reported a *fall* in serum potassium during cooling and used potassium chloride to *arrest* fibrillation in the cold heart, pointing out that much intracellular potassium was lost from the myocardium during fibrillation (Sealy *et al.*, 1954). Recently Melrose (1955) reported an increase in the Ca/K ratio, and noted that injection of calcium ions produced a spike at the S wave of the electrocardiogram which was a precursor of ventricular fibrillation: conversely, Swan *et al.* (1953*a*) have used calcium chloride successfully to treat cardiac arrest in a hypothermic patient. Another suggested cause is that during hypothermia acetylcholine production is depressed, so that, the pacemaker losing its dominance, ectopic foci tend to arise. In keeping with this Swan (1954) reported that Prostigmine had a powerful protective effect, but he ascribed it to the potentiation of potassium flow across the cell membrane.

It is of interest to note that hibernating animals can be cooled to 4° C. (Burton and Edholm, 1955; Juvenelle, 1954), a temperature which, in the non-hibernator, would certainly lead to ventricular fibrillation, and, as stated above, infants withstand cooling much better than adults; on this evidence it seems likely that the main basic cause of fibrillation is connected with the qualities of inherent cardiac rhythmicity and conductivity. It is possible

that drugs may be developed—e.g. Benodaine (Cookson *et al.*, 1952; Sealy *et al.*, 1954)—which will prevent this complication arising.

Should ventricular fibrillation occur cardiac massage is undertaken, and when the heart muscle is seen to be well oxygenated, defibrillation is attempted by means of repeated brief electrical shocks of 1·5 to 2·0 amps. Brewin (1954) has recently advocated the injection of 1 ml. of 1 in 3,000 adrenaline into the ventricular cavity followed by massage; when cardiac tone improved a single 1/5 second electric shock of 1 amp. was given: after a short pause a co-ordinated beat reappeared.

Potassium and calcium solutions have also been used with success, Swan using potassium chloride to arrest fibrillation and following with calcium chloride to restart the heart. On occasion an artificial pacemaker may be useful.

It follows from this review of the hypothermic heart that continuous electrocardiographic control is an essential part of the technique. A sinus bradycardia with normal complexes has usually been seen in our cases. A bundle branch block may occur, A.V. block and ventricular extrasystoles are regarded as danger signals.

(6) *After-cooling.*—In the rewarming period "after-cooling" may occur; this is presumably due to opening up of the circulation in the very cold outer shell of the body (Burton and Edholm, 1955). Very cold blood from the periphery thus enters the main circulation. This further fall in central temperature may lead to ventricular fibrillation and death. It is obvious that the danger of this "after-drop" will be greater in methods involving surface cooling than in extracorporeal cooling of circulating blood. The fact that temperature gradients can be set up in the body raises the question as to the best site at which to assess the body temperature. Most workers have hitherto observed the *rectal* temperature by means of a thermocouple: it is obvious that the cardiac temperature is of the greatest importance and pharyngeal or œsophageal temperatures are probably more reliable guides to the degree of cooling. With regard to the rewarming process, experimental work shows that this should preferably be as rapid as possible, for example, by immersion in a hot bath or by means of an inductothermy apparatus.

(7) *Limit of time available.*—The studies on the heart imply that at the present time 25° C. is about the lowest temperature that can be safely induced. This factor limits the time available for circulatory arrest if anoxic sequelæ are to be avoided and Bigelow *et al.* (1954) have tabulated the period of circulatory interruption and the body temperature likely to be required for various operations. Bailey *et al.* (1954) have reported a case of complete circulatory interruption for twenty-two minutes at 21·6° C.; there was no evidence of cerebral damage thirty hours after the operation. Rob has described an operation under hypothermia in which occlusion of the thoracic aorta for two hours was followed by definite but minimal spinal cord damage.

Methods of Inducing Hypothermia

(1) *Surface cooling.*—The patient may be immersed in a bath of cold water or merely covered with wet sheets and cooling promoted by means of electric fans. At Westminster Hospital a special cooling blanket is used to cover the patient. Water at a temperature of 2–4° C. is circulated through tubes incorporated in the blanket (Scurr, 1954; Inglis *et al.*, 1954).

(2) *By circulating* blood from an artery (e.g. subclavian or femoral) through a long plastic tube immersed in a cooling mixture and returning the blood into a vein (saphenous) (Delorme, 1952). In other centres a vein-to-vein circulation incorporating a pump has been used (Ross, 1954).

Surface cooling methods are in general slower in action and more liable to the dangers of cold injury, of shivering and the development of thermal gradients, and overshoot; it is also said that metabolic changes and hæmoconcentration are more marked. This technique is, however, simple and avoids cannulating an artery with the attendant threat to a limb; in small infants the cannulation may be a difficult undertaking and in such cases surface cooling is obviously to be preferred.

Extracorporeal cooling is more rapid and also saves time by enabling cooling to proceed *pari passu* with the opening of the chest (or even after the chest has been entered). In this way the total duration of cooling is reduced and cardiac massage is immediately possible should it be necessary. However, this rapid cooling may increase the tendency to ventricular fibrillation; and, furthermore, platelet loss due to extracorporeal circulation may predispose to troublesome hæmorrhage.

Description of Technique

At Westminster Hospital hypothermic anæsthesia has been undertaken in a number of children for various operations as shown in Table I.

TABLE I.—OPERATIONS UNDER HYPOTHERMIC ANÆSTHESIA

Initials	Age years	Age months	Age weeks	Operation	Lowest temperature during operation °C.
J. M.	4	11		Blalock's	23
M. S.	2	2		Blalock's	24
A. M.	1	5		Blalock's	25
W. M.		6		Blalock's	24·5
D. G.		6		Thoracotomy—investigation—pulmonary valvotomy	23
M. D.	2	2		Division of large patent ductus (window)	23
L. P.	6			Thoracotomy—attempted pulmonary valvotomy	23
T. L.			6	Removal of œsophageal cyst	28
R. S.			7	Ligation of patent ductus	25·5
K. C.	3			Thoracotomy for pulmonary valvotomy	25·5
M. H.	9	4		Pulmonary valvotomy	29
G. C.	13			Pulmonary valvotomy	28

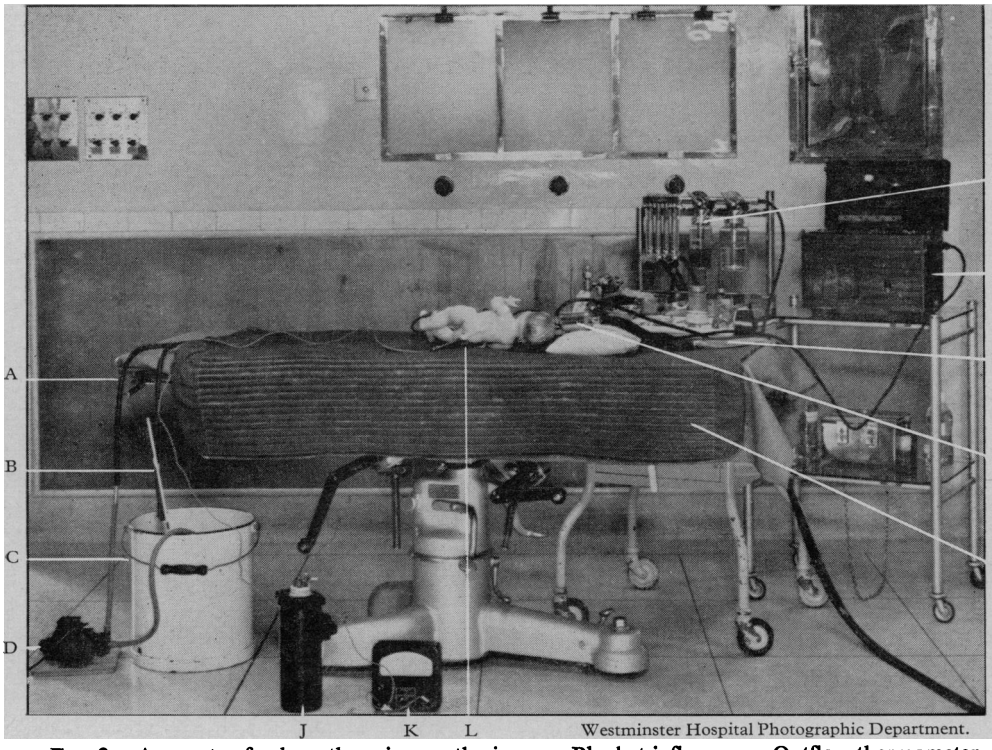

FIG. 2.—Apparatus for hypothermic anæsthesia. A.—Blanket inflow. B.—Outflow thermometer. C.—Reservoir. D.—Pump. E.—Anæsthetic machine. F.—ECG apparatus. G.—Breathing bag. H.—CO_2 absorber. I.—"Freezing blanket". J.—Zero junction. K.—Galvanometer, and L.—Rectal junction: thermocouple.

The apparatus used is as shown in Fig. 2, the child is anæsthetized and intubated in the usual way and then placed on the cooling blanket. The thermocouple and electrocardiographic leads are attached and an intravenous drip is set up. The blanket is then closed and the circulation of cooling fluid is continued. Light anæsthesia is maintained, e.g. with cyclopropane or ether and *oxygen*, or thiopentone gas and oxygen with relaxant so as to prevent shivering. The child's temperature falls as shown in Fig. 3 recording the course of a Blalock's operation in a child (J. M.) aged 5 years.

At 27° C. the anæsthetic may be discontinued and 100% oxygen used for the inflation. Shortly afterwards the operation is begun, relaxants being given as necessary during the thoracotomy.

The following points are noteworthy:

(1) The pulse falls in this instance to between 30 and 40 per minute. Continuous electro-

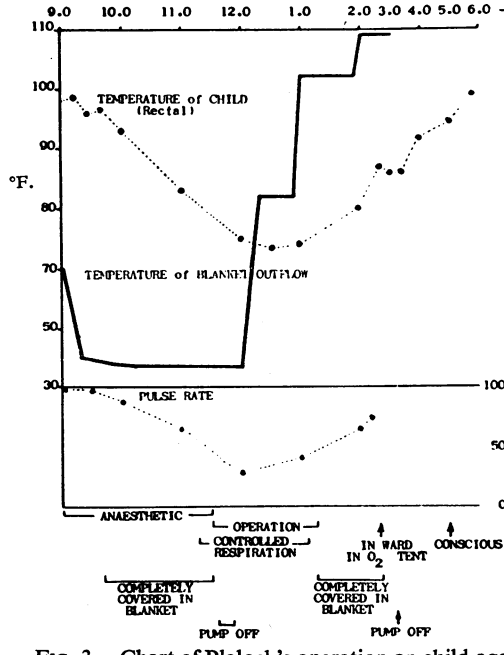

FIG. 3.—Chart of Blalock's operation on child aged 5.

cardiographic control was used and no serious cardiac abnormalities were seen despite the bradycardia which is probably less disturbing than the severe tachycardia common in these cases when conventional anæsthetic methods are used.

(2) At the start of cooling there is usually some apparent increase in respiratory activity. Later respiratory depression occurs—the temperature at onset of respiratory arrest varies, being higher in direct proportion to previous administration of respiratory depressant drugs. During emergence respiratory activity usually returns at a lower temperature level than that of apnœa during cooling. During cooling adequate controlled respiration should be started as soon as respiratory depression becomes evident. It is worth noting that the pupils are very widely dilated throughout the hypothermic period.

(3) Despite cessation of the pump and even substitution of warm fluid in the blanket the child's temperature continues to fall for half an hour or so. If this is not borne in mind the desired level may be overshot. This drift is worse after rapid cooling by immersion in a bath.

(4) These cyanotic babies as a rule become pinker when cooled. Estimations of arterial oxygen saturation confirm this observation as shown in Fig. 4. It is a great advantage to be able to inflate them with 100% oxygen. The reduced metabolic demand for oxygen must be balanced against reduced oxyhæmoglobin dissociation at low temperature. The balance is probably favourable to the method.

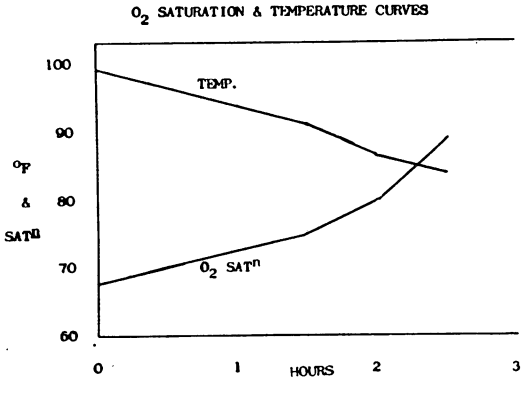

FIG. 4.—Case G. C., showing improvement in oxygen saturation with fall in temperature (arterial blood specimens estimated by hæmoreflector).

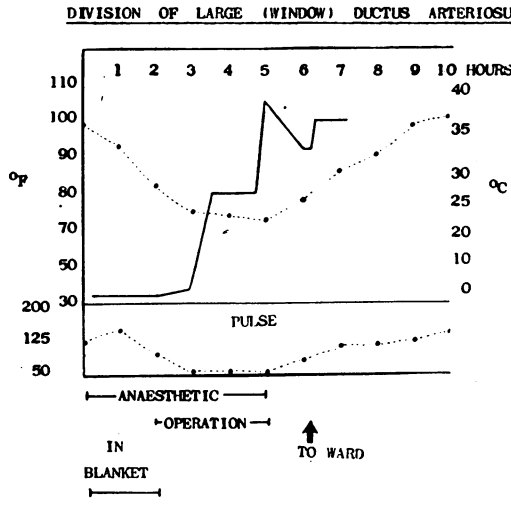

FIG. 5.—M. D., aged 2 years 2 months; weight 18½ lb.

(5) Reduced bleeding in the operative field is not a marked feature of this method—as noted, coagulation may, indeed, be retarded. Details of a similar case are shown in Fig. 5.

(6) The simplicity and rapidity of producing hypothermia by surface cooling and the improved operative course have made us prefer this method for infants and children with congenital cyanotic heart disease. In cases involving deliberate circulatory arrest hypothermia is essential. Hypothermia may well be a valuable adjunct to the use of the mechanical heart-lung.

In closing I should like to thank Dr. I. W. Magill for stimulating us to construct our first improvised cooling blanket after he had seen a transposition operation performed under hypothermia (Magill, 1953). I am also grateful to Dr. B. Cookson who visited us at the start of this work and gave us much helpful guidance. Finally, I am indebted to Mr. Charles Drew, the surgeon whose cases these were, and to Dr. J. R. E. Jenkins, my registrar, for his invaluable technical assistance.

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Dr. T. Cecil Gray:

Introduction.—The series of cases which I shall discuss have been collected by 7 anæsthetists working in association with my Department and I am grateful to them for enabling us to "pool" all our resources in order to get a clearer idea of our present position.

Over 110 cases have been collected in less than three years, with a further 20 that I can add. This number would seem to be a very eloquent reply to those who suggested in the past that we had been using this technique on occasions when there has been little justification.

With any new advance or method, the information that is sought, apart from the basic information which has been given us by Dr. Scurr, is: I, the method employed, II, the results which have been obtained, and III, its indications. I hope to answer these questions in the main.

I. METHOD

All our cases have been cooled by the surface technique. Of extra-corporeal cooling I have no experience, although I believe that it is a technique which carries its own risks which may prove in time to outweigh any advantages. The technique of cooling infants has been amply described by Dr. Scurr. Of the adults, for the first 40 cases in this present series we followed the French technique using the chlorpromazine-Phenergan-pethidine mixture although eliminating the use of a host of other drugs which were employed across the Channel. We found the technique unsatisfactory in that the period of cooling was prolonged

and the freedom from shivering was far from certain. Our present technique was devised by Dr. J. W. Dundee, and we have found it satisfactory. It is reasonably predictable, avoids shivering completely, and permits the required fall in temperature to occur in an average of one-and-a-half to two hours.

The basis of the technique is the use of extremely light anæsthesia and moderate doses of chlorpromazine to prevent shivering and vasoconstriction. Light anæsthesia alone, even with curarization, we have not found to give such satisfactory results.

The night before operation, the patient is given 50–100 mg. of chlorpromazine by mouth. One-and-a-half hours before cooling is to commence, 50 mg. of chlorpromazine is given intramuscularly with Hyalase; this may be combined, if the patient is unduly apprehensive or nervous, with 50 mg. pethidine or Phenergan to provide sedation. It is remarkable that, although we have given over a thousand of these intramuscular injections of chlorpromazine, we have not had a single instance of severe reaction or abscess formation despite the highly irritant properties of the drug. One-and-a-half hours later, anæsthesia is induced, in the case of abdominal and thoracic surgery with a dose of d-tubocurarine chloride of the order of 30 mg. and thiopentone 150–200 mg., and maintained with nitrous oxide and oxygen. An electrode from a thermocouple is inserted into the rectum, or, if that is inconvenient, into the œsophagus and a further electrode placed on to the skin, usually on the forehead. The cooling is brought about either with some form of blanket through which iced water can be circulated or for my own personal cases I have simply used ice packs. The ice bags must be applied all round the patient as cooling of the ventral surface alone results in considerable delay. The purpose of the skin electrode is to enable us to compare the rate of cooling on the surface with that in the body cavities. If the surface temperature is falling more rapidly than the rectal temperature, we would regard that as due to vasoconstriction and as an indication for the administration intravenously of 10–20 mg. of chlorpromazine. Only small amounts of chlorpromazine are required.

A further refinement of technique has been the changing of the patient's position every fifteen minutes in order to lessen the possibility of the pooling of cooled blood in any one part of the body with the aim of reducing the amount of after-drop of temperature. "After-drop" is the fall of temperature which takes place after the application of ice has been stopped and is no serious disadvantage provided it is remembered that it occurs. Fig. 1 shows the degree of after-drop in 37 neurosurgical cases. As can be seen it varies from 0° to 3·5° C., and depends on the type of patient. The well-built or obese have a pronounced "after-drop" and will cool slowly, whereas the lean, thin or emaciated patient cools rapidly and has no further fall in temperature after cooling is stopped. Children are a dangerous exception to this general rule in that they cool rapidly and usually have a pronounced after-drop. This can lead to trouble and it is doubtful whether it is safe to cool children unless there is some readily available method of warming them up quickly in case of too pronounced a fall in temperature. There will be other factors, of course, which will influence the amount of after-fall of temperature such as the room temperature and the degree of vasodilatation, but there is no doubt that build and age are of great importance in making the estimation as to when to stop cooling (Fig. 2).

II. Results

This series (Table I) has been collected by 7 anæsthetists over a period of three years, and

Table I.—Cases Operated under Hypothermia 1953–55.

Intrathoracic	Mitral valvotomy	1	
	Coarctation of aorta	1	
	Aortic aneurysm	1	
	Congenital cardiac	6	
			9
Neurosurgical	Vascular lesions	17	
	Tumours	22	
	Miscellaneous	2	
			41
General surgery	Total cystectomy	7	
	For portal hypertension	8	
	Œsophageal obstruction	5	
	Gastrectomy	6	
	Intestinal obstruction	2	
	Colectomy and abdomino-perineal	5	
	Pelvic evisceration	1	
	Others	12	
			46
Therapeutics		14	
	Total of series	110	

consists of 110 patients to which one could add a further 20 neurosurgical cases which have been treated since this Table was drawn up. Before considering these cases in greater detail according to their indication, I will review the complications.

Firstly, *the non-fatal complications*—we have had one inhalation of vomitus which was a case anæsthetized with the "lytic cocktail". A junior anæsthetist had not appreciated that the patient who was so sedated, might, if he had pyloric obstruction, regurgitate his stomach contents. He recovered after bronchoscopy. We had one burst abdomen; 3 cases had skin burns due to burst ice bags and direct contact of the ice with the skin, 2 had venous thrombosis in the arm due to the use of undiluted chlorpromazine, 1 temporary anuria lasting for three days, and 3 temporary auricular fibrillations. The auricular fibrillation occurred in elderly patients, commenced in the region of 34° C. and continued as the temperature fell to 30° C. The irregularities continued until, during rewarming, a temperature of 34° C. was reached when normal rhythm was restored. This occurrence in old people we would not consider as an indication to stop cooling.

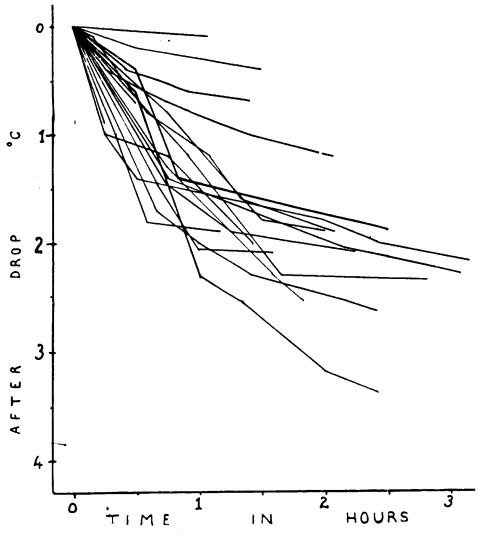

FIG. 1.—This shows the degree of "after-drop" in 37 neurosurgical cases.

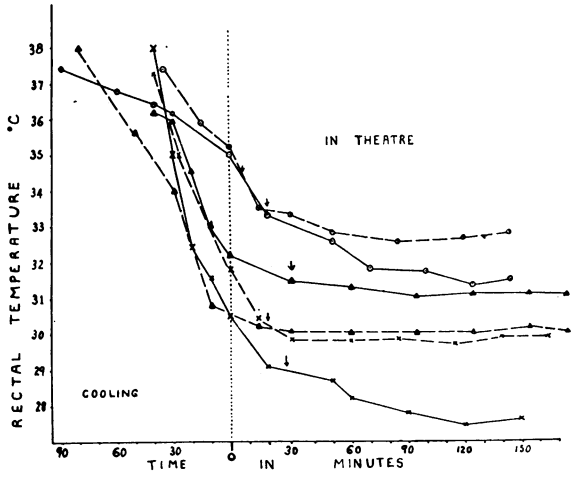

FIG. 2.—"After-drop" in three varieties of patients. O=2 well-built or obese. ▲=2 thin patients. X=2 children. The dotted line indicates the time of removal of ice-bags. The arrow indicates the commencement of the operation.

Secondly, *the deaths* we think may be associated with the cooling are listed in Table II.

TABLE II.—DEATHS

Pulmonary	? Bronchopneumonia (hæmatemesis)	1
	Pulmonary embolus .. .. .. (2*)	3
Cardiovascular	Ventricular fibrillation	1
	Cardio-pulmonary insufficiency	4
	Heart block (cerebral hæmorrhage)	1
	Cardiac failure and peritonitis	1
	Continued hæmorrhage (? transfusion reaction)	1
Others	Paralytic ileus and peritonitis	1
	Total	13

There have been 3 cases of pulmonary embolus. This might be regarded as particularly threatening because 2* of these cases were neurosurgical and this is a complication never seen in neurosurgery. They were, however, both patients who had been kept refrigerated for some days in the post-operative period because of extensive brain trauma during the operation. The one case of ventricular fibrillation occurred in the only patient with rheumatic myocardial damage. 4 cases labelled cardiac and respiratory insufficiency were neurosurgical patients who collapsed post-operatively. The case who died from hæmorrhage was definitely a hypothermic death. This patient had a porta-caval anastomosis. He had severe liver damage, and his coagulation time was so much increased at low temperatures

that he bled to death in spite of continued transfusions. The case of peritonitis died of paralytic ileus following a total cystectomy and transplant of the ureters. Ileus in total cystectomy cases has proved a hazard of the operation, but, except for this patient, death has occurred a considerable time after operation, and we have no evidence that cooling has predisposed to this complication.

III. Indications

We have classified our series under headings according to the indication for this type of anæsthesia.

A. *Intrathoracic.*—This group in our series is small because we believe that the majority of children with ordinary congenital cardiac defects can be operated upon with conventional forms of anæsthesia. Cooling is, in our opinion, only indicated where circulatory arrest must be achieved or perhaps, in extreme cases of Fallot's tetralogy in which cardiac failure is present or imminent. Our experience with open heart operations has so far not been encouraging and of the 13 deaths of the series, 5 have occurred in this group. In rheumatic heart disease, hypothermia may well be contra-indicated. One seriously ill patient for mitral valvotomy was cooled at the surgeon's request in the belief that lowering the temperature would improve the patient's oxygenation. As the temperature fell, the heart action became feeble and on opening the chest the heart was seen to be greatly dilated and beating sluggishly. Dilatation of the valve at a temperature of 25° C. resulted in irreversible ventricular fibrillation. Experiments which we have been able to carry out with the Starling heart-lung preparation in dogs, may have some bearing on this case. Under conditions of constant peripheral resistance in this preparation the cardiac output is maintained as low as 20° C. Starling found this to be the case only to 28° C. As there is bradycardia at low temperatures, the maintenance of output is due to an increasing stroke volume. However, these experiments have also shown that when the venous return to the heart is increased at low temperatures in adult dogs, the myocardium loses its power to compensate by increasing the stroke volume, so that at high venous flows the cardiac output is not maintained. This would seem to indicate that at temperatures below 30° C., there is interference with the efficiency of the heart muscle. Starling's "Law of the Heart" no longer applies. It would seem reasonable to expect that this myocardial "damage" would be much more serious in its significance in diseased states, as for example in rheumatic disease. It is interesting that the puppy's heart maintains its power to compensate for an increasing venous return even as low as 20° C.

B. *Neurosurgery.*—Patients who require prolonged hypotension to facilitate or permit neurosurgical procedures, particularly if they have to be operated upon in the semi-upright position, will obviously benefit from hypothermia. Our neurosurgical unit has had some remarkable results in the treatment of vascular tumours and aneurysms of the brain and Mr. C. B. Sedzimir has been able completely to occlude the middle cerebral artery for periods up to twenty minutes without producing apparent cerebral damage.

C. *Therapeutic indications.*—This particular series includes 2 cases of thyrotoxicosis, the remainder being patients in whom there has been severe cerebral damage accompanied by œdema and/or hæmorrhage. Where cerebral anoxia might be prolonged or perpetuated by cerebral œdema, reduction of the oxygen demand of the brain is indicated and our experience has shown that such patients benefit by reduction of temperature. Of the 2 cases of severe thyrotoxicosis, one was in crisis and the other had been presented for operation on two previous occasions but had been returned to the ward because of the circulatory condition. Both responded well to hypothermia.

D. *General surgery.*—In general surgery, I consider there are two indications for hypothermia. The first of these is when some degree of hypotension is required in patients for whom lowering of the blood pressure at normal temperature would be considered hazardous. An example was an old man of 72 who had a bilateral inguinal hernia which extended down to knee level. He had been bedridden for six months, was œdematous, had marked arteriosclerosis but was otherwise cheerful and willing to undergo anything to make his lot more tolerable. Unfortunately, no blood could be found with which he was compatible and as his hæmoglobin was only 65%, it was clear that some measures would have to be taken to reduce the blood loss in what promised to be a vascular and hæmorrhagic operation. He was operated on under hypothermia and is now ambulant and living a reasonably normal life (Figs. 3 and 4).

My second indication for hypothermia in general surgery, which I put forward very tentatively, is to protect the patient against the aggression of surgery as manifested by that syndrome which for years has been labelled "shock". A great deal has appeared in the literature drawing attention to the excellent condition of patients who have undergone very extensive surgery under so-called "artificial hibernation". The time has surely come

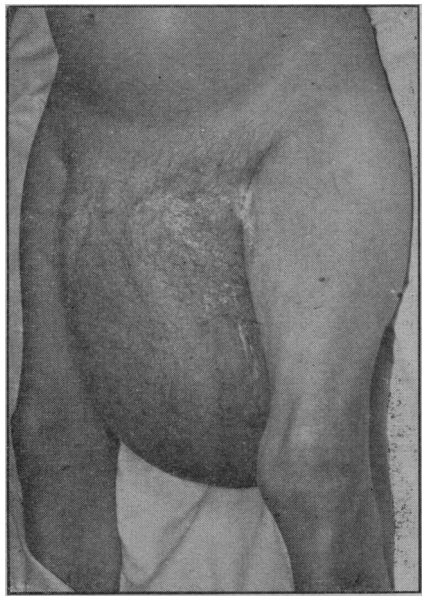

FIG. 3.—Before treatment.

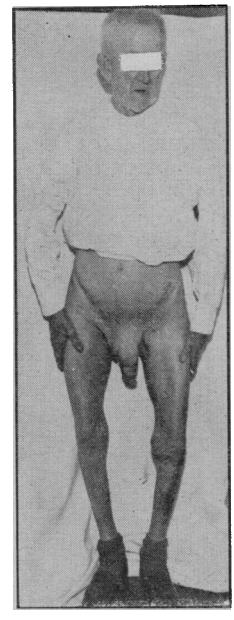

FIG. 4.—After treatment.

to cease using this term. There are two entities. One is the depression of various autonomic reflexes and responses by drugs such as, for example, chlorpromazine, and the other is a reduction of metabolism by hypothermia. It is a combination of these two as practised by French schools, which has been labelled hibernation, although it bears only the most distant relationship to the hibernating animal in which there are extensive endocrine readjustments.

There is undoubtedly a widespread impression among clinicians that patients who are submitted to these techniques are in some way "stabilized" so that, provided their blood loss is replaced, surgical trauma produces no apparent change in their circulatory condition. How difficult it is, however, to demonstrate objectively such an indefinable entity as "protection from shock."

In an attempt to find some objective evidence to refute or support this clinical impression, we have initiated a programme of observations of which we are only at the moment on the threshold. Our object is to discover whether or not the recognized responses of patients and animals to the stress of operation might not provide us with the necessary yardstick with which we could compare patients under hypothermia with those under the conventional forms of anæsthesia. In this we have been lucky enough to be assisted by Mr. Ian MacPhee of the Department of Surgery.

A first approach was made in the clinical field to investigate the changes in blood eosinophil counts and electrolyte balance which, it is believed, reflect the responses of the adrenal cortex to injury. Observations of hypothermic patients revealed no difference in their eosinophil response to operation and the electrolyte changes after operation were identical with those described by Moore and Ball (1952) and MacPhee (1953) under conventional anæsthesia. A little thought led us to believe that this was perhaps only what might be expected. The changes in electrolyte excretion are a reflection probably of the outpouring of steroids, particularly aldosterone, from the suprarenal cortex which occurs as a result of ACTH secretion by the pituitary gland. These endocrine secretions are "fired off" by the "stress" of the operation. But this reaction could also be initiated in the recovery period, even if it were suspended at the actual time of operation by our anæsthetic technique. In fact there is evidence (MacPhee, 1955) that the very anticipation of an operation is sufficient to fire off these hormonal activities and produce changes in electrolyte excretion. It seemed to us, therefore, that we must turn to animals if we desired to discover whether hypothermia was affecting this particular response to operation.

We, therefore, undertook to observe the electrolyte and steroid responses in dogs who were operated on under hypothermia and who were maintained hypothermic for the minimum of three days, which period is required for the changes to be manifested. If during these three days characteristic changes in electrolyte excretion occurred and the total steroid

output from the suprarenal cortex increased, then we could conclude that our technique was providing no cover, but if, on the other hand, these changes did not occur or seemed to be modified then we were doing something which might well be beneficial to our patients.

We have so far been able to undertake seven such experiments in dogs. In these dogs we have measured the total steroid output in the urine every twenty-four hours as well as changes in serum and urine electrolytes. I do not wish to describe the details of these experiments here but Fig. 5 shows the results in one of these dogs and demonstrates that,

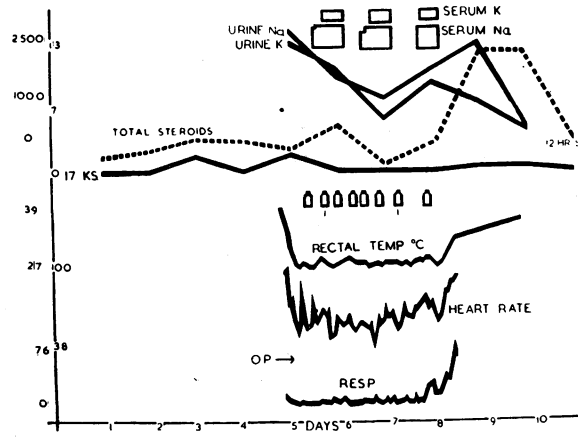

FIG. 5.—Chart summarising experiment on Dog 6. The excretion of total steroids and 17-ketosteroids is shown during the control period, during the period of hypothermia (27° C.) and during recovery. The "flasks" indicate bottles of 500 ml. of fluid. The "steroids" are measured in mg./twenty-four hours.

during the period of hypothermia, there is no adrenocortical response as evidenced by excretion of adrenocortical steroids, but as soon as the temperature is allowed to rise the response becomes evident. If this observation is correct, and it would seem to be so, it could be that by hypothermic anæsthesia we are preserving the adrenocortical responses to stress for the recovery period and not depleting the reserve of the patient during the operation.

CONCLUSION

It would be pleasant to be able to speak on one's subject with authority and unqualified enthusiasm. I would not dare to claim authority on the basis of a series of cases which is so small compared with those great series which have introduced or supported other anæsthetic procedures, nor can one claim authority on the grounds of our experimental work which is only at its very inception. Our enthusiasm is qualified by this lack of knowledge, but we know enough to appreciate that hypothermia is certainly no new anæsthetic technique with wide applications. We are, in fact, feeling our way, exploring new territory to discover whether it holds promise and new hope for the very sick and disabled. Let us regard hypothermia as a procedure which, like induced hypotension, can be utilized with benefit in exceptional circumstances and only in centres where there is the necessary special equipment, experienced personnel and, above all, adequate nursing facilities.

ACKNOWLEDGMENTS

I must express my very great gratitude to members of my Department and others associated with them who have permitted me to include their cases in this review, in particular to Dr. Jackson Rees, Dr. John Dundee and Mr. C. B. Sedzimir and other members of the Liverpool Neurosurgical Unit, and to Mr. John Shepherd for permission to quote the case of inguinal hernia. I am also grateful to Mr. Riddle, the physiologist in the Department of Anæsthesia, and to Mr. Ian MacPhee, Senior Lecturer in Surgery, for their help with the experimental work.

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Section of Obstetrics and Gynæcology

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[*April* 22, 1955]

DISCUSSION ON THE HAZARDS OF ANÆSTHESIA IN OBSTETRICS

[*Abstract*]

Mr. A. J. Wrigley: For some years I have felt that whereas enormous advances have been made in the nature and safety of anæsthetics and their administration in most other branches of medicine, what I may term "ordinary obstetric anæsthesia" has stood still.

The problem must be considered in two distinct categories—that of hospital and domiciliary obstetrics. About one-third of all babies born in this country are still born at home under the care of the family doctor and midwife. The former now receives little or no training in suitable anæsthetics to administer to women in labour and frequently this results in resort to the use of chloroform. Is this a good plan and can our anæsthetic colleagues suggest a safe and equally efficient method of anæsthesia for such patients?

In hospital too often the administration of anæsthetics to women in labour is left in the hands of the most junior member of the anæsthetic team. It is felt that this is not correct as so frequently these patients present a most difficult anæsthetic problem; they are tired, they have lost blood, and from an anæsthetic point of view are most inadequately prepared.

Therefore, a plea is made that a major problem exists which merits the serious and urgent consideration of the Faculty of Anæsthetists.

Dr. Derek Wylie: Some details of 31 anæsthetic deaths occurring in hospital and domiciliary obstetric practice are described. Particular attention is drawn to 15 of these, which were associated with vomiting or regurgitation. Death can be caused by acute anoxia or the results of aspiration into the lungs, but irreparable damage may be done to both mother and child even in cases where there is never any question of a fatal outcome. The frequency of vomiting with general anæsthesia in obstetrical cases is discussed, and five points are considered as a basis for tackling this problem: the use of local analgesia, the preparation of the patient, the anæsthetic, the posture of the patient, and the anæsthetist.

Although a wider use of local techniques would help to avoid the risk of anæsthetizing an unprepared patient, they cannot be the whole answer to the problem since there will always be occasions when a general anæsthetic is essential. It is not good medicine to starve or deprive of fluid for long periods a woman who is in labour, and the use of a stomach tube would therefore have to be routine to eliminate every chance of aspiration. This seems unjustifiable.

Special emphasis is laid on equipping the labour ward in the manner of an operating theatre, particularly in relation to the use of suction and an ability to posture the patient. A modified "Oxford" bed, which can be quickly tilted into either a head-down or a head-up position is described.

If all ancillaries are to hand there would seem to be no reason why an experienced anæsthetist should not successfully deal with the labour ward cases by methods he habitually uses for general surgery. The use of a cuffed endotracheal tube has much to recommend it.

Many obstetrical deaths due to anæsthesia can without doubt be prevented, and this is particularly true of those due to vomiting. The standard of labour ward anæsthetics should be brought up to that of the operating theatre, so that both mother and child can benefit from advances of the last decade. In the final event this will only be achieved by more experienced anæsthetists dealing with these problem cases.

Mr. John Peel: Has the obstetric patient benefited as much from the great progress in anæsthetic technique and knowledge as the surgical one? Maternal deaths due to anæsthesia have increased, proportionately if not absolutely. Anæsthesia plays a part in maternal morbidity because of pulmonary complications, and is also a cause of fœtal mortality and morbidity by reason of anoxia as well as the true action of the anæsthetic drug.

A rough estimate is that there are 50,000 forceps deliveries a year, and probably a fifth of these in the patient's own home, all requiring full surgical anæsthesia. Maternal deaths from anæsthesia occur both in domiciliary and hospital confinements.

Too many anæsthetics in hospital are given by juniors and in general practice by doctors inexperienced in anæsthesia. Not enough consideration is given by obstetricians and midwives to the preparation of the patient.

The following points are briefly mentioned as bearing upon safety of obstetric anæsthesia:

(1) The left lateral position for low forceps.

(2) Anæsthesia should be continuous once induced until the completion of the third stage.

(3) The more difficult obstetric operations following delayed labour are also the more hazardous from the anæsthetic viewpoint and require experienced personnel in both spheres.

(4) Special techniques such as caudal block have specific indications, but cannot be employed unless experienced anæsthetic personnel is available.

(5) The importance of blood pressure recordings in relation to anæsthetic risk is stressed.

(6) An adequate anæsthetic service for domiciliary midwifery is vitally important.

(7) Anæsthetic personnel is at least as important as anæsthetic agents.

(8) More anæsthetists, trained and interested in obstetric anæsthesia are needed, not only to administer anæsthetics, but to teach and to research into newer methods.

The following took part in the discussion: **Dr. E. H. Seward, Dr. R. B. Parker, Mr. O. Lloyd, Dr. D. A. Buxton Hopkin, Dr. O. P. Dinnick, Mr. G. H. Bancroft-Livingston, Mr. A. Walker, Dr. M. D. Nosworthy, Mr. E. D. Y. Grasby, Mr. J. V. O'Sullivan, Mr. G. F. Gibberd, Mr. W. Hawksworth, Mr. A. J. McNair.**

[*May* 13, 1955]

Spontaneous Uterine Rupture During Labour.—NORMAN MORRIS, M.D.

A specimen was shown of a uterus which ruptured spontaneously during labour. The patient, aged 25, had experienced 4 previous normal pregnancies and labours.

This, her fifth labour, was seemingly normal lasting just over two hours. The infant was born alive and the placenta delivered spontaneously. Shortly after this the patient became profoundly collapsed, although there was no associated post-partum hæmorrhage. A total hysterectomy was performed and she survived.

Careful scrutiny of this patient's previous history produced no evidence of any condition likely to predispose to the uterine rupture.

Rupture of the Uterus Occurring at the Time of Removal *per vaginam* of a Pedunculated Uterine Fibroid.—R. W. GRAYBURN, M.B., M.R.C.O.G.

The patient was a nullipara aged 52. Careful examination failed to reveal evidence of inversion of the uterus. The fibroid, as large as a golf ball, was removed easily by torsion and subsequently a ragged wound 1 in. in diameter was found in the uterine fundus. Hysterectomy was performed. It is thought that the "pedicle" of the fibroid was in fact a very localized and attenuated inversion of the uterus.

Rupture of a Pyosalpinx Associated with an Intra-uterine Pregnancy.—LYNN A. J. EVANS, F.R.C.S.

3 cases were described. The first presented a general peritonitis associated with a 14-week pregnancy. Recovery, complicated by a paralytic ileus, followed left salpingo-oophorectomy. The second patient had increasing lower abdominal pain with eight weeks' amenorrhœa. A large left pyosalpinx was excised. The corresponding ovary and appendages of the opposite sides were normal. Abortion occurred forty-four days and six days post-operatively respectively. The third died of peritonitis and septicæmia following rupture of a right pyosalpinx with a uterus didelphys, the left half containing a 24-week pregnancy.

Vaginal Metastasis of Hypernephroma.—N. GOURLAY, M.R.C.O.G.

A brief report of a patient whose only symptoms were related to a pedunculated vaginal tumour which was subsequently found to be a metastasis from a hypernephroma of the left kidney. Multiple pulmonary metastases precluded any treatment other than local removal of the tumour.