HIBERNATION ANAESTHESIA IN MAJOR SURGERY

A REPORT OF 36 CASES

BY

ANGUS SMITH, F.F.A. R.C.S., D.A.

Consultant Anaesthetist, Charing Cross Hospital

AND

J. G. FAIRER, M.R.C.S., D.A.

Registrar in Anaesthesia, Charing Cross Hospital

In major surgery, particularly in the case of malignant disease, where the patients are often cachectic and very ill, it is often not possible to contemplate surgical intervention. If an operation is started, after an hour or two of traumatic surgery the patient's condition deteriorates, and, however carefully the cardiovascular system is supported by intravenous transfusions, a state of shock develops. The completion of the operation may become an urgent matter, and the extent of the operation may have to be modified. Under effective "hibernation" anaesthesia the patient does not react in any way to the surgical stimulus, however severe or long-continued. Furthermore, intravenous transfusion is confined to replacing only the volume of blood lost. This is surprisingly small when measured, amounting to 300–400 ml. in extensive pelvic clearances. The body temperature drops to between 95 and 96° F. (35 and 35.6° C.), but this is only an indication that the autonomic blockade has succeeded, and it returns to a degree or two above the pre-operation level in six hours. The state of the patient approaches in many ways that found in the mammiferous hibernating animal, but it is not a truly comparable condition.

The defence mechanisms of the body for the preservation of the *milieu intérieur* of Claude Bernard against stress, aggression, or change in the external environment are largely the function of the autonomic nervous system. The hypothalamus, with its connexions with both the cerebrum and the autonomic system, has thus a large part in the control of the internal environment.

Conventional methods of anaesthesia attempt to modify these autonomic defences. This is done by depressing the cerebral functions, and in this way modifying the thalamic and hypothalamic control of the autonomic system; or, working from the periphery, by obtunding the stimuli that call the defence mechanisms into action. In the vasomotor system the defence mechanism, working through the mediation of the autonomic nervous system, causes the shutting of the pre-capillary sphincters and the opening of the arteriovenous shunts (Chambers *et al.*, 1943). This increases the circulating blood volume and also increases the venous oxygen tension, in order to combat the aggression. In the central nervous system, experimental work would indicate that the shunt mechanisms are not present; consequently, following aggression the oxygen supply to the vital centres is not diminished and may even be increased. In the peripheral circulation, if the stress is at all long-continued, these same defence mechanisms result in capillary dilatation, and the increased pressure at the venous end of the capillary loops is followed by fluid loss into the tissues, with diminution of the circulating blood volume. This leads to anoxia, building up of acid metabolites, and, finally, atony of the peripheral vessels—the fatal peripheral failure which no amount of intravenous or intra-arterial infusion will reverse. In this way the patient dies as a direct result of his attempt to preserve his *milieu intérieur*.

Physical Cooling

For many years attempts have been made to modify the reaction of the body to surgical aggression by means of physical cooling. It has been found by Prec *et al.* (1949), Bigelow *et al.* (1950), and Bigler and McQuiston (1951), and others that when the body temperature has been finally reduced by physical means the oxygen consumption of the tissues is markedly lowered. It is then possible to undertake surgical operations requiring the exclusion of the heart, or lungs, from the circulation for several minutes, without anoxic damage to the tissues.

However, the application of ice-packs, refrigerated blankets, and other external cooling in itself constitutes a stimulus which calls the defence mechanism into action. This is shown by increased oxygen consumption and heart rate, and by shivering in order to maintain body temperature. Only when the defence mechanism is overcome do the body temperature and the oxygen consumption drop (Prec *et al.*, 1949; Jaulmes, 1953). It is at this stage, on the way to final dissolution of the subject, that these operations can be performed.

The artificial hibernation technique evolved by the French workers, Jaulmes, Laborit, Huguenard, and others owes little to physical cooling of the subject from without, but depends on the specific neuroplegic effect of drugs, mainly those of the phenthiazine group on the autonomic nervous system. The phenthiazine derivatives include the antihistamine drugs promethazine hydrochloride ("phenergan") and promethazine-8-chlortheophyllinate ("avomine"), which has a central action, particularly upon the vomiting centre, and chlorpromazine ("largactil"), which has no antihistaminic action. This drug seems to act centrally on the autonomic system as a neuroplegic, and it has a pronounced anti-adrenaline effect and a direct depressant action on the temperature-regulating mechanism.

Laborit *et al.* (1952) have described a detailed plan for producing a state of artificial hibernation which has guided us in our efforts to ameliorate the condition of patients subjected to major surgical procedures. He relies on the use of a "lytic mixture" consisting of 50 mg. of promethazine, 50 mg. of chlorpromazine, and 100 mg. of pethidine, which is administered intravenously in divided doses in the hour before operation. The hibernant state is maintained by giving, intravenously, one of three "cocktails" containing, among other drugs, aneurine, pethidine, promethazine, chlorpromazine, diethazine hydrochloride, sparteine sulphate, ascorbic acid, ethyl alcohol, and procaine. In addition acetosterandryl, neostigmine, and heparin are given intramuscularly.

Present Investigation

We have attempted, so far as is practicable, to avoid the polypharmacy of our French colleagues. The technique which we now adopt and which has given excellent results in our hands in a variety of major surgical procedures is as follows. The patient is given 50 mg. of promethazine-8-chlortheophyllinate by mouth two hours pre-operatively. One hour later this is followed by a subcutaneous injection of 100 mg. of pethidine with 1/150 gr. (0.43 mg.) of hyoscine hydrobromide. The patient is brought to the anaesthetic room and the mixture of promethazine, pethidine, and chlorpromazine, in the proportions advocated by Laborit, is given in divided doses in the half-hour preceding operation. During the injection the pulse rate rises at first but later settles to a level a little above the resting rate, and remains unaltered despite the duration or severity of the surgical procedure. The respirations become shallow and may increase in rate, while the systolic blood pressure tends to fall and is maintained in the region of 100 mm. Hg. At the conclusion of the injection the patient is somnolent and apathetic but can still be roused. A small dose of 5% thio-

pentone, 2–3 ml., is given to produce unconsciousness, and tracheal intubations may then be performed with ease.

The patient is transferred to the theatre, where small doses of relaxants are given when required. Oxygen is administered if the respiratory excursion is inadequate, particularly in those cases requiring the steep Trendelenburg position. In prolonged operations, if the pulse rate begins to rise we have been able to re-establish control by a small supplementary dose of the original mixture. Great care is taken to replace any blood lost, as the patient is not able to compensate for gross diminution or increase of circulation blood volume. Our experience so far has been of patients aged from 28 to 76 years, and has included the following operations: gastrectomies, Wertheim's hysterectomies, hysterectomies, total colectomies, anterior pelvic exenterations, adherent malignant ovarian cysts, laminectomies, bilateral mastectomy and a second operation of prostatectomy on the same patient, together with less extensive operations in patients who would normally be considered poor risks.

Case Reports

Case 6.—A married woman aged 76, weighing 8 st. 4 lb. (52.6 kg.), had had two operations for carcinoma of the body of the uterus. She was admitted for symptoms of large-bowel obstruction with a large tumour arising from the pelvis with ascites. B.P. was 180/120. Six hours after admission she developed gross cardiac irregularity and electrocardiography indicated a coronary infarction. She was thought to be unfit for operative intervention. Two days later her condition became grave and fibrillation was occurring at a rate of 140, with a pulse deficit of 10–20 beats at the wrist. She was treated by the technique described above. Operation entailed the removal of a large adherent malignant ovarian mass involving the sigmoid colon, which was resected, and an anastomosis was performed, with a colostomy above. During the operation, which took three hours, she received 400 ml. of blood to replace the estimated loss. Her pulse rate remained irregular throughout at 90–100 a minute. Her rectal temperature was 96° F. (35.6° C.) at the conclusion of the operation. She was rousable within three hours of the end of the operation and regained consciousness after six hours. Her rectal temperature rose to 100.2° F. (37.9° C.) during this period and her pulse rate remained irregular at the same rate. She has made an uneventful recovery.

Case 23.—A man aged 46, weighing 8 st. 6 lb. (53.5 kg.), had generalized Paget's disease with involvement of the spine. He had had spastic paraplegia and loss of sphincter control for eight months. A myelogram showed a spinal block at the level of the fourth dorsal vertebra. We obtained an autonomic blockade by the method described, and an extensive decompression of the spinal cord was undertaken by performing a bilateral laminectomy from the fourth to the eleventh dorsal vertebra. Blood loss was very rapid and was replaced by a transfusion of 4 pints (2.3 litres). His pulse remained steady at 90–100 a minute and his systolic pressure was sustained at just over 100 mm. Hg. Recovery was uneventful and his neurological condition was improving.

Conclusions

It is impossible to assess statistically the advantages of any anaesthetic technique. From the small series of 36 cases involving really major surgery we have been impressed by the excellent condition of the patients, however extensive or long-continued the operation. We have had no deaths due either to the use of the method or to the operations performed. At no time during any of the procedures or during the post-operative period has the condition of the patient caused any anxiety. Furthermore, there has been no post-operative vomiting, nausea, or headache. The patients require less nursing care than normal, heavy post-operative sedation is not required, and there have been none of the post-operative complications which might have been expected to follow such major surgery. The patients are contented with this technique, for, although they can be roused, most of them have complete amnesia from the time they leave the ward until six to eight hours after the operation. The freedom from post-operative pain and restlessness during this period seems to aid their recovery, for when the autonomic blockade has worn off they are cheerful, rested, and relatively free from pain.

The great advantage of this modification of Laborit's technique has been that we are now able confidently to undertake the anaesthetic care of patients who previously would have caused great anxiety, or would have been considered unfit to withstand major surgical intervention.

Summary

A brief account is given of a simplified method of producing autonomic blockade, as a method of preventing surgical shock during and immediately after major operations. The patient's condition has been better, both during and after the operation, than when conventional anaesthetic techniques have been used.

We would like to thank our colleagues and the nursing staff of the hospitals at which this work has been done for their sustained interest, and also Messrs. May & Baker Ltd. for supplying the drugs used.

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THE BACTERIAL CONTENT OF HUMAN SMALL INTESTINE IN DISEASE OF THE STOMACH

BY

JUDITH CREGAN, B.Sc.

E. E. DUNLOP, M.S., F.R.C.S., F.R.A.C.S.

AND

NANCY J. HAYWARD, M.Sc., Ph.D.

(School of Bacteriology, University of Melbourne, and the Royal Melbourne Hospital)

It has already been shown (Cregan and Hayward, 1953) that when the human intestinal tract is healthy the small intestine is not colonized by a resident flora. Such organisms as are found there are so few in number that they must be regarded as transient contaminants passing through with the ingesta. The present work was undertaken to determine the effect of disease of the stomach on the flora of the small intestine. The results showed that neither a low gastric acidity nor the presence of a profuse flora in the stomach necessarily lead to the development of a resident flora in the small intestine. The antibacterial mechanism operating in the small intestine is therefore independent of the gastric germicidal barrier.

Experimental

The patients chosen for the experiment were undergoing operation for gastric or duodenal ulcers or gastric carcinoma. In addition, there was one patient with a subtotal gastrectomy of two years' standing and a small oesophageal hiatal hernia. He was operated on for recurring haematemesis and melaena. All had been given light nourishment and had then fasted for at least four hours before the operation.