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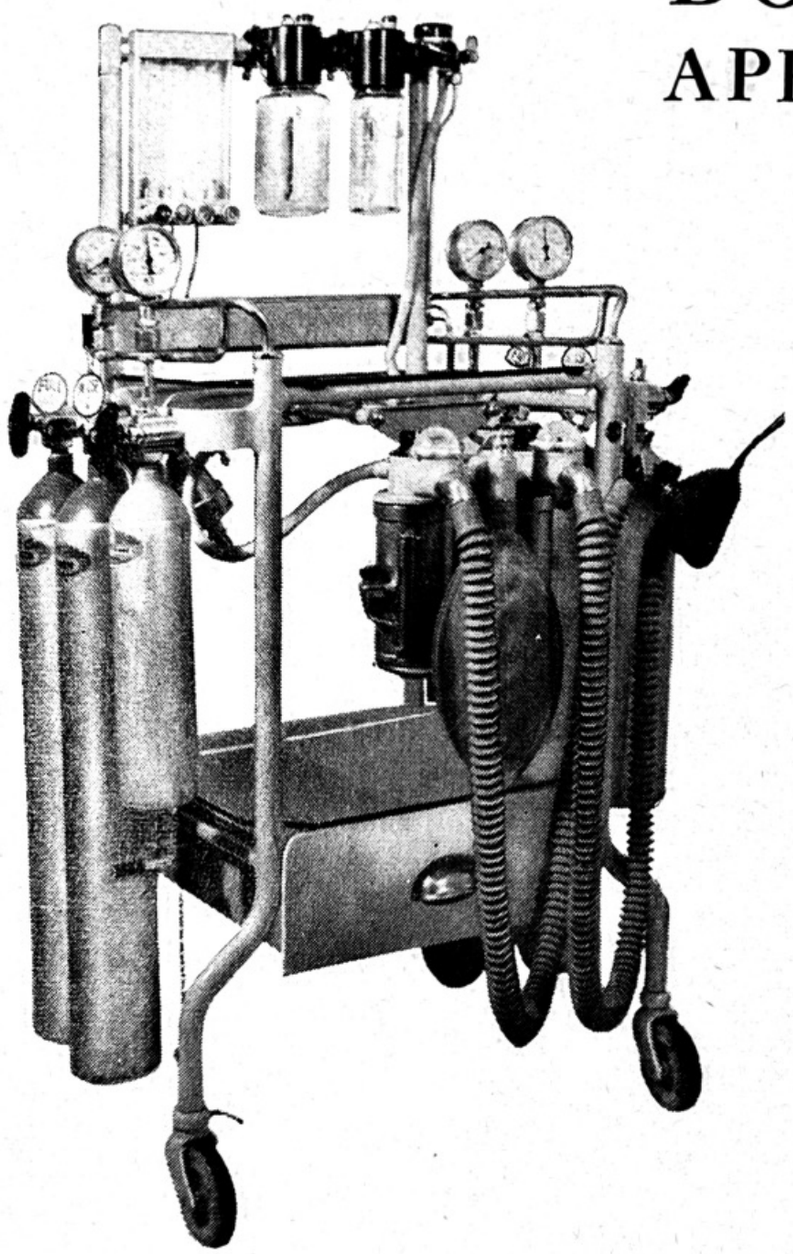
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ANNUAL MEETING

HOTEL VANCOUVER VANCOUVER, B.C.

June 14—15, 1954

CONTENTS

	Page
Executive Officers and Council	3
Editor's Note	4
Studies on Anaesthetics with Prolonged Action—Madelaine O. Maykut, M.A.	5
Blood Volume: An Important Factor in Anaesthetic Management—Charles M. Barbour Jr., M.D.	18
Equilibrium of the Autonomic Nervous System in Anaesthesia—Bernard Paradis, M.D.	24
Artificial Hibernation—Fernando Hudon, M.D., F.R.C.P.(C) and André Jacques, M.D., F.R.C.P.(C)	33
A Report of the Use of Succinylcholine in Anaesthesia—R. A. Gordon, M.D., F.R.C.P.(C) and I. M. MacKay, M.D.	44
Hexamethonium Chloride for Controlled Hypotension During Operation—Roland Duchesne, M.D.	51
The Arteriotomy Method of Producing and Controlling Hypotension—Elizabeth Martin, M.D.	57
Morbidity, Mortality and Pathology in Induced Hypotension—S. L. Vandewater, M.D.	62
Carbon Dioxide in Anaesthesia—Lucien E. Morris, M.D.	65
Contribution of Anaesthesia in Thoracic Surgery for Tuberculosis—Jean-Paul Dechene, M.D. and Fernando Hudon, M.D., F.R.C.P.(C)	72
Resuscitation of the Newborn: A Method and a Machine—John Mann, M.D.	81
Cardiac Resuscitation—Round Table Discussion—*Chairman*: Shirley A. Fleming, M.D. *Members*: Lucien Morris, M.D., Carl Stoddart, M.D., S. M. Campbell, M.D.	91
Blood Plasma Substitutes with Emphasis on Polyvinyl-Pyrrolidone (P.V.P.)—René Létienne, M.D., F.R.C.P.(C)	98
Physiological Requirements in Equipment Related to Anatomical Factors in Children—H. M. Slater, M.D.	103
A Preliminary Report on the Use of Hydrogenated Ergot Alkaloids in Obstetrics—P. B. Percheson, M.D. and John Carroll, M.D.	112
Nitrous Oxide-Demerol-Mecostrin Anaesthesia—F. A. Walton, M.D.	119
Analeptics and Vasopressor Substances—Harold Cameron, M.D.	124
Controlled Respiration as an Adjunct to General Anaesthesia—Richard N. Terry, M. D.	130
Index to Advertisers	xvii

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EDITOR'S NOTE

This second volume of the PROCEEDINGS OF THE CANADIAN ANAESTHETISTS' SOCIETY contains, in addition to the papers presented at the annual general meeting of 1953, certain selected papers from the meetings of the Divisions across Canada. We feel that these presentations are of real value, and it is our sincere hope that more of such contributions will be made available in the future.

The résumés in the French language will, I hope, adequately convey the salient features of each paper. These résumés have been provided by the authors themselves in the case of the French speaking authors, and I am indebted to Dr. René Létienne of Montreal and Dr. David Lévy of Toronto for translations of the remainder.

R. A. GORDON,
Editor.

STUDIES ON ANAESTHETICS WITH PROLONGED ACTION

MADELAINE O. MAYKUT, M.A.*

A local anaesthetic preparation which would have a prolonged action to take care of both the operative and post-operative periods up to 24 hours or more, is desirable in some surgical procedures. Some commercial products are marketed for this purpose. This study deals with an investigation of these products with respect to duration of anaesthesia and local tissue reactions following subcutaneous, intradermal, and intramuscular injections.

METHOD

The shaved backs of white guinea pigs weighing 400–500 Gms. were used for the subcutaneous and intradermal injections of the various test preparations. One side of the mid-line was injected with the test solution while the other side was injected with physiological saline as a control. The amount injected subcutaneously was 2 cc. of a solution or suspension; intradermally 0.1 cc. was injected to discover whether local damage such as ulceration or sloughing might occur. The test used for the index of the degree and duration of anaesthesia was the animals' response to a light touch of a pin point in the anaesthetised area as compared with an unaesthetised area. The type of response was (*a*) squealing of the guinea pig, (*b*) twitching of the skin, or (*c*) jumping away from the source of annoyance. These tests were performed once every 24 hours, since the desired local anaesthetic period sought was longer than this.

Other animals such as the rat and rabbit were used to settle the questions of species specificity with respect to skin reactions to the various local anaesthetics.

The quadriceps muscles of the hind limbs of guinea pigs were used for intramuscular injections (0.5 cc.) to investigate the type of reaction which might occur in muscle when a long-acting local anaesthetic was used in surgical procedures such as herniorrhaphies. Histological studies were made on excised tissues in all experiments.

A few preliminary experiments using the retrobulbar block technique (1) were carried out in guinea pigs. The length of time that the pupil of a guinea pig's eye remained dilated after the injection of 0.2 cc. of an anaesthetic preparation was noted; procaine hydrochloride 2% was used as a standard for comparison.

Animal experimentation was supplemented by experiments on human volunteers who received 1 cc., 2 cc., and 5 cc. of various preparations subcutaneously on the forearm. The boundary of each injected area in these latter was marked with ink and tests were made by means of pin pricks as previously described.

*Department of Pharmacology, University of Toronto and the Shouldice Surgery, Toronto.
Read at the Annual Meeting of the Canadian Anaesthetists' Society, Montebello, Quebec, June 1, 1953.

Materials

Table I shows the compositions of the various commercial preparations tested which, with one exception, utilize procaine in some form. The substances tested were: procaine base 2%, aluminum hydroxide 2%, merthiolate 1:5000, butesin 5%, propylene glycol 78%, benzyl alcohol 5%, cyclaine 2%, procaine amide hydrochloride 2%, procaine amide 2%, and procaine hydrochloride 2%. The foregoing materials were made up in physiological saline.

TABLE I

Composition of Commercial Preparations

Duracaine: pH 7.3	
Procaine base	2%
Merthiolate	1:5000
Methocel	0.5%
$Al(OH)_3$ gel	2%
Distilled Water	q.s.
Efocaine: ph 8.9	
Procaine	1%
Procaine HCl	0.25%
Butyl-p-amino-benzoate (Butesin)	5%
Polyethylene-glycol-300	2%
Water for injection	20%
Propylene glycol	78%
Preserved with	
Sodium Metabisulfite	0.1%
Phenyl Mercuric Borate	1:25,000
Proctocaine: pH 8.4	
Procaine	1.5% w/v
Butyl-p-amino-benzoate (Butesin)	6% w/v
Benzyl Alcohol in Oil	5% w/v
Analcaine: pH 4.1	
Procaine HCl	1%
Isoamylhydrocupreine Dihydrochloride (Eucupine)	1:500
In Ringer's Solution	
Diothane Hydrochloride:	
1% Solution, pH 5.9	
Diperodon Hydrochloride	1%
Piperidinopropanediol diphenylurethane hydrochloride in aqueous solution	

Results and Observations

Table II presents the duration of anaesthesia of a subcutaneous injection of the various materials listed, as well as the reactions noted upon gross examination after subcutaneous and intradermal injections. All substances showing anaesthetic properties by the pin prick method gave immediate anaesthesia upon

TABLE II
GUINEA PIG EXPERIMENTS

Substance	*Apparent duration of anaesthesia upon subcut. inject.*	*Retrobulbar block*	*Subcut. react.*	*Intraderm. reaction*
	Days	Min.		
Duracaine	1–8	206–246	+	+
Procaine base 2%	2–4		0	0
Aluminum hydroxide 2%	0 (hypersensitive)		+++	++
Merthiolate 1: 5000	0		0	+
Efocaine	9–22	359–406	++	+++
Butesin 5%	4		+	++
Propylene Glycol 78%	15 (+)		++	+++
Proctocaine	8		++	+++
Benzyl Alcohol 5%	5–12		++	+++
Benzyl Alcohol 5% in Almond Oil	0 (hypersensitive)		++	+++
Diothane hydrochloride 1%	14–16		++	+++
Analcaine	18–22		++	+++
Cyclaine 1%	4		0	+
Cyclaine 2%	7 (+)		0	+
Procaine amide hydrochloride 2%	1 (delayed effect)		0	+
Procaine amide 2%	8–12		0	+
Procaine hydrochloride	0.1	51–56	0	0

Subcutaneous reaction: + slight thickening
++ very thick
+++ hard raised lump
Intradermal reaction: + slight reddening
++ very red
+++ ulceration and sloughing

subcutaneous injection except procaine amide hydrochloride, which required 10 min. for onset of anaesthesia in guinea pigs. A typical gross appearance of an animal injected intradermally with a material causing ulceration and sloughing may be seen in Fig. 1.

Similar skin reactions were noted in the rat and the rabbit following subcutaneous and intradermal injections of the test substances.

Histological studies of skin sections from guinea pigs injected with the test materials are presented in Table III.

When a retrobulbar block was performed in the guinea pig, procaine base 2% had a duration (206–246 min.) four times that of procaine hydrochloride (51–56 min.); the complete block achieved with efocaine had a duration approximately eight times (359–406 min.) that obtained with procaine hydrochloride and twice that found for procaine base. In human experiments the duration of anaesthesia for 2% procaine base (8 hours) was four times the duration of procaine hydrochloride 2% (2 hours).

Human Experimentation

The subcutaneous injection (2 cc., 5 cc.) of a suspension of procaine base 2% in physiological saline in 4% (Knox) gelatin solution into human volunteers brought about immediate anaesthesia as evidenced by the testing with pin

pricks. A distinction had to be made by the volunteer between the sharpness of the pin point and pressure with which the pin was applied when testing the anaesthetised area. Our interest was concerned with the presence or absence of sharpness of an object since pressure could always be distinguished. Numbness in the whole of the injected area persisted definitely for 8 hours; some insensitive spots remained within the injected area for 24 hours but most of the sensation had returned by this time. Unfavourable reactions such as reddening or thickening of the injected area were absent upon gross examination. Some mild deep tenderness, disappearing the next day, was reported in 2 cases.

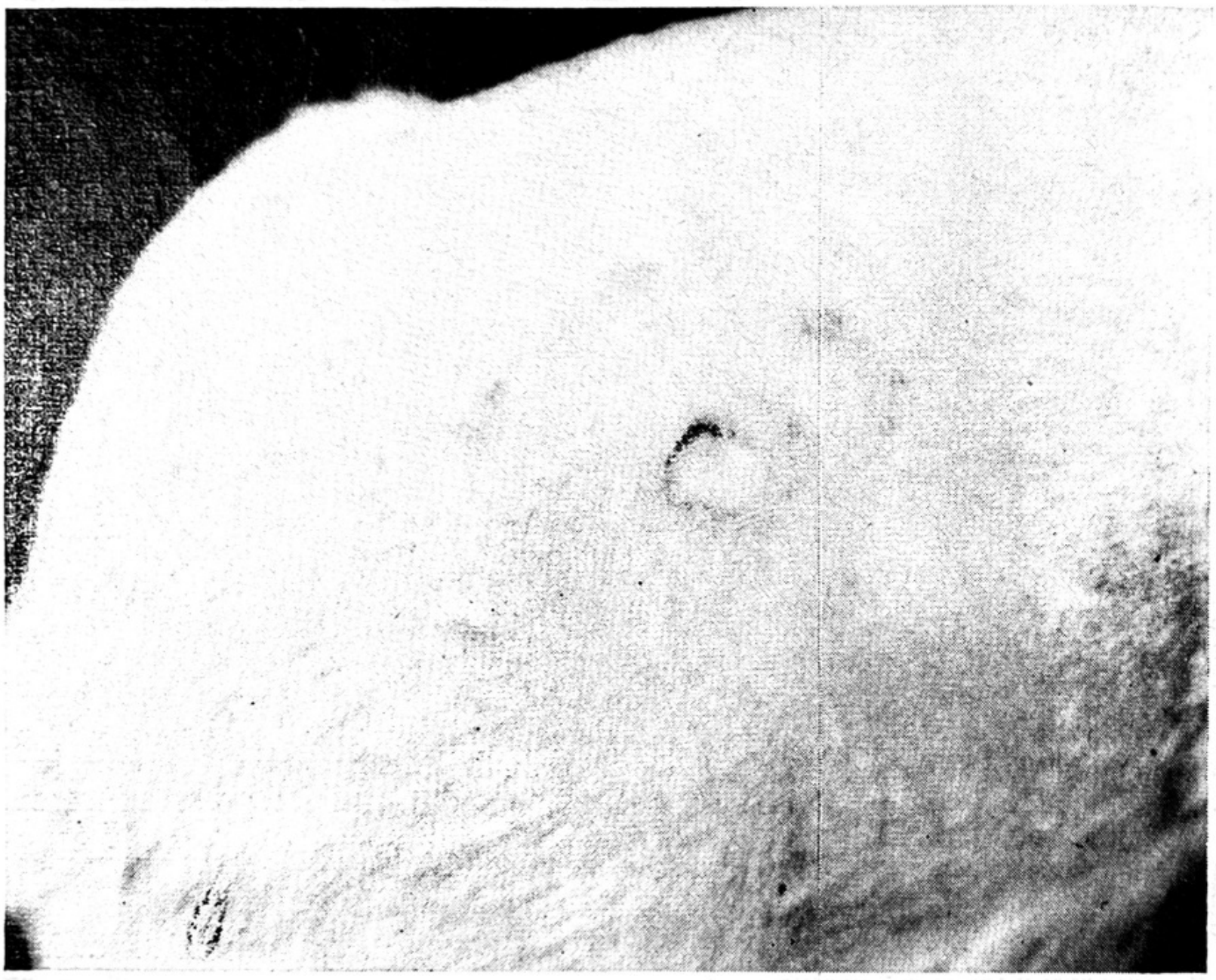


FIG. 1. Efocaine: 5 day period.

The subcutaneous injection of merthiolate (2 cc. of 1:5000) into human volunteers gave rise to edematous red areas which spread to twice the original injected area in 24 hours. This area became tender and sore.

An ulnar nerve block performed on a human volunteer using 5 cc. of a 1% cyclaine solution lasted (135 min.) five times that found with 1% procaine hydrochloride solution (25 min.). Initially the injection of cyclaine was quite painful; an aching and uncomfortable feeling persisted for 24 hours.

DISCUSSION

The prolonged period of apparent cutaneous anaesthesia obtained in the above experiments on guinea pigs, may be due to (i) the anaesthetic substance, (ii) thickening of the tissue, or (iii) destruction of the nerve fibres. The anaesthetic material itself apparently has a relatively short duration of action,

TABLE III

HISTOLOGICAL STUDIES

Fig. No.	Subcut. Inject. of 2 cc.	Period after injection Days	Histological Findings
2	Physiological saline (control)	10	Normal section showing all layers of skin including subcutaneous tissue down to muscle (bottom) with ovoid hair follicles (top).
3	Site of injection	11	In most instances site is in subcutaneous muscle (strip diagonally through middle); in this case the fat is involved (lower centre).
4	Duracaine	13	Muscle degeneration and replacement with fibrous tissue.
5	Procaine base 2%	14	Some edema (top) and some mild muscle degeneration with fibrotic replacement (lower centre); much less reaction seen than with other agents used; similar picture seen with an intramuscular injection.
6	Aluminum hydroxide 2%	12	Muscle necrosis; relatively normal muscle (top); destruction (middle) and liquefaction (bottom) of muscle fibres.
7	Merthiolate 1:5000	10	Destruction of fat cells; infiltration of inflammatory cells (lower right hand corner).
8	Efocaine	17	Fibrotic reaction with muscle degeneration, some giant cells (upper), and necrosis (lower).
9	Propylene glycol 78%	15	Fibrosis with some muscle degeneration and some edema; replacement of muscle with fibrous tissue; definite giant cell formation with mononuclear reaction (resembling Efocaine).
10	Diothane HCl 1%	11	Fibrosis; some replacement of muscle with fibrous tissue; no giant cells; inflammatory cells infiltrated into fatty layer separating fat cells.
11	Analcaine	7	Fibrous reaction; muscle degeneration and replacement.
12	Cyclaine 2%	7	Mild fibrosis; disappearance of muscle striations (lower left hand corner).
13	Procaine amide 2%	12	Mild fibrosis; some infiltration of fibrous tissue into muscle tissue.

as indicated by the retrobulbar block experiment and by the human experiments. Therefore the prolonged duration obtained in guinea pigs could be due to damage to the nerve fibres, or to the swollen tissue which may impair nerve functioning. A report by Duncan and Jarvis (2), which leads one to believe that the lasting effect is due to nerve degeneration, demonstrates that further investigation is needed. Swelling itself, as observed when aluminum hydroxide was injected, did not induce anaesthesia.

Intradermal injections of local anaesthetics are not made as a rule. Their purpose in the above experimentation was to ascertain if a reaction would

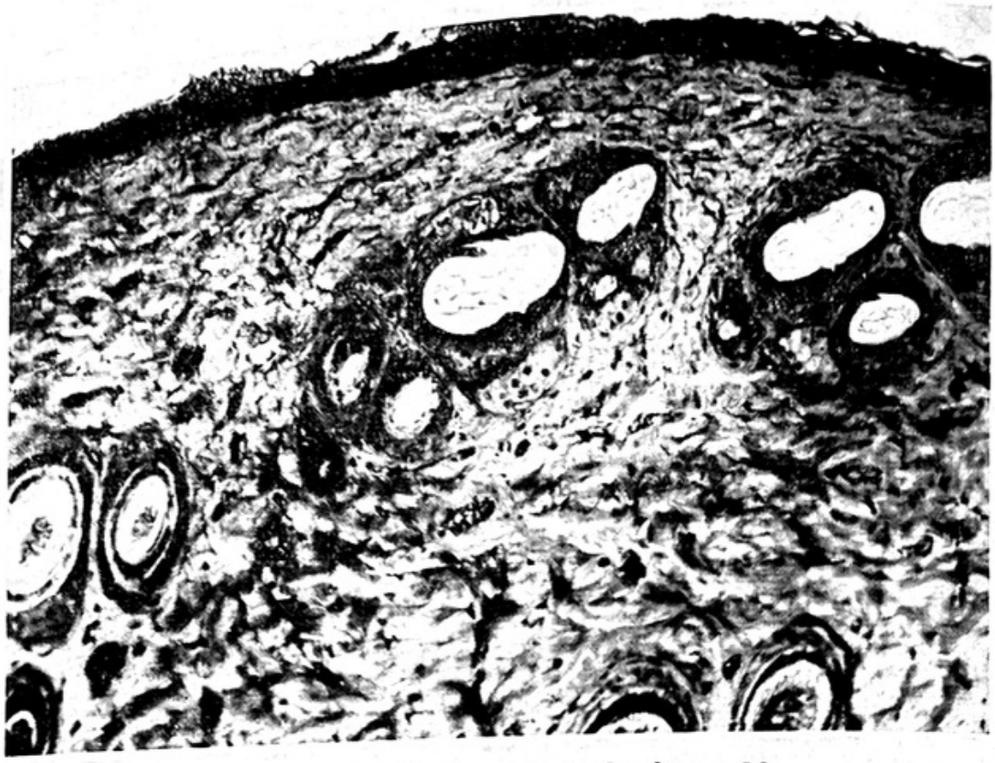


FIG. 2. Control: physiological saline x 80.

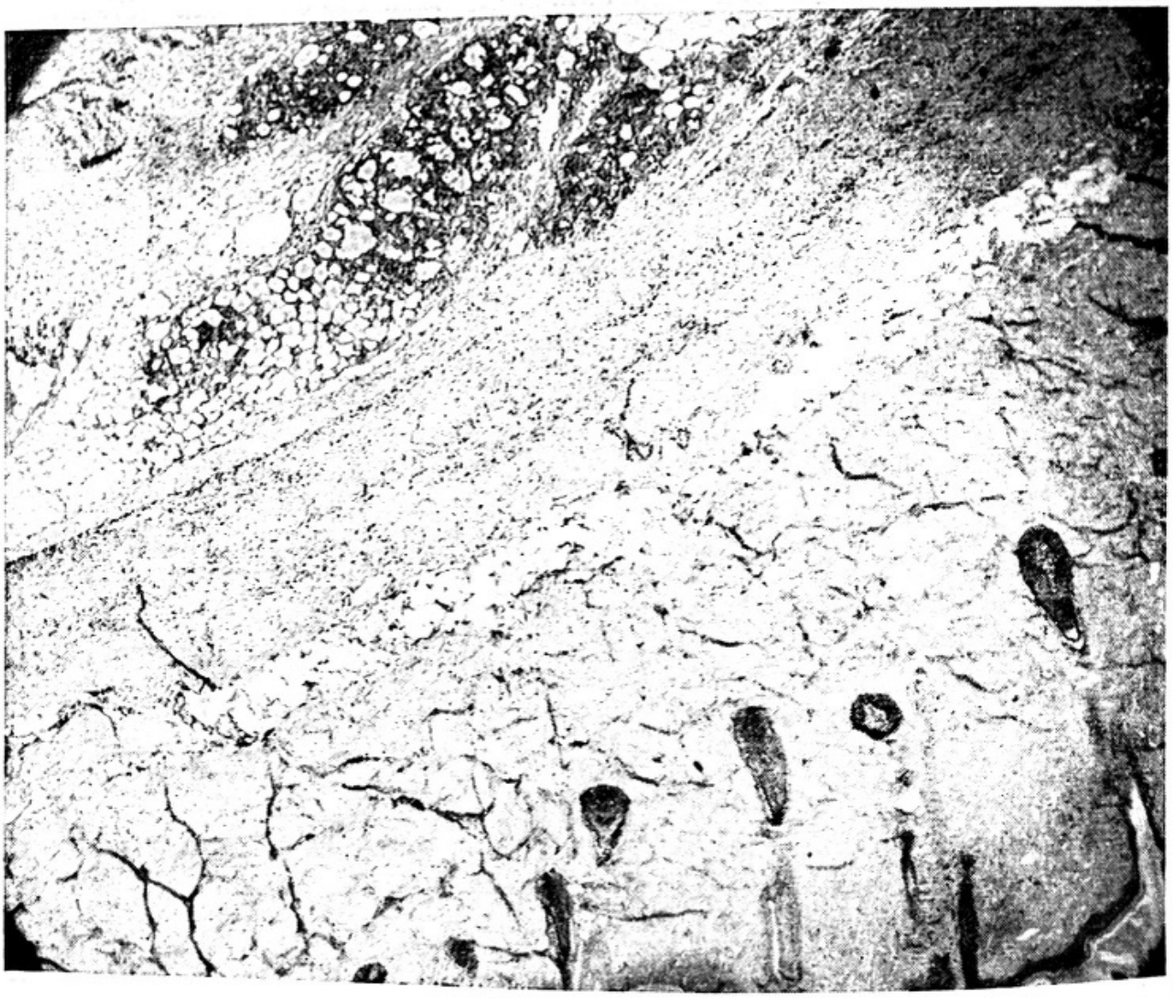


FIG. 3. Diothane HCl x 20. Site of injection.

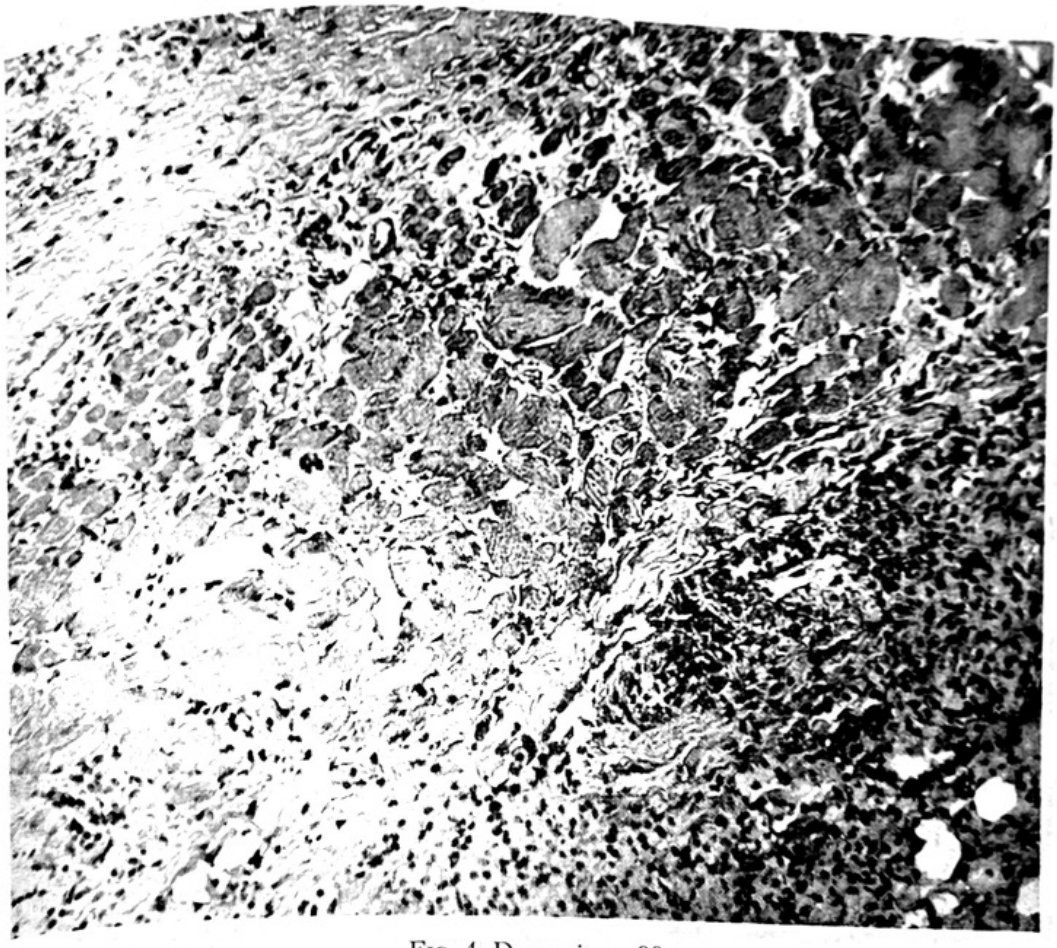


FIG. 4. Duracaine x 90.

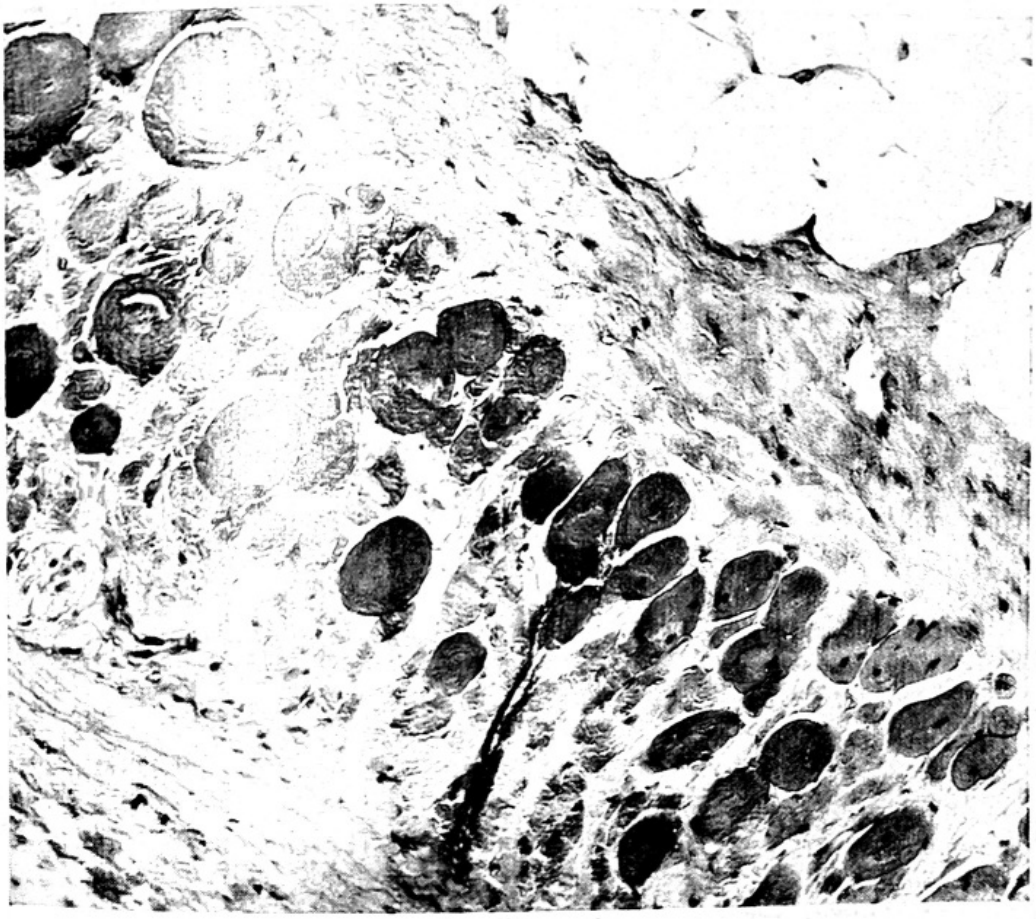


FIG. 5. Procaine base 2% x 90.



FIG. 6. Aluminum Hydroxide 2% x 90.

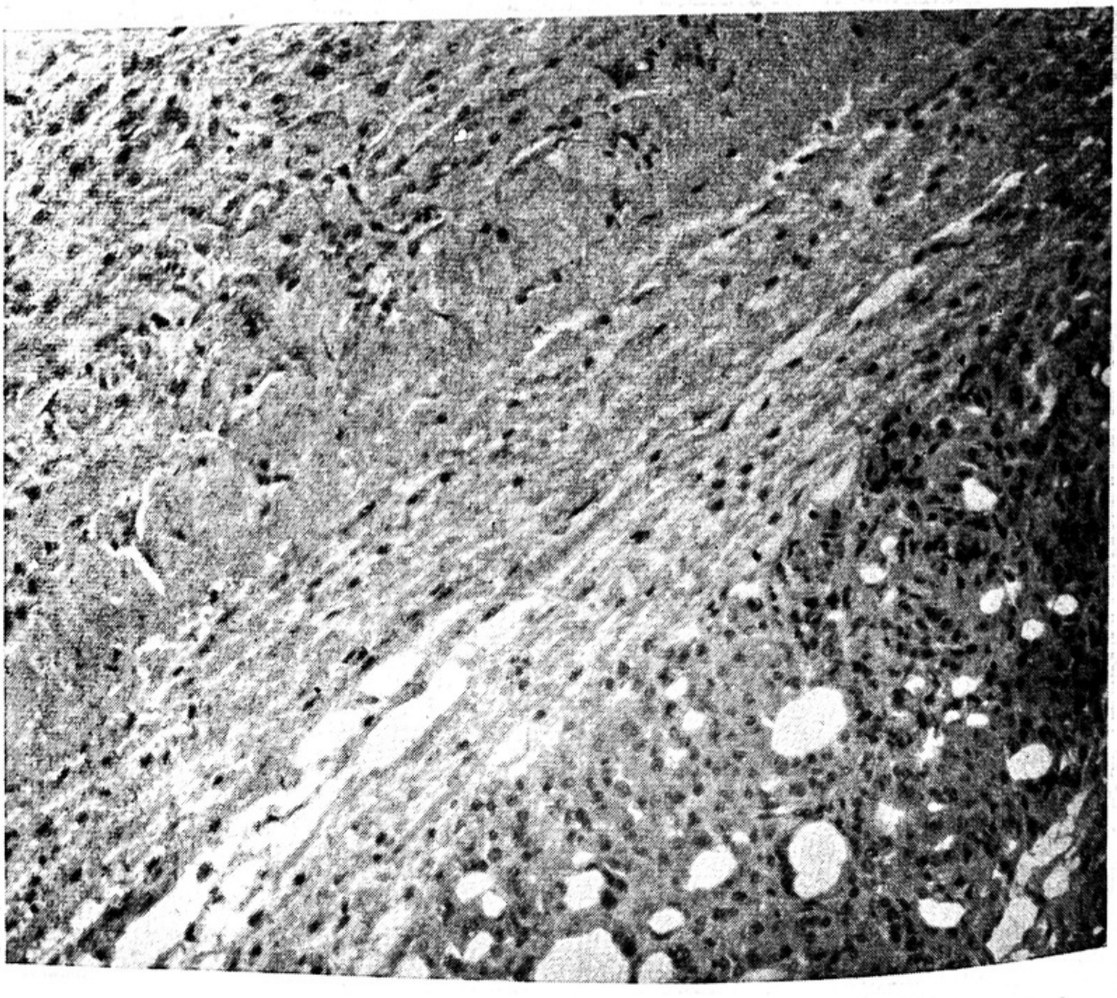


FIG. 7. Merthiolate 1:5000 x 100.

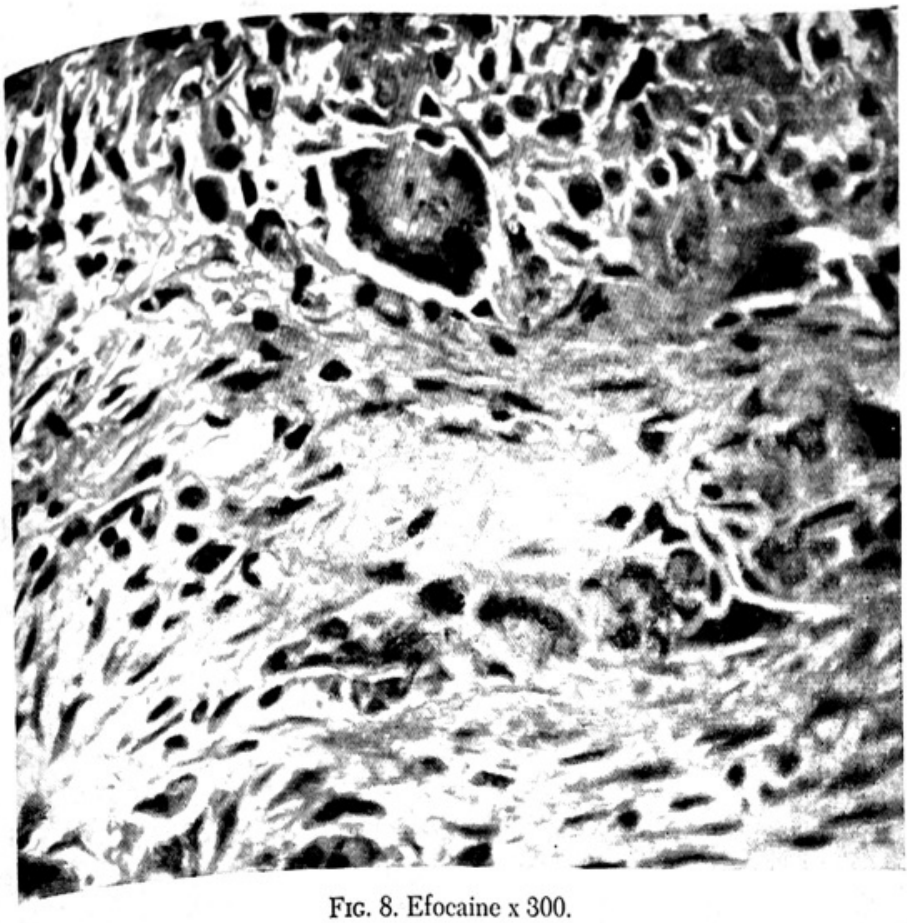


FIG. 8. Efocaine x 300.

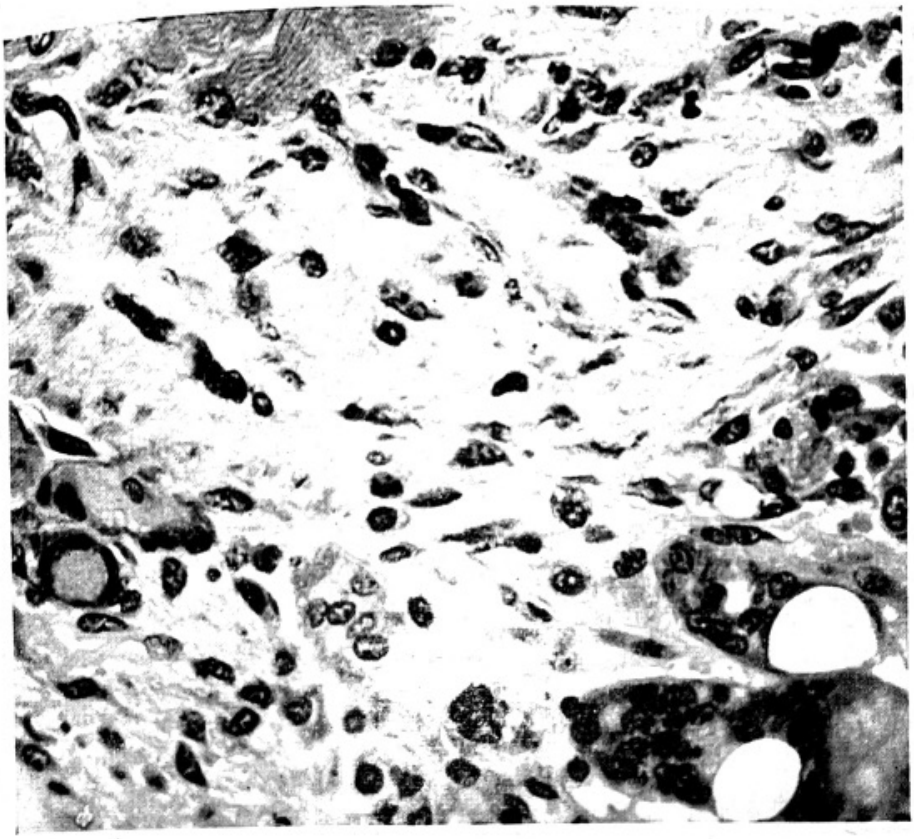


FIG. 9. Propylene glycol 78% x 300.

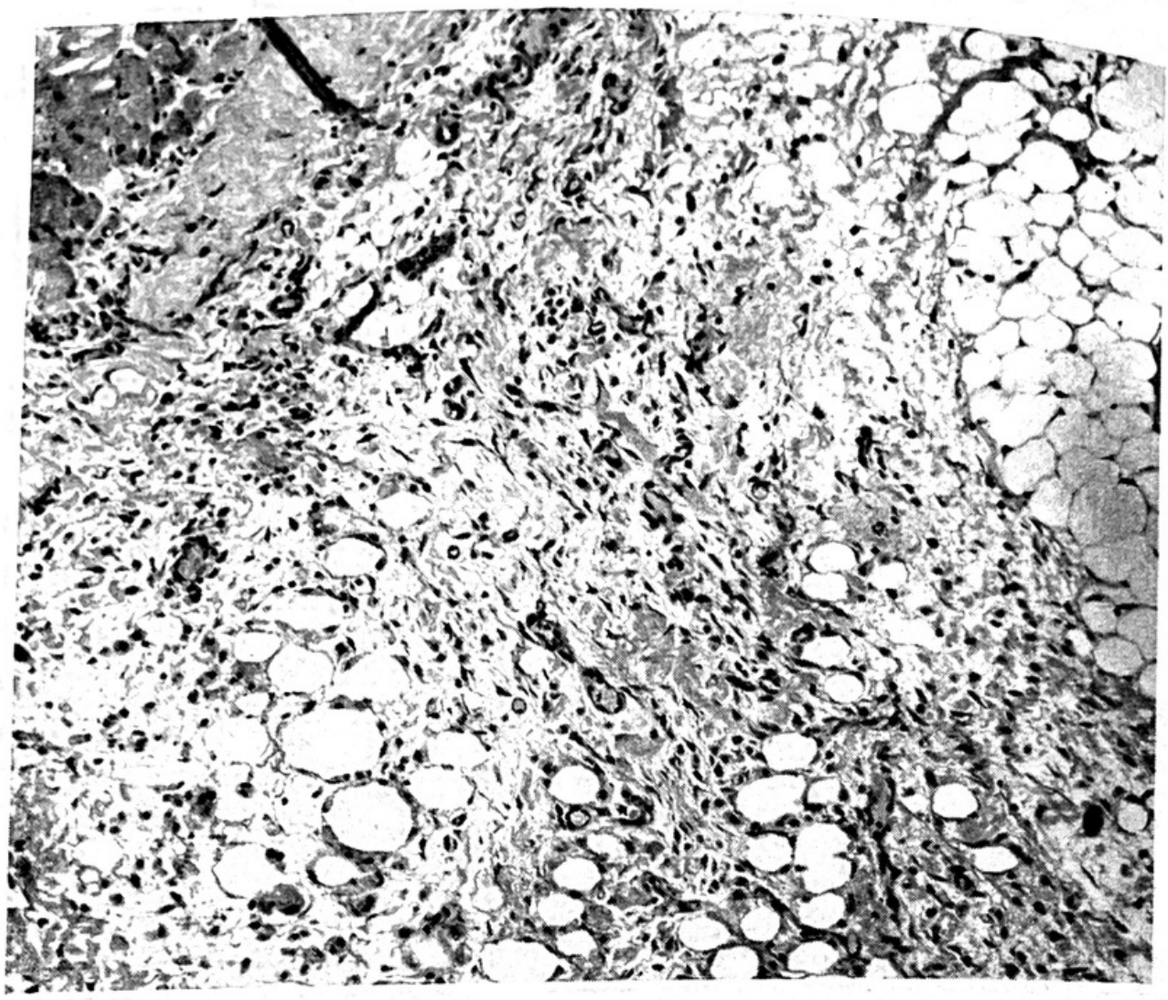


FIG. 10. Diothane HCl x 80.

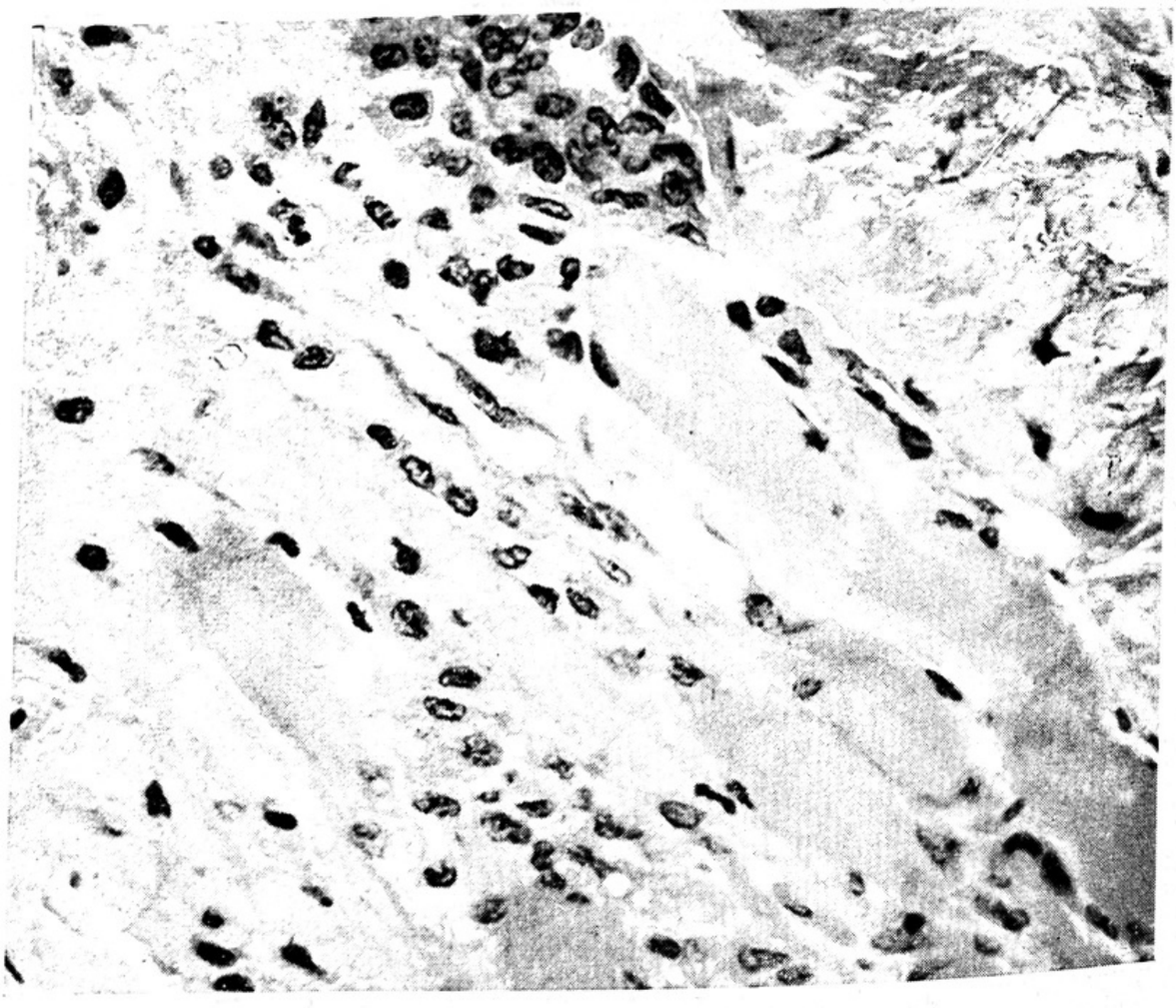


FIG. 11. Analcaine x 300.

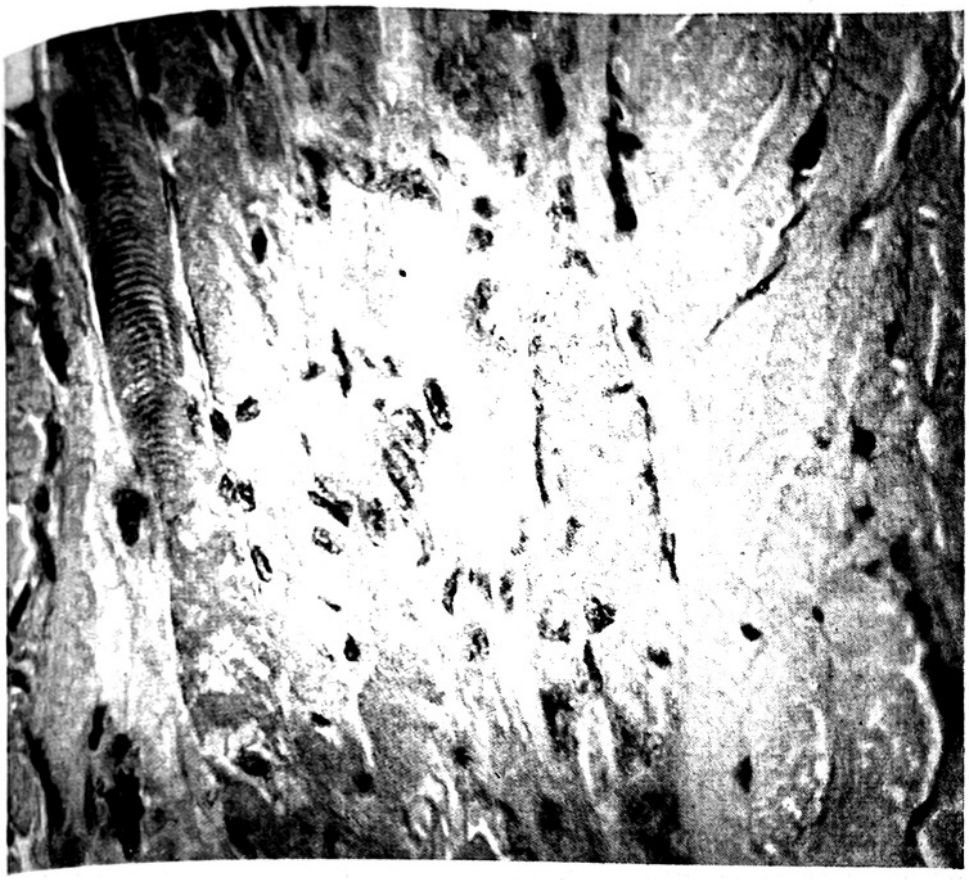


FIG. 12. Cyclaine 2% x 300.

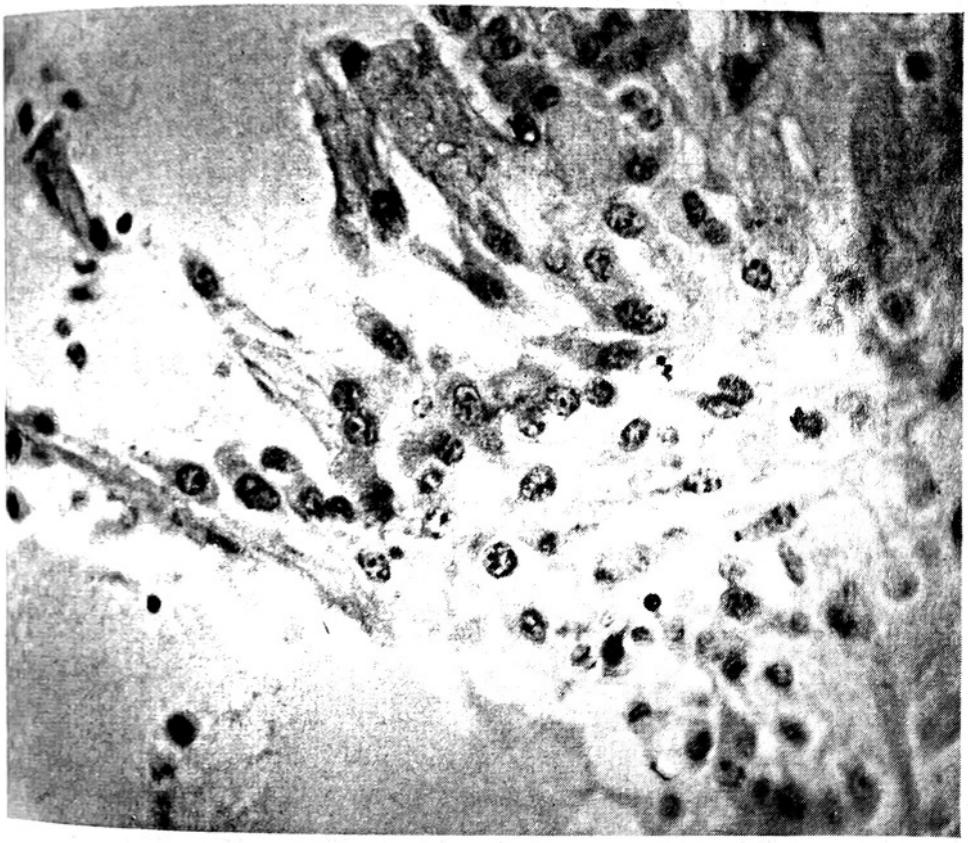


FIG. 13. Procaine amide 2% x 300.

follow; if it did, it could be inferred that interference with healing in the skin might follow the use of long-acting anaesthetics.

In animals, in some instances, prior to anaesthesia, immediate pain, as indicated by struggling and squealing, was aroused during the injection. This occurred with efocaine, propylene glycol 78%, diothane hydrochloride 1%, cyclaine 1%, and remains unexplained to date.

Both cyclaine and procaine amide which appear to be quite interesting at a first glance, because of their potency and duration, require further investigation. The greatest disadvantage of cyclaine is the pain upon injection and the uncomfortable aching sensation which ensues. Patients suffering pain might not object to the injection of these drugs in view of the relief they could expect.

Summary

1. The available commercial products marketed for the purpose of prolonging local anaesthesia all evoked unfavourable local reactions in the quantities employed for infiltration anaesthesia. The suspending agents (aluminum hydroxide) or solvents (propylene glycol) used in the preparations appeared to be responsible for the untoward reactions.

2. From the few preliminary experiments performed it appears that the retrobulbar block method in the guinea pig may give a better indication of the duration of anaesthesia to be expected in the human; whereas, the subcutaneous injection method reveals the type of local tissue damage which may occur.

3. Procaine base appears to be the least noxious substance used in the commercial preparations. Although this material prolongs the anaesthetic effect by some hours, its main effect is to provide immediate anaesthesia.

4. From these experiments it appears that the prolonged action of the long-lasting local anaesthetic products, presently on the market, is not due solely to the anaesthetic substances present such as procaine base and butesin but appears to be associated with the tissue destruction produced by the other ingredients present in the commercial preparations. Further studies to correlate nerve degeneration and long-lasting effects of local anaesthetic preparations are essential.

Acknowledgements

I would like to express my appreciation and thanks to all those who have assisted in any way with this work and would particularly like to acknowledge my indebtedness to Dr. J. K. W. Ferguson and Dr. G. H. W. Lucas of the Department of Pharmacology for their advice and facilities made available for this work (photographs of guinea pigs taken by Dr. Lucas); to Dr. E. E. Shouldice for his full financial support of this project as well as assisting in the clinical research part of the problem, together with Dr. E. A. Ryan; to the Staff of Shouldice Surgery for volunteering for some experiments; to Dr. S. Hartroft of the Banting and Best Department of Medical Research for the pathological studies contributed (microphotographs of slides taken by Dr. Hartroft); and to Dr. R. Chaplin of the Toronto East General Hospital for supplying a volunteer

for the cyclaine injection. I am indebted to the pharmaceutical firms mentioned below for Duracaine (Harvey Laboratories), Efocaine (Fougera), Knox special gelatin solution (Knox Gelatine Protein Products Inc.), and Diothane HCl (Merrell).

Résumé

Un anesthésique local dont les effets sont prolongés, couvrant les temps per et post-opératoires, durant vingt-quatre heures ou davantage, peut être avantageux dans certaines interventions chirurgicales. Plusieurs préparations commerciales sont offertes à cette fin, sur le marché. Le présent travail étudie ces préparations, tant au point de vue durée qu'au point de vue des réactions locales observées après injections sous-cutanées, intra-dermiques et intra-musculaires.

Toutes les préparations dont nous disposons occasionnèrent des réactions locales importantes avec les quantités couramment employées en anesthésie locale. Les agents de suspension (hydroxide d'aluminium) ou les solvants (glycol propylique) employés dans ces préparations semblent être en cause quant aux réactions locales notées.

La procaine basique semble être la moins dommageable des drogues vendues sur le marché. Quoique l'action anesthésique soit prolongée de plusieurs heures, le principal avantage de la procaine basique découle du fait que l'analgésie s'installe immédiatement.

D'après nos observations, il semble que l'action prolongée des anesthésiques locaux à effets-retard ne soit pas uniquement attribuable aux substances anesthésiques locales telles que la procaine basique ou la butesine, mais soit associée à une destruction tissulaire causée par les autres agents qui entrent dans ces préparations commerciales. D'autres études devront être poursuivies pour établir les rapports qui existent entre la dégénérescence nerveuse et les effets des préparations d'anesthésiques locaux à longue action.

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BLOOD VOLUME: AN IMPORTANT FACTOR IN ANESTHETIC MANAGEMENT

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Deviations from the normal of blood volume constitute the most common abnormality encountered among surgical patients. Deficits and excesses of blood volume alter efficiency of bodily functions so markedly that their recognition and correction are essential requisites to good anaesthetic and surgical care. Otherwise optimal physiologic function cannot be maintained during and following performance of anaesthetic and surgical procedures. Studies of blood volume provide the essential information not obtained by employment of other hematologic procedures currently in use. Clinical application of this technique promotes detection of quantitative and qualitative deficits and excesses of blood volume which escaped recognition in the past. Correction of these abnormalities have resulted in more adequate preparation of patients for operation and marked improvement of anaesthetic and surgical management. Anaesthesiologists are granted wider range of selectivity of agents and techniques. Surgeons are offered greater peace of mind. Patients are guaranteed greater safety. Reduction in the incidence of operative and postoperative complications is made possible.

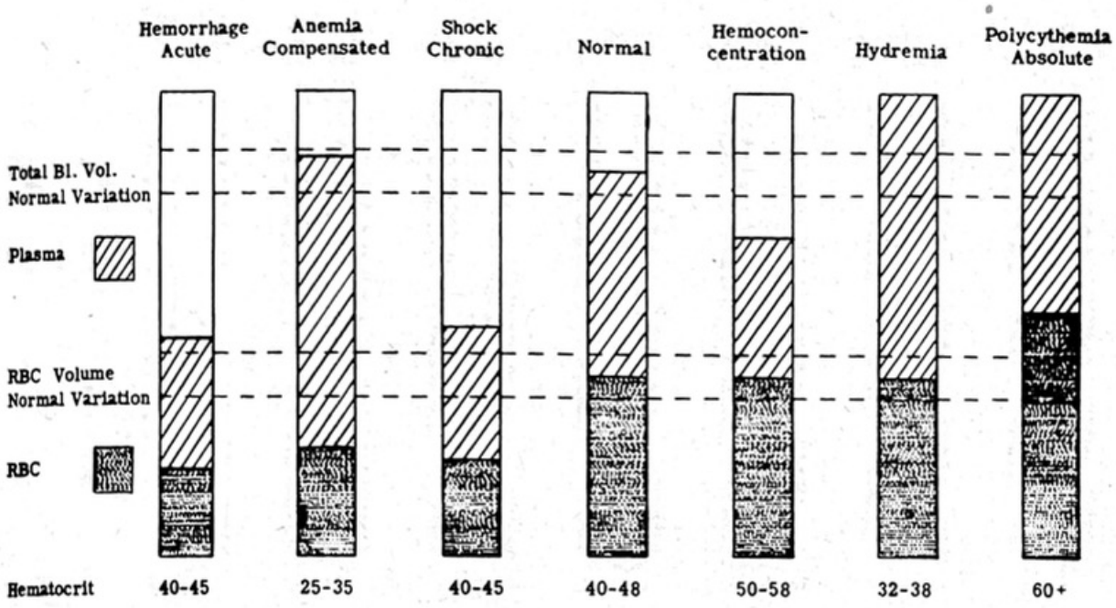
There are six common abnormalities of blood volume encountered among surgical patients. Deficits of blood volume include acute hemorrhage, compensated anemia, the syndrome of chronic shock and hemoconcentration due to dehydration. Hydremia and absolute polycythemia account for the excesses of blood volume. For descriptive purposes consider the seven schematic representations to a hematocrit tubes into which one's volume of circulating blood has been placed. (Figure 1.) The volume of red cells is represented by the blackened areas below. The cross-hatched portions above indicate the volume of plasma. Limits of normal red cell volume are depicted by the lower two interrupted horizontal lines. Normal range of plasma volume falls within the upper two interrupted horizontal lines. In the center is the schematic representation of the blood volume of a normal patient. To the left are the three common causes of deficits—acute hemorrhage, compensated anemia and the syndrome of chronic shock. Hemoconcentration is placed among the excesses because the characteristic elevation of the hematocrit readily confuses dehydration with absolute polycythemia. Hydremia and absolute polycythemia constitute the two actual causes of hypervolemia.

Immediately following acute hemorrhage and in the presence of the syndrome of chronic shock deficits of red cell volume and plasma volume co-exist. Values for the hematocrit remain within the limits of normal and are therefore not indicative of existing deficiencies. Compensated anemia is characterized by an excessive volume of plasma and a deficit of red cell volume. Values for the

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hematocrit, percentage of hemoglobin and red cell counts are low. Again they are not reliable guides for replacement therapy because hemodilution exaggerates the magnitude of the anemia. Hemoconcentration due to loss of circulating plasma produces the exact opposite hematologic picture. Marked elevation of the hematocrit results due to deficits of plasma in the presence of a normal volume of red cells. The possibility that this indicates the presence of polycythemia must be eliminated. Hydremia is characterized by excessive volumes of plasma in the presence of normal red cell mass. Values for the hematocrit and other tests of concentration are low. Hydremia therefore simulates the clinical and hematologic findings of compensated anemia. Excessive volume of red cells is the characteristic feature of absolute polycythemia. Primary polycythemia or



polycythemia vera is further characterized by a normal volume of plasma and an elevation of the platelet count. Secondary polycythemia as found in patients with chronic pulmonary, chronic or congenital heart disease, and with some renal and adrenal tumors may have excessive volumes of red cells and plasma.

These illustrations emphasize the significant fact that values for the hematocrit, percentage of hemoglobin and red cell counts are not truly indicative of deficits or excesses of blood volume. These laboratory procedures cannot be accurate unless the total volume of circulating blood is within limits of normal. It has been demonstrated that normal values for the hematocrit exist immediately following acute hemorrhage and in the presence of the syndrome of chronic shock. Deceptively low values are found with compensated anemia and hydremia, while abnormally high values exist in the presence of both dehydration and absolute polycythemia. It is obvious that in the absence of studies of blood volume grave errors of replacement therapy will be made.

Acute Hemorrhage

Management of acute loss of blood as presented by patients with bleeding peptic ulcers, traumatic rupture of a viscus, fractures of the femur and due to operative or postoperative hemorrhage demands prompt administration of whole

blood. While values for the hematocrit are of no value as guides to replacement therapy, studies of blood volume indicate the quantity of whole blood required to prevent development or continuance of shock. Thirty per cent reductions of total blood volume in the normal patient are accompanied by onset of shock unless appropriate therapy is administered promptly. Patients with existing deficits of blood volume develop vascular collapse with the loss of smaller amounts. Studies of blood volume are also of value in the differential diagnosis of shock due to causes other than loss of blood—such as bacteremia.

Immediate treatment of acute blood loss differs from that required after four to twelve hours have elapsed. In the past we have overlooked the fact that fluid from the interstitial compartment enters the vascular tree to compensate for blood lost during hemorrhage. Studies of blood volume brings to light glaring errors made in replacement therapy. Information they provide now makes it possible to use blood more efficiently. Deficits of blood volume are recognized and replenished according to specific indications. Improved physiologic conditions for operation therefore prevail. Transfusions of packed red cells rather than whole blood for anemic individuals whose volume of plasma is normal is a refinement which promotes better surgical care.

Compensated Anemia

Compensated anemia differs from acute hemorrhage in that within eight to twelve hours following acute loss of blood fluid from the interstitial spaces enters the circulation in an attempt to restore total blood volume to normal. Depending upon the time that has elapsed following hemorrhage three gradients of total blood volume restoration exist. Early in the process total blood volume is partially restored; within twenty-four to forty-eight hours the volume of circulating blood is usually normal. After forty-eight hours have elapsed the process of hemodilation may have over-compensated for the deficit. These gradients of plasma replacement are reflected by decreasing values for the hematocrit. Only when total blood volume has been restored to normal will the hematocrit indicate the actual degree of anemia. Otherwise the hematocrit will either approach normal values and fail to reveal existing deficits, or else it will exaggerate the magnitude of anemia because of excessive hemodilution. Studies of blood volume will indicate the specific needs of the patient with regard to quantity and quality of blood. Transfusions of packed red cells, or red cells suspended in saline or glucose will avoid hypervolemia. Otherwise circulatory overload may lead to cardiac failure, pulmonary edema or cerebral edema. Replacement therapy for patients with compensated anemia must be qualitative as well as quantitative.

Chronic Shock

Studies of blood volume will avoid errors of clinical judgment in management of patients presenting the syndrome of chronic shock. As is true immediately following acute loss of blood, patients with this syndrome have sizeable deficits of red cell and plasma volume. Values for the hematocrit and other tests of concentration are within normal limits and are of no value as therapeutic guides.

Formerly these hematologic reports, when normal, were interpreted to indicate that patients possessed adequate amounts of blood. We are now aware that these patients failed to tolerate or survive operation because they went to the operating room having significant deficits of whole blood. The syndrome of chronic shock presents a treacherous situation. None of the signs and symptoms of shock are exhibited till the characteristic susceptibility to vascular collapse is made apparent by the added stress imposed by performance of anaesthetic and operative procedures, or the additional loss of but small amounts of blood. The syndrome is characterized by:

1. Loss of weight.
2. Reduction of Blood Volume.
3. Increased Volume of Interstitial Fluid.
4. Depletion of Tissue and Plasma Protein.

It is found in patients with chronic infection, malnutrition, and malignant disease especially when metastases are present. Preoperative replacement of existing deficits of whole blood permits these patients to undergo operation without vascular collapse. Administration of whole blood hastens wound healing and convalescence. In the presence of anemia fabrication of hemoglobin has priority over manufacture of tissue protein. The importance of accurate differentiation between hemoconcentration due to loss of circulating plasma and that produced by excessive red cell volume warrants emphasis. Grave errors of therapeutic management are possible unless dependable guides are utilized. Studies of blood volume will differentiate between hemoconcentration caused by dehydration and that produced by hypervolemia. Treatment of the two conditions differ markedly. For the one administration of plasma or solutions containing appropriate electrolytes are indicated, while performance of phlebotomies or destruction of the excess red cell volume is essential for the other. In the presence of plasma deficits studies of blood volume indicate the need for hydration to eliminate the harmful effects of increased viscosity. Of 460 patients having values for the hematocrit of 50 or more, twenty-five per cent had deficits of circulating plasma, or dehydration. It is our belief that thrombophlebitis, coronary and cerebral thrombosis may be precipitated or aggravated by hemoconcentration, or polycythemia. Their presence may play a significant role in the course of these diseases and suggests that we may be over-cautious in restriction of fluids for many of these patients.

Hydremia

Physiologic hydremia accounts for the apparent anemias of pregnancy. Pathologic hydremia is found in patients with cirrhosis of the liver, renal insufficiency, chronic leukemia and following excessive fluid therapy. Existence of excessive volumes of plasma makes circulatory overload a real hazard if one relies upon values for the hematocrit. Studies of blood volume are indicated to prevent injudicious intravenous therapy.

Absolute Polycythemia

Hemoconcentration produced by excess volumes of red cells may cause complications because of increased viscosity, slowing of circulation, intravascular coagulation, thrombosis and circulatory overload. Unless excesses of red cell volume are detected and corrected prior to operation induction and maintenance of general anaesthesia are rendered difficult. Respiratory function is laboured, cyanosis of the head, neck and shoulders is marked, hypertension and increased venous pressure develops and excessive bleeding ensues due to vascular congestion. This sequence of events is considered by some to be pathognomonic of hemoconcentration and hypervolemia. Its presence contraindicates the administration of general anaesthesia. Elective operations should be postponed to provide time to reduce blood volume to optimal levels. In emergency regional anaesthesia, including spinal anaesthesia, is indicated whenever possible. Otherwise the patient is subject to onset of serious complications such as pulmonary or cerebral edema, cardiac failure, coronary thrombosis, cerebrovascular accidents or the formation of postoperative hematomata. In our experience hemoconcentration and hypervolemia are not uncommon findings. Their presence must be considered potentially hazardous to the well-being of medical as well as surgical patients.

Both primary and secondary varieties of absolute polycythemia are characterized by an increased volume of red cells. In the presence of primary polycythemia the volume of plasma is normal. With secondary polycythemia it may or may not be elevated. Development of secondary polycythemia accompanies existence of chronic hypoxia caused by chronic pulmonary and chronic or congenital heart disease. This variety of hypervolemia is also found in the presence of some renal or adrenal tumors. In the absence of chronic or congenital heart disease repeated controlled phlebotomies are recommended. These can be performed without untoward effects provided normal fluid and electrolyte balance are maintained. For patients whose polycythemia is secondary to chronic or congenital heart disease controlled phlebotomies of 250 cc. every third day are advised. Total blood volume should be reduced to that level which permits optimal physiologic function. Onset of persistent weakness, dizziness or syncope is an indication of too rapid, or excessive removal of blood. Not infrequently a residual excess volume must be allowed. In our experience removal of renal and adrenal tumors have been followed by disappearance of the accompanying secondary polycythemia.

Summary

The need for greater reliance upon fundamental physiologic principles to guide intravenous therapy has been emphasized. That commonly employed hematologic procedures are frequently unreliable has been demonstrated. Values for the hematocrit and other tests of concentration cannot accurately indicate existing volumes of circulating blood unless the total blood volume is within limits of normal. A plea has been made for more widespread use of transfusions of packed red cells for patients whose hematocrit is low following loss of blood. In the absence of hydremia low values for the hematocrit are indications for the

use of this specific therapy. Awareness of the possible presence of hemoconcentration and hypervolemia and the value of prophylactic measure recommended warrant serious consideration. Utilization of studies of blood volume to facilitate specific quantitative and qualitative replacement therapy and to avoid onset of complications is recommended. Provided intravenous therapy is guided by this method more patients will be adequately prepared for safe conduct of anaesthetic and surgical procedures. Smoothness and rapidity of convalescence can be assured with greater certainty.

Résumé

Les variations du volume sanguin sont très fréquentes chez les opérés. L'auteur rappelle qu'il faut se baser sur les principes de la physiologie pour mener à bien toute thérapeutique pratiquée par voie intraveineuse. Souvent, il n'y a pas lieu de trop se fier aux tests hématologiques de routine. Les données fournies par l'hématocrite ou d'autres épreuves de concentration ne mesurent pas exactement un volume de sang circulant à moins que le volume sanguin total soit lui-même dans les limites de la normale. On devrait plus souvent utiliser les transfusions concentrées d'érythrocytes chez les malades ayant saigné et qui ont un hématocrite abaissé. En l'absence d'hydrémie, un hématocrite abaissé devient une indication particulière pour utiliser cette thérapeutique spécifique. Le fait qu'il y ait possibilité d'hémoconcentration et d'hypervolémie mérite considération, tout en se rappelant l'importance des moyens prophylactiques connus. Pour faciliter une thérapeutique de remplacement aussi exactement quantitative que qualitative et pour prévenir l'apparition de complications, il faut se baser sur des études du volume sanguin. Si une thérapeutique intraveineuse se base sur cette méthode, un plus grand nombre de malades seront aptes à subir l'anesthésie et à être soumis à l'acte opératoire. D'autre part, une convalescence facile et rapide sera assurée avec plus de certitude.

EQUILIBRIUM OF THE AUTONOMIC NERVOUS SYSTEM IN ANAESTHESIA

BERNARD PARADIS, M.D.*

The title expresses our efforts to decrease abnormal reactions of the autonomic nervous system, before, during and after a surgical procedure. In order to achieve this, one must have a proper understanding of the functioning of the neuro-vegetative system, and of its chemical mediators; and also, the mode of action of selective drugs upon it.

Anaesthesia is no longer a simple matter of depressing the sensory-motor system. It is now a complicated method to calm the patient, taking care to maintain the equilibrium of his neuro-vegetative system.

Newer conceptions of endocrinologists such as Selye, Reilly, Crile, demonstrate that a surgical operation is *an aggression against the neuro-vegetative system and against the neuro-endocrinian system.* This aggression brings about a syndrome which is called the *"Irritation Syndrome"*.

One may define this syndrome as follows: Irritation of the autonomic nervous system is transmitted to the diencephalon. This irritation of the diencephalon stimulates the neuro-endocrinian system: the pituitary, the thyroid, and the suprarenal glands. The intensity of the irritations and of the responses will vary with the concentration of the irritants, and will also vary with the individual functioning of the sympathetic and the neuro-endocrinian system.

I do not wish to undertake the study of Hibernation, its new drugs and its endocrine question. All I wish to do is to summarize for you what we have done in the last few years, to stabilize the autonomic nervous system, and to balance its chemical mediators. In order to facilitate the understanding of this study, permit me to summarize for you the anatomy and the physiology of the autonomic nervous system.

Beckman in his excellent new book entitled "Pharmacology in clinical practice" gives the following definition and description of the autonomic nervous system: "It is the complex of nerves, ganglia and plexuses innervating the so-called vegetative organs: heart, blood vessels, glands, thoracic, abdominal and pelvic viscera, and smooth vessels. These are important structures, subject to many disease processes. They respond to stimuli and drugs in a specific way, and at specific places. One does not know why, but there are only two places where drugs could act on the autonomic nervous tract. These are: the cells and synapses.

"In the central nervous system there are so many of these cells and synapses that it is extremely difficult to determine just where a drug exerts its action, but in the autonomic nervous system it can only act upon the first cell at the site of origin of the nerve, or upon the only other cell there is along the tract, namely, out in the periphery either in specialized ganglia or in the walls of the organ innervated. Knowing this, the subject becomes greatly simplified.

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"We will need to know only a few things: the reflex arc, the site of the first and second cell, the site of action of the drugs used, the power of these drugs, the toxicity and the fate of the drugs and their antidotes."

Generally speaking the anaesthetist using his drugs considers the autonomic nervous system *as an efferent nervous system*. There are however afferent fibers from the viscera to the higher centers carried in some of these nerves (v.g. the sensory portions of the vagus, splanchnic and pelvic nerves), but these are medullated, do not respond to autonomic drugs, and belong essentially to the somatic central nervous system. These afferent fibers are blocked by local anaesthetics and spinal anaesthesia.

This is one of the main advantages of spinal anaesthesia as will be shown later.

The efferent, motor, two-cell and two-fiber autonomic nervous system (cell of origin, then preganglionic fiber, then ganglion or peripheral cell, then the non-medullated postganglionic fiber) needs merely to be traced out to be understood.

The system is comprised of two anatomically and physiologically distinct parts: the sympathetic and the para-sympathetic. The actions of the two parts are in opposition in the same organ, and it is possible to play one against the other by the proper choice of the drug. In the normal individual, there is a balance between the both systems, which must be maintained. A serious disequilibrium between the two would bring about real danger.

"The parasympathetic system comprises the whole of the vagus cranial nerve (tenth) and some of the oculo-motor (third), facial (seventh), the pharyngeal nerve (ninth), and the second, third, and fourth sacral nerves. There are some who believe that there exists parasympathetic fibers coming off the cord between the cranial and sacral segments, carried out in the somatic nerves, called the cord portion of the parasympathetic system."

At the neuro-visceral junction, there is production of a chemical mediator called acetylcholine. At the same site an enzyme is also produced, called cholinesterase which practically instantaneously destroys acetylcholine when it appears. The first cells of the parasympathetic are at the origin of these cranial nerves and in the lateral horns of the sacral portion. The second cells are in the ciliary, sphenopalatine, otic and submandibular ganglia. For the vagus nerve the second cells are located in the arborizations within the walls of the viscera, because the whole vagus nerve is a "pre-ganglionic fiber".

The sympathetic system originates from cells located in the lateral horns of the gray substance of the medulla from the first thoracic and the third lumbar regions of the cord. The cells of origin are in the lateral horns of the cord, and, except in the abdominal cavity, (where the splanchnic nerves are really extended white rami-communicantes, or pre ganglionic ones. The coeliac, upper and lower mesenteric ganglia are gray rami-communicantes or post-ganglionic ones.) the second cells are in the ganglia lying in front of the cord.

From those ganglia, the fibers are distributed to the glands and the viscera. At the neuro-visceral junction, chemical substances are produced called "Sympathin E and I", also called adrenergic substances, because of their analogous pharmacological action with adrenaline.

The anaesthetist must also consider the action of the sinoaortic mechanism. Its action is similar to that of the para-sympathetic system. It is not directly influenced by autonomic drugs as it belongs to afferent pathways. It is however influenced by variations of pressure (intra-aortic and intra-carotid), and also by various concentrations of O_2 and CO_2 and by variations of the Ph of the blood.

I will now tell you a few words about the chemical mediators of the nervous influx. They are: Adrenaline, Acetylcholine and Histamine.

Adrenaline possesses an action identical to that of the sympathetic nervous system:

(*a*) Vaso-constriction and hypertension
(*b*) Cardiac acceleration
(*c*) Decrease in the tonicity of smooth muscular fibers of the digestive tract, except at the sphincters
(*d*) Dilatation of the bronchi
(*e*) Hyperglycemia
(*f*) Elevation of the B.M.R.

All adrenergic fibers are post ganglionic ones. Accordingly, drugs may act in two different places:

(*a*) At the end of the adrenergic fiber, that is upon the effector organ with sympathicolytics or drugs paralysing the sympathetic system.
(*b*) Between the pre and post ganglionic fibers by blocking the passing of the impulse through the ganglia.

Acetylcholine is the chemical mediator of:

(*a*) para-sympathetic nerves
(*b*) pre ganglionic sympathetic nerves
(*c*) pre pheo-chromic nerves
(*d*) somatic nerves for striated muscles.

Its action is a muscarine one i.e.

(*a*) Vaso dilatation and hypotension
(*b*) Slowing of the heart beat with decrease of cardiac output
(*c*) Contraction of smooth muscular fibers: bronchi, oesophagus, gall bladder, stomach, bladder, uterus and pupilla
(*d*) Increase of secretions
(*e*) Lowering of the B.M.R.

Histamine has:

(*a*) Vaso-motor effects:
  1. Vaso-dilatation of capillaries with hypermeability
  2. Oedematous infiltration
  3. Hypotension.

(*b*) Muscular effects:
  1. Spasm of the bronchi
  2. Spasm of the intestines.

(*c*) Secretory effects:
Increases secretions.

Summarizing, the purpose of the anaesthetic procedure is to balance the neuro-vegetative system by controlling the action of the chemical mediators upon the nervous influx. Adrenaline and histamine are the two most important mediators to control.

We have at our disposal three methods to obtain this purpose.

1.–Hibernation, pharmacologically speaking. It consists in blocking as completely as possible all the mediators.

2.–Spinal anaesthesia up to T4 which will block the splanchnic nerve and will control adrenaline excess. This procedure will block most afferent and efferent pathways of the sympathetic system. The para-sympathetic system will remain untouched.

3.–Partial blocking of the predominating autonomic nervous system according to whichever of the two appears to be getting a headway during the surgical intervention.

In order to understand the mode of action of these three methods, we must now study the site of action of the various drugs we have at our disposal. These drugs act on four different sites: (*a*) the Afferent pathways, (*b*) the cerebral Centers, (*c*) the Synapses, (*d*) the Efferent pathways.

SUMMARY OF THE SITE OF ACTION OF SOME DRUGS ON THE REFLEX ARC

1. AFFERENT PATHWAYS: Medullated nerves: travel through somatic nerves.
    1. Block by local anaesthesia, v.g. infiltration of the splanchnic nerve.
    2. Spinal anaesthesia.
    3. Affected by
        1. Lowering B.M.R.
        2. Biochemical variations of blood.
        3. Tensional variations.
        4. Actions on Cyon and Hering nerves.
        5. Actions on carotid body.

2. CENTERS:
    1. Influenced by:
        1. Novocaine i.v.
        2. Opium and its derivatives.
        3. Atropine and Scopolamine.
        4. Demerol.
        5. Diparcol, phenergan, largactil.
        6. Analeptics, hibernative drugs.
    2. Not-Influenced by:
        1. Curares and curarizing agents.
        2. Ganglioplegic Drugs.

3. SYNAPSES:
    1. Annihilated by:
        1. Curares and curarizing agents.
        2. Novocaine i.v. and Methonium salts.
        3. Hibernative drugs.
    2. Site of predilection:
        1. Ganglionic fibers of the sympathetic:
            (*a*) Curares and curarizing agents
            (*b*) Novocaine i.v.
        2. Ganglionic fibers of the para-sympathetic (diparcol).
        3. Ganglion cells of the para-sympathetic:
            (*a*) Methonium derivatives.
            (*b*) T.E.A.

4. EFFERENT PATHWAYS:
    1. Para-sympathetic:
        1. Depressors: Atropine.
            Scopolamine.
            Demerol.
            Hibernative drugs.
        2. Stimulants: Morphine.
    2. Orthosympathetic:
        1. Depressors: Novocaine i.v.
        2. Stimulants: Analeptics.
        3. Anti-Histaminic: Synthetic ones.
        4. Myoneural junction of striated muscles: Curares and curarizing agents.

When one knows and understands these various sites of action, one must necessarily believe that there is such a thing as "Reflex Shock". One understands that a light or deep anaesthesia when it is purely a sensory one, does not prevent the occurrence of this shock, as there is no blocking of irritative impulses from the operative field. On account of this absence of blockage, there occurs an irritation of the neuro-vegetative nervous system, with production of adrenaline in excess. This production of adrenaline has at first a favorable effect but eventually *the action of adrenaline becomes inverted and this inversion of its pharmacological properties together with the synergistic action of acetylcholine brings about a very unfavorable condition. At this point may I mention that Novocaine is about the only drug which may counteract the inversion of adrenaline, and potentiate its action.*

I also wish to point out that I have voluntarily omitted the subject of the humoral action of the pituitary gland and of the adrenals as this will be discussed in the following paper.

Summarizing again, the objective which one must have in mind during a

surgical intervention, is a pre-operative preparation of the patient which will eliminate the loss of balance of the neuro-vegetative system, and an operative period and post-operative condition during which time the balance of the patient will be maintained, together with elimination or correction of all irritations of the Autonomic nervous system. With this achievement *one prevents inversion of adrenaline and secondarily oedema and hyperpermeability of capillaries.*

In order to facilitate the understanding of this paper, I have prepared for your information a summary of a few clinical cases which I will now bring to your attention.

Let us go back to nine years ago, in 1944. This case is that of Mrs. R.S., 62 years of age who was to be operated on for toxic goiter. Her B.M.R. was plus 102%. The anaesthesia consisted of intravenous pentothal of which 4 grams were administered, oxygen through a nasal catheter without intubation. The operation lasted three hours. Six hours after the end of the surgical procedure I was asked to examine the patient. I was told that a few hours after she had regained consciousness, she had fallen back into deep sleep, her blood pressure had risen from 140 to 200 mm. of mercury. Clinically the respiration was not embarrassed by any appreciable amount of bronchial secretions. However bronchial aspiration was performed to eliminate the possibility of excess CO_2 as a cause of the hypertension. 50 cc. of thick mucus was aspirated and immediately the blood pressure fell back to normal and the patient regained consciousness.

This is an example of a purely sensory anaesthesia which we would now condemn. Had we had in those days the use of the drugs which we now possess such as: Curarizing agents, ganglioplegic drugs, anti-histaminics and others, the amount of pentothol used would have been considerably reduced, intubation would have been possible, secretions would have been more easily aspirated, recovery would have been shortened and the shock which appeared would probably not have occurred.

Four years later, in 1948, we had the advantage of using curare and procaine. This is the case of Mrs. M.G., 51 years of age. Her blood pressure was 250 mm. of mercury and she was to be operated upon for thoraco-lumbar sympathectomy and unilateral surrenalectomy. She was given pentothal-curare with intra-tracheal intubation, and nitrous oxide-oxygen inhalation. The patient behaved well during the thoraco-lumbar sympathectomy with a fall in the blood pressure to somewhere around 160. When the surgeon began his surrenalectomy, suddenly the blood pressure fell to 0, the pulse became imperceptible, the patient stopped breathing and the peripheral circulation disappeared. 20 cc. of procaine was immediately administered intravenously, and controlled step-up respiration with 100% oxygen started. To our great amazement, all of a sudden, the pulse started beating again, the blood pressure rose, spontaneous breathing appeared and the surgeon could continue his operation without any further embarrassment. We were then in the presence of a serious disequilibrium of the neuro-vegetative system which could have brought about the death of the patient. In our opinion, what really happened was either, *Reilly's phenomenon* or there occurred an *inversion of adrenaline which was counteracted by our*

immediate use of intravenous procaine. Even if it seemed illogical to use procaine which is a hypotensive drug, its use was well justified with our present knowledge of the action of the neuro-vegetative system in anaesthesia. Had we had in those days the use of drugs such as: ganglioplegic drugs, anti-histaminics, and hibernative drugs, it seems to us that this shock would probably not have occurred.

The third case is that of a man, Mr. M.G. age 40, who was to be operated on for perforated duodenal ulcer. He had perforated his ulcer six days previously. When the patient arrived at the operating room his blood pressure was at zero, the pulse was imperceptible. He had no peripheral circulation and the R.B.C. was at 1,000,000. In spite of his moribund condition we performed a spinal anaesthesia basing ourselves on a paper presented by Samain, in Courtrai, Belgium, which we shall explain later. A 26 gauge needle was used and 28 mgms. of pontocaine-dextrose at a concentration of ½%, and density 1018. Pure oxygen was given and intravenous perfusion containing methedrine was installed. 1500 cc. of whole blood were also administered. The condition of the patient gradually got better and we did not look forward to any appreciable rise in blood pressure. After one hour and a half the peripheral circulation was quite good, the pulse began to beat well at a rate of 100/min., the hematocrit was found to be at 51%. At the end of the surgical procedure, during which time a partial gastrectomy was performed, the blood pressure was found to be at 110 and the general condition was very good.

One may wonder why we decided to use a spinal anaesthesia in a case like this one when the blood pressure was at zero. A spinal was used knowing that when it is raised to T4, it is the only anaesthesia which will block the afferent pathways, by blocking the irritative impulses passing through the splanchnic nerve to the diencephalon. In this way secondary influxes from the diencephalon to the suprarenals were accordingly blocked, blockage necessary as the abnormal activity of the suprarenals threatened to kill the patient. Therefore the mechanism of action was *that of blocking both the afferent and efferent pathways*, a good type of anaesthesia in such a case. Spinal at T4 should be considered as a precious mean to prevent the irritative syndrome, to counteract it when this syndrome is established and in this way maintain the equilibrium of the Autonomic nervous system.

Summary

We are at this date in possession on the one hand, of drugs acting on the neuro-vegetative system, acting electively on the Reflex arc, and on the other hand, of a great variety of anaesthetic products. Each and all chemical agents used will be chosen having in mind a definite action in a particular and precise portion of the Reflex arc. They will also be used with regard to the clinical picture of each patient, be he an alcoholic or a patient suffering from hyperthyroidism, a moribund, a cardiac, a sympathico or a para-sympathicomimetic patient and others.

Admitting this, one does not wonder that anaesthetic techniques may be

multiplied to infinity. The proper understanding of the anatomy, physiology, and pharmacology of the Autonomic nervous system is therefore indispensable for the proper handling of modern up to date anaesthesia.

If, after having improved the condition of the patient during the surgical procedure, one continues the maintenance of the same equilibrium of the Autonomic nervous system post-operatively, he will be amazed at the almost complete absence of post-operative complications pertaining to irritative reflexes, pulmonary and nervous complications which belong to the vaso-motor group.

Résumé

Le titre du travail exprime les efforts faits pour diminuer les réactions anormales du Système Nerveux Autonome avant, pendant et après une intervention chirurgicale.

Ces conceptions nouvelles en anesthésie découlent des travaux récents des endocrinologistes, tels que Selye, Reilly, et Cril e. D'après eux, toute intervention chirurgicale est une AGRESSION envers le système neuro-végétatif et le système neuro-endocrinien. Le syndrome qui en découle est connu sous le nom de SYNDROME D'IRRITATION. Ce syndrome atteint le Système Nerveux Autonome, ainsi que les glandes endocrines, soit la pituitaire, la thyroide et les surrenales.—

Pour faciliter cette étude, un résumé de l'anatomie et de la physiologie du Système Nerveux Autonome et de ses médiateurs chimiques fut élaboré.—

Trois méthodes sont à notre disposition pour maintenir un contrôle certain du Système Nerveux Autonome, et de ses médiateurs chimiques, soit l'ardénaline et l'histamine.—Ces méthodes sont (1) l'hibernation pharmacodynamique et physique complète, (2) la rachianesthésie à la deuxième ou quatrième vertèbre dorsale, (3) et enfin l'anesthésie partielle, équilibrée et balancée du Système Nerveux Autonome et de ses médiateurs chimiques. Ces méthodes sont décrites en détail. Il est décrit également l'endroit précis d'action de certains produits pharmacodynamiques sur l'Arc Reflexe.—

Trois cas cliniques typiques illustrent chacune de ces trois méthodes.

En conclusion, cette conception nouvelle d'une anesthésie neuro-végétative plutôt que sensistive a pour avantage de prévenir le Choc Reflexe, de prévenir également l'INVERSION D'ACTION DE L'ADRENALINE, et par ce fait de diminuer ou éliminer toutes les complications par et post opératoires, complications pulmonaires, vasomotrices, ou reflexes.—

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ARTIFICIAL HIBERNATION°°

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Considered as a new therapeutic concept in anaesthesia, artificial hibernation is the result of a pharmacodynamic process which brings about a controlled inhibition of the vegetative nervous system, an homeostatic neuroplegy. Artificial hibernation is synonymous neither of general refrigeration, neither of hypothermic anaesthesia, neither of controlled hypothermia nor of induced general hypothermia. Artificial hibernation should also not be mistaken for total hibernation which assumes a generalized refrigeration.

Artificial hibernation is based on the fact that every stress be it traumatic, infectious, toxic, psychic, or surgical, induces in the organism a series of neuro-endocrine reactions of defence. The surgical operation is not all; its associated indirect sequelae constitute by themselves as many secondary aggressions. Pain, fasting, dehydration, resorption of small haematomas are less striking but more prolonged aggressions. That series of neuro-endocrine reactions aims often beyond measure to maintain, as Claude Bernard and Cannon have emphasized, the constancy of the internal environment of the organism or its homeostasis.

As a basic principle, artificial hibernation infers a physiological rest to calm the reactions of homeostasic regulation primarily of neuro-vegetative initiation. According to the phenomenon of Reilly, it appears to-day that all hypotheses so far suggested to explain many organic reactions and affections (vascular, toxic, metabolic, chemical) should give place to the likelihood of a common reflex mechanism of neuro-vegetative origin.

The blockade of the autonomic nervous system has to be as extended as possible to inhibit all known mediators at every level–periphery, synapses, centres. In fact, this disconnection has to affect the sympathetic system more than the parasympathetic. The sympatho-adrenal system is more concerned with the expenditure of energy and is not essential to life. To emphasize one of its untoward actions, the sympathetic mediator, adrenaline likewise, inhibits the secretion of heparin by the mastzellen. There is a synergism between the catabolic adrenergic impulse and the ACTH-gluco-protidic hormones, also catabolic. These hormones affect coagulation in the same way as adrenaline and sympathetic stimulation, and can be responsible of thrombo-embolic accidents.

On the other hand, a parasympathetic predominance has to be maintained, concerned as it is with the functions of conservation and restoration. In other words, artificial hibernation employed to facilitate anaesthesia is based on the stabilization of the autonomic nervous system in order to minimize the irritative reflexes which cause vaso-motor and capillary disorders, and to diminish also the hypophyso-adrenal-cortical reaction. By setting the neuro-vegetative system

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at rest, the tissue requirements are reduced and life is slackened, a condition next to that of animals in hibernation status.

Reviewing drugs in accordance with this stabilization of the neuro-vegetative system during anaesthesia and surgery, it appears that the use of morphia was the first step toward artificial hibernation. The cholinergic action of this alkaloid is well known. Already in 1948, an article on "Pentothal-curare-nitrous oxide anaesthesia" published by the Department of anaesthesia of the Hotel-Dieu de Quebec, was foreseeing the possibilities of artificial hibernation in saying: "During anaesthesia with pentothal-curare-nitrous oxide anaesthesia, the patient is in a state which is near to latent life, to hibernation. Like during natural sleep, the patient is in a state of vagotonia. His general aspect shows it: his teguments are pink, dry and warm; there is peripheral vasodilation, no diaphoresis, myosis; respiratory movements are slow, calm and regular; every sympathetic influence appears inhibited."

Since then, although anaesthesia with pentothal-curare-nitrous-oxide-oxygen remains a procedure of choice, many new drugs are used in conjunction with it to accentuate the stabilization of the neuro-vegetative system. The drugs most commonly used are the phenothiazine derivatives: Phenergan, Diparcol and Largactyl.

Primarily antihistaminic, Phenergan is secondarily a hypnotic and a central and peripheral analgesic. Its use is advocated as a pre-anaesthetic medication.

Apart from being an antiparkinsonian, Diparcol is vagolytic, an acetylcholinolytic drug. It is slightly myoresolutive. As a broncho-dilator, it is a respiratory analeptic. Like procaine, it causes arteriolar vasodilation. Differently, atropine produces capillary vasodilation.

Largactyl seems to be a more potent stabilizer and deserves a more elaborate description. Largactyl is but slightly antihistaminic. It has a true ganglioplegic action; the blood pressure is lowered with a well equilibrated pulse pressure. This slight hypotensive effect is accompanied by vasodilation and is less pronounced than with hexamethonium. It moderates the homeostatic response to aggression and diminishes capillary permeability. Administered intravenously it produces tachycardia with a regular pulse. The ECG tracings demonstrate nothing but a sinusal tachycardia. It is possible that this tachycardia might be effected by a Bainbridge reflex.

The anticholinergic potency of Largactyl is between Diparcol and Parsidol. It inhibits convulsions induced by nicotine. Largactyl is primarily a sympatholytic drug. The adrenergic blockade is dominant. Sympatholytic and adrenolytic, it annuls or inverts adrenal hypertension. This action is confirmed experimentally in dogs by a direct splanchnic stimulation with a faradic current. This drug is a potent spasmolytic and anti-irritative. It stimulates respiration by increasing its depth and reducing its rate. The respiratory movements are not jerky. The sensitiveness of chemoreceptors in the carotid body is diminished.

As an antishock measure, Largactyl provides a better tolerance toward hemorrhagic shock. A not immediately corrected blood loss does not induce an abrupt lowering of the blood pressure, thus giving an optimal margin of safety.

As to its influence on the central nervous system, Largactyl interrupts the synapses between the cortex and the diencephalon, inducing in a way a pharmacological lobotomy. It has also a direct action on the diencephalon, turn-table of multiple incitements arising from the periphery. This cortico-visceral disconnection produces a state similar to amnesia, a tendency to sleep, to hypnosis, to sedation. A sedation which is characterized more by a passing out of mind of the pain sensation than a true analgesia. It has also antiemetic, antipyretic and hypothermic effects. The body temperature is sometimes lowered around 96–95 without shivering. Largactyl influences the activity of the pituitary gland through the hypothalmus. The depressing action of this drug on the thyroid gland has been demonstrated experimentally on dogs, with radio-active iodine 131.

Most of all, this neuro-vegetative stabilizer intensifies and potentiates the action of the barbiturates without increasing the respiratory depression. It potentiates the action of some anaesthetics: nitrous oxide, ether and cyclopropane, of the hypnotics, of the analgesics, of the curare-like drugs, and of pronestyl the hypotensive effect of which it increases considerably.

Since a preliminary report presented at the meeting of the Ontario division of the Canadian Anaesthetists' Society last April and up to now, Largactyl has been used at an average dose of 50 mgs. for 212 cases in the Department of anaesthesia of the Hotel-Dieu de Quebec. It has been given either intravenously or intramuscularly. Tachycardia is more present when this drug is administered by the intravenous route. When it is injected intravenously, it is slowly injected through the tubing of an isotonic saline solution. An isotonic saline solution in preference to a dextrose solution which would probably not be metabolyzed because of a state of inhibited pancreatic secretion with Largactyl.

It has been administered before induction or during maintenance of general anaesthesia. General anaesthesia being either pentothal-curare-nitrous oxide-oxygen or cyclopropane-curare or nitrous oxide-oxygen-ether. In a few cases, the usual pre-anaesthetic medication was replaced by Phenergan and Gardenal.

Here are the characteristic signs that were noted:

–on the cortex: sedation, euphoria, indolence, sometimes sleep, even snoring.

–on the striated muscles: difficult to raise head.

–on respiration: depth increased, rate diminished.

–on the heart: tachycardia sinusal type as evidenced by ECG tracings taken in the recovery room.

–on blood loss: The blood loss is measured for all the surgical procedures. With Largactyl, the blood loss is less. It is necessary only to compensate the total measured blood loss. This is different from the ordinary general anaesthesia where sometimes the blood loss has to be overcompensated for reestablishment to normal and to overcome peripheral collapse. A study of the quantities of blood transfusions administered during similar operations shows an appreciable diminution in cases receiving Largactyl in comparison to those given the usual general anaesthesia. It seems that a slight deficit is well tolerated. The advent of the vicious circle of peripheral collapse appears to be considerably delayed; capillary permeability, one

of its elements, is absent. This effect is more evident when Largactyl is given before operation than after.

—on the general aspect of the patient: skin is dry, warm and pink; venodilation; ungual bed, ear lobes, lips pink; myosis; inhibition more marked on the sympathetic than on the parasympathetic system.

—on the post-operative stage: less need for immediate analgesics; rarity of atelectasis, of pulmonary embolism, of phlebo-thrombosis; precocity and easiness in the reestablishment of intestinal peristalsis; body temperature rise less pronounced.

Largactyl has also been used with good results to overcome post-operative excitement, to treat hiccough, and to stop shivering sometimes present in the immediate post-operative stage of endo-urethral resections.

Largactyl either combined with Phenergan or not was given during spinal or regional anaesthesia, and for fenestration under local anesthesia, in order to replace the usual analgesics and hypnotics. It was noticed that the patients are calm and often inclined to sleep; that the blood pressure is less prone to fall abruptly, and that the spinal or the regional seems to be prolonged in duration.

Four patients have received, without untoward effects, two doses of Largactyl 50 mg. at varied intervals: 3 days, 13 days, 20 days and 21 days.

In the series of 212 cases presented, there are three deaths:

1—Male 36 years old. March 25th: gastrectomy under pentothal-flaxedil-nitrous oxide-oxygen anaesthesia and Largactyl 50 mg. Total measured blood loss: 550 cc.

April 8th: sudden death. Patient was supposed to leave hospital on the following day. Post-mortem: coronary stenosis due to marked parietal sclerosis. Iliac and femoral arteries: marked sclerosis.

2—Female 69 years old. Cortone therapy during the eleven preceding days. March 23rd: surgical exploration of the biliary ducts, under cyclopropane-curare-ether-oxygen anaesthesia. Largactyl 50 mg. Total measured blood loss: 200 cc.

April 14th: death from pulmonary embolism.

3—Female 67 years old. Diabetic. April 8th: total hysterectomy under cyclo-propane-curare-oxygen anaesthesia. Largactyl 50 mg. Total measured blood loss: 525 cc.

April 29th: death from cerebral hemorrhage.

In these three cases, death happened at a distant post-operative stage: 14 days, 23 days, and 21 days. So much so that it does not seem easy to establish a connection between the anaesthetic procedure and this untoward result.

To conclude with regard to so spectacular an innovation, instead of formulating a general opinion which would venture of being premature if not inadequate, it seems more suitable to recall a few words of Laborit and Huguenard: "The prominent part of the therapeutist is not anymore to facilitate an arrogant struggle for the conservation of homeostasis. On the contrary, he must promote momentarily an artificial involution, slow down the factors which determine evolution, that is the neuro-vegetative system and the rate of the cellular

metabolism, every time that an aggression of the external environment chances of exceeding the reactionary possibilities of the organism".

This great problem is considered exactly inside out of the angle from which it used to be viewed until now.

Operations	*Number*
Total hysterectomy	33
Wertheim	3
Gastric resection	24
Thyroidectomy	15
Biliary ducts	45
Carcinoma (bowels)	28
Nephrectomy	4
Mastoidectomy	2
Mastectomy	3
Eventration	10
Pneumectomy	3
Lobectomy	2
Thoracoplasty	2
Ureterostomy	3
Herniotomy	7
Colpo-perineorraphy	4
Bone grafting	1
Salpingo-ovariectomy	4
Varicose veins	2
Splenectomy	1
Exploratory laparotomy	2
Facial plasty	1
Cystostomy	1
Caldwell-Luc	1
Colectomy	2
Endo-urethral resection	3
Sympathectomy	1
Anal fistulectomy	1
Radical neck dissection	1
Cataract	1
Retro-pubic prostatectomy	1
Pylorplasty	1
Total	212 cases

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« L'HIBERNATION ARTIFICIELLE »

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Considérée comme une nouvelle idée thérapeutique en anesthésie, l'hibernation artificielle est le résultat d'un processus pharmacodynamique qui détermine une inhibition contrôlée du système nerveux végétatif, une neuroplégie stable. L'hibernation artificielle n'est pas synonyme de réfrigération, ni d'onesthésie avec hypothermie, ni d'hypothermie contrôlée. L'on ne doit pas de plus confondre hibernation artificielle et hibernation totale, laquelle suppose une réfrigération générale.

L'hibernation artificielle est basée sur le fait que tout «stress» fut-il traumatique, infectieux, toxique, psychique ou fut-il chirurgical, provoque dans l'organisme une série de réactions de défense d'ordre neuro-endocriniennes. L'intervention chirurgicale n'est pas tout, ses suites constituent par elles-mêmes autant d'agressions secondaires. La douleur, le jeûne, la déshydratation, la résorption de petits hématomes sont moins agressifs mais sont la cause d'agressions plus prolongées. Ces réactions neuro-endocriniennes, comme Claude Bernard et Cannon l'ont noté, tendent à maintenir souvent outre mesure la stabilité de l'organisme. Comme principe de base, l'hibernation artificielle procure un repos physiologique qui calme les réactions du système nerveux végétatif. D'après le phénomène de Reilly, il semble aujourd'hui, que toute hypothèse jusque là suggérée pour expliquer plusieurs réactions ou affections organiques (vasculaires, toxiques, métaboliques, chimiques) devrait laisser place à la probabilité d'un mécanisme réflexe commun d'origine neuro-végétative.

Le blocage du système nerveux autonome doit être aussi large que possible pour inhiber tout médiateur connu à chaque niveau: à la périphérie, aux synapses et aux centres. De fait, la déconnection doit toucher le sympathique plus que le parasympathique. Le système sympathique a trait aux dépenses d'énergie et n'est pas essentiel à la vie. Pour mentionner un de ses inconvénients, le médiateur sympathique, comme l'adrénaline, inhibe la sécrétion d'héparine par les mastzellen. Il y a synergisme entre l'impulsion adrénergique catabolique et l'ACTH hormones gluco-protidiques aussi cataboliques. Ces hormones affectent la coagulation de la même façon que l'adrénaline et qu'une stimulation du sympathique et peuvent être responsables d'accidents thromboemboliques.

D'autre part, l'on doit maintenir une prédominance du parasympathique, intéressé qu'il est dans les fonctions de restauration et de conservation. En d'autres termes, l'hibernation artificielle, employée pour faciliter l'anesthésie, est basée sur la stabilisation du système nerveux autonome de façon à minimiser les réflexes irritatifs qui causent des désordres vaso-moteurs et capillaires et pour amoindrir aussi la réaction hypophyso-surrénalienne. En mettant le système neuro-végétatif au repos, les besoins des tissus sont moindres et la vie est ralentie, condition similaire à celle des animaux en état d'hibernation.

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En conformité avec cette stabilisation du système nerveux végétatif durant l'anesthésie et la chirurgie, si l'on passe en revue les diverses drogues employées, il semble que l'emploi de la morphine fut le premier pas dans la marche vers l'hibernation artificielle. L'action cholinergique de cet alcaloïde est bien connu. Déjà en 1948, un article sur l'«anesthésie au pentothal-curare et protoxide d'azote» publié par le département d'anesthésie de L'Hôtel-Dieu de Québec entrevoyait les possibilités d'une hibernation artificielle par ces mots: «Durant l'anesthésie au pentothal curare protoxide d'azote, le patient est dans un état qui est voisin de la vie latente, l'hibernation. Comme durant le sommeil naturel le patient est dans un état de vagotonie. Son aspect clinique en fait preuve: ses téguments sont roses, secs et chauds; il y a vaso-dilatation périphérique, pas de diaphorèse, myosis; les mouvements respiratoires sont lents calmes et réguliers: toute influence sympathique semble inhibée.»

Depuis lors, quoique l'anesthésie au pentothal-curare protoxide demeure un procédé de choix, plusieurs nouvelles drogues sont employées conjointement avec ce procédé pour accentuer la stabilisation du système nerveux végétatif. Les drogues les plus communément utilisées sont les dérivés de la phénothiazine: Phénergan, Diparcol, Largactil.

Antihistaminique d'abord, le Phénergan est secondairement un hypnotique et un analgésique central et périphérique. On l'emploie comme prémédication. En plus d'être un médicament anti-Parkinsonnien, le Diparcol est un vagolytique et une acétylcholinolytique. C'est un léger relaxant musculaire. Entant broncho-dilatateur, c'est un analeptique respiratoire. De même que la procaïne, il cause une vaso-dilatation artériolaire alors que l'atropine détermine une vaso-dilatation capillaire.

Le Largactil semble être un stabilisateur plus puissant et mérite une description plus élaborée. Légèrement antihistaminique, le Largactil est réellement un ganglio-plégique: il abaisse la pression artérielle et le pouls demeure plein. Cet effet hypotenseur léger s'accompagne de vaso-dilatation et l'hypotension est moindre que celle produite par l'hexamethonium. Il tempère la réponse de l'organisme à l'agression et il diminue la perméabilité capillaire. Administré par voie intra-veineuse, il produit de la tachycardie mais le pouls demeure régulier; d'ailleurs, l'électrocardiogramme ne révèle rien d'autre qu'une tachycardie sinusale. Il est possible que cette tachycardie soit la conséquence d'un réflexe de BainBridge.

La puissance anticholinerigique du Largactil se situe entre le Diparcol et le Parsidol. Il inhibe les convulsions provoquées par la nicotine. Sympatholytique et adrénolytique, le Largactil annule ou inverse l'effet hypertenseur produit par l'adrénaline. Cet avancé est prouvé expérimentalement chez le chien par stimulation directe du splanchnique avec un courant faradique. C'est aussi un anti-spasmodique puissant et un anti-irritant. C'est un stimulant respiratoire: il augmente l'amplitude et diminue la fréquence des mouvements respiratoires qui ne sont pas saccadés. Il diminue aussi la sensibilité des chimio-récepteurs du corps carotidien.

Comme prévention du choc, le Largactil fournit une meilleure tolérance vis-à-vis le choc hémorragique. Une perte sanguine non corrigée immédiatement

n'amène pas une brusque chute de la tension artécielle, ce qui procure une plus grande marge de sécurité.

Pour ce qui est de son influence sur le système nerveux central, le Largactil interrompt la contiguité entre le cortex et le diencéphale réalisant pour ainsi dire une lobotomie pharmacologique. Il exerce aussi une action directe sur le diencéphale.

Cette déconnection cortico-viscérale produit un état similaire à l'amnésie, une tendance au sommeil, à l'hypnose à la sédation. Sédation qui est caractérisée beaucoup plus par la non-interprétation de la sensation douloureuse que par l'analgésie réelle. Le Largactil est aussi anti-émétique, antipyrique et hypothermique. Il abaisse quelquefois la température du corps aux environs de 96–95 et cela sans frissons. Le Largactil influence l'activité de l'hypophyse par l'intermédiaire de l'hypothalamus. L'action dépressive de cette drogue sur la glande thyroidienne a été démontrée expérimentalement chez le chien avec l'iode radioactif 131.

De plus, ce puissant stabilisateur du système neuro-végétatif intensifie, potentialise l'action des barbituriques sans augmenter la dépression respiratoire. Il potentialise l'action de quelques agents anesthésiques: protoxide d'azote, cyclopropane, éther, des hypnotiques, des analgésiques et des curares, et du pronestyl dont il augmente aussi considérablement l'effet hypotenseur.

Depuis le rapport préliminaire présenté le 11 avril à la Société Canadienne d'Anesthésie, division de l'Ontario, à venir jusqu'à maintenant, le Largactil fut employé à la dose moyenne de 50 mgms pour 212 cas dans le département d'Anesthésie de L'Hôtel-Dieu de Québec. Il fut administré par voie intra-veineuse ou intra-musculaire. La tachycardie est plus fréquente lorsque la drogue est donnée par la voie intra-veineuse; on l'injecte alors par le tube d'un soluté salé isotonique. Le soluté salé isotonique est préférable au soluté glucosé qui ne serait probablement pas métabolisé à cause de l'inhibition de la sécrétion pancréatique par le Largactil.

Le Largactil fut donné soit avant, soit durant l'anesthésie générale qui se faisait au pentothal-curare-protoxide d'azote ou au cyclopropane-curare ou bien encore au protoxide d'azote-oxygène-éther. Dans quelques cas, la prémédication usuelle fut remplacée par le phénergan et le gardénal.

Voici les principaux signes cliniques que l'on nota:

–sur le cortex: sédation, euphorie, indolence, sommeil qui va parfois jusqu'au ronflement;

–sur les muscles striés: difficulté à se lever la tête;

–sur la respiration: augmentation de l'amplitude et diminution de la fréquence des mouvements respiratoires;

–sur le coeur: tachycardie sinusale révélée par les électrocardiogrammes enregistrés à la chambre de recouvrement;

–sur la perte sanguine: La perte sanguine est pesée pour toute intervention chirurgicale. Avec le Largactil, la perte sanguine est moindre et il y a lieu de ne remplacer adéquatement que le sang perdu. De là la différence avec l'anesthésie générale ordinaire où la perte sanguine doit être com-

pensée outre mesure pour la rééquilibration normale de l'organisme et pour prévenir le collapsus périphérique. Une étude comparative de la quantité de transfusions données pour les mêmes interventions démontre que, dans les cas où le Largactil fut employé, il y a eu diminution appréciable du nombre de transfusions. Il semble qu'un léger déficit soit bien toléré. Le cercle vicieux du collapsus périphérique semble considérablement retardé; une de ses composantes, la perméabilité capillaire est absente. Ceci est d'autant plus évident que le Largactil est donné avant l'intervention plutôt qu'après;

–sur l'aspect clinique du patient: la peau est sèche, chaude et rose; il y a dilatation des veines, les ongles, les oreilles et lèvres sont roses; il y a myosis; l'inhibition du sympathique est plus marquée que celle du parasympathique;

–sur les suites opératoires: les besoins immédiats d'analgésiques sont moindres; les cas d'atélectasies, d'embolies pulmonaires et de phlébothromboses sont plutôt rares; le péristaltisme intestinal est rétabli plus rapidement et plus précocement; la courbe thermique est moins accentuée.

Le Largactil fut aussi employé avec succès pour traiter l'agitation post opératoire, le hoquet et pour arrêter les frissons survenant quelquefois après les résections endo-uréthrales.

Le Largactil associé ou non au Phénergan fut donné durant l'anesthésie rachidienne ou régionale et durant la fénestration sous anesthésie locale dans le but de remplacer les analgésiques et hyponotiques usuels. L'on nota que les patients demeuraient calmes, qu'ils étaient enclins au sommeil, que la pression artérielle avait moins tendance à chuter brusquement, et que la durée de l'anesthésie rachidienne ou régionale semblait prolongée.

Quatre patients ont reçu, sans incidents fâcheux, deux doses de 50 mgms de Largactil, à intervalles variés: 3 jours, 13 jours, 20 jours, 21 jours.

Sur les 212 cas présentés, trois morts sont rapportés.

I–Un homme de 36 ans opéré le 25 mars pour résection de l'estomac et endormi au pentothal–flaxedil–protoxide d'azote–oxygène et Largactil 50 mgms. La perte sanguine se chiffrait à 550 c.c.

Le 18 avril ce patient, qui devait quitter l'hôpital le lendemain, meurt subitement. L'autopsie décèle une sténose coronarienne due à une sclérose pariétale marquée et une sclérose marquée des vaisseaux et fémoraux.

II–Une femme de 69 ans traitée à la Cortisone durant les onze jours pércédent l'intervention. Le 23 mars, elle subit une exploration des voies biliares sous anesthésie au cyclopropane–curare–éther–oxygène et Largactil 50 mgms. La perte sanguine fut de 200 c.c. Le 14 avril, elle décédait à la suite d'une embolie pulmonaire.

III–Il s'agit d'une femme de 67 ans diabétique. Le 18 avril, elle subit une hystérectomie totale sous anesthésie au cyclopropane–curare–oxygène et Largactil 50 mgms. La perte sanguine fut de 525 c.c. Le 29 avril, une hémorragie cérébrale l'emportait.

Dans ces trois cas, la mort survint assez longtemps après l'intervention, soit 14 jours, 23 jours et 21 jours, de sorte qu'il ne semble pas facile d'établir une relation de cause à effet entre le genre d'anesthésie et ces fâcheux résultats.

En conclusion à l'égard de cette innovation si spectaculaire, au lieu de formuler une opinion générale qui risquerait d'être inadéquate sinon prématurée, il semble plus convenable de rappeler ces quelques mots de Laborit & Huguenard: «le rôle principal du thérapeute n'est plus de faciliter une lutte arrogante pour la conservation de l'homeostasie. Au contraire, il doit promouvoir momentanément une involution artificielle, ralentir les facteurs qui déterminent l'évolution, c'est-à-dire le système neuro-végétatif et le taux du métabolisme cellulaire, chaque fois qu'une agression de l'environnement extérieur a des chances de dépasser les possibilités réactionnelles de l'organisme.»

Ce grand problème est considéré exactement sous un angle opposé à celui sous lequel il était envisagé jusqu'à maintenant.

A REPORT OF THE USE OF SUCCINYL CHOLINE IN ANAESTHESIA

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I. Introduction

In recent times it has been considered that the properties desirable in drugs used in general anaesthesia are ready controllability through adequate potency, rapidity of action and rapid elimination, with specificity of action and absence of undesirable side effects. These desiderata apply to drugs for the production of muscular relaxation in the same measure that they apply to anaesthetic agents.

Heretofore drugs used for the production of muscular relaxation during anaesthesia have all fallen short in at least some of these desirable qualities. Of the drugs available until recently the maximum effect did not appear until from three to eight minutes after administration (1, 2), the effect lasted a minimum of 10 minutes (2), and undesirable side effects such as bronchospasm, tachycardia, hypotension or hypertension, and excessive salivation occurred with the various drugs (2, 3, 4, 5). Prolonged respiratory depression was an occasional complication.

Our observations during the past year on the use of succinyl choline as a muscle relaxant in anaesthesia have indicated that this agent more nearly approaches the concept of the ideal drug for this purpose than others which we have used.

II. Chemical and Physical Factors

Succinylcholine was synthesized by Hunt in 1906 (6). The drug is prepared for clinical use in the form of a halogen salt, the anion being chlorine, bromine or iodine. The structural formula of the chloride is as follows:

$$\begin{array}{l} \qquad\qquad\qquad\quad Cl \\ CH_2 \cdot COO(CH_2)_2N(CH_3)_3 \\ | \\ CH_2 \cdot COO(CH_2)_2N(CH_3)_3 \\ \qquad\qquad\qquad\quad Cl \end{array}$$

It is instructive to compare this formula with that of acteycholine, which is as follows:

$$\begin{array}{l} \qquad\qquad\qquad\quad /OH \\ CH_3 \cdot COO(CH_2)_2N(CH_3)_3 \end{array}$$

It will at once be evident that this drug (succinylcholine) is composed of two molecules of acetylcholine, and may be designated as di-acetylcholine.

The halogen salts of succinyl choline occur as white crystalline odourless substances. They are readily soluble in water to form acidic solutions. In alkaline solutions this substance hydrolizes rapidly as the ester linkage, giving one

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molecule of succinic acid, and two of choline. Similar hydrolysis proceeds slowly when the drug is stored in solutions prepared for clinical use.

III. Pharmacology

The neuromuscular blocking action of succinylcholine was described independently in 1949 by Bovet (7) and by Phillips (8). It was later investigated by Castillo and de Beer (9, 10).

Succinylcholine produces relaxation through production of a prolonged depolarization of the muscle membrane at the motor end plate (11), perhaps equivalent to a flooding of the motor end plate with active acetyl-choline. Evans *et al* (12) postulate that this action is produced by neutralizing the action of cholinesterase, thus permitting the unopposed action of acetylcholine on the muscle end plate. When the drug is given rapidly it produces twitching of whole muscle groups, indicating a preliminary stimulating effect. In the conscious patient paralysis is preceded by painful muscle contractions. The action is extremely rapid, and the short duration is due to immediate enzymatic hydrolysis (9, 10, 12). In this it differs from the curarines, gallamine tri-iodide and decamethonium compounds, which are excreted unchanged. There is no evidence of any effect on the blood pressure, or of any histamine-like action. There is no apparent effect on the heart muscle, and the electrocardiograph tracings are unaltered by the drug (7).

Unlike d-tubocurarine and gallamine tri-iodide, the activity of this drug is not counteracted by the anticholinesterases such as prostigmine, eserine and "Tensilon". On the contrary, since the destruction of the drug depends on the presence and action of plasma pseudocholinesterase and acetylcholinesterase, these drugs will prolong its action (13, 14). Procaine also prolongs the effect of the drug by competing for the enzyme system (15). Succinyl-choline likewise has a prolonged action in individuals who have a low plasma cholinesterase level such as patients suffering from severe liver disease, anaemia, and poisoning by certain insecticides or "nerve" gases (13). Although ordinarily no clinical antidotes are required, it is of interest that, experimentally, atropine, Etamon, and certain anti-adrenaline compounds are antagonists.

IV. Clinical Report

Since 1 June 1952 we have recorded the use of succinyl-choline for muscular relaxation during anaesthesia in 170 major surgical cases and for 70 vaginal obstetrical deliveries. In addition it has been used for brief relaxation to facilitate the introduction of an endotracheal tube in more than 500 cases in our hospital. The major cases recorded in this series are those done by the authors alone. The methods used to administer the drug for the major cases have been intermittent injection and continuous intravenous infusion. For the obstetrical deliveries and intubations single intravenous doses have been given. Methods used and combination with anaesthetic agents are as follows:

1. Associated with Pentothal or Kemithal for induction and intubation only, followed by:

(*a*) Cyclopropane
(*b*) Cyclopropane and ether
(*c*) Ether
(*d*) N_2O and O_2
(*e*) Nitrous oxide/trichlorethylene/oxygen
(*f*) Nitrous oxide and some other relaxant
(*g*) Oxygen only.

2. Intermittent Injection associated with N_2O, trichlorethylene, or cyclopropane. (10 cases)
3. Continuous intravenous infusion with N_2O or Cyclopropane as the main agent. Concentration of infused solution 0.1% or 0.2%. (160 cases).
4. Single injection for obstetrical delivery with forceps in association with N_2O-Trichlorethylene-O_2 or cyclopropane. (70 cases)

The preparations used in this series have been the chloride salt, the bromide, and, in a few cases only, the iodide. They have been found to be equally satisfactory in all respects. Since the salts differ in weight, the equivalent doses are somewhat different, and the various preparations must be related to one another on the basis of the amount of active cation contained in a unit volume of solution. The relative doses are as follows:

Preparation	*Active Cation*	*Equivalent*
Chloride	100 mgm	125 mgm
Bromide	100 mgm	150 mgm
Iodide	100 mgm	180 mgm

The intermittent method of administration was used in the first few of our series. It was found to be almost impossible by this method to maintain an even plane of relaxation, and the method was quickly abandoned. Except for those patients who received only a single dose, the method employed in the remainder of the series was a continuous intravenous drip infusion of a solution of 0.1% or 0.2% in normal saline or in glucose 5% in distilled water.

The quantities of succinyl-choline used in this study varied from 20 mgm. to 1200 mgm. of the active cation, and the operating time from 10 minutes to 5½ hours. The usual amount used was approximately 200 mgm. of the active cation per hour, although this varied with the muscle mass of the patient and his general physical condition.

In obstetrical patients succinylcholine chloride has been used to facilitate forceps delivery and breech delivery. In these patients we have given a single dose of 30 to 40 mgm. of the chloride as the forceps were applied, or, in the case of breech delivery, when the obstetrician was prepared to deliver the baby. The resulting relaxation has been useful in reducing the size of episiotomy required, or in abolishing the necessity for episiotomy.

V. Discussion

We have used succinyl-choline in patients presented for all types of surgery without respect to age or physical condition. Due to the fact that children under

14 years of age are not ordinarily admitted to our hospital there are no patients of this group included in this series. We are of the firm opinion that when the dosage required is carefully regulated to the requirements of the individual, that this drug may be safely used for the production of any degree of muscular relaxation or paralysis in any patient, as long as due regard is paid to the maintenance of adequate oxygenation.

With the exception of the obstetrical cases, Pentothal sodium or Kemithal sodium has been used for the induction of anaesthesia in all the patients of this series. In 87 cases these drugs were continued as the sole anaesthetic agent or in association with Nitrous Oxide. In no case have we found a greater requirement for the barbiturate, as suggested by Foldes (14). On the contrary, we have found that the requirement for pentothal and kemithal appeared to be reduced when relaxation could be so thoroughly controlled through the use of succinylcholine.

In 17 cases in the series another relaxant was used during the operation. These were not administered until all evident affect of the succinylcholine had disappeared. In no case was any variation in action of these other relaxants noted which could have been attributable to the previous use of succinylcholine.

It has been our experience that the degree of relaxation could be varied at will and within a few seconds with this drug when the continuous infusion method was used. Relaxation following an initial adequate dose became maximal within 1 to 3 minutes. When apnoea was produced by a single dose, respiration returned within three minutes in every case, although they might remain inadequate for a further 2 to 4 minutes. The dose required to produce adequate relaxation in the average robust adult patient was 20 mgm. of the chloride and 30 mgm. of the bromide. Increasing these doses by 50% resulted in apnoea.

The rapid intravenous injection of these preparations in relaxing doses resulted in generalized muscular fibrillation. If the same dose were injected more slowly in dilute solution in an intravenous infusion visible twitching did not occur. Rapid administration of doses of the order of 40 mgm. of the chloride or 60 mgm. of the bromide would in some patients produce muscular disturbances approaching convulsive magnitude.

Most patients in this series who were relaxed adequately for abdominal surgery required assisted or artificial ventilation throughout the operation. Under these circumstances muscle tone may be recovered by a still apnoeiac patient, and this sometimes made it difficult to judge the requirement for more of the relaxant. In spite of the maintenance of a profound degree of relaxation with these drugs, sometimes over a period of hours, these patients recovered their muscle tone within 3 to 6 minutes after the infusion was stopped. In no case did we encounter the prolonged periods of apnoea which has been described in the recent literature (16, 17, 18). Several patients showed post-operative respiratory inadequacy, but this was not more than is occasionally seen in association with the anaesthetic agents used in these cases. No distinctive effects on blood pressure and pulse have been seen, except a rise in both associated with carbon-dioxide accumulation due to depressed respirations. One patient developed

hiccoughs which were intractable until cyclopropane was substituted for nitrous oxide as the anaesthetic agent.

Some patients exhibited an unusual amount of sweating, but we are unable to determine that this phenomenon was related to the succinylcholine.

Although there is probably no doubt that this substance is transmitted across the placental barrier into the foetal circulation, we have encountered no case of flaccidity in the baby after its use for obstetrical procedures, other than those which were obviously attributable to obstetrical difficulties, or obstruction of the infant's airway.

Contra-indications to the use of the drug are few. Poisoning with the "nerve gases", which include some of the newer insecticides, is a definite contra-indication, as is dystrophia myotonia congenita. We believe that it may be used in patients who have low cholinesterase activity from the other causes mentioned above, providing that the dosage is carefully controlled to the patient's requirement by using a drip infusion of dilute solution.

In cases where it is important that the fluid intake of a patient must be restricted, the continuous infusion technique should be avoided or modified by increasing the concentration of succinylcholine in the infused solution, so that the probable fluid tolerance of the patient need not be exceeded.

VI. Conclusions

We feel that succinylcholine is a most valuable addition to the armamentarium of the anaesthetist. The ready controllability of muscular relaxation by this drug, the absence of undesirable side reactions, and the rapidity with which complete recovery from its effects occurs, even after the administration of large doses over long periods of time, make it particularly valuable. We feel that, with the few specific contra-indications stated, it can be safely used in any patient providing that the rate of administration is controlled to suit the patients requirement for the relaxation necessary, and that due attention is paid to adequate oxygenation. We believe that this drug will probably not replace the longer acting drugs completely in anaesthetic practice, but it will undoubtedly replace them for many indications.

VII. Summary

1. Succinylcholine is an "ultra-short-acting" depolarizing muscle relaxant which has proved satisfactory for the production of muscular relaxation during anaesthesia in all types of surgical intervention.

2. In the cases studied in this report, no serious complications or side reactions have been encountered either during or following the use of this drug.

3. The rapid action, and rapid recovery from this drug result in a controllability of muscular relaxation which make it unique amongst drugs used in anaesthetic practise today.

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as "Scoline," by Burroughs Wellcome & Co., in the form of the chloride as "Anectine" and by Poulenc Ltd., in the form of the Bromide in their preparation "Brevidil M". A sample of the iodide was provided by Brent Laboratories.

Résumé

La succinylcholine est un relâcheur musculaire du type dépolarisant que présente les avantages de rapidité à la fois dans son action et sa destruction dans l'organisme. La rapide destruction est due à l'hydrolyse enzymatique de la substance en acide succinique et choline. L'action du produit peut être prolongée chez les malades ayant une basse activité de cholinesterase plasmatique, tels que ceux qui souffrent d'une grave maladie de foie, anémie et empoisonnement par certains insecticides ou «gaz des nerfs». L'activité de la drogue n'est pas contre-carrée par les anticholesterases telles que la prostigmine et le «Tensilon».

Les auteurs ont rapporté l'emploi de cette drogue en vue d'un relâchement musculaire dans 170 grandes opérations chirurgicales, 70 accouchements par voie vaginale et d'un court relâchement pour l'introduction d'une tube endotracheal dans plus de 500 cas.

Dans l'accouchement et l'intubation la succinylcholine était donnée en une seule injection intraveineuse. Quelques unes des grandes procédures chirurgicales étaient menées à bien par la technique de l'injection intermittente, mais dans la majorité des cas la drogue était administrée en goutte-à-goutte intraveineux (perfusion contenant de 0.1% à 0.2% de succinylcholine dans une solution saline ou glucosée à 5% dans de l'eau distillée). Les doses employées ont varié de 20 mgm. à 1200 mgm.

Pas de complications ni d'effets d'accompagnement ni pendant ni après l'emploi de cette drogue étaient rencontrées. L'action rapide et le rapide rétablissement conduisent à une facilité de contrôler le relâchement musculaire qui la rend unique parmi les drogues employées dans la pratique anesthésique.

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HEXAMETHONIUM CHLORIDE FOR CONTROLLED HYPOTENSION DURING OPERATION**

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This report is intentionally not an elaborate scientific document. I wish to report a few clinical experiences with one of the methonium salts, called hexamethonium chloride. The search for a drug that would produce a sustained hypotension and so reduce blood loss during surgery first led to the discovery of tetraethyl-ammonium chloride and subsequently of the two methonium compounds, pentamethonium and hexamethonium by Paton and Saimis (Paton, W. D. M. and Saimis, E. J. (1949) Brit. J. Pharmacology). The hypotensive action of tetra-ethylammonium salts and of the methonium compounds has been exploited by several workers. Hexamethonium chloride has become the drug of choice because of its more reliable action.

During the first six months of 1952, we have used this drug in over one hundred varied surgical procedures, our main objective being the reduction of blood loss. The cases totaled 155. The longest was of 5½ hrs. duration and the shortest lasted 35 minutes. The ages varied from 14 to 81 years. Two hundred and eighty mgs. was the maximum amount given in a single case. The surgical cases were those encountered in a general hospital. As the pooling of blood in the dilated vessels is dependent upon posture, the cases selected were those in which postural drainage was possible by elevating the surgical site; operations on the lower extremities using the Trendelenburg position. Thoracic and upper abdominal surgery could also be done with minimal bleeding when the patient was placed in reverse Trendelenburg. Operations on the liver and the kidney were accompanied by less bleeding if that part of the body was raised.

Even in the horizontal position bleeding is less severe when the systolic blood pressure is around 60 mm. of Hg. However for minimal bleeding, postural drainage is important. With a systolic blood pressure below 70 mm. of Hg and a good postural drainage a fair amount of blood can be saved. This is especially true in longer bloody surgical procedures. We do not think however that the saving of 200 or 300 or even 500 c.c. of blood warrants the use of hypotensive drugs unless the saving of such a small amount of blood could shorten the operating time considerably.

When hypotension has been produced by one of the methonium salts the peripheral vaso-constriction that is seen in hemorrhagic states, is almost non-existent. Due to the pooling of blood in the dilated vessels the skin of the lower part is usually pink, dry and warm, that of the elevated part is pale but also dry and warm. Even when bleeding has been quite severe the skin in the lowered part will keep its color, warmth and dryness contrary to the clinical

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picture of profuse hemorrhage. However, the blood pressure is still a reliable sign when vasomotor control has been removed; the loss of even a small amount of blood may lead to a considerable fall of blood pressure.

Sometimes both systolic and diastolic blood pressure completely disappear while the patient's general appearance is good. Fortunately the pressure can be quickly restored by adequate intravenous replacement. In most cases the systolic B.P. will *drop* or *decrease* more than the diastolic giving a small "differential" or pulse pressure between 20 and 35 mg. of Hg.

Hypertensive patients will often have a considerable fall even with small amount of hexamethonium chloride. The pulse usually remains between 80 and 100 and it is often of a bounding nature. Its normal reactions to blood loss are obtunded by the autonomic block. However an insufficient venous return to the heart and a decreased blood volume will give a weak pulse and a slight increase in rate.

There is no doubt that in suitable cases the blood loss is reduced considerably and this alone is good reason for using this method. But apart from this reduced blood loss, the protection afforded to the heart by the autonomic block is of a great interest.

The heart seems to be well protected against vagal reflexes and this in thoracic surgery is of great significance.

We have not used the blocking agent in enough thoracic cases to be able to draw definite conclusions. However, the few cases that we did (3) were free of any cardiac disturbances. Two of them had electrocardiographic tracings during the operation. It is possible that the autonomic block produced by the methonium salts may prove to be a better way to protect cardiac automaticity than is the use of procaine or procaine amide, and in that sort of surgery where cardiac irritability is apt to occur it is questionable which of these two is more important, the reduction of blood loss or the protection afforded to the heart. Fortunately both go on a par. Unfortunately in thoracic surgery with an open pleura, a good venous return and sufficient cardiac output are difficult to maintain. The pulse and the blood pressure will often disappear even after short periods of positive intra-pulmonary pressure.

The autonomic block has also been found useful in patients with thyrotoxicosis. Three patients in spite of a long preparation were still running a rapid pulse. It was thought that a thyroidectomy could be done without harm if the blocking agent was used. Pentothal and syscurine were injected for intubation and they were given C_3H_6/O_2 for maintenance. A slow and bounding pulse followed the injection of the blocking agent in each case. No cardiac irregularities were noticed. The bleeding was much reduced. Their postoperative course was good.

We think that when a patient's circulatory system has been deprived in part of its normal vaso-motor control, means should be taken to minimize as much as possible the deleterious effects that such a method could produce on vital organs. Some precautions should be taken, among which is the maintenance of good oxygenation. Whether or not the arterial oxygen content is decreased during that period of hypotension I do not know. We have noticed, however, that in the

absence of respiratory activity the pulse becomes weak and sometimes rapid and the blood pressure tends to fall, signs which disappear when the respiration returns to normal. Patients with induced hypotension seem very sensitive to even a small degree of hypoxia. Neither do they seem to tolerate well any decrease in venous return to the heart. So these patients need good oxygenation and respiratory excursions should be kept near normal to facilitate the venous return. Controlled or assisted respirations should be used when respirations become inadequate. This bears a greater importance in the reverse Trendelenburg position with the pooling of a large quantity of blood in the lowered part of the body. It is also important to appreciate the blood loss and to replace it accurately; the loss of a small amount of blood after vaso-motor control has been removed may lead to a considerable fall in blood pressure.

Much attention must be paid to the patient in the post-surgical period. Reactionary hemorrhage though seldom seen is a possibility. Before closing the thorax or the abdomen, we prefer to raise the blood pressure slightly by changing the position of the patient and as the case may be, by an intravenous infusion. This will help to identify any important bleeding spot. If the blood pressure is still low at the closure, it is better to raise it very slowly thereafter to prevent any reactionary hemorrhage. Our patients are kept in the recovery room until their blood pressure has practically returned to the preoperative level. This sometimes constitutes a problem, the recovery room being jammed with patients especially on days with large operative schedule. Vaso-constrictors are given only when intravenous therapy and the posture have failed to raise the blood pressure sufficiently. Patients with low blood pressure are given oxygen.

All patients do not react similarly to the drug. Some seem very sensitive; in the aged and the hypertensive group for instance a dose of 20 or 30 mgs. may lower the blood pressure considerably. On the contrary, some will show much resistance and large doses of the drug fail to lower their blood pressure to any important degree. Others will show abnormal reactions to the blocking agent. A 36-year-old white man was given 125 mg. of hexamethonium chloride in successive doses over a period of 1 hour. His pulse and B.P. rose over the preoperative level. The para-sympathetic part of his autonomic nervous system seemed to have been more influenced than the sympathetic part. On two occasions, large amounts of hexamethonium chloride were injected by mistake. Two hundred mgs. or 5 c.c. C6 instead of C 10 were mixed with 500 mg. of Two hundred mgs. or 5 c.c. C_6 instead of C_{10} were mixed with 500 mg. of 2½ of pentothal and injected to facilitate the intubation. The error was soon realized and the patient's condition was followed with great care. The diastolic pressure was unobtainable. In one case, a slight Trendelenburg elevated the B.P. slightly and 3 hrs. after this massive injection the B.P. was near normal. The second case was given a small dose of a vaso-constrictor and his B.P. was normal 3½ hrs. after the injection of the methonium salts. This I report only to show that large single doses of the hexamethonium salts may sometimes not be harmful.

When a drug is used that produces such an unphysiological condition one is

right in wondering whether or not some other functions will be disturbed. In other words, what are the risks of lowering the blood pressure? Those risks are not clearly defined yet but there is little doubt that coronary thrombosis could be precipitated in patients with advanced arterio-sclerosis. It is also possible that cerebral thrombosis could occur although we do not know much about the cerebral blood flow when widespread vaso-dilatation is produced by such drugs. For these reasons we think that elderly patients and those with a history of coronary disease should not be given the drug.

The production of a clot with obliteration of a large vessel is also apt to occur when a marked hypotension is combined with a prolonged compression of an artery or a vein; such was the following case. A 60-year-old white male was brought to the O.R. for a nephrectomy, because of a large gravitz tumor of the left kidney. Pre-operative studies revealed a moderate generalised arterio-sclerosis, chronic bronchitis and hypertension. His blood pressure was 190 systolic and 100 diastolic, his hematocrit was 42. Under anaesthesia the patient was placed in the right lateral position with the bar raised (kidney position). Excision of the tumor was difficult and large packs were inserted with probable compression of the abdominal aorta. The systolic blood pressure was maintained between 90 and 75 and the bleeding was minimum. The operation lasted 3 hrs. and total blood loss during the operation amounted to about 700 cc., all of which was replaced by whole blood during the operation. Pentothal and Syncurine had been injected to facilitate intubation. Cyclopropane and oxygen were given intermittently up to the last half hour. Nitrous oxide and oxygen in a semi-closed circuit were given during the last half hour. The patient's condition was good in spite of his low blood pressure. After the completion of surgery the patient was brought to the recovery room. One hour later, he was conscious enough to complain of pain in his left leg and thigh. The left lower extremity was then found to be pale and cold. No pulse could be felt even over the femoral artery. The surgeon was called and a diagnosis of occlusion of the femoral or the left iliac artery was made. A continuous paravertebral sympathetic block was instituted but it did not bring any improvement. An emergency removal of the clot was advised but the permission for a second operation could not be obtained from the patient's wife. He died 12 hrs. later. The postmortem revealed a long clot that was obliterating the left femoral artery, the left iliac artery and the lower third of the abdominal aorta. No suture or clamp seemed to have been placed on any of the arteries involved. It was our impression that the prolonged hypotension with its consequent reduced blood flow, associated with a prolonged compression of the aorta were most likely to be blamed.

Reactionary hemorrhage occurred once in the case of a 34-year-old female who had an abdomino-perineal resection for a carcinoma of the rectum. The operation lasted two hours. The systolic blood pressure was maintained between 60 and 80 mm. of Hg. The blood loss was about 600 c.c. Replacement therapy was given in the recovery room and the blood pressure rose slowly to a 110. The patient was then sent back to her room. Five hours after the end of the surgical procedure, bleeding started from the perineal incision. She lost about 1000 c.c. of

blood. The blood pressure was then 60–40. One thousand c.c. of whole blood had to be given to restore her blood volume. No vaso-constrictor had been used.

Kidney function was also a matter of worry because it had been reported by Aos and Bhegan in Sweden that glomerular filtration, renal blood flow and the excretion of urine were reduced by an injection of tetraethyl ammonium bromide in normal persons. As the hypotension produced by hexamethonium chloride is of a longer duration than that produced by tetraethyl ammonium bromide it is likely that excretion of urine would be reduced by the latter. The urinary output was checked in most of our patients receiving hexamethonium chloride and the findings were not in agreement with what we expected. The urinary output was greater than we expected ranging between 1200 c.c. and 1500 c.c. during the first 24 hrs. and this with an average intake of 2500 c.c. to 3000 c.c. The output could possibly be lower in patients with nephritis but we had no occasion to check it.

No case of paralytic ileus was seen and the incidence of vomiting and nausea has remained unchanged.

One patient presented a low blood pressure of two and a half days duration. He was a mild hypertensive 55 year of age, cystectomised for a carcinoma of the bladder. His B.P. previous to surgery was 165/95. During the operation the B.P. was maintained at 70/45 most of the time with a total of 150 mgs. of hexamethonium chloride. The blood loss amounted to about a 1000 c.c. and was still at 70/50 despite a slight Trendelenburg and intravenous fluids. His general condition, however, was good. Methedrine 30 mg. I.M. raised the B.P. to 140/50. During the next two days the B.P. could not be maintained at its normal level without the use of vaso-constrictors. The urinary output was good and the post-operative course was normal.

Conclusion

The production of hypotension during surgical operations by blocking the autonomic ganglia with methonium drugs can be of benefit to the patient and the surgeon. It can reduce blood loss considerably which in turn shortens the operating time. It has a place in long operations where blood loss is expected to be great.

Patients seem to be better protected against vagal reflexes when such an autonomic ganglion block is produced. The importance of good oxygenation and a sufficient venous return to the heart must be emphasized. The method seems to be unsuitable for those with poor vascular system. The methonium salts have yet no place in the routine management of patients though they may prove very useful in certain cases. There is no doubt that the drug is difficult to use but we must not overlook its valuable possibilities.

Résumé

On rapporte des expériences cliniques dans l'emploi de l'hexamethonium chloride pour produire une hypotension dans 155 cas. Les risques encourus rendent nécessaire de selectionner les cas où l'hypotension provoquée est guaran-

tie, i.e. où la conservation du sang est profitable au malade. La technique doit être evitée dans les cas avérés de maladie cardio-vasculaire, particulièrement d'artério-sclerose et chez les vieillards. L'importance d'une bonne oxygénation est mise en valeur car ces malades sont très sensibles à l'anoxie. Il n'y a pas de dosage standard puisque les malades réagissent différemment les uns des autres. La plus grande dose totale était 250 mgms. Il est important que le champ opératoire soit élevée pour assurer un champ sec. On rapporte l'importance de remplacer le sang en quantité égale au sang perdu, car les grandes hemorrhagies ne sont pas bien tolérées. Deux complications sont discutées avec des cas illustrés, une thrombose post-opérative et une hemorrhagie réactionnaire.

THE ARTERIOTOMY METHOD OF PRODUCING AND CONTROLLING HYPOTENSION**

ELIZABETH MARTIN, M.D.*

Clinical observations on removal of Olfactory groove meningioma had led Gardner (1) to the conclusion that if the patient's blood pressure could be made to fall first instead of last, then the blood withdrawn might be re-transfused, as well as the surgeons work made easier from the beginning. The clinical application of this idea was based on the experimental work of Page and his co-workers in 1943 through 1946 and his method has seen very little change since. Page has shown that peripheral vasoconstriction is an early and constant accompaniment of shock, and that during and for a short time after the initiation of shock, this vasoconstriction is neurogenic due to vasomotor reflexes. As the brief period of nervous irritation passes off, an unfiltrable substance appears in the plasma, which, when injected into the vessels of an isolated perfused rabbit's ear, causes severe and prolonged vasoconstriction. Thus, there is good reason to believe that the persistent nonneurogenic vasoconstriction in shock is due to the appearance of this substance in the blood. It is neither of renal nor of adrenal origin but arises from the site of tissue injury. They believe that it was chiefly this peripheral vasoconstriction which was responsible for the ease with which hemostasis was obtained. It is not necessary to reduce blood pressure to a dangerously low level in order to bring the peripheral vasoconstrictor mechanism into play.

The advantages of infusion into the artery in the treatment of shock are enumerated by Page, who stated that infusion by the arterial route delivers blood immediately to the myocardium and medullary centers and rapidly restores blood pressure to normal. Controlled induced hypotension by arteriotomy has been employed only in certain types of craniotomy and in the fenestration operation. In craniotomy the bleeding may be extensive and almost routinely demands blood transfusion during or after the operation. In fenestration, patients are subject to vexing and annoying hemorrhage which may interfere with a satisfactory result.

The Apparatus

This consists of a Y/shaped glass cannula and connections. One limb of the cannula (the bleeding tube) leads to a flask containing 50 cc. of 4.0 per cent sodium citrate solution and suitable for the collection of 500 cc. of blood. This flask when filled with the patient's blood is readily replaced by a similar one. A tube leading from the other limb of the cannula has three connections:

(*a*) an aneroid manometer for direct reading of the arterial pressure;

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the heart to undue violence. Based on our experience and recent work of Van Noate, we have performed cardiac operations (1) to test this method in thoracic operations, and (2) to obviate massive bleeding from opening heart cavities. On 8 dogs, we have performed section of the ventricles and attempted valvulotomy. We have undertaken bloodletting only during cardiac section, reducing to a minimum the period of hypotension. The deaths of 5 dogs in this series were due to errors in technique of operation or transfusion. From a surgical standpoint after releasing only a small quantity of blood, considering the pressure level, section of the heart muscle does not produce such a gush of blood at each systole. The heart appears more as a pouch, well filled, with the blood always oozing from the wound, but easily controlled by the surgeon. In our opinion, this is the most important advantage of the method of this type of operation. We have concluded that bloodletting to diminish bleeding during operation should not exceed one-third or one-fourth of the total blood volume. This amount suffices to maintain hypotension only for the brief period necessary for the operation. This is especially true in thoracic surgery. From the analysis it may seem strange that we have obtained such low hypotension even with withdrawal of small amounts of blood. According to our opinion, this can result from sudden arterial bloodletting, which acts just like a whipping. The sudden withdrawal, for example, of 200 cc. of blood in a few seconds does not allow the organism to adapt itself at once and prevents defensive compensatory mechanisms coming into play. From bloodletting until all reaction of these mechanisms a brief period ensues, during which the pressure falls and remains at a rather low level. This period corresponds to the stage of simple hypotension of Wiggers and denotes the beginning of oligoaemic shock. From a practical viewpoint, this method has appeared particularly useful in operations on the liver and the heart. Every surgeon knows the great difficulties of these operations from excessive and often uncontrollable bleeding. Less valuable results have been obtained in operations upon the lungs and the kidneys. The authors consider it contraindicated in all operations upon the spleen. It is of great help to the anaesthetist in diminishing greatly the quantity of anaesthetic to be administered, as hypotension in itself, is considered from special points of view, to be a form of anaesthesia."

Résumé

La méthode d'artériotomie dans la production et le contrôle de l'hypotension.

La première application clinique suivie de retransfusion fut pratiquée par Page et ses collaborateurs, au début de 1943. Ils croyaient que la vasoconstriction périférique qui suit l'artériotomie était responsable de la facilité avec laquelle l'hémostase était obtenue. L'artériotomie a été pratiquée dans certains types de craniotomie et défénestration avec réduction de la perte de sang et amélioration des conditions opératoires. L'appareillage et la technique sont décrits d'après Page. Les avantages sont réduction de la spoliation sanguine et diminution de la tension du cerveau. On opère plus facilement sur les aneurismes intracraniens et les tumeurs vasculaires sous basse pression. Un rythme respiratoire accru est

le signal d'alarme exigeant une retransfusion. Les réactions de transfusion ne surviennent pas et la ligature de l'artère radiale ne s'est pas manifestée en tant qu'inconvénient permanent. Un rapport de Borri et Natallis d'Italie est commenté en détails; il traite de l'emploi de l'artériotomie dans les opérations sur le foie, le rein et le cœur.

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MORBIDITY, MORTALITY AND PATHOLOGY IN INDUCED HYPOTENSION**

S. L. VANDEWATER, M.D.*

There have been numerous reports on the clinical use of induced hypotension in the literature, particularly the British, beginning with Griffiths and Gillies of Edinburgh in 1948 (1). When these articles are read, one gets the impression that induced hypotension is a common, safe, and everyday procedure. In most of these articles, a frank discussion of indications, contraindications and complications is conspicuous by its absence. Does one conclude then, that induced hypotension can be carried out with impunity on unselected cases? I believe this to be a dangerous conclusion. Induced hypotension is not without its hazards; and complications will inevitably occur with its indiscriminate use. I believe we can say now, that induced hypotension has its place in the practice of Anaesthesia, but a *limited* one, and the careful use of these methods carries with it a calculated risk. It is not a procedure for the casual Anaesthetist, nor for the Anaesthetist who is not fully informed in cardio-vascular physiology and pathology.

When induced hypotension was first introduced in Edinburgh (3), considerable horror was voiced by the physicians, particularly the cardiologists, and I am sure this has been true in all medical centres. All sorts of complications and deaths, due to myocardial ischemia, venous thrombosis, liver and renal failure, and reactionary haemorrhage were predicted. In the past five years, these predictions have been partly correct. The complications, although relatively few, have nevertheless occurred.

The results of a recent survey by Yale University (2) of a questionnaire sent to British Anaesthetists, indicated 601 complications (other than deaths) in 21,125 cases of induced hypotension, an incidence of 2.8%. This figure is meaningless, but the list of complications make the figure interesting, as they can all be attributed directly to the hypotension. e.g.—Anuria (54), oliguria (30), cerebral thrombosis (20), retinal thrombosis (2), coronary thrombosis (15), reactionary haemorrhage (164), visual difficulty (126), delayed recovery (190).

This same report gives a total mortality related to the hypotension procedure as 46, i.e.—1 in 459 cases. e.g.—renal failure, cerebral thrombosis, coronary thrombosis, cardiac arrest.

Organe mentions two cases of cerebral damage following the use of arteriotomy and several patients with post-operative renal impairment (although occurring in malignant hypotensive cases). Organe also illustrates an important point, previously noted by Gillies of the danger of giving pentothal to a patient under induced hypotension with a sudden fatal termination.

In the year 1950–51, three cases of cardiac arrest, occurred in Edinburgh (3),

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two were successfully resuscitated, one was not. Dr. Gillies in a recent communication (3) pointed out, that in the use of "total spinal" one must accept "the irreducible minimum of post-operative neurological complications associated with it." He has had two cases of peripheral nerve palsies.

In my own series of one hundred cases in the past year I can report one cerebral thrombosis, one reactionary haemorrhage, and one death related to hypotension. This was in a carefully selected series where the patients had to satisfy four requirements, besides the indication for hypotension. Briefly these requirements are:

1. Upper age limit of 55.
2. Reasonably good physical health with no debilitating disease, dehydration, toxicity or suspected low blood volume.
3. No history of cardiovascular disease.
4. Minimum haemoglobin of 65%.

These requirements are those taught by Dr. Gillies, and again recently confirmed by him (3) in a personal communication, except that he raises the minimal haemoglobin figure to 80%.

Death due to hypotension may be classified as early or late. The early cause is cardiac arrest or failure due to inadequate coronary circulation, particularly where there is existing coronary artery disease, or secondarily to anoxia of the cerebral vital centres. The late causes, may be due to cerebral thrombosis, myocardial infarction, renal or hepatic failure. Shackman *et al* (4) of the Post Graduate School of London, recently showed in humans that the fall in cardiac output may on occasion be profound, with no relation to the observed level of the blood pressure. They mention one fatal case of liver necrosis.

The non-fatal complications, other than perhaps haemorrhage, are due to altered hemodynamics during hypotension with decreased rate of flow, and tissue anoxia. It is quite possible that a normal cardio-vascular system can function and deliver an adequate blood supply under low pressure to sustain life, but this is an unknown quantity with athero-selerotic vessels, diseased myocardium, decreased blood volume, and decreased hemoglobin. Bigelow (5) has recently pointed out to me the possibility of blood sludging at low pressures in acutely ill, toxic patients, or in the presence of infection or carcinoma, with its damaging effects on such organs as liver and kidneys.

The methods of inducing hypotension are four, arteriotomy, total sympathetic block, ganglionic blocking agents and finally deep anaesthesia with chloroform or the heavy use of thiopentone. The latter is mentioned only to be condemned without comment.

1. Arteriotomy differs from the other two methods as it produces hypotension with vasoconstriction. In effect it creates an artificial state of shock. The degree of hypotension reached with safety is probably not below 75 mm. Hg., below which one runs the risk of ischemia of the vital organs, and the procedure might easily become irreversible. It requires the use of rather complicated sterile apparatus and it is time consuming. The only place for its use is probably when

the patient is in a head up position as in posterior fossa exploration in neurosurgery.

2. Total spinal block either subarachnoid or epidural, particularly the former, is probably the most reliable of the methods. The latter may be technically difficult. Once the hypotension is established extreme positions are not necessary. It has the excellent advantage of abdominal relaxation, but does carry the minimal added risk of neurological complications, and the disadvantage of time limitation.

3. The use of ganglion blocking drugs are probably the most useful and adaptable method. Most writers give an average figure of 20% failure. Recently the use of procaine amide (6) has been advocated in those cases of failure where there is little drop in pressure even with extreme posture, with a marked tachycardia. The use of 0.5–1.0 gram of procaine or procaine amide, although effective in slowing the rate and dropping the pressure, is not without its dangers. Cardiac arrythmias may result, such as prolonged A-V conduction, partial to complete heart block and even cardiac standstill. In some cases a prolonged state of postoperative hypotension occurs which can be alarming. These drugs (i.e. the methonium drugs) should be used with caution in cases of renal impairment as the kidneys are the only source of excretion and this may lead to prolonged action.

Résumé

Des complications de l'emploi clinique de l'hypotension provoquée, surviennent plus communément qu'on est amené à le croire d'après la plupart des rapports dans la littérature. Ces complications attribuables à l'hypotension provoquée sont l'anurie, l'oligurie; thromboses cérébrale, retinienne, coronaire; hémorrhagie de réaction. La mort a été attribuée à la défaillance rénale, aux thromboses cérébrales et coronaires et à l'arrêt cardiaque. Des cas de défaillance hépatique et rénale ont été rapportés. L'auteur sent que l'hypotension provoquée occupe une place utile mais limitée dans la pratique de l'anesthésie. Les cas doivent être soigneusement choisis en ce qui concerne l'âge, l'état du système cardio-vasculaire, l'état physique en général, l'absence de maladie débilitante, déshydration et basse masse sanguine, l'hémoglobine devant être de 65% ou 80% de préférence. Le danger d'augmenter C6 avec de la procaine ou Pronestyl est décelé par la production de sérieuses arythmies cardiaques.

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CARBON DIOXIDE IN ANAESTHESIA

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One of the most frequent causes of serious difficulty during anaesthesia is simple respiratory obstruction and its consequent asphyxia. Asphyxia is a word which carries unpleasant connotations such as strangulation, suffocation, the inhalation of irrespirable gases, and death. More specifically, it connotes an interference with the normal transport system such that there is both a lack of oxygen and an excess of carbon dioxide in the tissues. In the oft repeated warnings against airway obstruction, treatment with oxygen has been properly emphasized as the treatment for hypoxia. However, this is only half the problem since there is also hypercapnia which can be eliminated only by adequate ventilation. The continual moment-to-moment excretion of the waste product carbon dioxide is hardly less important than the continuous supply of oxygen for metabolic use.

It is well to remember that normal respiration is brought about by the need for elimination of carbon dioxide. Excretion of carbon dioxide through the respiratory tract should not be hindered. However, all the anaesthetic agents and many of the methods of administration in use today, limit the ventilatory function of the anaesthetized individual, frequently to the point at which he can no longer adequately get rid of carbon dioxide. Additional contributing factors make undesirable accumulation of carbon dioxide during anaesthesia a daily hazard rather than an unusual or rare problem. It may, therefore, be well to enumerate the factors which may allow accumulation of carbon dioxide and to review the information which is available concerning its deleterious effects.

Causes of CO_2 Accumulation

The chief causes which singly or in combination lead to undue tissue accumulation of carbon dioxide are the unwise use of depressant drugs, the use of unsuitable anaesthetic techniques or apparatus, airway obstruction, rigid surgical requirements of position, quietude or relaxation, and occasionally, inherent disease of the patient. All these may interfere with the normal transport of carbon dioxide. The common denominator is the reduction in the ability of the patient to adequately ventilate his own alveoli. Assistance of respiration is, therefore, frequently necessary during anaesthesia.

Ventilatory function is lessened by all the general depressant agents in common use for anaesthesia today, either through reduced tidal exchange or decreased respiratory rate with a lowered minute volume. A similar reduction in tidal exchange results from peripheral interference with the activity of muscles of respiration following the use of either relaxant drugs or high spinal anaesthesia.

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The provision of flaccid relaxation for the surgical requirements in the upper abdomen by whatever means invariably embarrasses spontaneous respiratory efforts since the abdominal muscles have the same innervation as the intercostals and of themselves also function as accessory muscles of respiration. The decreased ventilation becomes even more marked if the diaphragm is splinted by severe abdominal packing, the presence of a large tumor (f.i. pregnancy), or the injudicious use of the trendelenburg position.

The operative position frequently contributes still more difficulties. It is easy to misuse both the gallbladder and kidney rests, while the unmodified lateral position in itself sometimes tends to severely restrict respiratory movement of the thoracic cage. In intrathoracic operations the combined factors of a partially collapsed lung with its apparent effect of an arterio-venous shunt, mediastinal shift, and mechanical disadvantage to the dependent lung, brought about by the operative position, make the opportunity for inadequacy of spontaneous respiratory effort very great indeed.

Normal ventilation is somewhat inefficient since it is accomplished by repeated partial dilution rather than by "draft" or "cross ventilation". Since no effective dilution or mixing occurs in the trachea and upper respiratory passages, this area is not effective in ventilation and has been, therefore, designated as dead space. The ventilation accomplished by any given tidal volume depends upon the relationship between the effective exchange volume of fresh air (tidal volume minus the dead space) and the volume of lung to be ventilated. Anything which allows an increased proportion of the exhaled volume to be rebreathed reduces ventilation by mechanically extending the dead space. Therefore, in anaesthesia apparatus rebreathing must be reduced to a minimum, or carbon dioxide must be removed from the re-inhaled gas volume. The early anaesthetists kept these facts in mind as they began to design equipment to facilitate the administration of ether and chloroform.

The inhalers designed by both Morton and Snow were each equipped with valves which precluded the possibility of appreciable rebreathing. Snow, himself, also tried rebreathing ether in a closed system using alkali to absorb the carbon dioxide, but apparently he did not use such a system on patients. Devices introduced by later anaesthetists disregarded these principles and allowed partial or even complete rebreathing. As a result of this, in many parts of the world pernicious rebreathing devices are still in daily usage. In the last thirty-five years increasing effort has been made to apply our knowledge toward the maintenance of normal physiology as nearly as is possible during the administration of anaesthesia. Established facts were combined in such a way by Dennis Jackson in the laboratory, and Ralph Waters in the clinic, to provide a reasonably efficient system for the absorption of carbon dioxide from anaesthetic atmospheres. The use of either the "to-and-fro" or "circle" systems has become a commonplace in modern operating rooms throughout much of the western world.

With universal adoption and usage of absorption systems it is perhaps inevitable that there should also be associated misuse and abuse. Some adaptations of the absorption principle are fundamentally inadequate in design or capacity.

Anaesthesia apparatus designed for the use of normal adults is frequently inadequate when used with abnormal adults, children, or debilitated individuals. A closed absorption system with the absorber turned off, or with soda lime inefficient or absent, will allow accumulation of carbon dioxide to more dangerous levels than an inadequate flow of gases in the older partial rebreathing methods. No matter how efficient the absorption system, there is invariably some mechanical addition to the dead space and, therefore, a higher percentage of carbon dioxide is present in the respired air of such a system than in normal breathing. In partial rebreathing systems where soda lime absorption is not used, carbon dioxide levels can be kept inconsequentially low only by the use of high flows of gases which exceed the minute volume of the patient (15–20 liters per minute). Some have combined more moderate gas flows (up to 5 liters/min.) with soda lime absorption in a semi-closed system, hoping thereby to reduce the likelihood of unwanted carbon dioxide accumulation. Avoidance of an elevation of carbon dioxide in the respired atmosphere is satisfactorily accomplished only by a properly used non-rebreathing system.

For a time it was in vogue to add carbon dioxide to anaesthetic atmospheres, or force the patient to rebreathe in a closed system, for the purpose of shortening the period of induction. We have abandoned this as an unnecessary practice and one which is not without the hazard of unwanted sequelae. Proponents of this type of induction suggest that anaesthesia is accomplished more rapidly because of the hyperventilation which moves a greater concentration of the anaesthetic agent into the alveoli. This is partly correct. However, not infrequently a considerable portion of the anaesthesia obtained is due to the narcotic effect of the carbon dioxide itself, and this at the expense of metabolic disturbances which may take a long time to return to normal.

Probably more dangerous than deliberate usage is unsuspected chronic accumulation. The hypoventilation which continues unnoticed in a partially curarized patient causes dangerous accumulation of carbon dioxide in alveoli and tissues of the patient just as surely as though compressed gas had been added from a tank. A concentration of 10% carbon dioxide in the respired air will produce unconsciousness in a normal individual. Yet we regularly expose anaesthetized patients to concentrations of carbon dioxide which equal or exceed this level. It has been shown (1) that during cyclopropane anaesthesia administered by the absorption technique a carbon dioxide tension of 75–80 mm. and a pH of 7.15–7.2 are a regular finding in arterial plasma. This means that the blood is equilibrated with 10–11% carbon dioxide in the alveolar air. Similar results have been observed during anaesthesia with ether, and barbiturates (2). Any depressant drug may bring about a similar situation, in which carbon dioxide is contributing to the depth of anaesthesia simply because of hypoventilation. Regular, intermittent assistance of respiration during anaesthesia would seem to be of merit in maintaining normal carbon dioxide levels.

It is well established that it is desirable to add oxygen to the respired atmosphere in order to be sure that its partial pressure is not reduced below normal by the presence of anaesthetic gas or vapor. However, in many places it has

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become customary to use oxygen as the sole diluent for the anaesthetic with the result that patients remain well oxygenated and the clinical impression is satisfactory even though excessive amounts of carbon dioxide are accumulated due to the lack of effective ventilation. The "pink" color of the patient is no guarantee against physiologic disturbance. Hypoventilation frequently allows accumulation of carbon dioxide to alveolar concentrations of as high as 10–15% and a value of 40% has been observed during anaesthesia (3). It seems certain that any excessive concentration for long periods of time subjects the patient to undue stresses and may possibly account for some otherwise unexplained acute circulatory accidents or for some of the disabling post-operative complications that are usually referred to other causes.

Effects of Carbon Dioxide Excess

The effects produced by abnormally high concentrations of carbon dioxide are manifold and depend upon many coincident factors of concentration, duration of exposure, degree of anaesthetic depression from other agents, and the condition of the patient. The usual signs of its accumulation in the otherwise unanaesthetized individual include quite marked changes in pulse, blood pressure, and respirations. Pulse rate shows a moderate increase. Blood pressure usually increases to a rather high level, maintains a plateau for several minutes and then, in severe increases of carbon dioxide, suddenly falls. The respiration is increased in both rate and depth with slight excesses of carbon dioxide but as concentrations increase there is markedly less stimulation and a depressant effect on respiration becomes increasingly evident (4). Twitching, spasms of muscle groups, and convulsions occur with increasing concentrations. Diaphoresis is usually present and the color of the patient is pink, flushed, or bright red due to the peripheral dilatation unless there is a concomittant oxygen lack (5).

The presence of anaesthetic agents may so modify the signs and symptoms of carbon dioxide excess that little or no warning may be provided of its presence. These signs and symptoms depend upon the ability of the patient to bring into play compensatory mechanisms which will minimize the effects of the abnormal atmosphere presented to the tissues. During anaesthesia it may not be possible for the body to call these mechanisms into play, or because of the anaesthetic, the surgical procedure, or the pre-existing conditions, some of them may be already functioning and there be no reserve capacity to either take care of the need at hand or provide warning symptoms. Thus, high degrees of carbon dioxide retention may occur during anaesthesia in the absence of the classic signs and symptoms (5).

Both vasoconstriction and vasodilation are produced by high carbon dioxide. Presumably the vasoconstriction is a central effect, while the direct peripheral action is one of vasodilation. These may tend to neutralize each other. The rise in blood pressure is generally attributed to the central effect, the constriction occurring in the visceral bed. This visceral vasoconstriction and the associated reduction in blood flow is reflected in a reduction of kidney function (6). In small animals exposed to carbon dioxide there is an increase in the recovery time

from barbiturate anaesthesia which is thought to be due to vasoconstriction in the liver and a consequent decrease in liver function (7). Recent studies of liver function in anaesthetized patients indicate a correlation between increased carbon dioxide concentrations and the frequency of liver damage. The severity of this damage appeared to be more marked when chloroform was the associated anaesthetic (8).

Frequently a pronounced fall in blood pressure has been observed to occur immediately after cessation of cyclopropane anaesthesia. This is now known to be associated with hypercapnia rather than an inherent fault of cyclopropane. There is evidence of a direct correlation between the severity of post-anaesthetic hypertension and the degree of hypercapnia developed in a closed system of anaesthesia with inadequate carbon dioxide removal (9). Cardiac irregularities appear to be more frequent in the presence of high carbon dioxide (5, 10). In addition, evidence is accumulating that in the period of reaccommodation to normal atmosphere after exposure to elevated carbon dioxide levels there may also be severe changes in cardiac conduction (10, 11). It has been shown that hypercapnia may greatly increase the effect of any vagal stimulation that might occur during operation (12). However, cardiac arrest could not be produced in this way experimentally except under concomitant conditions of extreme oxygen deficiency (13).

High carbon dioxide concentration produces a decreased tissue respiration in vitro (14). It has also been observed in acute experiments on rats that with 11% carbon dioxide the total oxygen consumption is reduced to three-fourths the control value in spite of increased muscle activity (4). Whether this represents an actual reduction in need or an interference with utilization is not clearly understood.

Muscle tone is increased by carbon dioxide accumulation to the point that it frequently represents deficient relaxation during a surgical procedure. This is a trap which frequently leads the anaesthetist to use an overdosage of the anaesthetic. It is a mistake to try to counteract this increased muscle tone by increased depth of anaesthesia or additional relaxant drug when it could be either prevented or corrected by adequacy of ventilation.

Carbon dioxide in excess produces a specific narcotic effect which has been demonstrated experimentally as depression of the monosynaptic pathway (15). Definite narcotic effects have been demonstrated in man and small animals at concentrations of from 5–10%. Moreover, animals are more resistant to high concentrations than man (4). General anaesthesia is produced in man by concentrations of over 10%, and with high concentrations there is evidence of depression of the central control of both respiration and circulation. Electroencephalograms show disappearance of electrical activity with increased concentration of carbon dioxide, which parallels the findings with other anaesthetic agents (16). There is a marked increase in cerebral blood flow and a rise in cerebro-spinal fluid pressure (17, 18). Convulsions occur less frequently in the anaesthetized than in the unanaesthetized individual. Whether these are cerebral, medullary or spinal in origin is not entirely clear (19). There is frequently a

premonitary warning in twitchings of muscle groups of the face or extremities.

Pathologic studies of tissues from small animals following both acute and chronic exposure to excess carbon dioxide show alterations in many tissues (20) (lung, liver, kidney, brain), but changes have been reported as being greatest in the thalamus, brain stem, and spinal cord. All gradations of damage were observed from swelling, chromatolysis, and vacuolization of cell body to complete disintegration. These findings are compatible with a generalized depression of oxidative processes in cells to the point of cellular anoxia. Cells which are anaesthetized early, such as in the cerebral cortex, are apparently protected from severe histopathologic changes. It is postulated that (in unprotected cells) prolonged activity in the presence of cell anoxia leads to severe damage (21). Thus, the primitive brain damage and the sparing of the higher centers.

Summary

It is evident that the undesirable effects of hypercapnia may be of considerable variety and magnitude. Since signs of carbon dioxide accumulation may be masked during the state of anaesthesia even the possibility of hypoventilation should be studiously avoided. Assistance of respiration during anaesthesia is frequently necessary in order to provide effective ventilation.

Résumé

Le gaz carbonique en Anesthésie

La respiration normale est entretenue par le besoin d'éliminer le gaz carbonique, et l'excrétion du CO_2 par le système respiratoire ne devrait pas être diminuée. La cause la plus commune d'accumulation de CO_2 est la diminution de pouvoir qu'éprouve le malade à ventiler convenablement ses propres alvéoles, cela est dû ordinairement à l'emploi de drogues dépressives. Une concentration de 10% de CO_2 dans l'air respiré produira un état d'un inconscience, et ces chiffres ou mêmes de plus grandes chiffres de CO_2 ont été trouvés dans les malades anesthésiés. Il semble certain que n'importe quelle concentration excessive pendant une longue période soumet le malade à des défaillances intempestives et peut s'ajouter à des accidents aigus du système de circulation ou à certaines graves complications post-opératoires. Les effets de l'excès de CO_2 sont discutés. L'aide de la respiration pendant l'anesthésie est fréquemment nécessaire à fin de pouvoir une effective ventilation et, ainsi, éviter ces effets.

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CONTRIBUTION OF ANAESTHESIA IN THORACIC SURGERY FOR TUBERCULOSIS

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The recent advances mde in Thoracic Anaesthesia have made possible chest surgery for a larger group of the far advanced cases of Pulmonary Tuberculosis. The Anaesthetists working in that field meet the problems before, during and after the operation.

After decision by Medico-Surgical Conference, the anaesthetist should become the crucial link between the internist and the surgeon and keep the patient in the best homeostatic conditions for that operative period.

Before the operation

In order to improve the patient's general condition, the anaesthetist should have a perfect knowledge of the physiologic condition of his patient. For this purpose the following examinations are considered very useful:

1. Clinical Findings and Physical Examination
2. Radiography (Antero-Posterior and Lateral Views)
3. Fluoroscopy (Diaphragms' Mobility)
4. Stereoscopy (Bilateral)
5. Some Cardio-Pulmonary Function Tests

Preoperative Laboratory Examinations:

1. Urinalysis
2. Blood Urea
3. Bromsulphalein
4. Phenolsulphonphthalein
5. Hematocrit
6. Prothrombin Time
7. Sedimentation Rate
8. Complete Blood Count
9. Rh Factor Determination
10. Type and Cross-Match Blood
11. Total Blood Protein
12. Bleeding and Coagulation Time

From the above findings, in cooperation with the surgeon, some special pre-operative cares could be set up and the anaesthetic technique settled.

1. Restoration of Fluid Balance and Blood Volume (Fluid and Transfusion)
2. Aerosoltherapy (Streptomycin and Vaponefrin)
3. Physiotherapy
4. Postural Drainage
5. Preoperative Sedation

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The day before the operation the anaesthetist sees the patient in order to evaluate the patient's state, and orders the premedication.

During the operation

For you the normal physiology of the respiration is well-known. When the slightest disorder occurs it brings and begets problems, which are common to every anaesthetist in thoracic anaesthesia: paradoxical respiration, mediastinal flutter, reduction of usable vital capacity, increase in residual capacity, reduction of tidal air, inadequate dynamic lung volume, lessening of cardiac output and blood volume, delay in the venous return, arterial-venous shunt, hypoxemia or anoxemia and not the least, the reflex problems.

Tuberculous patients represent more serious anaesthetic risks, avoidance of spread of the disease is imperative.

Surgeons work around the cardio-pulmonary area which is the most reflexogenic zone of the body. The anaesthetic agents, the surgical stimulus, or both may cause the reflexes. The prevention of such complications includes the following: a preoperative cyclaine 5% topical anaesthesia of the vocal chords and the mucus membrane of the whole tracheo-bronchial tree, a long acting (efocaine) intercostal nerves block before the opening of the thorax, a good plane of general anaesthesia, chiefly a good oxygenation of the patient and sometimes, intravenous injection of atropine, procaine or procaine amide. Recently we tried a new sedation of the autonomic nervous system, devised in France by Huguenard and Laborit, the "Cocktailytique": Nembutal, Demerol, Diparcol, 4560 R.P. (Largactil), intravenous injection of local agent (cyclaine, procaine) and curare drugs.

With thoracic patients, especially with tuberculous patients, we have reduction of blood volume and anaemia; if the blood loss is important as it occurs during a thoracic operation, the patient from being anemic becomes hypoxemic or anoxemic; thence, the importance to prepare the patient with blood, plasma, plasma expanders, and electrolytes must be strongly underlined.

Cardio-Pulmonary Function Tests should be performed to determinate the patient's ability to go through an operation. This includes: Barach's Index, Moot's Law, Henderson's Holding Respiration; spirometry, diffusion tests and sometimes bronchospirometry.

Arterial blood studies and the measurements of the venous pressure, of the circulation time and of the cardiac output by Fick Principle complete this physiological information.

To improve or maintain the respiratory reserves, aerosoltherapy and physiotherapy are very helpful.

In thoracic anaesthesia, except for minor cases, our preference goes to general anaesthesia with endotracheal or endobronchial intubations. The catheter allows a free airway, rapid lung inflation, which might be very important in the occurrence of cardiac arrest, and general anaesthesia unlike the high spinal maintains the patient's compensative mechanisms.

Paradoxical breathing and mediastinal flutter are serious problems; to

solve them some intubation techniques, controlled or assisted respiration and the face down position (Overholt) are very helpful.

As we said before in thoracic anaesthesia for tuberculous patients, we may have one more problem, the spread of the disease; that is why the endobronchial anaesthesia with Carlens' tube is our first choice. This double lumen catheter was constructed by Dr. Eric Carlens from Sweden for bronchospirometry, but has been adopted later for anaesthesia. This catheter is made of rubber and obtainable in two sizes; No. 39 for men and No. 35 for women. The lumen of each side has a diameter of 7 mms. for men and 6 mms. for women; the total outer diameters are thirteen and eleven respectively. The advantages of the technique are summarized by Dr. Carlens in "Anesthesiology" January 1953 issue:

1. Once the chest is opened, the diseased lung may be deflated to provide greater operating space when the lung is separated from the chest wall.
2. The lung can be inflated when lobar or intersegmental planes are developed.
3. The bronchus can be divided, whenever this is suitable during the resection and left open until it is convenient to close it. During the time the bronchus is open, a small plastic catheter is left in place for continuous suction, with suction close to the opening of the bronchus to collect blood and secretions.
4. It is not necessary to apply a clamp on the proximal part of the bronchus, thus, injury to the bronchial wall is avoided.
5. The bronchial tree may be inspected and aspirated by a small rubber catheter through the open bronchus.
6. Bronchotomies and resection of the carina and of the tracheal wall are facilitated by this method of endobronchial anaesthesia.
7. In wet cases during repeated aspirations one lung is always ventilated and the same plane of anaesthesia can be maintained more easily.

In some pneumectomy cases with empyema, we use endotracheal or endobronchial tubes associated to the Thompson's blocker. Before the time of Thompson's blocker and Carlens' tube we used simple intubations with endotracheal or endobronchial tubes. However in Children's Surgery, the tracheobronchial anatomy does not allow any other technique and we still use these simple intubations. A few months ago Dr. Carlens paid a visit to our hospital and told us that five thousand cases were done in Sweden with his catheter with many advantages but without any harmful incident.

Up to now at Laval Hospital, this technique of endobronchial anaesthesia (Carlens' tube) has been used in ninety cases of pulmonary resections and one hundred and thirteen cases of Thoracoplasties. We tend to agree with Dr. Carlens' remarks. Our cases of excisional surgery also include a few patients suffering from bronchogenic carcinoma and bronchiectasis.

This tube is also used at our hospital for bronchospirometry. Its introduction is relatively smooth. Nevertheless a bronchoscopic examination previously performed is helpful.

Now the intubation techniques used at our hospital are known. Regarding anaesthetic substances it is a matter of choice. When the surgeons are using cautery, we are limited to intravenous anaesthetic substances, curare-like drugs and Nitrous Oxide, Oxygen technique administered with controlled or assisted respiration. For one reason or another, after good understanding with the surgeon, the cyclopropane or ether technique may be used for some special cases.

As intravenous substances we use: Demerol, Pentothal and recently Surital, with which we find the following advantages:

1. Almost an absence of laryngeal and pharyngeal reflexes
2. With less respiratory depression oxygenation is easier
3. Less circulatory depression
4. Recovery more rapid
5. Little postoperative discomfort to the patient.

We also use most of the usual curare like drugs: d-Tubocurarine, Flaxedil, Metubine, Syncurine and succinylcholine (Anectine, Brevidil). With the last two our experience is not very large, but we may say that they are the best relaxants we have used up to the present time. There is great ease to control dosages, especially for lung operation and there is complete absence of toxicity particularly in the immediate postoperative period.

Actually, we are more and more interested in potentiated anaesthesia technique as devised by Laborit and Huguenard in France. These authors use several drugs to stabilize the autonomic nervous system and to lessen the hormonal reaction. They combine: Phenergan, Demerol, Diparcol, Pentothal, procaine and curare in a whole complex called "Cocktailytique". Anaesthesia with the combined action of all these drugs is much more facilitated and the risk of shock and hemorrhage are lessened. In the Diparcol-Phenergan's series, the Rhone-Poulenc Laboratories have lately found a new product; this drug is known under the name of 4560 R.P. Its potential properties are great and its actions are numerous. This drug brings a complete disconnection of the autonomic nervous system; it works as a pharmalogical lobotomy on the patient, by decreasing the cortical action of the diencephalic centers. Moreover, this drug is neuroplegic, vagolitic, sympathicolytic and somewhat antihistaminic. One intravenous injection of 4560 R.P. (25–50 mgms.) before surgery gives the following responses: the patient becomes completely relaxed, the pulse rate is usually increased, lesser quantity of hypnotic drug and during the anaesthesia period lesser quantity of pentothal or surital will be needed. The neuroplegic action gives a slight fall in blood pressure; that is why we have to be careful with aged hypertensive patients. Its vagolytic action protects against laryngospasms and bronchial spasms. The 4560 R.P. also minimizes the hypophyso-adrenal reactions which occur during the immediate preoperative anxiety and during the surgical stress.

With this drug our experience in thirty-three cases is summarized in the following:

Cases	*Age*	*Anesthetic Technic*	*Preoperative Dose: 4560 R.P. Oral*	*Preoperative Dose: 4560 R.P. I.V.*
Pleural-pneumectomy (3)	39	Penthotal or	25 mgms.	27.5 mgms.
Pneumectomy (2)	39	Surital	25 mgms.	37.5 mgms.
Lobectomy (10)	28	Curare Drug (Anectine) or	25 mgms.	38.2 mgms.
Segmentary Resection (2)	30	(Brevidil)	25 mgms.	40.0 mgms.
Pleurectomy (1)	30	Nitrous Oxide Oxygen or	25 mgms.	50.0 mgms.
Thoracoplasty (8)	30	Cyclopropane, Ether Technic	25 mgms.	35.0 mgms.

At the present time we tend to believe that this drug has the following properties:

1. Reduction of the amount of curares and anaesthetic agents
2. Full protection against pleural and pericardial reflexes
3. Reduction of blood loss
4. Slight fall in blood pressure
5. Slight harmless tachycardia, but when given intra-muscularly we did not note any tachycardia.

For the immediate postoperative period:

1. Perfect analgesia
2. Better ventilation
3. The immediate postoperative pulmonary complications (atelectasis) have almost completely disappeared.

In summary, we feel that this drug might give an easier intubation and maintenance of anaesthesia with better postoperative course.

The functions of an anaesthetist are not limited to the choice of a good anaesthetic agent. He must also pay close attention to the heart action and to the arterial oxygen saturation. In this the cardiotacoscope and the oximeter may prove to be of a great help.

In the occurrence of a cardiac arrest, the anaesthetist should immediately look for a close cooperation between the members of the surgical team. Without delay the surgeon performs cardiac massage for adequate circulation. The anaesthetist, on the other hand, administers oxygen under positive pressure.

Everyone knows that thoracic surgery often means a large amount of blood loss; this may be approximately estimated by the weighing of sponges. Following the work of Drs. Pierce, Boyan and Masterson of New York, we recently started to replace blood according to the variation of venous pressure.

To control the blood lost three methods are used at our hospital:

1. Continuous sympathetic block by Peridural Technique
2. Hypotensive anaesthesia by Methonium Compounds
3. More recently 4560 R.P.

After the operation

For the anaesthetist the recovery period is as important as the operative one. During the first postoperative hours, the anaesthetist stands by the patient as long as he needs his services. In the following days, in cooperation with the surgeon, the anaesthetist supervises: oxygenation, blood transfusion, fluid balance, sedation, aerosoltherapy and physiotherapy.

The pulse rate serves as a guide to oxygenation; a pulse of one hundred or over is an indication of extending the oxygenation for two hours.

According to fluid balance, the anaesthetist orders fluid and electrolytes solutions.

Anaesthesiologic Department, in our hospital, is also responsible for the Blood Transfusion Service. About one hundred transfusions monthly are given on active surgical wards.

We routinely try to use the less depressive sedatives (demerol, dromoran), infiltration blocks with cyclaine or xylocaine, 5% alcohol solution given intravenously. According to Dr. Mary Karp of Wesley Memorial, Chicago, 5% alcohol solution given intravenously increases the caloric intake, has a special value in patient with inanition and reduces by thirty to fifty per cent the need of narcotics postoperatively.

The most serious respiratory complication: atelectasis, is minimized by carbon dioxide inhalation, associated with physiotherapy in the immediate postoperative period, aerosoltherapy (steptomycin, vaponefrin, alevaire) and bronchial toilet by aspiration, are also helpful. But the use of some anaesthetic techniques have greatly reduced the postoperative respiratory complications for our patients.

In conclusion let us say, that the more the anaesthetists have a good knowledge of the difficulties encountered in Thoracic Surgery, the more this field will progress.

Résumé

Les succès actuels de la Chirurgie Thoracique en Tuberculose sont, dans une grande mesure, dus aux progrès de l'Anesthésie Thoracique moderne.

Dans ce champ d'action, les anesthésistes ont à résoudre de multiples problèmes relatifs à la préparation du malade, à l'anesthésie elle-même et à la réanimation post-opératoire.

I–Préparation du malade:

Dans le but d'améliorer l'état général du patient, l'anesthésiste doit porter un grand intérêt à l'examen clinique pré-opératoire et aux examens routiniers des fonctions sanguine, rénale, hépatique et surtout cardio-respiratoire.

Suivant les renseignements que lui ont fournis ces investigations, il doit décider, de concert avec les chirurgiens, de la technique anesthésique à employer chez ce malade et des traitements pré-opératoires à instituer:

1° Restauration de l'équilibre électrolytique et du volume sanguin;

2° Aérosolthérapie;

3° Physiothérapie;
4° Drainage postural;
5° Sédation pré-opératoire.

II—Anesthésie du malade:

D'abord, un mot des problèmes communs de l'anesthésie thoracique en général. Nous parlerons par la suite de ceux qui sont particuliers à l'anesthésie thoracique en tuberculose.

Problèmes communs:

Respiration paradoxale,
Ballottement médiastinal,
Réduction de la capacité vitale,
Augmentation de la capacité résiduelle,
Réduction de l'air courant,
Diminution du débit cardiaque et de volume sanguin,
Retard dans le retour veineux,
Court circuit circulatoire,
Hypoxémie ou anoxémie,
Réflexes.

En tuberculose, ces problèmes ne font que s'aggraver. Le plus important de tous est celui de la dissémination de la maladie du côté malade au côté sain.

Pour prévenir les réflexes, nous recommandons: une anesthésie topique (cyclaïne 5%) des cordes vocales et de l'arbre trachéo-bronchique, une infiltration intercostale (Efocaïne) avant l'ouverture de la cavité thoracique, une anesthésie générale adéquate, quelquefois l'injection d'atropine, de novocaïne. . . . et surtout une bonne oxygénation.

Récemment, nous avons employé une nouvelle sédation du système nerveux autonome préconisée en France par Huguenard et Laborit, le «Cocktailytique» et le 4560 RP (Largactil).

Pour combattre l'anémie, restaurer le volume sanguin et l'équilibre électrolytique, nous recommandons le sang, le plasma, le «Subtosan» ou le «Dextran» et les solutions électrolytiques.

Pour apprécier un risque opératoire et anesthésique, les divers tests de physiologie cardio-respiratoire sont d'une grande utilité.

L'aérosolthérapie et la physiothérapie augmentent les réserves respiratoires.

Sauf pour les cas mineurs, nos préférences actuelles vont à l'anesthésie générale avec intubation endo-trachéale ou endo-bronchique. La respiration contrôlée ou assistée est employée pour lutter contre la respiration paradoxale et le ballottement médiastinal. La sonde «Carlens» est notre premier choix comme technique d'intubation. Nous avons aussi employé dans certains cas d'empyèmes, le bloqueur «Thompson» associé à la sonde endo-trachéale ou endo-bronchique. Chez les enfants, l'anesthésie endo-trachéale simple est seule employée et alors ces sujets sont placés dans la position d'Overholt. Nos chirurgiens utilisant le thermocautère, nous sommes limités à l'emploi de substances intra-veineuses (de préférence «Surital» «Anectine» «Brévidil») associées au Protoxyde d'azote avec oxygène.

Nos tendances actuelles s'en vont vers l'anesthésie potentialisée. L'une des substances employées «Largactil» nous a semblé présenter les avantages suivants:

1° Diminution de la quantité d'agents anesthésiques,
2° Protection quasi complète contre les réflexes,
3° Diminution de la perte sanguine,
4° Bonne analgésie dans la période post-opératoire immédiate,
5° Meilleure ventilation et absence presque complète d'atélectasie.

Au cours de l'opération, le cardiothacoscope et l'oxymètre sont des aides précieux pour l'anesthésiste dans la surveillance de son patient.

En présence d'arrêt cardiaque, l'anesthésiste doit pourvoir à l'oxygénation du malade pendant les trente secondes qui suivent, et de concert avec les chirurgiens, diriger la thérapeutique médicamenteuse. Pour réduire la perte sanguine, nous employons tantôt une infiltration continue du sympathique, tantôt les médicaments hypotenseurs (Hexamethonium), tantôt le «Largactil».

III–Réanimation post-opératoire

Immédiatement après l'intervention, l'anesthésiste demeure auprés de son malade aussi longtemps que son état l'exige. Dans les jours suivants, en collaboration avec le chirurgien, il prend charge de l'administration de l'oxygène, du Service de la transfusion et de l'équilibre liquidien, de la sédation post-opératoire, de l'aérosolthérapie et de la physiothérapie.

Les succès de la chirurgie thoracique tuberculeuse se feront d'autant plus sentir qu'un plus grand nombre d'anesthésistes comprendront ces problèmes.

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RESUSCITATION OF THE NEWBORN
A METHOD AND A MACHINE

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Much has been written in recent years on resuscitation of the newborn. There exist a great many theories, and controversial points. No attempt will be made in this paper to review the literature which has recently been admirably done by Little and Tovell (1).

There are however, certain fundamental facts which will bear restatement and offer a basis for our outline of a method and a machine which have proved eminently satisfactory over a period of more than two years at the Toronto General Hospital.

It has been frequently stated that undue emphasis has been placed on the necessity and indications for resuscitation. This, in part, is true; and if certain precautions were taken, such as prevention of over sedation of the parturient etc., the problem of resuscitation of the newborn would be greatly reduced.

However, in spite of caution in our teaching, sedation will continue to be used, and sometimes indiscriminately. This, and other factors arising in childbirth beyond the most skillful control, will always supply a demand for efficient methods of resuscitation. Countless methods and devices are still in vogue, many of which are dangerous and even lethal. Children have survived, in many cases, in spite of the treatment they received and not because of it; and because they managed to survive the ordeal of slaps and bangs, hot baths and cold ones, the treatment was given the credit. Doubtless some have succumbed to the ill-advised use of some of the methods that might have survived if only nature had been given a chance.

There are many etiologic factors responsible for the production of asphyxia neonatorum, and as a rule, a combination of factors will be found in almost every case.

Apart from the previously mentioned effects of over sedation of the mother during labor and constitutional disorders affecting the mother such as cardiac and pulmonary disease, toxaemia, etc., there are other conditions directly affecting the infant. Some of these are immaturity of the child, abnormal presentation and position of the foetus, medical inductions, the length and type of labor, foetal circulatory disturbance due to placental pathology and mechanical obstruction in cord circulation, the type of delivery, i.e., amount of manipulation as against spontaneous delivery, the anaesthetic agent used, etc.

Under congenital debility, Little and Tovell mention congenital malformations of the respiratory and circulatory systems etc. In addition to anatomical abnormalities, the writer is firmly convinced that *histologic aberrations exist which result in a lung or parts of a lung that are quite incapable of expansion, either spontaneously or by any artificial method.* If this theory is correct there must be

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a percentage—difficult to determine—of children born with lung tissue which is incompatible with life. This mortality we will have to accept just as we do those with defective development of the central nervous system.

It is hoped that work now under way in our department in conjunction with the department of pathology, might verify this theory or at least shed light on a situation that, to date, has simply been accepted as atelectasis. The word atelectasis simply means a collapsed lung. But why?

Classification

Of all the methods suggested to describe the degree of oxygen lack in the infant, that by Flagg (2) provides the best working classification for the immediate problem of resuscitating the asphyxiated child. He outlines three stages.

1. *The stage of depression*, where the baby does not breathe well. There is a tendency to recurring cyanosis or duskiness. The infant is depressed but capable of being aroused; the respiratory centre, circulation, muscular tonus, and reflexes are all depressed from anoxemia but are easily stimulated to normal activity.

2. *The spastic stage*, where respirations are irregular, gasping, or shallow, and occur at long intervals. There is marked cyanosis of the lips. There is reflex reaction to aspiration within the pharynx and an active glottic reflex is present. Froth or fluid appears in the mouth and pharynx.

3. *The flaccid stage*, where respirations occur either at long intervals or cannot be demonstrated. There may be either cyanosis or pallor. There is complete flaccidity of all the musculature; the jaw is completely relaxed, the glottic structures are collapsed and there is no resistance on exposure of the pharynx. Fluid is found in the hypopharynx. All reflexes are in abeyance. Cardiac pulsation may or may not be demonstrable at the apex. The circulation is failing.

The importance of the anoxic state in the newborn is emphasized by the chemical changes in the blood described by Eastman and co-workers (3, 4, 5). The direct effect of this altered chemistry is a degenerative change in the cells of the central nervous system. How far this reaches into the realm of mental inferiority which manifests itself at later stages of child, adolescent, or even adult life is open to conjecture.

Method of Resuscitation

Little and Tovell state that the fundamental problem in resuscitation is that of initiating an inspiratory gasp and starting the lungs to expand. Quite true, but too many people get impatient about obtaining the initial inspiratory gasp and often resort to overzealous and sometimes disastrous methods. It must be kept in mind in experimental research, that the problem of the lung that has once been areated is one thing. The lung which has not yet been expanded is another. In the first case we are dealing with a lung that we know will expand and the introduction of oxygen is easy. The lung can be artificially ventilated until the function of the respiratory centre is restored. In the case of the newborn child, we may have no way of knowing the histologic structure of the lung

tissue or how much of the lung tissue is capable of expansion and how much is congenitally defective and incapable of expansion.

The problem in the newborn may or may not be respiratory centre depression. It may be entirely in lung structure. Normally constructed alveoli expand with the inspiratory gasp at atmospheric pressure, abnormally constructed alveoli do not, and it is here that attempts to inflate the lung with higher pressures can only do damage, because the normal tissue will be destroyed before any dilatation can possibly be produced in the collapsed area. The suggestion that has been made of applying *momentarily* higher pressures is unsound physics. Regardless of the duration of the increased pressure, the gas will take the path of least resistance. As collapsed alveoli offer more resistance than normal lung tissue the increased pressure is simply directed to the already distended alveoli and the damage is done. The fact that the increased pressure may just be applied momentarily does not alter the consequences. The lung tissue is torn at its weakest point and surgical emphysema involving the mediastinum and cellular tissue of the neck is the result.

The theory underlying the method to be described is to supply oxygen to the alveoli which *are* open. The range of the positive and negative pressures supplied overcomes the surface tension of the collapsed alveoli (that is, those which are collapsed but *capable* of expansion). Respiratory movements are eventually initiated, but in the meantime (a very important time) vital oxygen is supplied *in the absence of respiratory movements*. To quote Eastman, "There seems to be only one urgent indication in the treatment of asphyxia neonatorum and that is to introduce oxygen into the circulating blood of the infant."

One of the greatest objections to mechanical resuscitators in general, is that their design, and accompanying instructions for their use, causes them to be applied to the infant without any thought or investigation of the condition of the air-way. It must be glaringly obvious that any machine applied to a child with an obstructed air-way is not only ineffective but often fatal.

The establishment and maintenance of a free air-way is of first importance; without it, no method can succeed. The entire respiratory tract must be cleared of obstructing fluid or mucus. Obstruction due to spasm of the glottis, if present, must be overcome. This condition may result from an irritating mucus plug or from certain types of anaesthetic agents administered to the mother. Infants in the stage of flaccidity with collapsed glottic structures and absent reflexes may also have obstructed airways. Intubation of the trachea is the *only* method of dealing with these situations.

There is considerable controversy over the ease or difficulty and safety of intubation. Much of this controversy is a result of a gross misunderstanding of the problem at hand.

There are two points to be made:

1. In the cases where, to use Little and Tovell's expression, "intubation is mandatory", then it must be done whether it is easy or difficult.

The procedure of intubating the infant has been made unnecessarily difficult due to a lack of understanding of a few simple principles.

Valve control

The administration of oxygen and the switch to negative pressure is regulated by a manual control, marked positive and negative. The *rate* of alternation from positive to negative pressure is entirely under the *operator's control*, which is a distinct advantage over automatic control.

The manual control regulates the *rate* of alternation only. When on positive, the pressure is always 12 mm. Hg.—never more and never less. Similarly, on

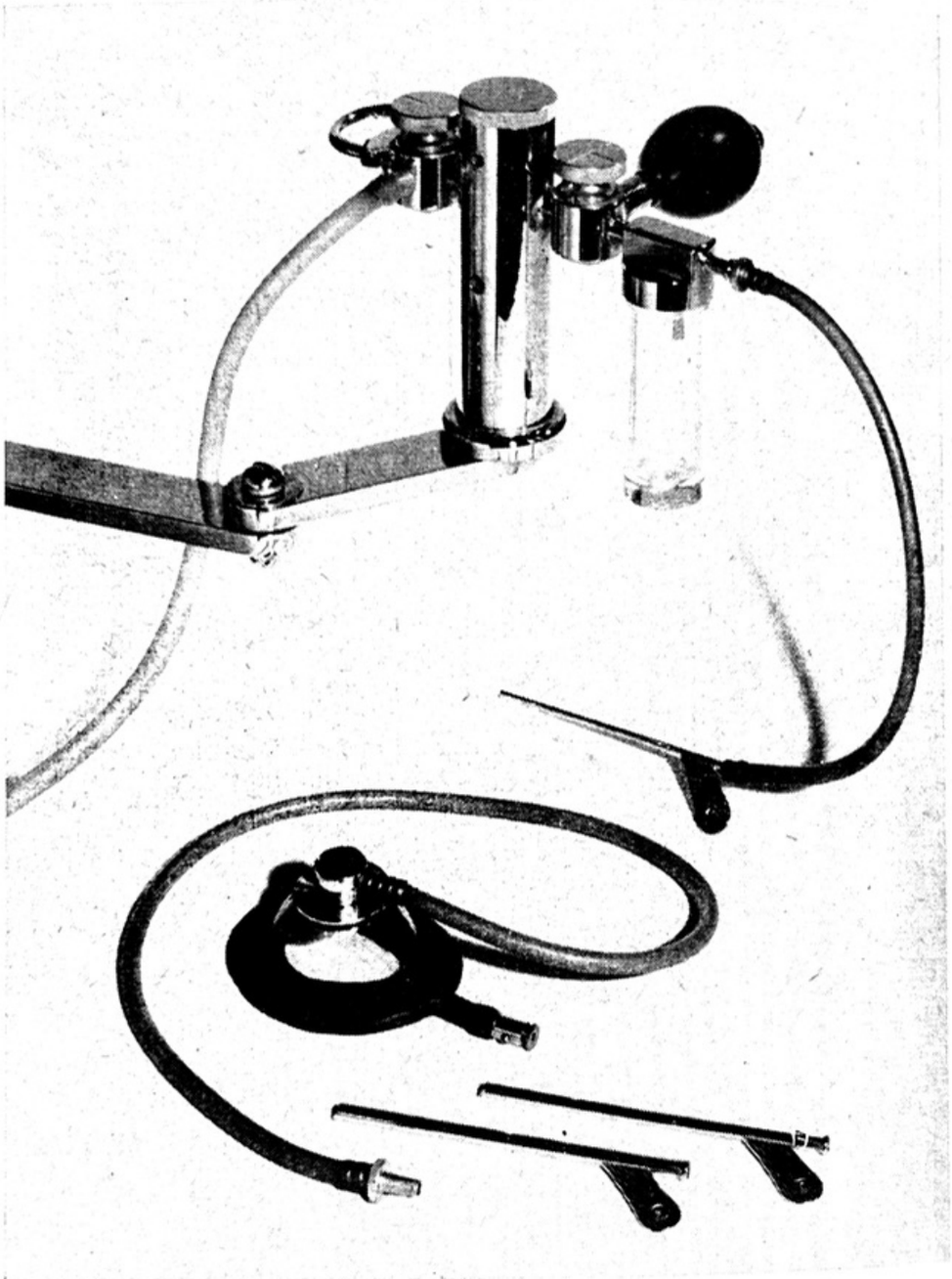


FIG. 2. Enlarged picture of the resuscitating head of the machine with mask and catheters provided.

negative, the pressure is always 8 mm. Hg.—never more and never less. There is no *neutral* or dead spot on the control. It is either positive or negative. (The negative pressure is created from the positive reduced tank pressure by the Venturi attachment.)

No two resuscitation problems are alike. Each case requires individual treat-

ment which cannot be accomplished by *automatic* mechanical devices. The sooner this fact is realized and accepted, the sooner will resuscitation salvages increase and disasters be avoided.

Application of the Apparatus to the Method of Resuscitation

As soon as the child is delivered, mucus should *routinely* be removed from the nasal passages and pharynx.

If the infant does not breathe spontaneously there is no use wasting time with obsolete, not to mention dangerous methods. Nor is it permissible to attempt the administration of oxygen to an infant until a clear airway has been established.

The passage of an intratracheal catheter is a procedure which requires more gentleness than skill. The minimal amount of dexterity required for introducing the catheter can readily be accomplished by anyone who has arrived at the station of assuming the responsibility for the care and management of the newborn infant. The catheters supplied with the apparatus greatly facilitate this procedure.

The catheters are supplied in graduated diameters and the length from hilt to tip is designed to permit of adequate descent into the trachea without encroachment on the carina. They are metal and designed to prevent trauma. The metal construction provides rigidity to facilitate control and the thin wall permits a maximum lumen. The hilt provides a side handle which removes the operator's fingers from obstructing the field of vision during insertion.

With the catheter in place the suction valve is opened, bulb suction is applied to remove mucus and the suction valve then closed.

With the reducing valve registering about 3 to 4 L. p.m. flow of oxygen the alternating positive and negative pressures to instigate respiratory movements are under the operator's control. Alternations of 10 to 15 per minute are adequate and give the child a much better chance of establishing his own respiratory rate than more rapid artificial movements. As long as the child's color is improving, the depth of respiratory movements is of *no* concern. We are dealing with a child which was designed to live on air and the apparatus is delivering to the lung alveoli 100% oxygen. When respirations are established the catheter is removed. If the child is not robust and additional oxygen is indicated it may be administered with the face mask. A longer tube for attachment to the mask is provided for administering continuous oxygen to the child in the crib if necessary.

This apparatus and method of resuscitation is accepted and endorsed by the Department of Obstetrics and Gynecology, and the Department of Anaesthesia, University of Toronto, Canada. In the two years that the instrument has been used in the Toronto General Hospital it has never been found out of order. There have been no mechanical breakdowns of any kind, and no maintenance or service work required. This continued performance may be expected indefinitely. There has been no occasion to alter in any way the original design of the machine.

For the verification of the tracheal catheter measurements the author is

indebted to Dr. R. C. Ritchie, Department of Pathology, Hospital for Sick Children, Toronto, who obtained measurements on a series of autopsies.

The writer also wishes to thank Mr. Percy Hermant and his staff at the Imperial Surgical Company, not only for assuming the cost of building the pilot model of the machine, but for their active co-operation and keen interest as well.

To my friend Paul Aldwyn of the same company I am deeply indebted for invaluable technical assistance.

I would like to take this opportunity to thank Professor D. E. Cannell, of the Department of Obstetrics and Gynaecology, University of Toronto, Dr. H. J. Shields, retired Chief, and Professor S. M. Campbell, the present head of the Department of Anaesthesia, University of Toronto, and my colleagues of both departments for their acceptance of this apparatus, and the encouragement to make it available to the profession.

Résumé

Réanimation du nouveau-né
Une méthode et une machine

Pour le réanimation du nouveau-né, le rapport esquisse une méthode et décrit une machine qui se sont avérées éminemment satisfaisantes sur une période de plus de deux ans à l'Hôpital Général de Toronto.

L'excès de sédatifs à la parturiante est reconnu comme une cause majeure dans la création des problèmes de réanimation et l'emploi abusif de sédatifs pendant le travail est proscrit.

Cependant d'autres facteurs affectant la mère pendant le travail sont maladies cardiaque ou pulmonaire, toxémie etc. D'autres facteurs affectant directement l'enfant sont la prematurité, la présentation et position anormales, longueur et type du travail, troubles de la circulation fétale dûs à la pathologie placentaire, à l'obstruction mécanique de la circulation du cordon et au type d'accouchement.

Sous une débilité congenitale, l'auteur mentionne la possibilité d'anomalies histologiques dans le tissu pulmonaire qui pourrait être un facteur dans le manque d'expansion et le problème de la réanimation du nouveau-né peut être une dépression du centre respiratoire ou une anomalie du tissu pulmonaire. Le danger d'appliquer des pressions plus élevées que celles indiquées par la machine décrite est bien mis en évidence.

La machine qui est entièrement actionnée à la main a été conçue pour vaincre les objections faites aux conceptions automatiques dont un bon nombre contiennent une multiplicité de pièces, le résultat en est que la machine est fréquemment hors d'usage. Toujours prête est une qualité essentielle pour une machine employée en urgence.

Une pratique dangereuse—aux résultats souvent désastreux—s'est développée dans la fourniture d'oxygène provenant de machines aux enfants par administration sous masques, sans essayer de chercher et d'établir une voie respiratoire libre. La fourniture d'oxygène à l'enfant qui a une voie respiratoire obstruée n'est pas seulement inutile mais le danger est flagrant.

La machine est pourvue d'un équipement pour intubation trachéale pour permettre le nettoyage de la voie respiratoire par succion et l'administration directe d'oxygène intratrachéal. Les attaches du masque sont également fournis au cas où l'administration intrachéale n'est pas nécessaire.

La valve de contrôle

L'administration d'oxygène et le changement aux pressions négatives est réglée par une manette positive ou négative. Le mode de changement de la pression positive à la pression négative est entièrement sous le contrôle de l'opérateur, ce qui est un net avantage sur le contrôle automatique.

Le contrôle manuel règle seulement le mode de changement. En positive la pression est toujours 12 mm Hg—jamais plus et jamais moins. De même, en négative la pression est toujours 8 mm Hg—jamais plus et jamais moins. Il n'y a pas de point neutre ou mort sur le contrôle. Il est ou positif ou négatif. (La pression négative est crée à partir de la réduction de pression dans le réservoir par une attache de Venturi.)

Il n'y a pas deux cas de réanimation qui se ressemblent. Chaque cas demande un traitement particulier qui ne peut être fait par les conceptions automatiques. Le plus tôt on s'en rendra compte et l'admettra, le plus tôt les sauvetages en réanimation augmenteront et les désastres seront évités.

Description de la machine

La machine est un ensemble qui se contient lui-même monté sur une lourde base avec des casters tournant librement. L'oxygène est fourni par 2 réservoirs, l'un en action, l'autre en réserve, toujours disponible. L'oxygène est fourni à la tête à réanimer à travers une valve réductrice. Un petit meuble en bois contient un laryngoscope et des piles de rechange, 4 tubes intratrachéaux aux diamètres gradués 4, 5, 6, 7 et une masque de face.

La tête consiste en une ampoule de succion actionnée à la main pour ôter le mucus et un conduit de drainage en plastiques transparent et amovible. Le mucus ne peut entrer dans la valve administrant l'oxygène. La valve de réanimation est de la plus simple construction. C'est simplement une valve de sécurité, positive et négative.

La valve est d'un type de balle, en construction de bronze. Il n'y a pas de laveurs, écrous ou autres pièces qui s'usent ou qui demandent à être remplacées. La valve est conçue pour fournir une pression positive d'oxygène de 12 mm. Hg. et une pression négative de 8 mm. Hg. Aucune installation n'est nécessaire et aucune variation de ces pressions peut être effectuée. Même avec des chiffres de pression élevée sur la valve de réduction, ces pressions positives et négatives appliquées à l'enfant ne peuvent changer. N'importe quel excès d'oxygène s'échappe dans l'air.

Application de l'appareil à la méthode de réanimation

Dès l'expulsion de l'enfant, le mucus devrait être retiré du rhino-pharynx, par routine.

Si l'enfant ne respire pas spontanément, inutile de perdre du temps à des méthodes dangereuses; il n'est pas permis non plus d'essayer d'administrer de l'oxygène à un enfant avant d'avoir établi une voie de passage libre.

Le passage d'un tube intratrachéal est une procédure qui exige plus de douceur que d'adresse. La moindre dextérité manuelle exigée pour introduire un cathéter peut être possédée par quiconque est arrivé à la position d'assumer la responsabilité des soins et traitements du nouveau-né. Les cathéters fournies avec cet appareil facilitent grandement cette procédure. Les cathéters sont fournis en diamètres gradués et leur longueur d'un bout à l'autre est désignée pour permettre une descente facile dans la trachée sans accrochages sur la carina. Ces cathéters sont métalliques et dessinés pour éviter tout trauma. La construction métallique donne de la rigidité et facilite la manipulation et la paroi fine permet une lumière maxima. A l'embase il y a un manche sur le côté qui repousse les doigts de l'opérateur et les empêchent d'obstruer le champ de vision pendant l'insertion.

Le cathéter en place, la valve de succion est ouverte, l'ampoule de succion est mise à ôter le mucus et la valve de succion ensuite fermée.

Quand la valve de réduction marque environ 3 ou 4 litres d'oxygène par minute, les pressions changeables positive ou négative pour stimuler les mouvements respiratoires sont sous le contrôle de l'opérateur. Des changements en nombre de 10 ou 15 par minute sont adéquates et donnent à l'enfant une bien meilleure chance d'établir son propre rythme respiratoire plutôt que les mouvements artificiels plus rapides. Tant que la couleur de l'enfant s'améliore la profondeur des mouvements respiratoires n'est d'aucun intérêt. (Rappelez-vous que nous avons à faire à un enfant qui était destiné à vivre à l'air et l'appareil fournit 100% d'oxygène aux alvéoles pulmonaires.) Quand les respirations se sont établies le cathéter est ôté. Si l'enfant n'est pas robuste et si un supplement d'oxygène est indiqué il peut être donné avec le masque de face. Un tube plus long pour l'attachement au masque est pourvu pour administrer continuellement de l'oxygène à l'enfant dans le berceau si nécessaire.

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CARDIAC RESUSCITATION*

Round Table Discussion

Chairman: Dr. Shirley A. Fleming

Members: Professor Lucien Morris, Iowa
Dr. Carl Stoddard, Halifax
Professor Stanley Campbell, Toronto

The discussion opened with a consideration of the etiology of cardiac arrest.

Dr. Stoddard: When it is considered that the anaesthetic drugs are the most potent depressant agents employed in medicine, it is not too surprising that serious difficulties are sometimes encountered during their administration. Illustrative cases may serve as an introduction to the causes of cardiac arrest. An instance is recalled when cardiac arrest occurring during ethyl chloride ether anaesthesia was considered due to sensitization of the heart by overdosage of the ethyl chloride. Another case is remembered of ethyl chloride ether anaesthesia, when laryngospasm occurred producing anoxia with vago vagal reflexes, resulting in cardiac arrest. Another case of cardiac arrest was due to hypoxia resulting from sudden severe haemorrhage with sensitization of the heart to vagal reflexes. There have been instances when there was cardiac arrest due to trauma to the heart or great vessels. An air embolus may be the factor.

Dr. Morris: It is a popular conception that agents such as ethyl chloride and chloroform may cause cardiac arrest by sensitization of the heart, and that the individual's own epinephrine may be the activating agent. It seems to me that this idea should be challenged, since death from these agents is almost invariably due to overdosage. The overdosage may have been relative rather than frank in a great many of the accidents with these agents, but, nonetheless, I believe it is overdosage and not sensitization of the myocardium to epinephrine which is the mechanism to be indicted. It must be remembered, too, that other agents which sensitize the myocardium are cyclopropane, trichlorethylene and cocaine.

There is no doubt that patients die at all ages, and some of them quite suddenly, so that cardiac arrest during anaesthesia may be a coincidence. Who can be sure that a patient who dies of coronary occlusion or pulmonary embolus during an anaesthetic might not have died in bed at home had no anaesthetic been given? Isolated instances are well known in which patients have died just before operation or at a time which would have been during the operation had it not been postponed for some reason or other.

The condition of the patient is a definite factor. If a sufficient number of patients in poor physical condition are anaesthetized, sooner or later a fatal accident will occur. It may be, however, that some of these accidents are due to poor judgment on the part of the anaesthetist. In some patients overdosage is dangerously easy to achieve. When individuals are not very much alive, it does

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not take much of any drug to depress what little vitality they have. It is easy to be fooled and misjudge the resistance of an individual patient. In practice the anaesthetist can be guided only by his estimate of the response of the patient to the amount of the depressant drug already administered, and increases or reduction can then be made accordingly. Some accidents are known to have been precipitated by unwise positioning, or by rough handling of a susceptible patient. It is sometimes difficult to assign a definite cause for a cardiac arrest since several factors of etiological significance may play a part. However, the effects of anaesthetic overdosage, and obstruction which leads to asphyxia can be most often indicted, but, in fairness, all the major factors concerned in operating room deaths should be considered.

Dr. Campbell: I heartily agree with the previous speaker's statement that hypoxia is the precursor of cardiac arrest.

Dr. Morris: The consideration of cardiac arrest must begin with prophylaxis. The anaesthetist must take the onus upon himself to do something about it. Ignorance and inattention must be replaced by knowledge, care and judgment. It is important that a constant awareness of the state of each patient's vital functions is maintained. This is best done by physical contact—continual palpation of the pulse leaves no room for doubt. The anaesthetist who by constant and continual palpation of the patient's facial pulse maintains close physical contact throughout the entire period of anaesthesia will have fewer accidents than one who does not. It is not enough to take pulse and blood pressure every five minutes. Changes in pulse rate and volume leading to cardiac syncope may occur at any instant, and, if not recognized until the next stated five minute interval has elapsed, the time of opportunity for reversal of the process may be completely wasted. It is evident that the anaesthetist whose attention wanders is not taking the best possible care of his patient. The practice of the anaesthetist leaving his patient in order to understudy the surgeon, or to go out for a smoke, or look at the morning paper, or for any other purpose, is to be severely criticized.

Avoidance of airway obstruction is constantly necessary. Only a few years ago cessation of a patient's respiration was cause for alarm and patients died because respiration was not continued. To-day there is less concern, indeed we often produce apnoea in order to facilitate the ease in performing the surgical procedure, and artificially ventilate in a physiologic manner until the patient resumes control of his own respiration. A means of control over the ventilation portion of the transport system has been learned.

When circulation fails in its function of oxygen and carbon dioxide transport, substitution therapy is not so familiar. When the pump fails there is an immediate breakdown of the transport system. All efforts must then be directed toward support of the circulation.

Cardiac arrest occurs suddenly, but there is a warning which may be of only seconds duration—bradycardia becoming asystole—indicating the cessation of circulation. Oxygen must be given, carbon dioxide and the anaesthetic removed. If artificial ventilation is not adequate then an artificial circulation is necessary.

An effective heart beat and peripheral evidence of an adequate circulation are only achieved by cardiac massage not by the administration of drugs. Nothing less than a peripheral pulse and blood pressure is acceptable. In experimental animals artificial circulation can maintain only about half of mean normal blood pressure.

Dr. Campbell: I should like to speak about the use of drugs in cardiac resuscitation. When ventricular fibrillation has occurred it is pharmacologically wrong to use epinephrine because fibrillation is intensified. However, multiple ventricular foci of contraction is very frequently the condition present in so-called cardiac arrest, and can only be distinguished from ventricular fibrillation electrocardiographically. If the heart muscle is soft, cardiac massage will not be effective in producing any cardiac outflow, so that a drug which will cause contraction of the heart muscle is necessary. Epinephrine will do this. The dose used has been 1 cc. of a 1/10,000 to 1/20,000 solution, injected into the left ventricular wall.

Procaine and procaine amide have been enthusiastically used and then dropped. These drugs apparently cause some weakening of the cardiac muscular contraction which, along with the peripheral dilatation produces a drop in blood pressure. However, 100 mgms. of procaine in 1 cc. is injected into the heart muscle along with the dose of epinephrine previously mentioned, to lessen cardiac irritability.

Of the electrolytes, calcium produces contraction of cardiac muscle, so in the case of a heart stopped in diastole it has been our habit to inject into the heart 7½ cc. of 10% calcium chloride solution. Theoretically it should be effective and our surgeons, while not enthusiastic, feel that it may be of some value.

Atropine has been used intravenously in large doses to eliminate the vagal inhibitory reflex. If the heart has stopped I doubt if it is of much value. Where the heart is definitely slowing in its action or has just been restarted, and is beating at a rate below sixty per minute, atropine intravenously may be of some value.

Quinidine produces amongst other things a decrease in cardiac tone, so that I am rather loathe to use it in an emergency.

Where there is a definite diagnosis of auricular fibrillation in a heart which has been restarted intravenous digitalis is of value.

Dr. Morris: Drugs will not accomplish the transportation of oxygen to the tissues. They should only be used, if at all, after an effort has been made to produce an artificial circulation.

Occasionally epinephrine seems to better the situation. It must be used in very dilute solutions as suggested by Dr. Campbell. Its danger is that it may produce ventricular fibrillation.

Procaine gives very little if any protection.

An electric defibrillator is of questionable value. In fact, a home-made makeshift seems to be as effective as a manufactured fancy gadget.

Dr. Campbell: I agree.

Dr. Stoddard: I like to use diluted adrenalin and procaine. The injections are into the right auricle.

I have noticed that patients having intrathoracic operations seem to do better

when resuscitation is required than those having other types of surgery. Probably this is because the heart is easily seen and accessible for massage.

The floor: When there is trouble with heart cases, the heart is in asystole not fibrillation.

Dr. Morris: Sudden cessation of circulation may be associated with surgical trauma, either directly as by mechanical interference with the heart and great vessels, or indirectly as by stimulation of the pericardium. It may occur secondarily from anoxia, due possibly to pulmonary emboli or to severe haemorrhage. In some instances, the disease of the patient is of such a nature that the reserve pulmonary function is very low, and during the surgical procedure anoxia or asphyxia may occur in spite of efforts to prevent it.

Dr. Campbell: Intra-arterial transfusion can be a lifesaving procedure in producing an effective blood pressure, especially where cardiac massage is not adequate because of haemorrhage. This can be intraaortic to produce the maximum effect. Also, one must not forget to place the patient in a head down position to maintain cerebral circulation.

Dr. Morris: Saline has been injected directly into the heart.

Dr. Campbell: I recall a case where intraarterial blood appeared to be the determining factor in a successful resuscitation.

Dr. Morris: It is said that replacement intravenously is sufficient if it is as rapid as intraarterial.

To bring up another point. Would lowered body temperature help?

The floor: From experience with animals in hibernation with a temperature of 70 degrees Fahrenheit, it should help. Largactil may serve this purpose. With refrigeration using no blocking drugs oxygen demand decreases. Dogs would go for an hour without breathing under such circumstances.

From experience with cardiac surgery in children, it appears that if the temperature rises there will be more deaths.

Dr. Stoddard: I should like to suggest a plan for treatment when cardiac arrest occurs.

1. Inform the surgeon what you suspect.
2. Perform artificial respiration with 100% oxygen.
3. Ask the surgeon to prepare for a thoracotomy and to perform artificial circulation.
4. Place the patient in the trendelenberg position.
5. Start an intraarterial transfusion if there has been severe haemorrhage.
6. If there is cardiac standstill then start cardiac massage.
7. If there is cardiac standstill give adrenalin and procaine.
8. If heart is fibrillating do not give adrenalin, but pronestyl, quinidine or an electric shock may be used.

The proper way to massage the heart is to place two or three fingers, as size permits, above and below the heart, and milk the organ from the apex to the base until there is evidence of peripheral circulation.

Should the rate of massage be one hundred or forty per minute?

Forty is inefficient, fifty or sixty per minute is attempted.

The floor: Shouldn't it be faster?

Dr. Stoddard: If seventy is possible you are lucky.

Dr. Campbell: How forceful should the massage be?

Dr. Stoddard: As gently as possible.

Dr. Campbell: Does it need to be strong? It must be strong enough to establish a peripheral circulation.

The floor: Should the massage be one or two handed?

Dr. Campbell: That is determined by the room available.

The floor: How long should massage be carried out?

Dr. Morris: Until the heart can provide adequate circulation itself. If the heart stops after thirty seconds begin to massage again. The heart may need aid for four, five or ten minutes after it starts to beat.

The anaesthetist should be in charge in this emergency because he is in the position to see more cases. For preventive purposes and to be ready for emergencies have this question discussed in staff meetings.

Readiness to expose the heart is important. Thoracotomy must be done with care during artificial ventillation, to avoid incision of either lung or the ventricle of the dilated heart. Massage must be done hard enough and fast enough to get results, and that depends on how good the venous return is.

The floor: A case is reported where after failure for an hour to resuscitate the patient, noradrenalin was successful.

Dr. Morris: In two cases a gram of pronestyl has reversed ventricular fibrillation to asystole. I do not think drugs should be used for a flabby heart.

The floor: Is cardiac arrest more common than it used to be?

Dr. Morris: No, I do not believe so. Newer and more difficult fields in surgery are being explored with resultant more challenging anaesthetic problems, often in patients whose physical condition will admit of only the gentlest management of anaesthesia. There is also a freer discussion of cases.

The floor: Is light anaesthesia a factor?

Dr. Morris: No, I do not think so. Hypoxia and the other factors given are still the chief ones.

The floor: In cases of tracheobronchitis in children there is severe hypoxia and cardiac arrest might be expected, but so far in our experience has not occurred.

Dr. Morris: It was implied earlier that the occurrence of cardiac arrest is often associated with human error. In a recent report by the oldest of the existing Anaesthesia Commission Groups, the belief is stated that nearly two out of every three deaths submitted to it for appraisal were associated with improper anaesthetic management. Certainly, none of these are instances of willful mismanagement, but are associated with a less than adequate degree of knowledge, care and judgment. There are few of us indeed who have not wished to be more adequately endowed with wisdom and experience.

Dr. Fleming: The members of the discussion group hope they have given you food for thought, and that too dismal an outlook has not been produced, for some of these patients requiring cardiac resuscitation have been saved, and so will others if prompt action is taken when required.

Résumé

Les principaux facteurs étiologiques qui mènent à l'arrêt cardiaque dépendent du surdosage de l'agent anesthésique et de l'hypoxie. Une notion en vogue soutient que certains agents, tels le chlorure d'éthyle et le chloroforme, causent l'arrêt cardiaque par sensibilisation du myocarde à l'épinéphrine, cependant que le Dr. Morris émet l'opinion qu'avec ces drogues la mort est presque toujours due au surdosage. Il faut se rappeler que le myocarde est également sensibilisé par le cyclopropane, le trichloriéthylène et la cocaine. Il y a aussi possibilité que, par coincidence, le malade meure au cours de son anesthésie. L'état du patient est un facteur à ne pas oublier. Si plusieurs malades en mauvais état sont anesthésiés, des accidents graves surviendront tôt ou tard. Le surdosage est fréquent chez ces patients. Certains accidents sont attribuables à une position défavorable ou à des manipulations intempestives. Le surdosage anesthésique et l'obstruction allant à l'hypoxie sont les causes principales de l'arrêt cardiaque.

Prévenir demeure le point capital. Il appartient à l'anesthésiste de remplacer l'ignorance et l'incurie par des connaissances, des soins et un jugement sains. La palpation continue du pouls est essentielle. La lecture du pouls et de la tension artérielle aux cinq minutes ne suffit pas car des altérations aboutissant à une syncope cardiaque peuvent survenir incessament et la période d'alarme qui permettrait de juguler ces signes avertisseurs peut échapper à jamais. L'arrêt cardiaque survient brutalement, quoiqu'il existe une phase d'alarme de quelques secondes, avec bradycardie, évoluant en asystolie.

S'il y a fibrillation ventriculaire il n'y a pas lieu d'utiliser de l'épinéphrine car celle-ci intensifie la fibrillation. Toutefois, on note souvent la présence de multiples foyers de contraction ventriculaire durant les soit-disant états d'arrêt cardiaque et seule l'électrocardiographie peut les différencier de la fibrillation ventriculairevraie. Si le muscle cardiaque devient mou, le massage cardiaque demeure ineffectif. Il faut utiliser une drogue qui augmentera la contraction du myocarde. On emploie 1 cc. d'une solution d'épinéphrine à 1/10,000 au 1/20,000 injectée dans la paroi du ventricule gauche. On injecte aussi 100 mgms. de procaine. Si l'arrêt cardiaque se produit en diastole, an pratique une injection de chlorure de calcium (7½ cc. à 10%). Si le coeur qui a recommencé de battre ralentit, l'atropine par voie intraveineuse est utile; la digitale l'est aussi pour un coeur qui a repris ses battements et qui demeure en fibrillation. Le Pronestyl et la Nor-adrénaline ont également été employés avec succès.

Directives pour la ressuscitation cardiaque:

1—Avertir le chirurgien;
2—Respiration artificielle avec 100% d'oxygène;
3—Demander au chirurgien de procéder à une thoracotomie et de pratiquer la circulation artificielle.
4—Placer le malade en Trendelenburg;
5—Pratiquer une transfusion intraartérielle s'il y a eu hémorragie;
6—Pratiquer le massage cardiaque s'il n'y a pas de contractions;
7—Administrer de l'adrénaline et de la procaine s'il y a arrêt cardiaque;

8–Si le coeur est en fibrillation, ne pas donner d'adrénaline mais du pronestyl ou appliquer un choc électrique.

Pour pratiquer le massage cardiaque, il faut «traire» le coeur depuis sa pointe jusqu'à la base, assez vigoureusement et assez rapidement pour obtenir une circulation effective. La thoracotomie doit se pratiquer avec soins pour ne pas inciser dans le coeur ou les poumons.

En resuscitation, la clef du succès dépend d'une action prompte.

BLOOD PLASMA SUBSTITUTES, WITH EMPHASIS ON POLYVINYL–PYRROLIDONE (P. V. P.)

RENÉ LÉTIENNE, M.D., F.R.C.P.(C)*

The clinical features of shock, a term used in medical parlance to describe almost any condition associated with sudden or rapidly developing weakness, were clearly stated more than a century ago and the similarity of its signs with those of haemorrhage were also recognized. Theories to account for it, based more on logic than on experimental data, were submitted hesitantly as efficacious therapeutic counter measures remained helpless or unsuitable.

To-day, much remains to be done even if great strides have been achieved in the prevention and treatment of this extremely common condition. In the short span of thirty years, two wars have further forcibly focussed our attention on this problem of matching the challenge created by shock.

Three hundred years ago, Harvey described circulation. Christopher Wren used quills to introduce fluids parenterally and Denys performed blood transfusions on human beings. Within the last century, Wood and Pravaz developed the hollow needle, Pasteur rendered safe the introduction of foreign substances into the body while Richet studied the phenomena of anaphylaxis and other allied systemic reactions. In 1900, by observing the differences existing between the bloods of normal individuals, Landsteiner laid the cornerstone for adequate treatment of haemorrhage and shock.

Conditions of occurrence of shock have been gradually elucidated, as well as its early recognition, its prevention and treatment. Whether it be primary or secondary, shock is the product of a reduction in the circulating blood volume following the loss of blood or plasma. Thus, the primordial oxygen carrying function of the erythrocyte becomes severely hampered. Although the exact mechanism of shock remains baffling, it is agreed that a marked decrease in the total circulating blood volume is one of its outstanding features. Through information gathered from clinical data and laboratory observations, the rationale for its control and prevention was established, along with other measures of less magnitude.

Painstaking, delicate tests, either qualitative or quantitative, have become standard routine to firmly diagnose shock and to corroborate or to alter the course of treatment, particularly during the last twenty years, thanks to facilities made available by well equipped laboratories and qualified personnel.

The present keen interest in blood plasma substitutes is easy to understand. Even if it were always employed parsimoniously, in conditions where no other known substitute might be used judiciously to produce a lasting or temporary restorative effect, stocks of human blood will never fulfil all the calls for it. Despite all the laudable efforts made by national organizations, by local groups, scientific and philanthropic societies, supplies of blood will remain limited, even under ideal conditions. Experience from the last world war demonstrated the

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limitations of blood banks and our present way of living, with its ever impending catastrophes, only bears up this fact.

Since blood is life-saving, it must only be used where there is a definite need for it. There exists no doubt that it remains the best remedy against shock, even if its administration entails certain risks, demands time and raises problems as to its conservation. On the other hand, substitutes may well tide over patients who do not necessarily require whole blood to recuperate normal functions, following thermal burns or crush syndromes, for instance, where haemoconcentration values basically determine correct treatment. Obviously blood could frequently be economized and substitutes used to combat shock, particularly when physical rather than biologic properties will determine the immediate usefulness of the replacement agent.

Moon, Scudder, Trueta, Van Slyke and several other investigators, have made exhaustive studies demonstrating that with the immediate development of shock, the high state of permeability of the altered capillary wall leads to a diminution of blood volume, along with consequent reflex vaso-constriction, haemoconcentration, hypotension, interference with the circulation of oxygen-carrying erythrocytes, tissular anoxia and acidosis. Physical and biochemical standards are soon involved in this general systemic upset. Restoration of the depleted circulating blood volume logically appears as an essential and integral step towards adequate correction, provided it can be maintained long enough and without disturbing the physiological range of components found in body fluids.

Around the turn of this century, many unsuccessful attempts had been made to find substitutes for blood. Interest faded away with Landsteiner's discovery of blood groups, with technical improvements in the collection of blood and in the use of anticoagulants. World War I brought new impetus in the study of substances which might replace blood in certain modalities of shock. Bayliss, in 1916, introduced a 6% gum acacia in normal saline solution which proved far more efficient than the crystalloid solutions. The pendulum soon swung the other way again as results definitely proved to be superior with blood. Moreover, impurities frequently caused anaphylactic, allergic or pyrogenic reactions and possibly, blocked the reticulo-endothelial cells of the liver.

Similar disadvantages were to be encountered with other substitutes, such as gelatin, pectin, isinglass, bovine plasma, bovine albumin, etc. . . None, of course, can act as a vehicle for oxygen. Attempts to use hemoglobin solutions turned out to be dangerous on account of renal complications. Until recently, human plasma stood as the sole dependable substitute available, but dangers of sensitization, of virus hepatitis, lack of adequate supplies prompted research to look for cheaper, safer, easily produced colloid substances which would satisfactorily improve and sustain venous return, cardiac output and blood pressure.

Requirements of Plasma Substitutes

Some essential qualities are desirable if a substitute is to be of any practical value.

On initial or repeated administrations, whether in small or in large amounts,

substitutes must exhibit a minimum of variable physical, chemical, biochemical and biological characteristics which determine their suitability whilst not seriously affecting vital processes which otherwise would not be disturbed from their use.

Solutions should be fluid at ordinary temperatures, indefinitely stable, of a constant composition, well tolerated in tissues, causing no ionic interaction. Molecular weight approximating that of serum albumin is desirable for colloid solutes in order to be longer retained in the general circulation. Solutions should also have an osmotic pressure and a viscosity similar to that of plasma. Their fate should be known as they must not be stored too long in tissues. To be safe, pyrogenic, toxic or antigenic reactions must never occur. Furthermore, kidney, liver and blood functions must not be altered; should dysfunction be present, it ought to be detected easily while being essentially of a temporary nature.

To be usefully employed on a large scale, the preparation of substitutes should be relatively easy, inexpensive and available under all circumstances. Finally, they should effectively maintain the osmotic pressure of the circulation until their replacement by plasma proteins.

Poly-Vinyl-Pyrrolidone

Perhaps, it may be worthwhile to give a brief description of the physical and chemical properties of this product.

P.V.P. is a synthetic polymer, a white, hygroscopic, very soluble substance, giving a viscous, clear, yellowish, indefinitely stable solution with a pH of 4.0 to 7.0. Molecular weights of this polymer are not unique and vary in size from 30,000 to 60,000. In 3.5% Solution, colloidal osmotic pressure and viscosity are about of the same order as that of blood, thus reducing the risk of haemolysis or of deformation of red cells.

Investigation has shown that this nontoxic preparation can be recovered in the urine (80% after ten days) and following histological studies, there is no evidence of accumulation in tissues. Only large quantities of hyperviscous solutions (never approaching clinical uses) can be damageable, as one may easily presume. No sign of remote toxicity has, so far, been accounted for.

Solutions of P.V.P. being inert pharmacologically, non-pyrogenous and non-antigenous, their use presents no real problem. However, biochemical alterations may be detected and are not to be overlooked if use of P.V.P. is anticipated.

Although it is claimed that no interference with blood grouping or cross matching exists, we cannot completely rule out the fact that rouleaux formation can be present. In our experience rouleaux formations appeared only following several or massive administrations of P.V.P. Of course, such rouleaux formations can be expected following the administration of any large molecule, whatever its chemical nature; Hyperglycemic patients, for instance, frequently exhibit rouleaux formation.

Therefore, in case of emergency P.V.P. may safely be given without previous blood-typing. Where time permits, the taking of a blood sample as a precautionary measure is perhaps advisable. The risks are comparable with the use of O. group blood in patients of undetermined grouping.

Sedimentation rate is also modified, showing an increase for a period of two to three weeks.

Likewise, high concentrations act as reducing agents and values for blood sugar may be modified, despite the rapid excretion of poly-vinyl-pyrrolidone. False quantitative and qualitative values for albuminuria are rather common.

In conditions where Subtosan (Plasmosan—trade name in Great Britain) is generally indicated, the apparent physiological upsets mentioned above have little meaning, for they are transitory in nature, easily estimated. Ionic balance and its maintenance, together with adequate control of intravascular circulating fluids, remain the chief indication of this replacement therapy.

Clinical Experience with P.V.P.

Our first experiences with Subtosan (a 25% solution of P.V.P.) were begun in 1947. This preparation was used as a retarding agent, very satisfactorily, in more than one hundred cases. The idea was to control or to reduce total dosage of certain drugs while obtaining adequate and sustained response, when using Procaine intravenously particularly. Subtosan was felt to be an extremely valuable adjunct.

Case Report: Sedation proved to be almost beyond therapeutic limits in a case of Delirium Tremens. During a twelve hour period, this patient had received nine grains of Nembutal orally, two hypodermic injections of HMC no. I, 150 mgms. of Demerol, an undetermined amount of Chloral hydrate and one gram of Pentothal sodium I.V. in 500 cc. of 5% Dextrose. All this to no avail, only his state of agitation turned for worse.

Therapy was entirely discontinued for 6 hours. He was then given 20 cc. i.v. of Subtosan, followed by another gram of Pentothal sodium i.v. in 500 cc. of 5% Dextrose. This patient fell asleep after 0.30 gm. had been administered. The drip was slowed down and he managed to sleep for 24 consecutive hours. The following three days, after adequate oral feeding, the same procedure was repeated with equally gratifying results.

The fact that Subtosan "retarded" certain drugs led us to believe that it could be employed to retard the elimination of electrolytes, where plasma or blood were not available to maintain adequate intravascular volume. Twenty to thirty cc. of Subtosan would be injected i.v. prior to the administration of routine fluids. This assumption, of course, was not correct as P.V.P. does not interfere with glomerular or tubular resorption, and is not stored in any particular tissue. In fact, this retarding effect is selective in action, and its duration seldom lasts, more than 12 to 24 hours. Various concentrations in saline and dextrose, were tried nevertheless with some rather good responses, lasting a few hours at least, until we became aware of the very extensive work that had been carried out mainly in Germany and in France with solutions of P.V.P. as substitutes for human plasma.

With clinical work covering well more than one million infusions, a safe and effective solution has been marketed under the trade-name of Subtosan (Plasmosan) its composition is as follows:—

Polyvinyllpyrrolidone	3.5	g.	per 100 ml.
Sodium	361	mg.	" " "
Potassium	22	mg.	" " "
Calcium	9	mg.	" " "
Magnesium	0.06	mg.	" " "
Chloride	582	mg.	" " "
Bicarbonate	17	mg.	" " "
Dissolved Carbon dioxide	75	mg.	" " "

Our frequent use of this solution only corroborated the numerous publications which have devoted attention to this product, namely that it can appropriately replace plasma, without contraindications. Like many others, we feel that it should be adopted for current therapeutic measures and that it should be available in every laboratory, in every practitioner's shelf. On strictly practical grounds, Subtosan (Plasmosan) can always safely carry on where plasma is scarce or not existant.

You may well all wonder why no reference has been made to another valuable development in the field of plasma augmentors. I refer of course to Dextran the polysaccharide compound. From published data it is seen that this product would appear a most useful blood plasma substitute. However, after five years investigation with Subtosan there are still many points which we would like to establish, and we would prefer to know all there is to know about one product, rather than half as much about two.

I have been careful to mention Subtosan* or Plasmosan in this paper as opposed to P.V.P. as this is the brand that I am most familiar with. The type of P.V.P. available varies according to the method of Polymerisation adopted by the manufacturer, and molecular weight mean depends upon this of course. As stated, therefore, we have confined ourselves to the product which we know does not alter as far as the method of polymerisation is concerned.

Résumé

Le traitement du choc par le sang et par le plasma, constitute une arme de première valeur. D'autre part, ni l'un ni l'autre sont à notre disposition en quantités suffisantes. Les chercheurs ont donc orienté leurs travaux pour trouver des substituts qui posséderaient au moins les qualités physiques du plasma.

Le Subtosan semble doué de ces avantages, n'exhibant aucune toxicité ni aucun effet d'accumulation, tout en aidant à restorer de façon durable une circulation défaillante. A date, son usage n'a donné lieu à aucune réaction prouvée comme délétère et a permis d'aider de nombreux malades qui, autrement, auraient été privés d'une médication anti-choc de valeur réelle, à défaut de sang et de plasma.

*Subtosan: trade-name of a P.V.P. preparation, kindly supplied by Poulenc Laboratories, Montreal, Que.

PHYSIOLOGICAL REQUIREMENTS IN EQUIPMENT RELATED TO ANATOMICAL FACTORS IN CHILDREN**

H. M. SLATER, M.D.*

INTRODUCTION

Paediatric Surgery and Anaesthesia today have become specialties within specialties, attributable to the ever advancing progress of medicine and surgery. Within a relatively short period, both the research laboratory and the clinical investigation have produced for the paediatric anaesthetist, a wider range of techniques, equipment and drugs to facilitate and assure successful surgical interventions. The significance of physiology, pharmacology, biochemistry and anatomy soon became apparent when "heroic surgery" was instituted in infants and children. Much thought is presently being expended on the various physiological problems which have attended our procedures, many of which are directly related to the anatomical structures of infants and children.

BASIC PRINCIPLES

Basically, all techniques must assure the infant or child an adequate supply of oxygen and an easy elimination of carbon dioxide. These two factors alone have influenced our conceptions of proper paediatric equipment and agent administrations. A better understanding of breathing patterns, especially in infants, and more attention to details have enabled the anaesthetist to overcome many seemingly major problems. Although it is said that newborns can withstand hypoxia or anoxia, we are quite aware that a superimposed surgical condition and operation adds greatly to the risk involved. We know that such children are, or become candidates for an acidotic condition which is created by the increased carbon dioxide in blood and tissues. We are also cognizant of the associated dangers of heat accumulation caused by the increased metabolism. A child will not tolerate for long, any lacking assistance to his basic needs; he will simply give up. By assistance is meant the proper application of anaesthetic equipment and management; regard for differences in anatomical structures; and the prevention of undue metabolic upsets.

The *dead space* in an average adult is approximately 150 cc. That of a newborn infant is in the neighborhood of 8 cc. Therefore it becomes obvious that ordinary small adult face or ether masks with a capacity of 125 cc. or over, will add greatly to the accumulation of carbon dioxide. An adult is better equipped to move gases in breathing systems. Not so with the baby. The infant soon tires, perspires, has tachypnoea and tachycardia—and finally quits. Reduction in total dead space precludes such a finale.

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Resistance too, has added its share to the many unnatural circumstances to which a child is subjected during an anaesthetic. The cross-sectional diameter and length of infants' tracheae and bronchi reveals the fact that resistance amounts to almost 256 times that of the adult. The child must then compensate by breathing rapidly. Prematures at the rate of 58 per minute; Newborns at 44 per minute and 5-year olds at 26 per minute. Therefore, any technique applied should not increase the respiratory volume per minute nor the mechanical energy for pulmonary ventilation.

Let us now consider in more detail the relevancy of these principles to paediatric anaesthetic equipment.

Equipment

Endotracheal Tubes: The value of an endotracheal tube as a reliable airway need not be challenged. It provides for proper ventilation and resuscitation. Troublesome secretions are easily aspirated thereby preventing an acute or chronic hypoxia. This assured airway has enabled the anaesthetist to overcome the difficulties created by enlarged adenoids and tonsils, large tongues, micro-agnothia, and in short, all abnormal anatomical situations in the mouth and throat. Interference with breathing caused by difficult posturing is alleviated by intubation together with assisted respiration.

An endotracheal tube reduces the total dead space by a significant amount. This is well illustrated in a baby, two months of age, with an anatomical dead space of 8 cc. The dead space is reduced to ¾ cc. by the introduction of an 18F portex tube 10 cm. long. (Table I and 2). The tube need not be too long, otherwise there is the hazard of passing it too far into the trachea and blocking a bronchus. Furthermore, excess lengths extraorally add to the dead space. The internal diameters must be the maximum allowed without jeopardizing the flexibility or non-kinking qualities of the tube. A kink adds greatly to resistance during inspiration and expiration. Polyvinyl catheters mould well at body temperatures with the oropharyngeal and tracheal contours thereby preventing undue irritation of the larynx and trachea. Rubber tubes do not have this faculty. Strict attention to the position of the bevelled end prevents unnecessary blockage distally. Bevels should be at the side and not anteriorly or posteriorly. Otherwise there is a tendency for the open end to become approximated with the tracheal mucosa creating a valve-like action during respiration.

Face Masks: The face masks available for children still leave much to be desired. The conventional masks have a dead space far greater than that of the child. Hence they become a major problem in carbon dioxide accumulation. (Table 4). A flat triangular shape similar to the Bennett type is preferable. And with a soft cushioned edge, contours of the child's cheeks, nose and chin, are not injured by the pressure of the mask on the face. Again, the size of the mask must be in accordance with the size of the patient's face. The average infant face piece has a capacity of approximately 40 - 50 cc. as compared with an average adult's of 150 cc. Hence it behooves one to seek ways and means to lower the carbon dioxide concentration possible under a mask. The solution is

to afford a high flow of incoming gases together with a suitable exit, the entrance and exit of gases being located in close proximity to mouth and nose. Cumbersome spring or gravity type exhalation valves offer much resistance to the efforts of a child on expiration. A simple port which can be opened or closed easily and through which air is prevented from entering by virtue of the high gas flow is more desirable. Recently, a new non-rebreathing type of face mask

TABLE 1
SIZES OF ENDOTRACHEAL TUBES FOR VARIOUS AGES

Age	*French Size*	*Magill Rubber Tubes*	*Portex (Vinyl Plastic) Magill Tubes*	*Length in centimetres* *S (Short)*	*M (Medium)*	*L (Long)*
Birth to 3 mos.	13	00	0	10	11	12
	16		1			
3 to 9 mos.	17	0	1A	10	11.5	13
	18		1B		11.5	13
9 to 18 mos.	20	1	2	11.5	12.5	14
18 to 2½ yrs.	22	2	2A	12	13.5	15
2½ yrs. to 5	24	3	2B		14.5	16
	25	3	3		16	18
5 to 7 yrs.	26	4	4	15	17	19
8 to 9 yrs.	27	5	5	16	18	20
	29	6	6	16	18	20
10 to 12 yrs.	30	7	7	17	19	21
Over 12 years	31 to 38	8 & 9	8, 9 & 10	18	20	22

Short and medium lengths are for oral intubation. Long lengths are for nasal intubation.

The numbered sizes of tubes vary from one type to the other; but they can be measured on a French size scale and numbered accordingly to make the numbering common to both types of tubes.

The sizes suggested above are only approximate for each age group; the next smaller or next larger size might have to be used in certain instances, depending on the size of the child.

These lengths are for oral endotracheal tubes. The short length is correct for most individuals. The long length could be used for nasotracheal, although may be a little short in some cases.

Rough guide to tube length for an individual case (orotracheal) is to compare tube with earlobe to nose-tip distance (EN) of the patient, allowing an extra 1–2 cms. in the smaller sizes (up to 4 years) and 2–5 cms. in the larger. Nasotracheal tubes should be approximately 1¼ EN for infants and children up to about 4 years. 1½ EN for older patients.

has been developed for infants and children. Here the directional valves within the mask are so light that a 5-pound infant has no difficulty operating them. Such a system aids in the reduction of accumulated carbon dioxide, since there is no rebreathing into a bag. However, unless the patient has sufficient respiratory effort, some of the exhaled gases may remain in the mask. Non-rebreathing masks have a minimum of resistance and permit a supply of fresh gases with each breath. It is recommended that the chimney pieces to masks should not be cumbersome and heavy—again to reduce the total dead space.

Accessory Connectors: In his quest for a glorified technique, the anaesthetist may become over-zealous in his efforts and proceed to create wierd forms of

apparatus. The more apparatus that is added to a child's breathing system, the greater is the chance for increased dead space (TABLE 3) and *resistance*. Endotracheal tube connectors, rubber connections, elbow joints, etc. are contributors: therefore they should be kept to a minimum in number as well as in size and length. Acute angles in connectors cause turbulence of gases, which, it is said, increases the intrapulmonary negative pressure. This form of resistance cannot be tolerated by infants or acutely ill children over long periods, as witnessed by the indrawing of the suprasternal notch and lower intercostals. Any constriction or sharp bend with local turbulence is to be avoided anywhere in the breathing system. Where flows are laminar, resistance is dependent on the

TABLE 2
SIZE OF ENDOTRACHEAL TUBES WITH CORRESPONDING CAPACITIES

	Size Number	*Length in cm.*	*Capacity in c.c. H_2O* (Average)
Portex Endotracheal Tube (Oral)	00 (16 F)	10	0.58
	0 (18 F)	10	0.78
	0	12	1.1
	1 (20 F)	11	1.05
	1	12.5	1.42
	1 A	12.5	1.6
	2 (22 F)	14	1.8
	2 A	14	2.2
	2 B	14	2.3
	23 F	15	2.8
	24 F	15.5	3.3
	26 F	15	3.8
	26 F	17	4.1
	27 F	17.5	4.8
	27 F	21	6.5
	30 F	20	7.5
Magill Rubber Nasotracheal Tube	00	14	1.1
	0	15	1.8
	1	16	2.6
	22	19.5	4
	24	21	5.5
	27	24	7.6
	28	25	9.4

diameter of connectors and tubes—rising sharply as the diameter decreases. Obtuse gradual curves are recommended whenever changing the direction of gas flows. Strict attention to the size of infant tube connectors is vitally important.

Rebreathing Bags: Any rubber rebreathing bag can be adapted to paediatric use, but certain factors must be borne in mind. The larger the bag the greater is the flow of gases required to maintain its fullness. This is wasteful and uneconomical. Resiliency of the bag is important to facilitate manual compression or to allow it to distend with a minimal expiratory effort. Therefore it is recommended that a 1-litre bag be used for infants up to 4 months of age; a 2 litre bag for infants from 5 months to 5 years; and a 5 litre bag may be used for children over that age. The size again is determined by the child's minute volume. Experience has taught us that in high flow techniques the minimal gas flow is 4 litres and the maximum is eight litres without causing accumulation

of carbon dioxide or overdistension of the reservoir bag. Infants up to the age of 12 months require 4 litres; 1 - 4 years need 5 litres and over this age, 8 litres is well tolerated. Needless to say, it is preferable to have the bag close to the

TABLE 3

CATHETER CONNECTORS

	Nasal		*Oral*	
	Number	*Capacity c.c.*	*Number*	*Capacity c.c.*
Magill Type (Tapered)	9	1.2	1	0.7
	10	1.2	3	1.1
	11	1.9	4	1.9
	12	2.2	5	2
Magill Type (Corregated End (and Tapered)	7	0.3	1	0.6
	8	0.4	2	0.8
	9	0.9	3	1.2
	11	1.9	4	1.6
	12	2.1	5	2.3
			5 A	3.3
			6	4.2

	Inside diameter mm.	*Length cm.*	*Capacity c.c. H_2O*
Magill (Foregger)	3	4.5	0.5
	5	5.2	1
	6.5	6.5	1.5
	6	7	1.5
	4.5	4.2	0.5
	6	5.6	1
	7	6.8	2
	7.1	7	2.5
	8	4.2	1.5
	8.5	6.4	3

	Number	*Capacity c.c. H_2O*
Foregger "8" (Slipjoint)	14	2
	20	2.2
	26	2.3
	30	3
	35	3.4
	40	4.2

	Inside diameter mm.	*Capacity c.c. H_2O*
(Elbow)	5.5	1.4
	7	2.2
	10.5	4.1

	Number	*Capacity c.c. H_2O*
Foregger "8–C"	60	0.3
	80	0.4
	62	0.4
	82	0.4
	83	1

head in order to reduce the respiratory effort. If it is at some distance, the conduction tube should be of adequate calibre. In such instances, a well placed, light valve will prevent rebreathing along the tube.

Ether Masks: Ether masks come in all shapes and sizes. While some are

simple, others are complicated. Essentially the only pre-requisites of a good mask for children are: (a) proper size to cover mouth and nose; (b) sufficient covering to enable ether vapour to pass through and carbon dioxide to be eliminated effortlessly; (c) a minimum of "wetting" and draining into the child's face. The modified Ferguson mask has these qualities. For rapid inductions, a towel

TABLE 4

FACE MASKS

Make	*Size*	*Capacity c.c. H_2O*
		(Approximate)
Heidbrink	Adult, medium	135
"	Child, medium	125
"	Child, small	90
"	Infant	35
Bennett	Adult, medium	80
"	Infant	10
Foregger	Adult, No. 17-A	250
"	Child, No. 18-E	125
"	Infant, No. 18-D	40
"	Infant with face piece connector (No. 56)	60 (Average)
New Plastic	Adult, regular	150
"	Adult, large	225
McKesson	Adult	190
"	Child	120
British Oxygen Company	Adult	150

wrapped around the base of the mask will enhance the ether concentrations. Caution must be observed in the matter of carbon dioxide accumulation as there is considerable dead space in all masks (TABLE 5). This is best avoided by periodically lifting one edge and allowing the exhaled air to escape, or by

TABLE 5

OPEN DROP MASKS

	Dimension cm.		*Capacity c.c. H_2O*
Yankaver	9 × 5 × 5		110
Yankaver	10 × 5 × 6		125
Ferguson	13 × 10 × 6.5	Adult	650
Ferguson	12.5 × 9.5 × 7	Child	610
Ferguson	11 × 8 × 8		500
Infant Ferguson	9 × 7.5 × 5		200
Infant Ferguson	9 × 6 × 4.5		150
Infant Ferguson	7 × 5 × 3.5		50
Cannister (Water's To and Fro)	Large, Metal		700
	Medium, Metal		520
	Small, Metal		305
	Infant, Metal		200
	Infant, Plastic		130

placing a mouth hook underneath and insufflating with 1 - 2 litres of oxygen. Such a procedure precludes the onset of convulsions.

Absorption Apparatus: Absorption apparatus, whether of the "circle" or "to and fro" type, has one outstanding contra-indication in paediatric anaesthesia—namely, heat accumulation. Our present day concepts require that this be

reduced to a minimum. Indeed, the cooler the better, because the oxygen requirement of the child will be less and metabolism is maintained at near normal physiologic levels. The standard circle type of equipment creates somewhat less heat in the child by virtue of the dissipation occurring along the breathing tubes; but children especially under the age of five, must exert their own breath force to move the gases over a distance and through resistant directional valves. Furthermore, there is always a certain degree of diffusion of gases in and around the face piece. Therefore it would be preferable to have non-resistant valves located adjacent to the mask. Difficulties which are created by lazy breathing and prolonged operations are easily overcome by manual assistance. The Leigh type of circle filter for infants is ideal for short operations no longer than 45 minutes to 1 hour. Soda lime granules if too small may become a source of increased resistance in the breathing system, the optimum being 4–8 mesh. Further resistance is influenced by increased tidal volumes; if this is raised, the child is obliged to force more gas through the same space in the same time interval.

TABLE 6
FACE PIECE CONNECTORS*

Standard Partial Rebreathing (Foregger)	40–42 c.c.
Chimney Y to Circle Filter (Foregger)	50
Y—Piece only	30–50 c.c.
Connell Elbowjoint	45
Adaptor to Cannister, straight	10
Adaptor to Cannister, angular	18
Chimney Y and Angular Adaptor and Slipjoint	55 c.c. (total)

*The above are only a few of the many varieties available.

New Stephen-Slater Non-resistant Non-rebreathing Valve
Dead Space of 10 c.c.

Normally, the dead space in a "to and fro" system is slightly less than that of the circle type, but as the soda lime becomes exhausted, the dead space is increased proportionately. The "to and fro" method has the advantage of less resistance due to the absence of valves. The main disadvantage is that of greater heat accumulation. This can be controlled by frequent changes of cannisters (every 15–20 minutes) and the application of ice bags to the unit when in use. Small size cannisters are now available for infants, which have increased the efficiency of the technique.

Once again, stress is made on the reduction of the resistance originating from moving mechanical parts in absorption systems. All valves should be light and not affected by moisture. Spring action or gravity types are undesirable. The best location for exhalation and inhalation valves is as close to the mouth and nose as is possible.

Insufflation: Insufflation of anaesthetic mixtures can be accomplished either orally or endotracheally. The oral method is probably one of the oldest, although unpredictable in its efficacy. The gas flows must be adequate to maintain anaesthesia and wash out carbon dioxide. Too great a flow acts as a "gas barrier" against which an infant refuses to breathe. The endotracheal form of insufflation

is best exemplified by the Ayres' Technique in which the child breathes in fresh gases from one arm of a "T" piece and exhales to the outside air through another. There are no valves to increase resistance and rebreathing can be prevented depending on the length of tube fixed to the exhalation opening and the flow of gases delivered. The Ayres' method was first devised for cleft lip operations where it was realized that an endotracheal tube reduced the anatomical dead space and the "T" piece assured an escape for carbon dioxide. The only disadvantage is the possibility of uneven maintenance due to inhalation of air from the outside or due to too great a flow or pressure of gases. The method is not suitable for older children.

Valves: As indicated previously, valves offer an excellent source for increased resistance. Any metal, plastic or mica disc which operates with the assistance of gravity and the child's inhalation effort is inefficient when turned upside down. In the opposite position, the patient must breathe against gravity. Any faulty valve therefore adds tremendously to the resistance in the apparatus, resulting in increased fatigue on the part of the individual. The non-rebreathing and non-resistant valve which incorporates delicate rubber discs so designed that a 2-pound infant is able to breathe with freedom, is more desirable. It is efficient in all positions and is so designed that it is virtually impossible to accumulate carbon dioxide. The valve is applicable to children of all ages and has demonstrated the gratifying property of being able to assist in maintaining lower body temperatures because of the escape of body heat through the exhalation valve. The new non-rebreathing valve now has a small dead space of 9–10 cc.

Laryngoscopes: Although laryngoscopes per se do not maintain anaesthesia, they do however facilitate certain techniques. Due attention to size and shape of blades, weight of handles, and position of the head renders intubation less difficult. Anatomically, an infant's larynx is more superior and anterior than that of the adult. The tip of the epiglottis is close to the glottis. Therefore by introducing a curved tipped blade as far as the velecula without lifting the epiglottis and by suspending the jaw, trauma to larynx is avoided and the hazard of eliciting harmful reflexes is eliminated.

Oxygen Therapy: Even oxygen equipment has been streamlined to accommodate infants and children. Small plastic hoods with facilities for high humidity and oxygen concentrations are necessary for infants with pulmonary infections. Children with inflammation of the larynx, trachea, and bronchi do not need as much oxygen (maximum 50%) as they do humidity. Tents such as the Croupettes are then indicated. One must use ice freely to maintain lowered temperatures in either type, thereby reducing the patient's metabolism and consequently the oxygen demand. The oxygen flows of 7–9 litres per minute will provide enough oxygen in a hood and will simultaneously aid in eliminating carbon dioxide gas. The liberal and judicious employment of oxygen therapy to children postoperatively oftimes precludes the advent of undue complications.

Gas Machines: Any standard gas machine which is versatile in its possibilities in accordance with the numerous techniques is suitable for paediatric anaesthesia. There is only one exception and that is the demand type of machine.

Children up to the age of 4 or 5 are easily fatigued when called upon to withstand prolonged anaesthesia with this equipment. Any inherent resistance in the mechanism can be overcome by manual or mechanical assistance. Much thought is being given to the possibility of creating a "suck and blow" apparatus wherein our problems of resistance, dead space and ventilation will be overcome.

Conclusion

As good anaesthesiologists we should be constantly reminded that the proper use of equipment of any type is governed by our good sense and good teachings. We must always strive for the physiologic normal and never become addicted to "watchful waiting". Anticipation and preparation for the problem at hand rewards us with a healthy patient and a satisfied surgeon.

Résumé

Fondamentalement, toutes les techniques anesthétiques doivent assurer au nourisson ou à l'enfant un apport approprié d'oxygène et une facile élimination de gaz carbonique. Nous reconnaissons que l'acte opératoire et les conditions chirurgicales en général augmentent considérablement les risques d'anoxie et que les enfants sont aptes à développer un état d'acidose dû à la rétention du gaz carbonique. Nous admettons aussi les dangers de la chaleur emmagasinée.

Les conditions de l'anesthésie chez l'enfant sont satisfaites par un équipement où tout est prévu pour réduire au minimum le temps mort et la résistance respiratoire. Cet équipement particulier comprend l'emploi de tubes endotrachéaux dont le but est de réduire le temps mort et d'assurer une respiration libre dans les positions défavorables; masques faciaux spécialement conçus pour enfants et ayant le plus petit mort possible; des valves à sens unique pour les masques et les tubes endotrachéaux; des connecteurs endotrachéaux dont les angles sont obtus plutôt qu'aigus; un fonctionnement facile des valves dans l'appareil d'absorption, placées de préférence près de la face.

Nous devons toujours nous efforcer d'approcher la physiologie normale et ne jamais s'habituer à la routinière formule "attention vigilante."

L'anticipation et la préparation du problème en cause nous donne la récompense d'un malade en bon état et d'un chirurgien satisfait.

Les tables donnent la capacité (temps mort) des différentes pièces figurant dans l'équipement anesthétique.

A PRELIMINARY REPORT ON THE USE OF HYDROGENATED ERGOT ALKALOIDS IN OBSTETRICS

P. B. Percheson, M.D. and John J. Carroll, M.D.*

Cervical spasm and uterine inertia are two of the major problems in obstetrics. These conditions are grouped under the heading of 'Disordered Uterine Contractions'. The mechanism of production of these disordered uterine contractions is not easily explained. A re-orientation in regard to the accepted concepts of the nerve supply of the uterus is necessary in order to elucidate these problems.

The "anatomical" sensory and motor nerve supply of the fundus is located in the thoraco-lumbar sympathetic division of the autonomic nervous system. That of the cervix is situated in the sacral parasympathetic division of the autonomic nervous system. The somatic, pudendal and perineal nerves supply the outlet of the birth canal. This concept implies that the sympathetic controls the fundus of the uterus and the parasympathetic the cervix, and that pain due to the dilatation of the uterine cervix reaches the cord via the second, third and fourth sacral parasympathetic segments.

Cleland (6) has incontrovertibly proven that the pain of the first stage of labour (including that of the fundus and the cervix) is abolished by blocking the 11th and 12th thoracic segments of the sympathetic. His work proves that the uterine fundus and cervix have identical pain pathways, and implies that the sympathetic nervous system plays the dominant role in mediating the motor functions of both during labour.

Sauter (4) in 1948 published some interesting conclusions concerning the effects of the sympathetic nerves on the pregnant uterus at term and during labour. He stated that atropine elevated the basal tone of the entire uterus, including the cervix. His observations led him to conclude that during labour both the cervix and the body of the uterus were stimulated to a state of spasm by sympathetic overactivity. He believed that this state of affairs resulted in decreased uterine contractions and in cervical spasm, i.e. disordered uterine contractions.

Snyder (8) states that apart from the birth of the child, the greatest suffering in labour is experienced during the first stage. When the cervix is fully dilated and the foetal head has descended low into the pelvis the pains alter in character and usually are tolerated better. It is quite apparent that when the latter part of the first stage is prolonged due to cervical spasm and related conditions, abnormally severe pain is commonly experienced, even though the force of the uterine contractions may be less than usual.

Read (5) epitomises these concepts in his teaching that a tense patient means a tense cervix, and that a tense cervix means a prolonged and painful labour. He claims that in the presence of fear, either conscious or subconscious,

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sympathetic overactivity causes a spasm of the circular inhibitory fibres of the cervical sphincter. In an effort to overcome this spasm, the longitudinal fibres of the upper segment are stimulated to a state of tonic spasm and the pain is thus excessive.

To date many analgesics and uterine anti-spasmodics have been tried in an attempt to overcome cervical spasm. The results on the whole have been disappointing. The use of uterine stimulants such as Pitocin has its advocates; but this practice can be hazardous to both mother and child. Signs of foetal distress are often detected in these patients and, in the face of a rigid cervix, the obstetrician is forced to do a Caesarean section or to try some of the above mentioned drugs. In cases where the foetus is not in distress, the long drawn out first stage exhausts and disheartens the mother, and she often becomes hysterical and uncooperative and most difficult to manage. The most common treatment for this state has been additional sedation with the hope that a period of rest and sleep might re-establish a normal pattern of uterine contractions and cervical relaxation.

Since all attempts to overcome cervical spasm with other drugs have, on the whole, proved disappointing, we have studied the action of Dihydroergotamine* (DHE) in a small series of cases.

The natural ergot alkaloids are known to possess the following pharmacological actions (*a*) a direct effect on smooth muscle, and (*b*) an inhibition of sympathetic activity. The oxytocic effect of natural alkaloids is well recognized and this action has tended to overshadow their sympatholytic and adrenolytic actions.

In 1943 Stoll and Hoffman (10) synthesized DHE. The hydrogenation of ergotamine produces a marked change in its pharmacological properties. The oxytocic action is either markedly reduced or completely abolished, and the sympatholytic and adrenolytic actions are markedly enhanced.

Rothlin (9) states that, in animals, DHE not only has no oxytocic action but is capable of inhibiting the oxytocic powers of ergotamine and ergometrine. He claims that the sympatholytic and adrenolytic actions of this drug are increased in the presence of sympathetic overactivity and excess of circulating adrenalin. His experiments on animals showed that DHE was relatively non-toxic as compared to the natural alkaloid ergotamine.

In 1948, Sauter (4) published his report on the use of DHE in 43 selected cases of cervical spasm. Good results were obtained in 30 of the cases. The remainder he reported as partial or complete failures. He used the drug by intramuscular injection in doses of from .25 to .5 mgs. He claimed that, in his series, the drug exhibited no oxytocic effect.

Sauter further states that the drug was not toxic to the foetus and that it did not inhibit the action of the oxytocic agents on the human uterus.

Gill and Farrar (3) were impressed with the beneficial action of DHE in selected cases of delayed labour. The majority of the patients on whom they used this drug presented disordered uterine contractions characterized by uterine spasm, and a cervix, which instead of dilating, either remained tense and unchanged or was observed to contract with the pains. They took as a standard of

delay a 24 hour period from the commencement of labour. They were careful to exclude any cases of disproportion in their series of 43 cases. The drug was given in doses of 0.25 to 0.5 mgs. intramuscularly. In some of their cases the injections were repeated at intervals of approximately 4 hours. In 80 per cent of their cases the drug produced a noticeable relaxation of the cervix, but in the remainder it proved to be of little value. No adverse effect on blood pressure, pulse rate or fetal heart was observed, and, in quite a few instances, by its lowering of the resting tone of the uterus, the drug was beneficial to a fetal heart which was showing signs of distress. They concluded that the drug takes effect in from one half to two hours after the intramuscular injection and that the response to a single injection wears off in approximately 4 hours. Subjectively, some of their patients reported that the pattern of their contractions had improved.

Baskin and Crealock (2) reported on the use of DHE in the treatment of cervical spasm. They gave 1 mgm. of the drug intravenously and combined this with 50 mgms. of demerol in patients who had no previous sedation. They believed that demerol was effective in preventing gastro-intestinal upsets which might complicate the use of large doses of DHE. Twenty-three of the patients received an injection of Methylergobasine intravenously at the time of delivery of the head, and the desired oxytocic effect was observed in every instance. They were of the opinion that DHE shortened the pain interval but that it did not increase the duration of the pains. They reported that no elevations of maternal blood pressure, no cervical tears, no fetal anoxia, no retained placentas and no post-partum hemorrhages were observed in their series. They found that DHE was relatively ineffective if given before the cervix was 5 to 6 cms. dilated. They obtained equally good results in 4 cases of persistent posterior and two breech presentations.

In another series (1), these workers employed DHE in several cases of secondary inertia in an attempt to shorten the duration of labor. They noticed that good pains were usually re-established in these cases, and that this effect was more dramatic in those patients who showed signs of fear and emotional distress.

Our results with DHE differ somewhat from those reported by the above-mentioned investigators, and this report deals with a series of 50 cases in which we have used this drug. There were 20 primiparas and 30 multiparas in this group. In 13 instances the drug was given by intramuscular injection in doses of from 0.5 to 1 mgm. In 4 cases of this series the drug was of no apparent value; but in these failures the DHE was injected when the cervix was only 2 to 4 cms. dilated. In the remaining 9 cases cervical dilation was noticeably affected and found to be complete on an average of 38 minutes after the injection of the drug.

In the remaining 37 patients, to whom the drug was given intravenously, excellent results were obtained in all but one. In this case the drug was administered when the cervix was only 2 cms. dilated. We used the drug in doses of 1 mgm. diluted to 10 ccs. with sterile water or saline and the injection was given

intermittently over a period of 3 to 8 minutes depending on the response to the test dose of 1 cc. of the diluted solution.

In our intravenous series, the average time from the injection of the drug (calculating from the time the test dose was administered) until the cervix was fully dilated was 10 minutes, and the average time from the injection of the drug until delivery of the baby was 25 minutes. We found the response to be most dramatic and constant in cases where the cervix was at least 6 cms. dilated and where the mother showed signs of emotional turmoil and sympathetic over-activity.

There was no appreciable slowing of the fetal heart in the intramuscular series, whereas, when given intravenously, the fetal heart was observed to slow down considerably in 60 per cent of these cases. It was our impression that there was some increase in the intensity, amplitude and frequency of contractions of the uterus when the drug was used intramuscularly. These effects were more definitely and more constantly apparent when the drug was given intravenously. In a few of these cases, the contractions became continuous indicating an oxytocic action. DHE had no appreciable effect on the maternal blood pressure, but in most of the intravenous series it did slow the maternal pulse. There were two stillbirths and one infant death in this series. None of these deaths could be attributed to the effects of the drug.

The majority of the patients in our series were the tense, nervous types with marked evidence of cervical spasm and uterine inertia. A few of the patients in this group had delayed labor from no apparent cause and the drug was tried in an attempt to evaluate its effect on shortening labor. We were not impressed with the action of the drug in these cases.

Discussion

It is our impression that in almost all of the cases where DHE was used intravenously and where the cervix was at least 6 cms. dilated, there resulted a rapid softening of the cervix and complete dilatation within 10 minutes. In a few instances where fetal distress had developed before the cervix was fully dilated, we believe that this drug permitted us to deliver a living baby which otherwise would not have survived.

Where the cervix was less than 4 cms. dilated, we were unable to detect any appreciable softening or increased dilatation within 30 minutes from the start of the injection. We believe that the drug has a definite but weak oxytocic action and increases the amplitude, intensity and frequency of uterine contractions. In a few instances, in the intravenous series, the drug produced tonic contractions of the uterus resembling spasm. In certain types of inertia this oxytocic effect may be an advantage since our obstetricians consider the resulting contractions to be more effectual.

We do not feel that DHE is an innocuous drug since it causes a bradycardia, in most cases, not only of the fetus but the mother as well. This action on the fetal heart has caused us some concern, since, even if it is a benign central vagal

action, our most useful sign of fetal distress is lost. In our series, the fetal heart rate returned to normal as soon as the baby was delivered and had taken its first normal breath.

Since the drug is most efficacious in cases of cervical spasm and primary uterine inertia, we do not feel that it should be used routinely to expedite a normal labor for the convenience of the obstetrician or the comfort of the patient. We were not favourably impressed with the intramuscular use of this drug.

Conclusions

1. DHE has proved to be a valuable adjunct in the treatment of primary uterine inertia and cervical spasm.
2. By the intravenous use of this drug in doses up to 1 mgm., the average time to achieve complete dilatation of a 6 cms. dilated and spastic cervix was 10 minutes from the administration of the test dose.
3. Intramuscularly, DHE did not produce the desired effect as consistently as when given by the intravenous route; but it was characterized by fewer side reactions such as fetal bradycardia and uterine spasm.
4. We do not believe that this drug should be used to expedite normal labor for the convenience of the obstetrician or the patient because it possesses oxytocic properties and decreases the fetal heart rate.
5. In our series there were no complications directly attributed to the use of DHE, and, in some instances we believe that it enabled us to deliver a living baby where fetal distress was detected in the presence of cervical spasm.
6. Because the incidence of Caesarean section and fetal wastage is unduly high in cases of primary uterine inertia and cervical spasm, we believe that the use of DHE in these carefully selected cases is fully justified.

Since the writing of this paper, another hydrogenated ergot alkaloid, Hydergine, has been placed on the market. Hydergine is composed of the methane sulfonates of dihydroergocornine, dihydroergocristine and dihydroergokryptine. It possesses vasodilatory properties by virtue of its adrenolytic and sympatholytic powers combined with its central vasodilatory action. In this latter action it differs from DHE which has a mild vasoconstrictor effect on peripheral vessels and direct action on smooth muscle.

We have used Hydergine in a few cases of cervical spasm and uterine inertia and it is our impression that it will supplant DHE for this purpose. Hydergine had no undesirable action on the uterine muscle in the few cases where it was used by us. Our series is too small as yet to justify any definite conclusions.

Acknowledgment

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Résumé

Manifestement, lorsque la dernière phase du premier stage du travail est prolongée à cause d'un spasme cervical ou pour d'autres raisons, des douleurs particulièrement pénibles sont ressenties, même si la force des contractions utérines est moindre que d'habitude. Les auteurs ont étudié l'action de la Dihydroergotamine dans une série de 50 cas, pour vaincre ce spasme cervical douloureux.

L'hydrogénation de l'ergotamine amène des modifications profondes dans ses actions pharmacodynamiques, l'action oxytocique étant particulièrement réduite ou abolie, alors que ses effets sympatholiques et adrénolytiques sont de beaucoup augmentés.

On compte vingt primipares et trente multipares dans cette série. Dans treize cas, la drogue fut administrée par voie intra-musculaire à la dose de 0.5 à 1 mgm. Pour quatre de ces cas la drogue ne sembla d'aucune valeur apparente alors que pour les neuf autres cas, la dilatation cervicale fut affectée visiblement. Chez les trente-sept autres patients à qui la drogue fut administrée par voie intra-veineuse, les résultats furent excellents sauf dans un cas, où la drogue avait été donnée alors que la dilatation n'était qu'à 2 cms. La drogue fut donnée à la dose de 1 mgm, diluée dans 10 cc d'eau en de solution salée, l'injection étant pratiquée de façon intermittente, durant une période de 3 à 8 minutes, suivant la réponse à 1 cc de la solution diluée, comme dose d'épreuve. Pour les cas où l'injection fut pratiquée par voie intra-musculaire, la dilatation se compléta 38 minutes après l'injection, en moyenne, dans 9 cas; par voie intra-veineuse, la moyenne pour arriver à une dilatation complète fut de dix minutes. Les résultats les plus soutenus et impressionnants se manifestèrent alors que la dilatation était d'au moins 6 cms et que la mère exhibait des signes d'agitation émotionnelle et d'hyperactivité sympathique.

Lorsque la voie intra-veineuse fut utilisée, on observa, dans 60% des cas, un ralentissement considérable du cœur foétal, en même temps qu'une augmentation marquée de l'intensité, de l'amplitude et de la fréquence des contractions utérines.

Les auteurs sont d'opinion que le DHE vaut dans le traitement de l'inertie utérine primaire et la spasme cervical mais ne croient pas que la drogue devrait être utilisée pour accélérer un travail normal ni pour accommoder l'obstétricien ou la malade.

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NITROUS OXIDE-DEMEROL-MECOSTRIN* ANAESTHESIA

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Most doctors are aware that the millennium has not been reached in the art and science of anaesthesia. Even the modern anaesthetist using the latest equipment and techniques is not infrequently faced with the fact that his patient has been adversely affected by the anaesthetic in one way or another. This is particularly true of the long cases where muscular relaxation is needed and in the poor risk patient. Pentothal tends to cause or aggravate laryngo-spasm and broncho-spasm. It also produces variable myocardial depression and hypotension. Prolonged administration may leave the patient depressed for many hours post-operatively. Cyclopropane has many undesirable features such as cardiac irregularities, including ventricular fibrillation, increased bleeding and post-operative shock; not to mention its explosive nature. Ether's ill effects on the liver and kidneys and the gastro-intestinal system are well known, as well as its ability to cause oedema of the brain. Chloroform is largely discarded today. Nitrous oxide in non-hypoxic concentration is remarkably non toxic and free from ill effects and is eliminated rapidly. Used by itself however it usually has to be given in definite hypoxic percentages. It has been known for many years now that the administration of adequate pre-operative analgesics reduces the amount of anaesthetic needed for surgical intervention. Logically, this knowledge has led to the use of analgesics *during* as well as before and after surgery. This move has had a natural impetus because of the increased use of relatively non-toxic drugs with little or no analgesic power such as pentothal, curare and nitrous oxide. The ease of measurement of dosage of the above drugs has also facilitated the accumulation of accurate knowledge concerning the effectiveness and dosage of the analgesics used.

Haroun et al (1) in 1946 published a series of cases where nitrous oxide and curare anaesthesia was supplanted by opiates. They considered that the patients did better than similar cases anaesthetized by ether, cyclopropane or continuous spinal. Brotman and Cullen (2) published a large series of cases in 1949 who were given pentothal, nitrous oxide, curare, supplemented by demerol. They used demerol because it is superior to morphine in several respects; to wit, there is less respiratory depression, it is a bronchodilator rather than a bronchoconstrictor, there is less cardiovascular depression, and also less post-operative nausea and vomiting. Its action is also shorter which makes it more flexible to use. Michael Johnstone (3) of England showed clinically that it is easier to inflate the lungs after the administration of demerol and that it relieves bronchospasm after intubation.

*d-tubocurarine dimethyl ether chloride.

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Where relaxation is needed for intubation or for the surgical procedure it is common to use a muscle relaxant drug, of which there are a great variety. Of the longer acting drugs I now use mecostrin (d-tubocurarine dimethyl ether chloride) almost exclusively, reserving flaxedil for asthmatics where relaxation can't be obtained by other means, and for cases where one might expect difficulty with the intubation or bronchospasm afterwards. Mecostrin is used because of the conviction that it occasions less respiratory depression than any of the other long acting muscle relaxants. Sadove et al (4) have shown this to be true and also that the duration of its action is shorter (and therefore more flexible), and that it is more predictable in its action than some other drugs, e.g. syncurine. Also Wilson et al (5) have shown that there is less cardiovascular depression, especially in long cases, and that it is easier to inflate the lungs than is the case when using d-tubo-curarine chloride. They consider that this is because less histamine is released.

It has been argued that respiratory depression runs pari-passu with abdominal muscle relaxation, and that this is also theoretically true inasmuch as the intercostal muscles are supplied by the same nerves as the abdominal muscles. Practically, experience shows this idea to be false, (6) and theoretically, one remembers that respiration is also mediated by the diaphragm. Also, we have all seen profound abdominal muscle relaxation under spinal anaesthesia with good intercostal activity. This differential resistance of the intercostal neuromuscular apparatus may be of an evolutionary nature, developed to protect the individual and the species, through preservation of this vital activity "to the last breath." Complete abdominal relaxation then can often be obtained without sacrificing adequate spontaneous respiration. Also, with this differential in mind there is no postulate that different drugs may not affect the components of the respiratory mechanism in different degrees. Some anaesthetists have argued that the factor of respiratory depression is of no consequence because controlled or assisted respiration is so readily performed. However, there are many instances where it is very desirable to have spontaneous respiration, and also to have as little respiratory depression as possible. Examples of this are, where intubation proves difficult, where it is hard to fit a face mask, where the anaesthetist is assisting at the operation, where open ether is being administered, where the anaesthetist is inexperienced in assisted or controlled respiration, unsuspected myasthenia gravis, short operations, electro-shock therapy; or where relaxant drugs are being used therapeutically in spastic states such as neuro-musculoskeletal disorders, pain syndromes, tetanus etc. In any case it is surely desirable to have a choice in the matter.

In view of the above I believe the method to be described has some advantages because of the relative lack of respiratory depression combined with the low toxicity of the drugs used. One hundred cases (selected to correspond with my flaxedil curare series (6) as far as possible) who were given this type of anaesthetic between September, 1950 and June 1951, are analysed. There were twenty-one upper and thirty-nine lower laparotomies in the series.

Method.

Premedication usually consisted of demerol 100 mgm. or morphine gr. 1/6 with scopolamine 1/150 gr. or atropine 1/150 gr.

Pentothal 2% is used for induction only. In some cases (e.g. tonsils) it is preceded by intravenous demerol (50–100 mgm.) given over a period of not less than two minutes, in which case the amount of pentothal is less than halved. If intubation is to be performed the pentothal is preceded by an estimated dose of mecostrin. Intubation is always preceded by manual inflation of the lungs with oxygen. With this technique one sometimes encounters palatal expiratory obstruction. (7) Following intubation or induction without intubation the patient is given N_2O and O_2 usually in the proportion of 5/2 litres per minute for a few minutes and then carried throughout with a proportion of 3/1 litres per minute. It was found that a proportion of N_2O — O_2: 5/2 for long periods leads to excessive drying out of the respiratory passages with tracheobronchitis as a sequel. Demerol is now given in divided doses of 12 to 50 mgm. at a time or occasionally as a drip. The demerol is administered *in relation to the respiratory rate*, the aim being to keep the rate between 12 and 16 per minute. A rapid respiratory rate indicates that pain impulses are getting through. However if the patient is very light breath holding may occur, usually accompanied by movements and an increase in the pulse rate and blood pressure. Even with a respiratory rate of as low as four per minute oxygenation is usually adequate as the respirations are very deep at this rate. Mecostrin is given as needed for muscular relaxation. Cyclopropane was used near the end in thirteen cases and a small amount of ether in two cases.

Dosage and Age:

The average dose of demerol used in this series was 102 mgm.; the largest dose being 270 mgm. and the smallest 25 mgm. The average total dose of mecostrin used was 7.2 mgm; the largest 20 mgm. and the smallest 3 mgm. The average dose of mecostrin (corrected)* needed for intubation of patients between the ages of 20 and 60 was for males 8 mgm., and for females 6.5 mgm. The average dose of pentothal was 314 mgm. One case received no pentothal at all. The largest dose was 1240 mgm. Only four cases received more than 500 mgm.

The average age was 37 years, the oldest being 87, the youngest 7. There were eight cases who were 70 or over.

Operative Course.

The average duration of operation was 92.6 min.; a little longer than in the flaxedil and curare series (6) reported earlier. Despite this the total time that assisted or controlled respiration was needed was 480 minutes as compared with

*"Corrected." The figures given for intubation were arrived at by adding or subtracting anything from none to 1½ mgm. of mecostrin to the dose actually used, in the light of the patient's reactions.

988 minutes total in the flaxedil series. Many more cases in the present series needed controlled respiration for a time than in the flaxedil and curare series as, due to a change in emphasis in technique, many more cases (59) were intubated, with necessarily deeper anaesthesia for a while, and on occasion, breath holding. It was noted however that in the cases that were not intubated that controlled respiration was practically never needed and assisted respiration only occasionally. The average operative pulse rate was 87 per min. which is close to the rate seen when using d-tubo-curarine chloride. The average operative systolic blood pressure was 123 mm. of mercury which also approximates the curare level. Twenty-three cases had a systolic blood pressure of under 100 mm. of mercury at some time during the operation. This approximates that seen with d-tubocurarine also and is in contrast with the sustained blood pressure seen when using flaxedil. This fall of blood pressure was not prolonged nor serious in any case in this series.

Post-operative Course.

Nearly all cases were cared for in the post-anaesthetic recovery room where repeated blood pressure readings etc. were done. According to the nurses notes forty-five cases were conscious on arrival in the P.A.R.R. and the average time taken for the remainder to regain consciousness was 28 minutes. The average time before the patient needed a hypodermic was four hours post-operatively and twenty cases didn't need any sedation post-operatively. Restlessness was remarkable by its absence. Twenty cases vomited at least once post-operatively and five needed catheterization, which is similar to the flaxedil or d-tubocurarine cases. Six cases had an increase over their pre-operative respiratory morbidity. There was one case of thrombophlebitis. The systolic blood pressure was below 100 mm. of mercury in only three cases at any time which would indicate that carbon dioxide retention was not a factor in these cases and that therefore respirations during the operations were adequate. There was one death, four days postoperatively. She was an old lady in very poor condition who developed a thrombosis of the superior mesenteric vein following a pancreatectomy.

Discussion.

The above method is now used routinely by the majority of the anaesthetists in this hospital and it is felt that it has some advantages over other methods. At least 1000 cases have been anaesthetized here by this means with satisfaction. The dosage of demerol usually doesn't exceed by very much the amount used when supplementing block or spinal anaesthetics. Unexpected prolonged respiratory depression or apnoea doesn't occur as with d-tubo-curarine and syncurine. Bleeding in operations *above the clavicle* is thought to be less than when using flaxedil which raises the blood pressure and accelerates the pulse rate in many cases. The patients wake up soon and quietly with little or no pain. An occasional patient may develop post-operative inspiratory stridor (8) but this can usually be prevented and in any case is easily treated.

Since selecting the cases for this paper this method has been used for two emergency partial gastrectomies, each of seven hours duration. Mecostrin dosage approximated 30 mgm. and demerol dosage was over 500 mgm. in each case. Both patients were in poor condition, one in incipient shock and suffering from chronic bronchitis and emphysema.

Mecostrin is supplied in 10 c.c. bottles with one mgm. to the c.c. and it is felt that 4 c.c. of mecostrin (4 mgm.) is equal in power to 3 c.c. of d-tubocurarine (9 mgm.). It is thus a little weaker per c.c. and this is important to keep in mind as otherwise one tends to under dose the patient.

Résumé

L'auteur analyse une série de cent malades anesthésiés au protoxide d'azote-Demerol, employant le Mecostrin (Chlorure de di-méthyl-éther-d-tubocurarine) comme relaxant musculaire. Cette série comprend vingt-une laparotomies hautes et trent-neuf laparotomies basses. Une solution de Pentothal à 2% est utilisée pour l'induction seulement, parfois précédée par du Demerol intraveineux (50–100 mgms), injecté en jamais moins de deux minutes. S'il faut pratiquer l'intubation, une dose calculée de Mécostrin précède celle du Pentothal, et l'intubation n'est faite qu'après insufflation manuelle des poumons, à l'oxygène. Le Demerol est administré en doses fractionnées de 12 à 50 mgms au cours de l'anesthésie, l'administration étant ajustée pour maintenir une respiration de 12 à 16 à la minute. Le Mécostrin se donne à la demande, pour obtenir le relâchement musculaire. Dans cette série, la dose moyenne de Demerol a été de 102 mgms, la plus élevée étant de 270 mgms et la plus faible de 25 mgms. La dose totale moyenne de Mécostrin a été de 7.2 mgms, la plus élevée de 20 mgms et la plus faible de 3 mgms. Cette méthode semble être avantageuse à cause de l'absence de dépression respiratoire et de la faible toxicité des drogues employées. Les états de dépression respiratoire prolongés et soudains, pas plus que l'apnée, n'ont été notés. Le réveil des malades s'installe rapidement, sans agitation, avec peu ou pas de douleurs.

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ANALEPTICS AND VASOPRESSOR SUBSTANCES

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This title has been chosen with the intention that a clear distinction be drawn between the true analeptic drugs, and the cardiovascular stimulating agents which we use to raise the blood pressure. These two groups to a certain extent overlap, but the analeptic drugs are those whose predominant action is stimulation of the central nervous system, and whose main therapeutic usefulness lies in their ability to reverse drug depression.

In this part of the discussion devoted to analeptics it is convenient to consider the central nervous system stimulants as a group, and by their site of action on the cerebrospinal axis it will be clear which ones are most useful as analeptic agents, in the true sense of the word. Certain drugs exert their main action on the spinal reflexes, others upon the medullary centres, causing stimulation of respiratory, vasomotor, and vomiting centres, and others affect the cortex, bringing about a greater degree of mental alertness.

Strychnine.

Strychnine acts by increasing the excitability of the nervous tissue. Its main effect is upon the spinal cord, but it also sensitizes the cortex, and in large doses, the medulla, to stimuli. After small doses of strychnine muscles respond in an exaggerated manner to the normal environmental stimuli, and in higher dosage the subject may be thrown into a tonic convulsive state with opisthotonus. Strychnine has no effect upon the cardiovascular system except reflexly in the doses in which it stimulates the medulla. From the foregoing it is clear that this drug exerts its main effect upon the spinal reflexes and is of no value as an analeptic agent.

Picrotoxin.

Picrotoxin is the most potent analeptic available. Its site of action is higher than strychnine, its main effect being upon the medulla and midbrain; it also stimulates the cortex, and in very high doses the cord is also affected.

Most authorities state that Picrotoxin is rapidly destroyed in the body and should therefore be used in small frequent doses, watch being kept upon the reflexes and the breathing. It has recently been pointed out however (1) that the latent time of action of picrotoxin may be as long as ten to thirty minutes after intravenous injection.

Metrazol.

The stimulant action of Metrazol is mainly upon the higher centres but all parts of the cerebrospinal axis are stimulated to some degree. The medulla is

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stimulated by larger doses, and the reflex activity of the cord is increased to a definite but limited extent.

The result of administering metrazol is an increase in respiration. The circulation is also improved indirectly through medullary stimulation. It has no direct effect upon the heart or the coronary circulation, although the heart may be slowed due to vagal stimulation.

Coramine–Nikethamide: Anacardone:

The mode of action of coramine is not clearly understood. It is primarily a respiratory stimulant, and is thought to act reflexly via the carotid body, but some authorities believe that it interferes in some way and at some point in the enzyme systems concerned with nervous tissue metabolism.

Lobeline.

Alpha-Lobeline is frequently used in the resuscitation of the newborn. Its actions are essentially those of nicotine. Goodman and Gilman consider that its it increases mental awareness. In larger doses however the medullary stimulant and any benefits are followed by an even more pronounced depression.

Camphor.

Intramuscular injection of camphor is used as a respiratory stimulant, and its effects, if any, are due to reflex stimulation from pain.

Caffeine.

The main action of caffeine is on the cortex, where, in the conscious subject it increases mental awareness. In larger doses however the medulary stimulant effect is manifested, the respiratory, vasomotor and vagal centres being affected. The action on the respiratory centre is a direct one; it sensitizes the respiratory centre to CO_2.

Caffeine is usually administered as Caffeine Sodium Benzoate which contains 50% Caffeine.

N-Allyl Nor Morphine (Nalline–Merck)

This is an interesting new drug which was introduced into clinical practice by Eckenhoff and Dripps in 1952 (2) as an antagonist to morphine, demerol, and the opiates. It is closely related chemically to morphine, a methyl group in the morphine structure being replaced by an allyl group. The drug itself has a weak analgesic action and a depressent effect upon respiration when given to a normal individual, but its main therapeutic interest lies in its power to combine with the receptors on which morphine acts, preventing the action of subsequently administered morphine, or actually displacing morphine and therefore reversing its effects.

In doses of 5–10 mgm administered to a patient who is suffering from respiratory and circulatory depression from a gross over-dosage of morphine it will reverse these effects and maintain the reversal, but it does this without

actually awakening the patient. Within 20 seconds of the IV administration the respiratory rate is doubled or tripled. The minute volume reaches a peak within 2 minutes, and then subsides but remains above the depressed level. Circulatory effects are slower in onset, the heart is slowed; if BP is normal, there is no effect. If it has fallen, it is raised again. These cardiovascular effects are maintained.

By improving respiration and circulation it is therefore considered to be a useful antagonist, even though it does not awaken the patient. It has been tried out in the resuscitation of the newborn with promising results, but again it must be stressed that a diagnosis of opiate depression must be accurately made. In depression from other agents, normal allyl nor morphine will merely add its own inherently depressant action, and the patient will be that much worse.

Sodium Succinate—Soduxin.

The brain derives its energy from the oxidation of glucose. This oxidation goes on with the aid of a complicated chain of enzyme reactions by which carbon dioxide and water are ultimately formed. It has been shown that in the presence of barbiturates this oxidation of glucose is incomplete and it is believed that the barbiturates interfere with the chain at the flavoprotein to cytochrome level. It has also been shown that the oxidation of succinate is unaffected by barbiturates, and an attempt was made to shorten barbiturate narcosis by supplying succinate to the brain as an alternative substrate to glucose, thereby allowing cellular oxidation to continue. The results reported by various workers are conflicting. Barrett is the original protagonist of the drug, but many others have failed to achieve the same success as he did. One thing should be borne in mind–to be of value the succinate must reach the brain in adequate quantity, and must continue to reach it over the necessary period of time. This entails the administration of large quantities of sodium, to which the succinate is bound, and one death at least has been ascribed to this.

Amphetamine (Benzedrine).

Amphetamine may be looked upon as the link between the analeptics and the vasopressors. It is a sympathomimetic amine, and exhibits the cardiovascular stimulating properties of that group, but of that group it is the most potent in its action upon the central nervous system. It is a cortical stimulant, and will lighten narcosis when given to an anaesthetized patient. It stimulates the medullary centres, and causes an increase in the rate and depth of respiration; its dilating effect or bronchial musculature enhances this action. In common with other sympathomimetic amines it causes a rise in blood pressure due to peripheral vasoconstriction and increased cardiac output.

Amphetamine is now considered the analeptic of choice in many centres (1) in the treatment of barbiturate poisoning, and the reports from these centres stress its safety. Even in large doses convulsions have not been reported.

Vasopressors

The term "vasopressor" is used to indicate one of the drugs which are given to raise the blood pressure. The blood pressure is a function of the Cardiac

Output and the Peripheral Resistance. A vasopressor drug may act in one or more of a number of ways.

1. It may increase the peripheral resistance by a direct action on the arteriolar muscle.
2. It may stimulate the myocardium and cause an increase in cardiac output.
3. It may stimulate the vasomotor centre in the medulla, causing peripheral vasoconstriction.
4. It may constrict the veins and muscles.

Before using a vasopressor drug, a careful analysis of the factors which have brought about the hypotensive state should be made. Having decided from this that a vasopressor drug is indicated, the choice should be based upon a knowledge of the pharmacological actions of those drugs which are available.

Certain of the drugs have undesirable side effects. Pitressin, for example, causes coronary constriction. Other drugs stimulate the myocardium, and, added to the sensitizing effect of cyclopropane anaesthesia may lead to cardiac irregularities. This property appears to be related to chemical structure and there are two groups of drugs which exhibit this side effect. Adrenaline, Nor-adrenaline and Cobefrine contain in their structure a catechol nucleus, and by virtue of this, they exert a preferential stimulating effect on the conducting mechanism of the heart below the A-V node. In the presence of cyclopropane this may lead to ventricular tachycardia and fibrillation.

Ephedrine, Methedrine and Amphetamine belong to a group of primary and secondary amines with no hydroxyl group on the benzene ring, and these have a preferential stimulating effect on the supraventricular regions, causing auricular irregularities in cyclopropane sensitized hearts, a less serious complication than that produced by the first group.

It is convenient to note here that a third group, consisting of neosynephrine and methoxamine, are of a chemical nature such that they exact no effect upon the heart, when administered along with cyclopropane anaesthesia.

Adrenaline and Nor-adrenaline

These two closely related neurohormones, with a vasopressor action, are best dealt with together, so that their differences may be highlighted. Both adrenaline and nor-adrenaline (3) are secreted by the suprarenal medulla, the latter making up 25% of the total. Nor-adrenaline is the precursor of adrenaline, the addition of a methyl group producing it. In this mixture, the action of adrenaline is predominant.

Adrenaline was for long considered to be a vasopressor by virtue of its vasoconstrictor action. The clinical picture of pallor, and the use of adrenaline locally to reduce bleeding would both seem to support this view. Nevertheless, the overall picture of the affect of adrenaline administration (4) (5) is one of vasodilatation, with a decrease in total peripheral resistance. The rise in blood pressure is due to an increased cardiac output, partly from an increased heart rate, and partly due to alteration in the stroke volume.

The administration of nor-adrenaline on the other hand (7–14) causes an

overall vasoconstriction, and the renal vessels share in this. There is a reflex bradycardia due to the pressor action on the carotid sinus, but this can be abolished by atropine. L-Nor-adrenaline is marketed under the trade name of "Laevo-phed." "Arterenol" is the name for the racemic preparation. It is a very powerful drug with a very transient action, and is therefore used in a dilute intravenous drip. Careful watch must be kept upon the rate of administration and its effect upon the patient, to avoid the danger of extreme vasoconstriction, with excessive rise in pressure, and local tissue anoxia.

Ephedrine.

Ephedrine is a cardiac stimulant, a vasoconstrictor, and an analeptic. It closely resembles adrenaline in its pharmacological effects, and according to Gaddum's theory, it acts by inhibiting amine oxidase thus allowing the concentration of naturally occurring adrenaline to build up. Its cardiac stimulant action is exerted reflexly via the cardio-accelerator nerves, and it has no direct action on the heart. It is a coronary dilator, and this property was made use of at the Department of Pharmacology at McGill (18) (19) when they introduced a mixture of Pitressin and Ephedrine, the latter counteracting the constricting effects of the former upon the coronary vessels, the combination being a good vasopressor agent. The peripheral vasoconstrictor action of Ephedrine is manifested especially on the arterioles.

Ephedrine has a direct stimulating action on the respiratory centre, and also a cortical stimulant action. These properties are made use of when it is used as an antidote to avertin.

Neosynephrine.

Neosynephrine is another well known vasopressor drug closely related chemically to adrenaline. It acts by peripheral vasoconstriction, and there is a reflex slowing of the heart. The stroke is increased. The drug has no cerebral stimulant effect, and it has no effect upon the cardiac conducting mechanism, so, until the introduction of methoxamine, this was considered the vasopressor of choice during cyclopropane anaesthesia.

Methedrine.

Desoxyephedrine, or methyl amphetamine are the chemical names of the product which we know as "methedrine." (15) (16) The drug is therefore closely allied to ephedrine and to amphetamine, and possesses similar actions. It brings about an increase of blood pressure in the presence of a lowered peripheral resistance (17) suggesting an increase in the cardiac output. The heart rate is reflexly slowed. The coronary vessels are dilated, and so are the renal vessels, an important point in its favour. It also possesses an analeptic action. In correct dosage it produces a moderate rise in pressure of long duration.

Methoxamine.

"Vasoxyl" is the trade name by which we know methoxamine. It is chemically related to the other sympathomimetic amines, its characteristic being the pos-

session of two methoxy groups on the ring structure, and it is this arrangement which renders it safe from side effects when used along with cyclopropane anaesthesia. (20) On intravenous administration there is an immediate and sustained rise in blood pressure, associated usually with a bradycardia due to a reflex set up in the carotid sinus. This rise in pressure is accompanied by an increased peripheral resistance. (21) There is no increase in cardiac output. There is no cerebral stimulating effect. (22)

CONCLUSION

This presentation has been an attempt to state briefly the mode of action of the commonly used vasopressor and analeptic agents, and to separate them into their groups.

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CONTROLLED RESPIRATION AS AN ADJUNCT TO GENERAL ANAESTHESIA

RICHARD N. TERRY, M.D.*

For many years an elevated pCO_2 level has been known to be the rule and not the exception in patients undergoing general anaesthesia. Among those who have written on this subject are Dr. Neil Gillespie and Dr. Ben Etsten among the anaesthetists. Dr. Etsten observed that wherever Pentothal was employed respiratory depression was of sufficient degree to be invariably accompanied by an elevation in the arterial CO_2. Dr. Beecher observed a gradual and consistent elevation of arterial carbon dioxide throughout the performance of an open-chest procedure. The more prolonged the surgical procedure the higher the carbon dioxide elevation was observed to rise.

A few of the obvious reasons for an elevation of carbon dioxide during general anaesthesia are:

1. A depression of the respiratory mechanism directly by the effect of anaesthetic agents in sufficient concentration to produce surgical anaesthesia.
2. An incomplete removal of carbon dioxide by present day soda-lime absorbers.
3. The frequent interference with respirations by the surgical incision, the packs employed, the restricting effect of retractors, and not least of all the assistant's arm leaning on the patient's abdomen.
4. A contributing factor is usually the inanition of an acutely ill patient.

The undesirable effects of hypercarbia are well known. To list only a few:

1. Respiratory acidosis in the postoperative period contributes to nausea, fatigue, and electrolyte imbalance which is usually in proportion to the severity and duration of the surgery.
2. So-called postoperative anaesthetic shock known sometimes by the misnomer of "post-cyclopropane shock."

   Drips has demonstrated this to be associated with a rapid reduction of carbon dioxide levels when the gas machine is disconnected from a patient long under anaesthesia. The hypotension and the diminished ventilation is related to the elevated threshold which has been produced during the operative procedure by the respiratory acidosis, so that postoperative CO_2 levels are subthreshold in this respect.
3. An elevation of carbon dioxide is known to be associated with a dilatation in the capillary bed, especially the muscles, skin, and very obviously in the brain. This results in increasing and unnecessary bleeding in the surgical field.
4. Sweating associated with the retention of respiratory metabolite results in an excessive fluid loss.

*Buffalo, N.Y.

Presented at a meeting of the Ontario Division, Canadian Anaesthetists' Society, at Niagara Falls, Ontario, 11 April 1953.

5. An increase in cardiac irritability leads to the occurrence of cardiac irregularities during operative manipulation. More recently, Boniface and Brown have demonstrated a weakened myocardial contraction in proportion to the elevation of the carbon dioxide in the arterial blood.

In the past year Varco et al in Minneapolis have demonstrated cardiac arrest to occur in 9 out of 13 dogs subjected to sudden increases in carbon dioxide tension of the arterial blood, despite the fact that all the animals were well oxygenated.

As opposed to the foregoing, the desirable effects of normal or subnormal carbon dioxide levels produced by controlled respiration have been little dwelt upon. That a hypocarbic state, reduced arterial pCO_2 of a mild degree, may be produced by a moderate hyperventilation has been well demonstrated even in open-chest procedures by Maloney, Derrick and Whittenberger, Burford, Dundee of Liverpool, and others, including Dameron and Greene in our Buffalo General Hospital laboratory.

As opposed to the detrimental effects of an elevated carbon dioxide level, we may speak of what appears to be advantages in a subnormal, or reduced carbon dioxide level, during surgery in general anaesthesia. A reduction in capillary oozing may be anticipated, by obviating vasodilatation usually associated with hypercarbia. Also there is physiological evidence to indicate that even vasoconstriction in the peripheral bed may be attributable to a subnormal carbon dioxide blood level. Dr. Cullen of Iowa has graphically demonstrated this in his dogs with plexiglass cranial prostheses. This reduced bleeding may also be attributed, in some degree to the reduced cardiac work, when respiration is provided by other than the patient himself, since the heart need provide only for basal metabolism. Further, the patient may end the procedure in a rested state, as compared with one of exhaustion, where he has been called upon during the surgery to fight retractors, packs and surgical assistants. Another factor we might consider is the reduction of skeletal muscle tone afforded by a lowered carbon dioxide tension in the blood stream. This conclusion is confirmed by the fluctuation in abdominal muscle tone associated with normal breathing, there being an increase during the crest of CO_2 in respiratory cycles. There seems to be also a reduction in reflex pain irritability, which has been referred to by Sievers and may be associated with the syncope of voluntary hyperventilation. The reduction in reflex activity during hyperventilation appears to be both reflex suppression, and a decrease of cerebral blood flow during hyperventilation as noted by Schmidt and Ketty as an increased resistance to cerebral blood flow. A recently proposed intriguing feature called to our attention by Dr. Esplen appears to be an increased effectiveness of a single dose of Pentothal where the patient is in relative alkalosis. Brodie, Papper, Mark and Rovenstein in 1950, demonstrated that the plasma fat ratio varied with the PH of the blood, there being a relatively higher plasma concentration in the presence of a diminished carbon dioxide level.

In addition to the above a few personal observations of a clinical nature lend credence to the above observations. Where the level of anaesthesia has inadvertently been allowed to fall to the point of swallowing, retching and strug-

gling, we have resorted to vigorous hyperventilation to rapidly restore a quiet surgical field. The restoration has been more rapid and gratifying than adding to the level of anaesthetic drugs. Another feature has been the facilitation of intubation of preliminary hyperventilation. Originally this was intended to oxygenate the patient before intubation; however, the reflex obtundation following vigorous hyperventilation has produced a materially quieter and easier intubation. This might be attributed both to reflex suppression by mechanical hyperventilation, plus an elevation of threshold associated with the reduced carbon dioxide blood level. Since we have observed the restoration of a quiet field in a struggling patient in light anaesthesia by hyperventilation, we have extended the hyperventilation, as a substitute for deeper planes of drug-induced anaesthesia; vigorous hyperventilation producing a quiet field at unusually light levels of anaesthesia. This type of reflex obtundation has likewise been used to reduce the response to traction on the peritoneum at the time of closure, again obviating deepening of the anaesthetic.

In support of the above, has been the observation of prolonged narcosis in experimental animals in our laboratories, where the Burns valve has been employed to provide mechanical respiration. Following a single dose of Pentothal many of the animals will continue to sleep for an indefinite period if left on the mechanical hyperventilation during the recovery period. Dr. Dundee's article in the British Medical Journal last year concluded that the total dose of Pentothal was appreciably reduced in a series of patients where controlled respiration was employed as an adjuvant. In another of Dr. Dundee's series a statistically prolonged narcosis was observed from a single injection of Pentothal where controlled respiration was employed throughout the surgical procedure. Brennan, as quoted by Dundee, describes a prolonged narcosis from a single ½ gram injection of Thiopental, supplemented as it were, by continuous controlled respiration throughout the surgical procedure.

Inasmuch as respiratory acidosis appears to be a quite consistent accompaniment of inhalation anaesthesia which can usually be readily corrected by assisted or controlled respiration, almost universal assistance of the patient's respiration would seem to be in order. Manual controlled respiration by compression of the rebreathing bag on the gas machine is widely and well used by modern anaesthetists. It is, however, a manoeuver requiring the continuous attention of the anaesthetist, to whose lot has fallen a multitude of other tasks during the conduct of operation, such as clyses, records, blood pressures, adjustment of lights. etc. This, despite the fact that relaxant drugs are coming into very wide use, further limiting the patient's ability to ventilate himself. If minute adjustment of the assisting or compensating force applied to the rebreathing bag of the gas machine is to be maintained, the anaesthetist's duties will either have to be strictly limited, or the advantages of modern combined types of anaesthesia will have to be left incompletely utilized. There would therefore seem to be a case for the mechanically operated respirator in every day general anaesthesia.

The stage has been set for the use of mechanical respirators, first by the surgeon. Dr. Crafoord, of Sweden, in a recent paper reports that he has successfully used

a mechanical assistor for several thousand surgical operations, mostly intra-thoracic procedures, since 1937. Dr. Mautz of Cleveland, Ohio in 1940 was using continuous controlled mechanical respiration throughout intra-thoracic procedures with great satisfaction. Dr. Gibbon of Philadelphia reports recently 300 procedures carried out satisfactorily with mechanical ventilation. Anaesthetists have generally objected to the employment of mechanical ventilation on the basis that there would be a loss of the principal source of information as to the patient's condition, the signs of respiration. Further, anaesthetists are deeply concerned with the circulatory disturbance associated with an elevation in intra-thoracic pressure. However, neither of these objections have disturbed surgeons above mentioned in large series of patients, and have more recently failed to prove disadvantageous to a number of anaesthetists, among them Dr. Derrick of Boston, Dr. James in Australia, and a number of English anaesthetists. One might consider further that in the history of our civilization it is seen that anything done by hand generally can be done better by machine. Clearly, there is a place for a mechanical respirator capable of precisely meeting the requirements of pressure and cycling of respiration under anaesthesia. Irregularities of manual ventilation during open-chest procedures relative to the ancillary obligations of the anaesthetist lead to an occasional extravigorous effort which may push the packs out into the surgical field. Variations in respiratory assistance provided manually prevent the circulation from adjusting to this outside influence as consistently as might be with a regular mechanical performance of ventilation. Further with the ultra short acting relaxants, such as Succinylcholine, it is possible to supply the surgeon with an utterly relaxed field if only some consistently regular and deep mechanical ventilation may be supplied during the time when the anaesthetist is otherwise engaged than in assisting the ventilation.

Anaesthetic respiratory-assisting machines may be roughly divided into two categories; first, those which provide a very plain and simple ventilation by cam and gear, taking no account whatsoever of the patient's voluntary respiratory cycle; secondly, machines which are intended to respond to the patient's own respiratory cycle, such as the so-called assistor of Maloney, Derrick and Whittenberger, now produced commercially by the Emerson Company. The usefulness of this last machine will be somewhat limited, it might be supposed, by the lack of any purely mechanical means of initiating the respiratory cycle. This means that hyperventilation cannot be ordinarily supplied by this machine, since it does depend upon the patient's own respiratory pattern to initiate the respiratory cycle.

At the moment, a most promising looking machine devised by Dr. Esplen of Liverpool is in commercial production by M.I.E. It provides either assistance, (as the Emerson machine) or may cycle entirely automatically to provide ventilation in a totally apnoeic patient. A most ingenious new element, has been introduced in this mechanism to control the pressure of inspiration.

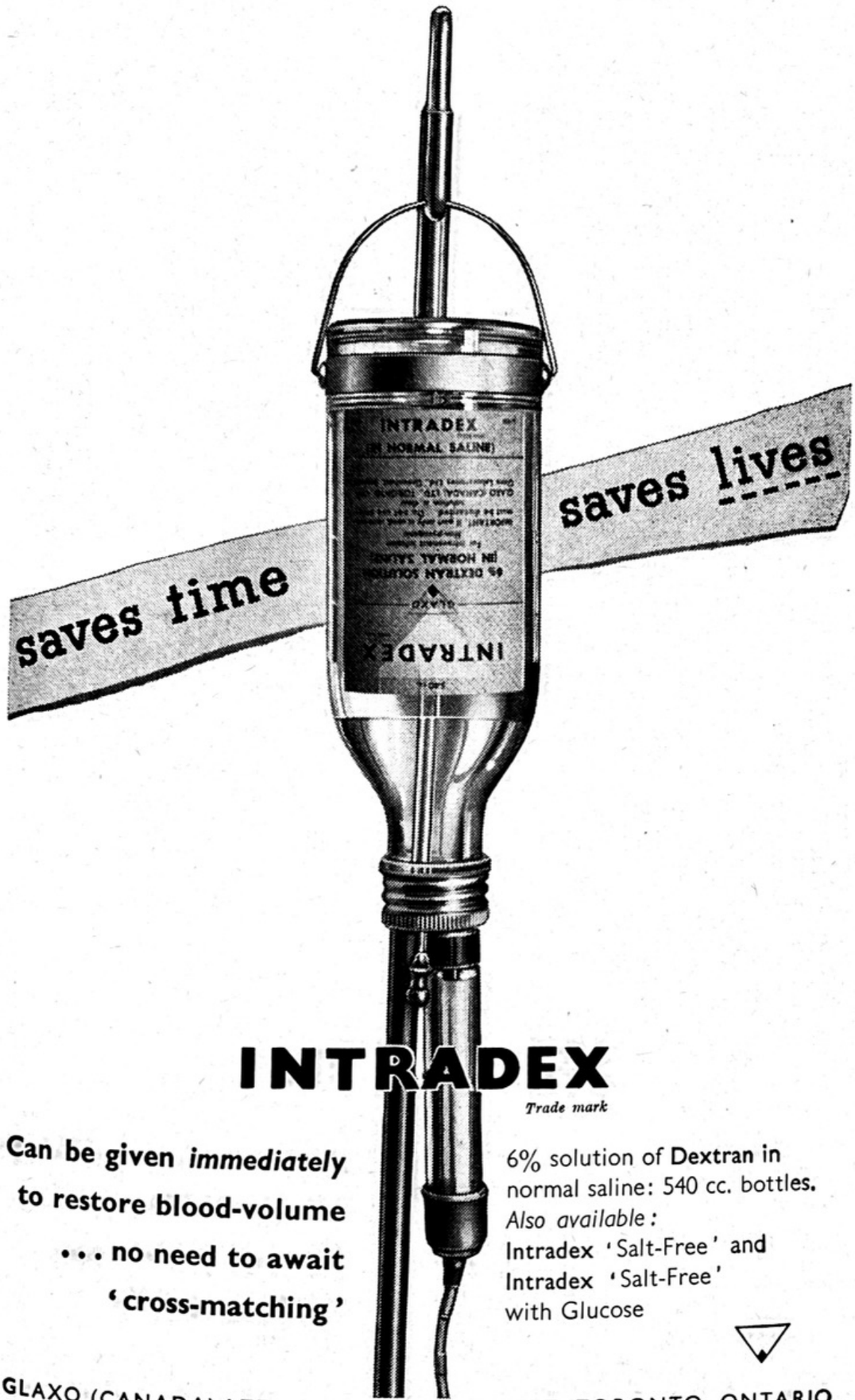
In conclusion, evidence has been assembled to indicate that controlled respiration and the associated reduction in blood carbon dioxide levels may be a valuable contribution to the daily performance of general anaesthesia, by the following

mechanisms; a reduction in general reflex irritability; a reduction in the requirement for relaxant drugs, yet a quieter surgical field; a decreased incidence in postoperative nausea, vomiting and shock may be looked forward to, as well as a decreased incidence of cardiac irregularity and an increase in the strength of the cardiac contraction. Further a reduction in cardiac work during general anaesthesia and surgery, providing safer anaesthesia for the poor risk patient. Last but not least, the anaesthetist's hands may be freed of a compelling task and be available for additional new duties connected with the administration of general anaesthesia.

Résumé

Depuis de nombreuses années on sait qu'un toux élevé de gaz carbonique est très commun chez les malades sous anesthésie générale. Les raisons en sont discutées. Les effets indésirables de cette hypercarbonie sont l'acidose respiratoire, nausées et vomissements post-opératoires, shock ("cyclopropane shock") post-opératoire, dilatation capillaire avec saignement augmenté dans l'endroit du traumatisme opératoire, transpiration et augmentation de l'irritabilité cardiaque.

En opposition à cela, les "avantages" d'un taux de gaz carbonique subnormal ou réduit sont une diminution du suintement capillaire, avec même une vasoconstriction capillaire, réduction du tonus musculaire due à la suppression des réflexes, tranquillité du champ chirurgical et diminution de la possibilité des arythmies cardiaques.



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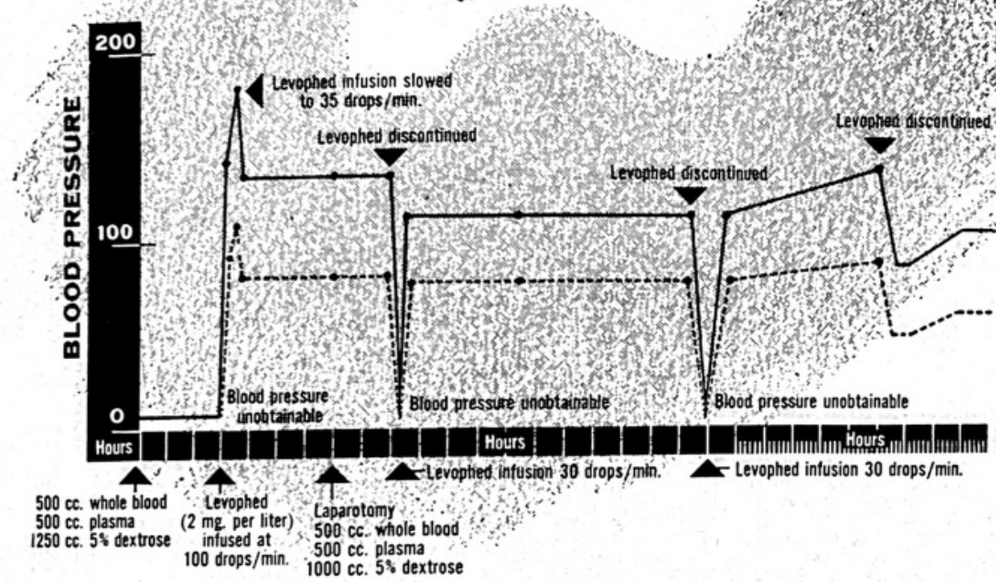
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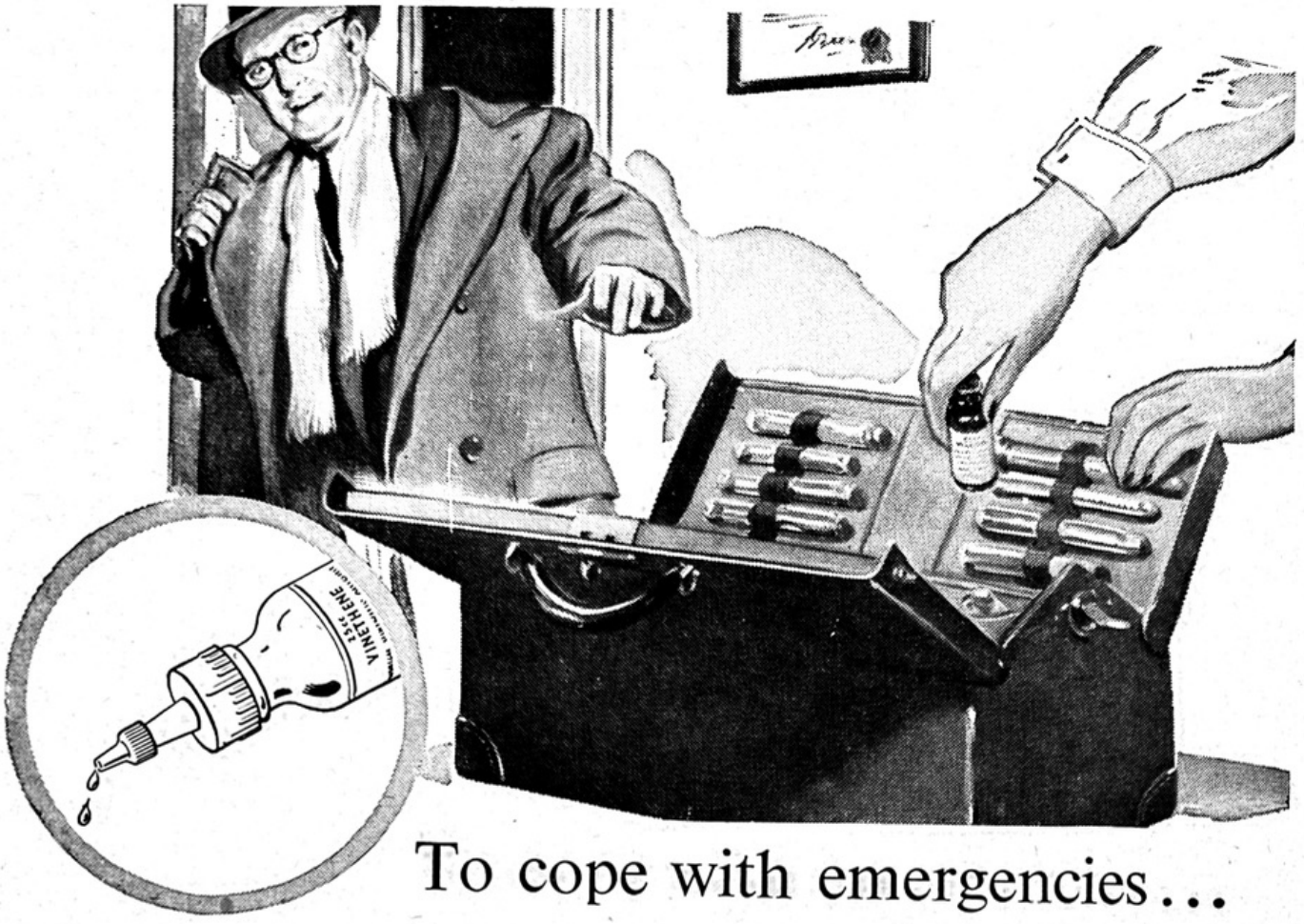
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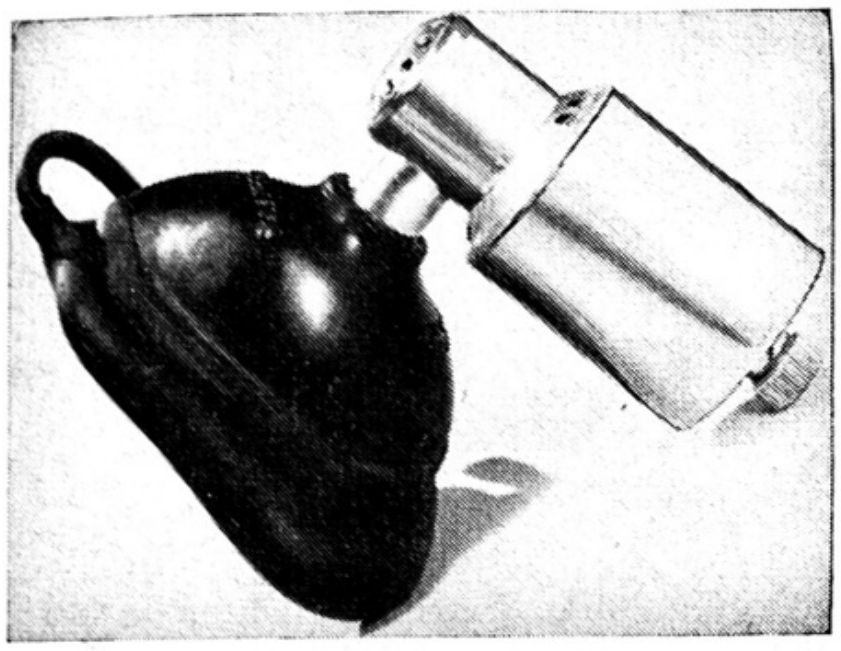
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INDEX OF ADVERTISERS

Allen and Hanbury's Company Limited	page xiii
Brent Laboratories Limited	page vii
British Oxygen Canada Limited	page iv
Burroughs Wellcome & Co.	page iii
Canadian Liquid Air Company Limited	page vi
Canadian Anaesthetists' Society, Inc.	page vii, xvi
Fisher and Burpee, Limited	page x
Foregger Company Ltd.	page ii
Glaxo (Canada) Ltd.	page ix
Hartz, The J. F. Co. Ltd.	page xv
Horner, Frank W., Limited	page xvi
Mercier, Pierre & Cie. Ltée.	page xiv
Merck & Co. Limited	page xiv
Poulenc Ltd.	page v
Squibb, E. R. & Sons of Canada, Limited	page i
Winthrop-Stearns of Canada, Ltd.	page xi
Wyeth	page xii