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Consideration of certain prominent rectal anesthetics with emphasis on the rectal administration of sodium pentothal

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A CONSIDERATION OF CERTAIN PROMINENT RECTAL ANESTHETICS WITH EMPHASIS ON THE RECTAL ADMINISTRATION OF SODIUM PENTOTHAL

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FOREWORD

At the present time, rectal anesthesia is receiving added impetus by the advent of the use of sodium pentothal as a basal anesthetic. This is a very new phase in this field and, as yet, its popularity is not very widespread.

In this paper, I will present material gathered from articles written by prominent individuals in the field of anesthesia, and also present three cases I have had the opportunity of personally directing. There will be no attempt to justify the position now held by rectal anesthesia, although the major advantages and disadvantages of rectal anesthesia will be presented. This is done, primarily, to give the reader something to base his judgment upon while considering the anesthetics discussed herein. The advantages and disadvantages of the individual drugs concerned will be presented, as well as the indications for each. Special mention is given to sodium pentothal as a rectal anesthetic since it seems to offer more advantages and fewer disadvantages then the other rectal anesthetics although, as yet, it has not been popularized to the extent that it seems to merit.

The reader should be forewarned that sodium pentothal per rectum is a new use of the drug, and that the

total number of cases reported upon does not exceed thirty thousand. This, in the mind of some, may not be a sufficient test of the use of the drug to allow it to be placed permanently with the time-honored rectal basal anesthetics now in use. This paper, therefore, is written in the hope that further light will be cast upon the rectal use of basal anesthetics.

HISTORY

The effectiveness of the intestinal mucosa of vertebrates and mammals as a transmitter of gases to and from the blood stream has long been recognized. As Gwathmey states, Erman established this fact as far back as 1808. In 1870, Paul Bert was said to have conducted an experiment upon a kitten in which he clamped the trachea of the animal and found it died of asphyxia in thirteen minutes, but if the intestine was inflated with air, life was prolonged for twenty-one minutes.

This fact being recognized by the early experimenters with ether, this route of administration was then attempted. The first mention in the literature of ether per rectum was made by Pirogoff in 1847 (35). Originally, Pirogoff planned to introduce the ether in the liquid form but being warned of the dangers involved, he devised a method in which only the vapors were brought into contact with the rectal mucosa. This was accomplished by placing the receptacle containing the ether in a hot water bath and conducting the gas through a tube lying in the rectum. He reported 81 cases; two of these died, but the cause of death was not given. In the same year, Reux, y'Yhede, and Duprey employed injections of liquid ether, pure or in aqueous mixture, with the result of producing complete anesthesia.

Pirogoff was especially enthusiastic about the rectal administration of ether, and even went so far as to think it might supplant the inhalation method (38). This method, however, disappeared from current literature, until 1884 when Molliere introduced a new technic in which he employed a Richardson hand bellows for forcing the ether vapor into the intestine (32). This method he soon abandoned, replacing it with the water bath method of Pirogoff.

The method again fell into disuse, not to be revived until 1903, at which time Cunningham employed it using air as a vehicle. In his article, which appeared in 1905, he reported 43 cases without untoward symptoms (9).

Stimulated by Cunningham's results, much more work was begun; advances were considerable during this period (10). Vidal added to the apparatus a provision for a continuous return flow of gas from the rectum, which before had been controlled by the finger of the anesthetist. One year later, Leggett added an exhaust tube which could be opened and closed at will. In 1909, Ligueu, Morel, and Verliac first reported the use of oxygen as a vehicle for ether vapor in rectal anesthesia.

Sutton developed the apparatus further by the use of a system of three parts: 1) a generator in which the mixture of oxygen and ether is produced, 2) an afferent tube which carries this product into the intestine, and 3) an afferent tube for the purpose of exhausting the contents of the gut. In 1910, Sutton published the results of a series of about 140 personally conducted cases, together with a description of the apparatus developed in the course of the work and the technic used in the application of the method at Roosevelt Hospital.

In 1913, Gwathmey reported the use of oil-ether at the Seventeenth International Medical Congress in London (15). The advantages of this method were considerable and, being such, afforded it fairly widespread popularity. Its popularity persisted until 1926 when a search for a less irritating rectal anesthetic was ended. It was at this time that Butzengeiger, a German anesthetist, made avertin available (28). Avertin grew in popularity until 1933, when it began a downhill swing, but it has since leveled off to hold the most prominent place of all basal anesthetics today.

In 1939, sodium pentothal was reported on by Weinstein as a rectal anesthetic (39). It has been

given little attention until the past two years, and now seems to be destined to a prominent position in the field of basal anesthesia.

GENERAL ADVANTAGES OF RECTAL ANESTHESIA

Monod's paper presented before the International Congress at Madrid stressed the advantages of rectal anesthesia, especially in operations in the upper portion of the body where it is not possible to use spinal or paraspinal anesthesia with reliable efficacy. Its most important advantage lies in the mild period of induction during which the patient passes into a pleasant, almost physiologic, sleep. It is without question the method with the least amount of disturbance and is preferable, therefore, to the oral administration of hypnotics, which very frequently produce gastric intolerance and are at times impossible to administer because of the bad state of absorption. It is also preferable to the intravenous method, which produces, in addition to the danger of the puncture itself, a certain apprehension on the part of the patient. There is also absence of the psychic insult which accompanies any form of inhalation or peripheral anesthesia. This is not only a tremendous advantage for rectal anesthesia from the point of view of satisfying the patient, but also of an additional advantage in that it does not lower his resistance (11).

Another important advantage in certain circumstances is the possibility of obtaining anesthesia without

the inconvenience or hindrance of a mask or apparatus which interferes with the operative field. The important indications of the rectal method are especially found in operations on the face, skull, neck, and back, in which local or regional anesthesia in inadequate. Still another favorable aspect of rectal anesthesia is that the lungs remain in a perfect state of rest. Even if the ether is eliminated through them, there is practically no reaction in the respiratory tract. For this reason, both ether and avertin administered by the rectal route have splendid indications in the presence of respiratory lesions, either pulmonic or pleuritic, of an acute or chronic nature. Insofar as postoperative pulmonary complications are concerned, they should be minimized if one follows the rules set down on the preparation and care of the patient.

DISADVANTAGES OF RECTAL ANESTHESIA

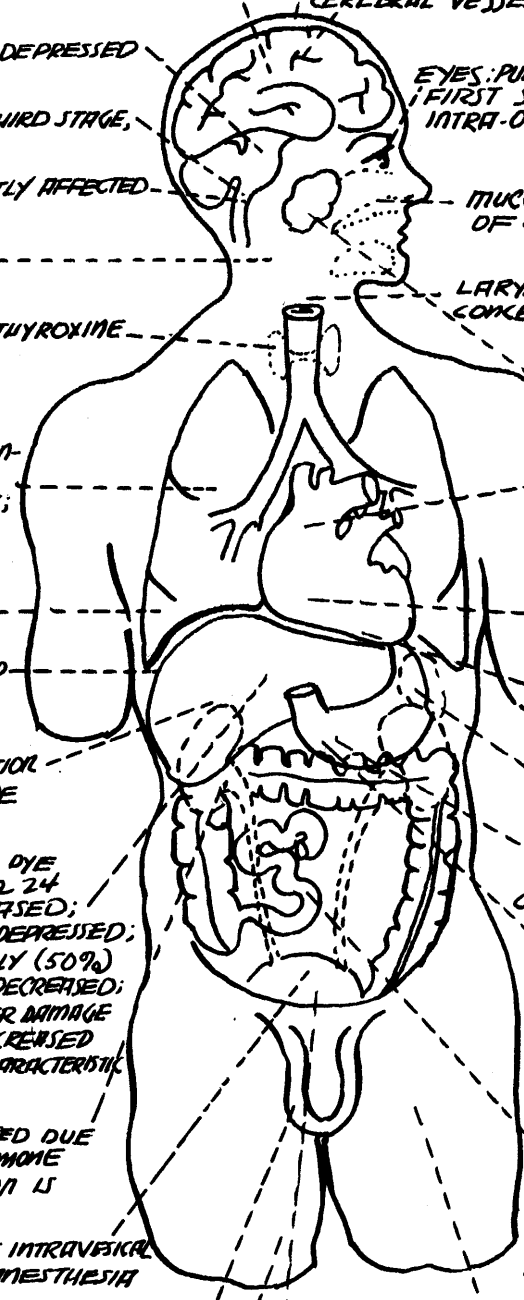
It is difficult to secure prompt elimination of the anesthetic when the patient shows signs of intolerance due to circulatory or respiratory depression. It is not easy to drain off the portion that has not been absorbed, and washing out the rectum, sigmoid and colon has but little effect. There is also a local irritation produced by the introduction of most substances by the rectal route. Dogliotti (11) asserted that certain pathologic conditions might contraindicate this method: "Even in the normal intestine the administration of the enema is not always free of danger and may produce secondary lesions, some of which are relatively frequent. In our experience this percentage has been very low, and we have never had disturbances of long duration or considerable seriousness".

The slowness of the absorption and elimination of the anesthetic, which is considered by many authors as one of the disadvantages of the method, may at times prove a favorable factor. It can be administered while the patient is still in his bed, thereby minimizing psychic shock or any apprehensive impressions.

On the other hand, even during the period of awakening, the prolonged return to normal is also an

advantage since it minimizes postoperative pain and reduces the quantity of analgesia or hypnotic necessary for the succeeding period.

ETHYL ETHER



CORTEX: LOWER PATHWAYS BLOCKED: CORTICAL ACTIVITY DECREASED; VOLTAGE AND FREQUENCY OF ACTION POTENTIALS DECREASED: DECREASED TISSUE OXIDATION OF SLICED CORTEX.

TEMPERATURE REGULATING CENTER DEPRESSED

VOMITING CENTER: DEPRESSED IN THIRD STAGE, FIRST PLANE.

VASOMOTOR CENTER: NOT DIRECTLY AFFECTED

CAROTID SINUS: DEPRESSED

THYROID: PRELIMINARY DOSES OF THYROXINE DO NOT ALTER NARCOSIS

LUNGS: RESPIRATORY MOVEMENTS INCREASED; HERING-BREUER REFLEX INTACT; BRONCHIAL MUSCLES RELAXED: BRONCHIAL SECRETIONS; INCREASED; ANAPHYLAXIS NOT PROTECTED.

METABOLISM: DECREASED

DIAPHRAGM: MOVEMENTS DECREASED IN DEEP ANESTHESIA

ADRENAL: SYMPATHETIC STIMULATION CAUSES DEPLETION EPINEPHRINE

LIVER: FUNCTION DECREASED BY DYE TEST, RETURNING TO NORMAL IN 24 HOURS; BILE SECRETION DECREASED; RETICULO-ENDOTHELIAL CELLS DEPRESSED; GLYCOGEN DECREASED RAPIDLY (50%) IN FIRST HOUR, THEN GRADUALLY DECREASED; UREA FORMATION NORMAL; LIVER DAMAGE GIVES INCREASED UREA FROM INCREASED PROTEIN METABOLISM: NO CHARACTERISTIC HISTOLOGICAL CHANGES.

KIDNEY: URINE VOLUME DECREASED DUE TO RELEASE ANTI-DIURETIC HORMONE FROM PITUITARY; RENAL FUNCTION IS DECREASED

BLADDER: CONTRACTS EARLY; INTRAVESICAL PRESSURE INCREASED IN DEEP ANESTHESIA

GENITALIA: CHOLESTEROL DECREASED IN TESTES

MUSCLES: RELAXATION OF SKELETAL MUSCLES SATISFACTORY; PARTIAL GLYCOGEN DEPLETION

BODY TEMPERATURE: DECREASED DUE TO DECREASED METABOLISM AND DEPRESSION OF TEMPERATURE REGULATING CENTER.

INTRACRANIAL PRESSURE: INCREASED IN EARLY ANESTHESIA

CEREBRAL VESSELS: DILATED

EYES: PUPILS USUALLY CONSTRICTED; DILATED IN FIRST STAGE AND IN DEEP THIRD STAGE: INTRA-OCULAR TENSION UNCHANGED

MUCOUS MEMBRANES; IRRITATED; ACTIVITY OF CILIA DECREASED

LARYNX: COUGH AND SPASM WITH HIGH CONCENTRATION DURING INDUCTION

SALIVARY GLANDS; STIMULATED DURING INDUCTION: DEPRESSED DURING ANESTHESIA

HEART: RATE NORMAL: CARDIAC OUTPUT INCREASED; NO EFFECT ON MUSCLE: OCCASIONAL VARIED ARHYTHMIAS: CARDIO INHIBITORY CENTER DEPRESSED.

BLOOD PRESSURE: SLIGHT INCREASE OR NO CHANGE

VENOUS PRESSURE: NORMAL BUT INCREASED DURING INDUCTION

SPLEEN: SIZE DECREASED: BLOOD FLOW NORMAL

PANCREAS INSULIN PRODUCTION DECREASED: BLOOD AMYLASE INCREASED 75-100%

STOMACH: MOVEMENTS DECREASED; MUSCLES MAY RELAX WITH DILATATION 15 MINUTES TO 1 HOUR AFTER ANESTHESIA EMPTYING TIME DECREASED 40%. GASTRIC SECRETION DECREASED: ACIDITY DECREASED; MUCOUS MEMBRANES IRRITATED.

INTESTINES: DECREASED PERISTALSIS AND SECRETION DUE TO SYMPATHETIC STIMULATION VESSELS DILATED WITH LOSS OF MUSCLE TONE: PERISTALSIS EXAGGERATED ON RECOVERY.

LYMPHATICS: ABSORPTION INCREASED THROUGH PERITONEAL CAVITY FROM INCREASED RESPIRATORY ACTIVITY IN PERITONITIS.

UTERUS: MOVEMENTS DECREASED: INTRA-UTERINE PRESSURE DECREASED; RELAXATION COMPLETE IN DEEP ANESTHESIA; DRUG PASSES THROUGH PLACENTA; ARTERIAL OXYGEN NORMAL IN FETUS

SKIN: TEMPERATURE INCREASED DUE TO PERIPHERAL DILATATION

Redrawn after Adriani

Figure I.

greatest part of the ether passes directly into the circulating blood, being absorbed by small capillaries and to a lesser extent by lymphatics. The capillaries in the lower portion of the rectum, which are tributaries of the inferior hemorrhoidal vein, pass directly into the right side of the heart. However, the greatest part of the ether is absorbed by the tributary capillaries of the portal vein. Consequently, it arrives at the inferior vena cava through the portal circulation and the liver. After the anesthetic passes through the liver, it goes through the vena cava to the right side of the heart. The anesthetic then passes through the pulmonary circulation, and here conditions are favorable for some of it to be expelled into the alveolar air.

In the lungs, the blood which is loaded with the anesthetic that has not been eliminated into the alveolar air then passes through the left side of the heart and is distributed throughout the entire body.

Elimination of the ether through the lungs is at first in a very small quantity compared to the amount absorbed through the rectum and colon, so that there is a progressive accumulation of the anesthetic in the blood and, consequently, a progressive action on the organism. However, when the elimination through the

pulmonary system is equal to the absorption, an equilibrium becomes established as to the quantity of ether in the circulating blood, and the anesthetic reaches a fixed level. This level is affected not only by the quantity of ether introduced by the enema, but is also influenced by a great number of other factors, not only from individual to individual but also during the very course of the anesthesia. There are many factors in addition to the numerous anatomic and mechanical ones which we have mentioned. Meyer, in 1924, stated the efficiency of the circulation, the condition of the intestinal mucosa, the body temperature, the ease of transit through the liver, and the variable conditions of the respiratory movements exert a profound influence (31).

Dogliotti (11) says there are three autoregulatory factors which regulate the concentration of ether in the blood. These are: 1) variation in the local body temperature of the mixture with corresponding variations in rapidity of evaporation, 2) progressive diminution of the power of absorption of the recto-colic mucosa, 3) elimination through the lungs, which increases as the quantity of ether in the blood rises. These factors of safety have been confirmed in clinical practice.

As Dogliotti (11) stated: "These automatic factors, which guarantee within wide limits against dangers of excessive dosage, may be insufficient when the organism, for some pathologic reason, is below the normal limits of resistance. In these cases, therefore, one may receive the greatest surprises, because after introduction of the mixture into the rectum it is impossible to withdraw efficiently the remaining ether, should the patient sink into an alarming state. When there is an arrest of the respiratory activity, it is impossible to remove the ether from the circulating blood".

Now let us consider the physiologic action of rectal etherization:

1. There is nearly always an absence of the period of excitement, some patients falling asleep within 15 to 20 minutes and arriving at a deep state of anesthesia without any movement whatever; in other cases, there is a moderate amount of movement of the extremities.

2. The respiration is modified but slightly, rarely reaching a frequency above 25 and 30 a minute. As a rule, the respiratory rate is between 20 and 24.

3. The pulse presents only slight variation and the blood pressure remains about the same throughout the entire course of the anesthesia.

4. There is practically complete inhibition of those reflexes which are produced by inhalation anesthesia due to the irritation of the vagus or trigeminal nerve ramifications. There is no coughing, rarely is there vomiting, and there is very little bronchial hypersecretion, such as usually accompanies or follows inhalation of ether vapors.

5. The postoperative course presents the same characteristic symptoms of tranquillity observed during the induction.

The anesthetic reaches its maximum point after 25 to 30 minutes, and with the average dose lasts from 1 to 1½ hours. The awakening is gradual and complete after a period of about 2 hours.

The reasons for this different action of the patient following rectal anesthesia in comparison with that found in inhalation anesthesia are the following: a) complete lack of the emotional and psychic factors, which, without doubt, have a great influence upon the period induction and subsequent spasms, b) with the more gradual and progressive advancement of the anesthetic, requiring about twice as much time as that by the inhalation method, one is able to produce the same degree of anesthesia, c) in less intense anesthesia obtained by this method, it is difficult to reach a

dangerous concentration, in contrast to that which one observes with inhalation anesthesia. In ether anesthesia by the rectal route even if large quantities are given, due to the above mentioned autoregulation mechanism it is practically impossible to have an overdose, provided the organism is in a relatively normal condition.

The technic of ether anesthesia by the rectal route presented here is essentially that of the Gwathmey procedure:

The patient is prepared by giving an enema the afternoon preceding the operation, even though a laxative has been given the night before. No enema should be given during the twelve hours preceding operation so as not to alter the normal absorptive power of the rectal mucosa. A hypnotic is given the night before, usually a barbiturate.

The formula which is advisable for individuals of middle age and of average resistance is the following: 2 gm. ether for each kilogram of body weight, and fresh olive oil, 1 gm. per kilogram body weight. Consequently, a man of 70 kilograms is given a preparation composed of 140 to 150 cc. of ether and 70 to 80 cc. of olive oil.

It may be necessary to change this formula according to Monod, Coleman (8), and other authors, who have recommended reduction of the quantity of oil with a slight increase in the quantity of ether in unusually vigorous, lean individuals of middle age. On the other hand, there should be a reduction in the quantity of ether and increase in the quantity of olive oil, even to the proportion of 50-50 in individuals whose general resistance is lowered and in elderly persons and children.

Gwathmey, Hogan, Howard, and Abajian (19) found, in 1939, that the addition of other substances to the mixture, such as paraldehyde, 5 to 8 cc., chloral hyfrate 0.6 to 0.7 gm., or the addition of stimulating substances, such as caffeine or camphor, or of substances which favor the retention of the enema, such as laudanum and small doses of atropine, is a debated point. It has been used in obstetrics by Axelrod (2) with barbital and quinine to some advantage, however.

The methods of administration vary from the rapid, large single dose, which takes 2 to 3 minutes, to the gradual and fractional administration by the Murphy drip method. An intermediate method is also used; that is, administration of the mixture in two successive doses at intervals of about 10 minutes. The first

dose is given 30 minutes before operation, giving one-third of the mixture; leave the rectal tube in place, pinch it off, and after 10 minutes give the remaining two-thirds. The mixture must be given slowly.

By introducing this mixture in two stages, rapid distention of the colon is avoided, and it is easier to judge dangers during the induction, especially of initial overdoses. Researches on the ether content of the blood following massive doses by rectum have shown that at first there is a very rapid rise which occurs within a few minutes after the termination of the enema. Then there is a falling off of the concentration regardless of the quantity of the mixture introduced, even if the ether is given by inhalation.

The apparatus required for this method is of the simplest. In addition to the beaker or graduate which is used to make the mixture, it is necessary to have a rectal tube, enema can, and a Petzer type catheter, or the Murphy tube for proctoclysis. The introduction of the mixture must be done at a low pressure and slowly, taking about 4 to 5 minutes. When the enema has been given, it is advisable to leave the rectal tube in place, pinching it off, so that if necessary, some of the introduced mixture may be permitted to escape, or, in order to favor elimination, the rectum and colon may

be washed free of the residual anesthetic. It must be remembered, however, that once the mixture has been introduced, the possibilities of its removal are not good. After 5 minutes, it is unusual to have more than one or two cc. escape, according to Dogliotti (11). Evidently the mixture rises in the colon, and due to the distention and paresis which follow the action of the ether vapor, it becomes increasingly difficult to expel it. This impossibility of reducing the quantity of the mixture that has been introduced is the one weak point in the method.

During the anesthesia, the patient must be strictly observed, the same as with any other method.

One may successfully administer supplementary doses of the mixture when the patient begins to show signs of awakening during the course of the operation. This is most convenient, unless there is some contra-indication, when a complementary inhalation anesthetic may be used to prolong the anesthesia.

Due to the fact that ether is primarily eliminated through the lungs, we must prevent, at all cost, the arrest of respiration, because if that should occur, there would be a fatal increase of the ether content of the blood due to continual absorption from the colon. Artificial respiration and stimulation with carbon

dioxide and lobeline must be practiced with much more energy than when the arrest is from inhalation anesthesia. When ether is given by inhalation, the respiratory cessation also represents stopping of elimination, but at the same time there is no increase in absorption.

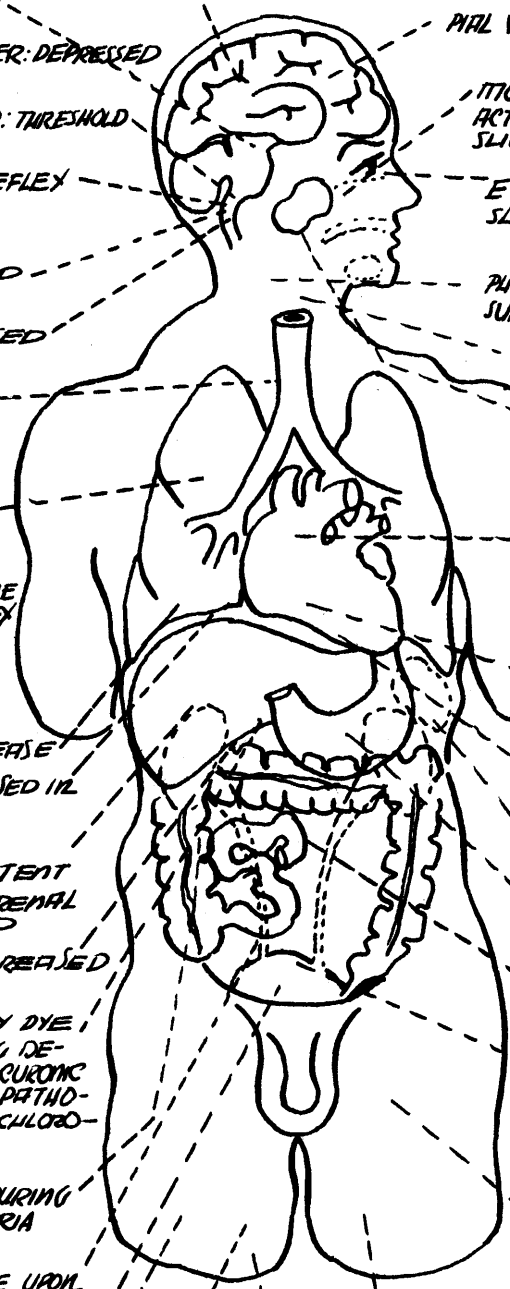
As has already been stated, although not very efficient, it is worth while attempting to wash out the residual mixture by irrigation of the rectum and colon with cold water containing caffeine, or using olive oil. By the introduction of half a liter or more of olive oil, it is possible to dissolve and retard the absorption of the residual ether. Dogliotti (11) has stated he has been successful in combating two cases which showed signs of depression due to overdose by this means.

When the enema does not give sufficient relaxation, the best form of complementary anesthesia, provided that no local complications exist (i.e., operations on the mouth or respiratory tract, or pulmonary complications), is inhalation ether anesthesia, using a semi-closed mask. One must remember that only a very small amount of ether is necessary by inhalation because it is added to that already present in the circulation. Besides, the semi-closed mask utilizes

part of the ether that is expired, and therefore part of the original rectal ether which is being eliminated through the lungs is reabsorbed. The use of the semi-closed mask with small doses of ether represents a stimulus to the respiration due to the accumulation of carbon dioxide. Ethyl chloride has the same advantage. It is, however, inadvisable to use chloroform because of its marked toxicity.

Dogliotti stated: "Combination of peripheral--local or regional anesthesia--with rectal ether anesthesia is also a method that may give optimum results. In such cases, the ether is a basal anesthetic and the peripheral anesthetic is used for the interruption of sensation. We have used this combination many times for operations on the brain, thorax, and upper extremities". (11)

TRIBROMETHANOL (AVERTIN)



CORTEX: DEPRESSED: LOWER CORTICAL AFFERENT PATHS IN TACT.

HYPOTHALAMUS: DEPRESSED

TEMPERATURE REGULATING CENTER: DEPRESSED

RESPIRATORY CENTER: DEPRESSED: THRESHOLD TO CO_2 INCREASED.

COUGH CENTER: DEPRESSED: REFLEX PRESENT IN DEEP HYPNOSIS

VOMITING CENTER: DEPRESSED

VASOMOTOR CENTER: DEPRESSED

THYROID: RESISTANCE TO DRUG INCREASED BY ADMINISTRATION THYROXINE 24 HOURS BEFORE ANESTHESIA

LUNGS: SLIGHT INCREASE IN RESPIRATORY RATE: DECREASE IN AMPLITUDE RESPIRATORY MOVEMENTS; DECREASED MINUTE VOLUME EXCHANGE: HERING-BREUER REFLEX INTACT: ALVEOLAR AND BRONCHIAL EPITHELIUM NOT IRRITATED: BRONCHIAL MUSCULATURE RELAXED

METABOLISM: UP TO 15% DECREASE

DIAPHRAGM: MOVEMENTS DECREASED IN DEEP ANESTHESIA.

ADRENAL: EPINEPHRINE CONTENT UNCHANGED; NECROSIS OF ADRENAL IN OVERDOSAGE REPORTED

GALLBLADDER: BILE FLOW INCREASED

LIVER: FUNCTION DECREASED BY DYE TEST: GLYCOGEN DEPLETED: DRUG DETOXIFIED BY CONJUGATION WITH GLYCURONIC ACID; CLOUDY SWELLING, ONLY PATHOLOGICAL CHANGE. (NEVER LIKE CHLOROFORM)

KIDNEY: ANURIA OR OLIGURIA DURING ANESTHESIA FOLLOWED BY POLYURIA AFTER HYPNOSIS

URETERS: RELAXATION OF MUSCLE UPON LOCAL APPLICATION

SPHINCTERS: NOT RELAXED EXCEPT IN DEEP HYPNOSIS.

NERVES: SUPERFICIAL AND DEEP REFLEXES PRESENT

BLOOD: CAPILLARY OOZE DECREASED DUE TO FALL IN BLOOD PRESSURE

INTRACRANIAL PRESSURE DECREASED: CONCENTRATION IN SPINAL FLUID IS ONE-HALF THAT IN BLOOD: SPINAL FLUID PRESSURE DECREASED

PIAL VESSELS CONSTRICTED

MUCOUS MEMBRANES: NOT AFFECTED CILIARY ACTIVITY DECREASED; MUCOUS SECRETION SLIGHT OR NONE.

EYES: PUPILS CONSTRICTED. MOVEMENTS SLUGGISH: INTRAOCULAR TENSION DECREASED

PHARYNX: REFLEX NOT ABOLISHED; TONGUE SUFFICIENTLY RELAXED TO CAUSE OBSTRUCTION

LARYNX: REFLEX NOT ABOLISHED

SALIVARY GLANDS: DEPRESSED

HEART: RATE INCREASES; CARDIAC OUTPUT DECREASED; RHYTHM SLIGHTLY CHANGED: EKG CHANGES ARE MINOR; LARGE DOSES SLOW HEART DUE TO DILATATION: DILATATION CORONARIES IN PERFUSED HEART

BLOOD PRESSURE: DECREASE OF 20% OR MORE DUE TO VASOMOTOR DEPRESSION AND PERIPHERAL VASOMOTOR DILATATION

VENOUS PRESSURE: DECREASED

SPLEEN: RESULTS NOT KNOWN

STOMACH: MOVEMENTS DECREASED

INTESTINES: DECREASED ACTIVITY

UTERUS: DECREASED CONTRACTIONS; ATONY AND RELAXATION OF MUSCLES; DRUG PASSES THROUGH PLACENTA TO FOETUS RESULTING IN SYMPTOMS OF ASPHYXIA: POOR RECOVERY OF INFANT AS LONG AS ONE WEEK.

SKELETAL MUSCLES: RELAXED WITH LARE DOSES GIVING COMPLETE ANESTHESIA

SKIN: TEMPERATURE INCREASED; DRUG EXCRETED IN SWEAT: DRUG IN ALCOHOLIC SOLUTION ABSORBED THROUGH IT.

BODY TEMPERATURE: FALLS DUE TO DECREASED METABOLIC RATE, DEPRESSION OF CENTER AND RELAXATION SKIN VESSELS.

Redrawn after Adriani

Figure II.

AVERTIN

Dogliotti (11) stated that "Avertin, or tri-bromethanol, is a tri-bromate ethyl alcohol with the formula CBr_3-CH_2OH. After numerous pharmacologic and clinical experiments (this at first was called E107), it was placed on the market under its present name in 1925, and one can say that it gained ground until 1933. From then on, its use became more or less limited. Whether this was due to the success of other methods, such as evipal by the intravenous route, or to the fact that it has shown factors of weakness and danger, is not known. It is commercially sold as a white crystal with a slightly irritating taste. It melts at 79 to 80 degrees Centigrade and decomposes rapidly under heat and light; when in a liquid form, it is dissolved in amylene hydrate".

Avertin is soluble in water in the proportions of 2.5 percent at ordinary temperatures and 3 percent at 40 degrees Centigrade. The aqueous solution decomposes rapidly if the temperature is above 40. A bromide acid is liberated, forming a dibromoacetaldehyde, a substance which may produce marked necrotic lesions of the tissues by direct local action. It is, therefore, of fundamental importance to prevent avertin from being

exposed to temperatures above 40 degrees or too long exposure to light.

The present method of controlling avertin is to add two or three drops of a 1 percent solution of congo red to the diluted solution when it is ready to be used. If traces of alteration exist, the orange color of the congo red will be changed more or less to blue. This important control must precede every administration of avertin. With each vial of avertin, the manufacturer furnishes a solution of congo red for this purpose (4).

Absorption of avertin takes place, as with other substances administered by the same route, through the mucosa of the rectum and colon. Its diffusion is limited, however, to the lower portion of the colon. By radiographic proof, it has been shown that, as a rule, the injected solution does not rise above the splenic flexure of the colon. Rarely does it reach the transverse colon, exceptionally the ascending colon, and then only in a very small quantity. The rate of absorption of avertin is also influenced by variable individual conditions, such as lesions of the intestinal mucosa. For this reason it is impossible to construct an exact chart of its absorption in all persons. It is absorbed much more rapidly than ether,

sleep taking place after five or six minutes. It requires about 20 minutes before the period of maximum efficiency is reached. The maximum concentration is 8 to 9 mg. per 100 cc. of blood, usually found at the end of about 10 minutes, after which there is a slight reduction. This peculiar ability of absorption of avertin makes it advisable to use fractional doses in order to avoid the dangers of overdosage.

Avertin is eliminated through the kidneys. It undergoes a transformation in the liver where it combines with the glucuronic acid, and in this state it passes through the kidneys (43). In animals, avertin injected intravenously at 0.08 gm. per kilogram body weight disappears from the general circulation in 10 or 12 minutes. Naturally, when the introduction is by the rectal route, elimination is slower because of the slower absorption. About four hours after the administration of the enema, 80 percent of the anesthetic is eliminated. After 24 hours, it is difficult to find any trace. In addition, avertin is eliminated in small amounts through the perspiration and in the urine as unchanged avertin. None is found in the stool or the expired air.

The pharmacologic action of avertin is predominately upon the cortex (6). Its action upon the mesen-

cephalic centers occurs only secondarily to excessive doses. It is easy to obtain deep sleep, which, however, can be very easily interrupted by external stimuli of slight intensity. In fact, it has been frequently observed that patients in profound sleep from avertin with generalized muscular relaxation react rapidly and with considerable energy when the operation is begun or when the periphery is strongly stimulated. This signifies that pain sensation resists the action of the anesthetic for a long time. Avertin essentially affects the cortical region and its associated psychic centers, but unconsciousness is rapidly lost when the patient is exposed to strong external stimulation.

The bulbar centers, on the other hand, are relatively sensitive to avertin, especially the respiratory centers. Depression of respiratory activity is, in fact, the most dangerous element of avertin anesthesia. This particular sensitivity of the respiratory center has been demonstrated largely by experiments and by clinical observation. Preoperative administration of morphine accentuates the depressive action of avertin upon the centers of respiration. The use of carbon dioxide and lobeline is less effective on syncope produced by avertin than that following any other anesthetic (11).

The arterial pressure is lowered, as a rule, 15 to 20 mm. Hg., and at times, even more. However, signs of marked hypotension or circulatory collapse are rare in comparison to the frequent alarming respiratory symptoms. The drugs used to combat hypotension are very effective in this form of anesthesia (21).

The efficiency of the circulatory system with avertin anesthesia is of vital importance, comparable to the respiratory activity in rectal ether anesthesia. In the latter, as has been stated, elimination of the anesthetic takes place through the lungs, while avertin is eliminated through the kidneys. If the arterial pressure falls and the circulation becomes less efficient, there is always increased danger of the accumulation of avertin in the blood when the secretion of urine is reduced or stops, the absorption of the avertin meanwhile continuing through the rectum. For this reason it is necessary with avertin anesthesia to prevent by all means the arterial pressure from going below certain limits. This is the most important reason, according to Johnson, Sheppard, and Haffey (24), why some form of complementary anesthesia should be given which has a tendency to produce hypertension, such as nitrous oxide or ether. The administration of carbon dioxide is very efficient, since it tends to activate

blood circulation and blood pressure besides stimulating the respiratory system.

The clinical course of avertin anesthesia is characterized by the fact that the period of excitement is almost completely lacking. After the administration of the enema, the patient passes most gently from the conscious state to that of sleep. He has the most pleasant recollection of this transition. Only in certain individuals is there any manifestation of motor agitation accompanied by incoordinated speech and complaints. In five or six minutes from the time of administration, the patient is asleep, and the respiration is tranquil, rhythmic, and of normal depth and frequency, at first slightly increased, later becoming normal or slightly subnormal. The anesthesia reaches its height about 20 minutes after its administration, at which time deep sleep is established and an even more or less marked condition of surgical anesthesia or analgesia. Larger doses for complete muscular relaxation with loss of reflexes are not advisable.

The color of the skin is pale and slightly cyanotic. This may be due to interference with the capillary circulation or to insuffiaient activity of the respiratory system. A loss of the pharyngeal reflexes with backward dropping of the tongue develops easily.

The deeper the anesthesia, the more superficial becomes the respiration. The pulse loses its tension and has an increased frequency, since the heart does not become directly affected by avertin. The tendon and skin reflexes are abolished, as are the conjunctival and corneal reflexes. However, the reaction of the pupil to light is usually present (1).

The awakening comes slowly after three or four hours of postoperative sleep. On the other hand, there is only a relatively short period of anesthesia available for surgery. This postoperative sleep presents characteristics similar to physiologic sleep in that the patient responds very readily and energetically to external stimuli.

In preparing the patient, it is necessary to evacuate the lower bowel, the same as when ether anesthesia is given by the rectal route. It is advisable to do this the night before, at the same time administering some form of sedative. It is inadvisable to give an enema for evacuation shortly before the operation. The patient may have the first dose in his bed and then be transported to the operating room where the second dose may be given. This is not advisable when used in combination with other anesthetics.

Whenever one uses avertin in the crystalline powder form, it is necessary to weigh the quantity; while if one uses the liquid, it is much easier to handle, and therefore more advisable, as the quantity can be accurately measured with a pipette or graduated syringe. One must remember that a gram of avertin in the powdered form corresponds to 1 cc. in the liquid form.

To use avertin as a basal anesthetic, a quantity of 0.08 to 0.10 gm. must be given for every kilogram body weight. A discussion of larger doses for obtaining complete muscular relaxation with avertin alone is avoided here since at the present time its use for this purpose is universally condemned.

The average quantity of 0.08 to 0.10 gm. per kilogram body weight is subject to minor variations, depending on the judgment of the anesthetist. A dose of 0.10 gm. per kilogram weight should be administered only to individuals of robust constitution, of middle age, and of good general condition. On the other hand, individuals in poor general condition, at an advanced age, or very obese, should be given smaller doses, such as 0.09 or 0.08 gm. per kilogram weight. In children, one may use the maximum dosage. In patients who are excessively thin but in good general condition, having the resistance of youth, doses of 0.11 gm. may be given

due to the fact that their body weight is less than that which it would be if the patient were of average nutrition. Slightly smaller doses are used in women (11).

Avertin is dissolved in distilled water. The quantity of water desired is poured into a glass beaker. This is heated over a hot water bath or directly with a flame over a metal screen. Care must be taken that the temperature does not exceed 40 to 45 degrees Centigrade. The avertin is then added and should be mixed energetically for four or five minutes until entirely dissolved.

The usual concentration of the avertin is 2.5 percent, so that every gram of the substance is dissolved in 40 cc. of distilled water. For a patient of middle age in good general condition weighing 60 kilogram, it is necessary to dissolve 6 gm. of avertin crystals or 6 cc. of the liquid avertin in 240 cc. of distilled water. It is preferable to exceed this quantity of water rather than to have lesser quantity, due to the fact that the solubility of avertin at a temperature of 40 degrees is but slightly above 2.5 percent.

The solution must be prepared fresh for each patient, and it is absolutely contraindicated to attempt to save it for the next day or even for one hour.

It is absolutely imperative that the test with congo red, which has been already described, be made to ascertain its purity. To do this, it is advisable to pour off a little of the solution and add 2 or 3 drops of the congo red which is sent by the manufacturer with the avertin. The resulting mixture should be a pure orange red. When there is some evidence of a bluish tint, the solution should be rejected. When one has a large quantity of liquid avertin, it is advisable to use it as soon as possible. It is inadvisable to have a vial open longer than 15 days. The flask must always be kept in a dark place.

The same procedure of administration is used as for the administration of ether by the rectal route. The rectal tube is inserted and the solution is injected slowly in two stages. Twenty minutes prior to the beginning of the operation, the enema is given to the patient while still in bed, administering about one-third of the mixture. The remaining two-thirds are given about 10 minutes later. The rectal tube must be left in place and pinched off, so as to be able to permit the residue of the solution to run off, or to wash the rectum, sigmoid, and colon if necessary.

It is advisable to limit the use of avertin so as to not reach a stage of deep anesthesia, due to the

fact that it will prove sufficient only in operations that do not entail severe and painful stimulation. When the operation, due to its extent, duration or unusual painfulness of the part which is to be operated upon, requires a more profound anesthesia with complete muscular relaxation, it is necessary to use some form of complementary anesthesia. The following, as Barlow, Fife, and Hodgins state (3), seem to be the most advisable to use in association with avertin:

Ether by inhalation with avertin is most widely used with good results. In fact, ether is easily administered by inhalation and does not give a dangerous summation with avertin. At the same time, it tends to produce slight hypertension and in moderate doses, stimulates the circulation and respiration. The quantity of ether administered will be a great deal less than that necessary with pure ether anesthesia. The semi-closed method of administration is particularly indicated, since it tends to increase carbon dioxide and therefore is a respiratory stimulant. Respiration is always depressed with avertin.

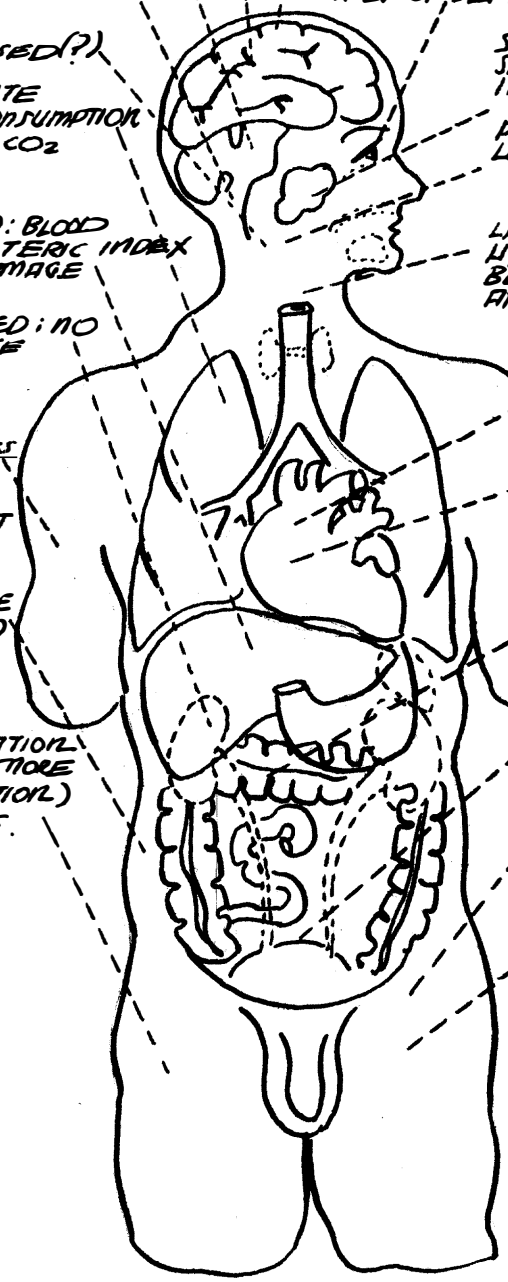
Ethyl chloride is also advisable because of its hypertensive action and rapid absorption and elimination. It is necessary to be prudent in patients with small margins of cardiac resistance, with toxemia or

sepsis, owing to its dangerous action upon the heart.

Nitrous oxide, narcylene, and ethylene are considered by many authors as the complementary anesthetics of choice to be used with avertin. These gases also produce a hypersensitive action which is beneficial during the course of avertin anesthesia, and also the body has a tremendous tolerance to these gases, which are rapidly eliminated. Monod, Desmarest, Gross, Domanig, and others consider this combination the best (11).

It is inadvisable to use chloroform, cyclopropane, or evipal, due largely to their depressing action on the circulatory system. It is also inadvisable, as a rule, to use avertin in combination with peripheral--local or regional--anesthesia, and especially with spinal anesthesia, because with the depressive action produced by local anesthetics, one may very easily have a dangerous summation with the avertin. Besides, avertin in average doses very frequently produces a motor excitability which is not influenced by local anesthesia.

THIOPENTOBARBITAL (PENTOTHAL)-N.N.R.



CORTEX: DEPRESSED: INHIBITS CONVULSIONS

VOMITING CENTER: NOT STIMULATED; POST ANESTHETIC VOMITING NOT COMMON

VASOMOTOR CENTER: DEPRESSED; BLOOD PRESSURE MAY FALL AS MUCH AS 40 MM. SYSTOLIC

CAROTID SINUS: DEPRESSED(?)

LUNGS: DECREASE IN MINUTE VOLUME EXCHANGE; O_2 CONSUMPTION DECREASED: TOTAL BLOOD CO_2 NOT CHANGED

LIVER: GLYCOGEN DEPLETED: BLOOD SUGAR RAISED SLIGHTLY; ICTERIC INDEX NOT CHANGED: HEPATIC DAMAGE DATA CONTROVERSIAL.

KIDNEY: N.P.N. NOT CHANGED; NO EVIDENCE RENAL DAMAGE

SPHINCTERS: RELAXED IN DEEP ANESTHESIA

REFLEXES: DEEP REFLEXES DEPRESSED IN DEEP ANESTHESIA: SUPERFICIAL REFLEXES MAY BE PRESENT IN LIGHT ANESTHESIA.

BLOOD: BLEEDING TIME NOT CHANGED: COAGULATION TIME UNCHANGED. W.B.C. NOT CHANGED CHOLESTEROL NOT CHANGED

SKIN: SLOUGH FROM SUBCUTANEOUS EXTRAVASATION DURING ADMINISTRATION (MORE FREQUENT WITH 5% SOLUTION) SKIN TEMPERATURE RISES.

INTRACRANIAL PRESSURE: NOT INCREASED: USUALLY DECREASED: MAY BE DUE TO FALL IN BLOOD PRESSURE

EYES: PUPILS IN MID-DILATATION; MOVEMENTS NOT ABOLISHED; EYE SIGNS NOT SATISFACTORY INDEX OF DEPTH.

SALIVARY GLANDS: NO STIMULATION OR SECRETION OF MUCOUS: NO IRRITATION TO MUCOUS MEMBRANE

PHARYNX: REFLEX NOT ABOLISHED: LOCAL STIMULATION ELICITS COUGH

LARYNX: REFLEX NOT ABOLISHED: HYPERACTIVITY OF REFLEX MAY BE PRESENT: SPASM MAY OCCUR AFTER INTUBATION

HEART: RATE INCREASED: NO DISTURBANCES OF RHYTHM WITH ADEQUATE OXYGENATION

BLOOD PRESSURE: FALL IN PRESSURE USED AS DIAGNOSTIC TEST IN HYPERTENSIVE PATIENTS ABOUT TO UNDERGO SYMPATHECTOMY

INTESTINES: CONTRACTION AND TONE DEPRESSED

UTERUS: ACTIVITY DEPRESSED IN DEEP ANESTHESIA; BARBITURATES PASS THROUGH PLACENTA

MUSCLES: RELAXATION POOR MUSCLE TREMORS MAY BE PRESENT DURING SURGERY

FATE: DESTROYED RAPIDLY IN LIVER; DETOXIFICATION BY OTHER TISSUES ALSO; MILD DEPRESSION PRESENT AFTER "AWAKENING", MAY BE DUE TO DEGRADATION PRODUCTS OF DRUG. CUMULATIVE ACTION RESULTS FROM SUCCESSIVE ADMINISTRATION.

Redrawn after Adriani'

Figure III.

SODIUM PENTOTHAL

The basic substances required for production of barbiturates are the various alcohols. Pentothal is the sodium salt of a barbiturate in which the oxygen has been replaced by sulphur. It is rapidly eliminated. The chemical structure of pentothal is sodium ethyl (methyl butyl) thiobarbiturate.

The physiological process of detoxification and elimination of the drug is still a debatable subject. Some investigators state that pentothal is detoxified by the liver and eliminated in the urine. It has been given to patients with severe liver disease without deleterious effect, and it has never been recovered as such from the urine, nor have its products of detoxification been found in any of the excretory products of the body (22).

Since 1938, the use of evipal sodium has been largely discontinued in favor of pentothal sodium as a rectal basal anesthetic. Pentothal sodium is the newest of the ultra-short acting barbiturates and is a sulphur derivative of pentobarbital sodium. It has been used quite successfully by many as an intravenous anesthetic. It is believed to be unquestionably the safest barbiturate we now have. This is attested to by numerous series of cases without a fatality, involving

intravenous administration of the drug; namely, 12,000 cases reported by Lundy, 100 cases reported by Murphy, 2,000 by Adams, 350 by Tovell and Thompson, 125 by Kassebohm, and 122 by Carraway. Also, recently Davidson reported 7,640 cases of intravenous administration of pentothal sodium, further attesting to its safety and salient traits (41).

In experiments with dogs and rabbits, it was found that large doses of pentothal sodium given rectally produced no evidence of local irritation or inflammation, and as compared with evipal sodium, larger doses of pentothal sodium could be given with more rapid elimination and less depression.

In 1939, Weinstein (39) reported 164 cases of rectal basal anesthesia with pentothal sodium, describing the drug and giving the advantages over evipal sodium as a basal anesthetic; and in 1940, in an article presented during the Clinical Congress of Surgeons in Chicago, Weinstein and Adams (40) made further observations on the use of this drug as a basal anesthetic, citing an additional series of 274 cases in which it had been used rectally.

Hooper (23) recently reported 113 patients given rectal pentothal sodium as a basal anesthetic, with favorable results and no detrimental complications.

Later Dr. Hooper stated his cases involving rectal pentothal sodium basal anesthesia now total over 350, with no unfavorable results.

Weinstein and Light (41) state "Most of our staff at Chicago Memorial Hospital are now employing rectal pentothal sodium as a basal anesthetic. To date, we have had over 1,500 cases involving the rectal use of this drug, with no deaths or serious complications which could be attributed to the anesthetic. Of these, approximately 50 percent were abdominal cases involving the gallbladder, appendix, and intestines, 25 percent miscellaneous procedures including operations on the genitourinary tract, thyroidectomies, mastectomies, bone surgery, and other procedures. Approximately 3 percent of the 1500 cases were children ranging in age from six months to fifteen years."

In most of their cases, the blood pressure remained stationary or slightly above the original reading, the respiratory rate was not appreciably affected, and no cyanosis occurred. Also, they found that with the use of rectal pentothal sodium, there is no prolonged sleep as with avertin or evipal. Elimination of the drug apparently is more rapid than with any other barbiturate, since it is completely destroyed in the body and the breakdown products are unknown,

none having been found in the urine. Scheifley and Higgins, as Weinstein and Light (41) state, conducted a research study showing that pentothal sodium resists destruction by the liver. Weinstein and Light also state simultaneously that Richards and Appel proved that liver damage does not prolong sleep after injection of pentothal sodium. Previously, it had been held that pentothal sodium is destroyed by the liver in its entirety. Partial hepatectomies were performed on rats, and it was shown that the duration of anesthesia produced by ethyl-o-ethyl-phenylurea and sodium pentobarbital is markedly prolonged. However, neither partial hepatectomy nor unilateral nephrectomy affected the duration of anesthesia with pentothal sodium, indicating that neither liver nor kidneys contribute to the destruction of the drug in the body.

As previously pointed out, it has been found that stridor is quite rare when a basal anesthetic is used with a supplemental inhalation anesthetic. Pentothal sodium as the basal anesthetic tends to allay shock and to keep the blood pressure at the normal level, and therefore aids in the prevention of stagnant anoxia. Also, with the use of the drug, respiration remains essentially unchanged and the drug is

so rapidly eliminated that histotoxic anoxia is not likely to occur.

At the present time, Weinstein and Light (41) are using pentothal sodium rectally as a routine basal anesthetic, supplemented with ethylene, cyclopropane, ether, nitrous oxide, local or spinal anesthetics, or intravenous pentothal sodium, at the Chicago Memorial Hospital. With its use, they have found a reduction of 25 to 50 percent is afforded in the amount of supplemental anesthetics necessary to relax patients for abdominal operation. One reason is the absence of the excitement stage, and another the apparent synergistic effect of the combined use of rectal pentothal sodium with nitrous oxide, cyclopropane, or ethylene.

As Weinstein and Light (41) reported: "We have found the necessity for ether almost completely eliminated since using pentothal sodium as a basal anesthetic. In two cases reported by Weinstein (39), one a multiple diverticulosis of the bladder with papillomata, and the other a wide perineoplastic repair with hemorrhoids, half the regular dose of the spinal anesthetic was used with gratifying results. We have found pentothal sodium given rectally in combination with a spinal anesthetic ideal in all procedures such as resections of the stomach, duodenum, jejunum,

ileum and colon, kidney surgery, pelvic operations, and many others. Ordinarily oxygen is unnecessary, but in desperate cases that are poor surgical risks and in patients with upper respiratory, pulmonary, or cardiac complication, rectal pentothal sodium as the basal anesthetic supplemented with a local or spinal anesthetic combined with oxygen inhalation is hard to surpass".

In a series of cases involving sodium pentothal, Thomas (38) noted that the blood pressure remained at the normal level or was slightly decreased, depending upon the speed of administration and depth of narcosis. In a far higher percentage of cases when spinal anesthetic was preceded by rectal pentothal sodium, the blood pressure remained at higher levels than when the spinal anesthetic was used with any other preanesthetic medication (40).

Rectal pentothal sodium combined with a local anesthetic of one percent procaine for removing tumor masses, as well as for ligation of the saphenous vein, has been used successfully.

In those cases requiring a very short period of anesthesia, as local radium insertion, cystoscopy with or without bladder fulguration, curettement, reduction of fractures and dislocations, removal of vaginal

and rectal polypi, biopsy procedure, opening abscesses, spinal puncture with or without lipiodol studies, and similar minor operations, rectal pentothal sodium basal anesthesia is sufficient and no additional anesthesia is required. Many such procedures have been done repeatedly in the same individual. One patient, cited by Weinstein and Light (41), has had his bladder fulgurated for carcinoma eight times within a period of four years, the same procedure and the same dosage of pentothal sodium being used each time without any supplementary anesthetic.

The elasticity of pentothal sodium is evidenced by a number of operative procedures in which rectal pentothal sodium was used as the basal anesthetic together with intravenous pentothal sodium as the supplementary anesthetic. This combination has proven very satisfactory, requiring for the supplementary anesthetic a smaller amount of the intravenous pentothal sodium solution than is ordinarily given with other basal anesthetics, such as narcotics and other barbiturates.

Pentothal sodium may also be used rectally as a sedative in obstetrics to replace chloral and bromides, ether-in-oil, and other drugs such as opium and the barbiturates of the slower acting groups.

Pentothal sodium has been used rectally in the obstetric department of Chicago Memorial Hospital in at least thirty cases, with no ill effects on the baby, no cessation of labor pains, no delirium, but with prompt sedation followed by moderately rapid dilatation of the cervix. The drug is destroyed quite rapidly so that repeated instillations may be given. The recommended dose in obstetrics is about one-half to two-thirds that for surgical cases, and this may be repeated as necessary (40).

For children, Schotz (37) reported that rectal pentothal sodium has proved the ideal premedicant for all types of surgery, affording all the advantages obtained in adults. Weinstein and Light (41) have had among children over 30 tonsil and adenoid cases, about 15 appendectomies, and a small number of fracture cases in which rectal pentothal sodium was used as the basal anesthetic with fine results.

Holly (22) states that "neither infancy nor age contraindicates the use of pentothal. We have administered this drug to a 10-day old infant for ruptured appendix. The abdomen was completely relaxed, color was good, skin warm and dry. The oldest patient to receive pentothal was a man 102 years old.

"I have given pentothal without harmful results to patients who had been taking large doses of the sulfa drugs before operation. It had been said that the sulphur in the sulfa drugs inhibits the process of detoxification of pentothal, thereby holding it in the blood for a long period. I have not found this to be a disadvantage, since if the drug is held in the blood, less anesthetic will be needed. Obesity is no contraindication to the use of pentothal. These patients take the drug as well as slender individuals."

No opiates or other barbiturates are necessary in combination with rectal pentothal sodium, which is used alone. No preliminary enema is required for the rectal administration; however, if an enema is necessary in preparation for operation, one of tap water or normal saline should be used and this is given several hours before operation. Weinstein and Light (41) found that soapsuds in the enema lessens the effect of the pentothal sodium.

The required amount of the drug is dissolved in one-half to one ounce of distilled water, and is instilled into the rectum by syringe through a catheter or by gravity with a funnel. This is done about fifteen minutes before moving the patient to the operating room.

The dosage rule is one gram, or 15 grains, for every 50 pounds of body weight. In addition, atropine sulfate gr. 1/150 hypodermically, or gr. 1/100 by mouth, is given one-half hour before operation. Occasionally, patients when brought to the operating room, especially those who have been receiving barbiturates over a period of time, are merely stuporous but not unconscious. They are relatively insensible to external stimuli, and on the administration of inhalation anesthetics, the excitement stage of anesthesia is absent. For nervous patients, children, and bowel and rectal cases, the amount of distilled water for administering the pentothal sodium rectally may be as little as 15 cc. For asthenic, overweight, anemic, and senile patients and for patients in shock, the dosage is reduced 10 percent. The dosage for children is the same as for adults, with even a slight increase being permissible. As previously stated, for obstetric cases, the recommended dose is about one-half to two-thirds that for surgical cases.

Within 15 to 20 minutes after the rectal administration of pentothal sodium, the patient is asleep or stuporous. The average duration of anesthesia is one to two hours. There is a smooth and slow return to normal during the awakening period, which averages one

to two hours, with a minimum amount of vomiting or nausea, which minimizes the amount of analgesic or sedative necessary in this period. Gwathmey and Abajian (20) have observed no excitement during either the induction or recovery with the use of rectal pentothal sodium except the ordinary restlessness which follows the average operation.

Weinstein and Light (41) reported "in our case, it has been unnecessary to resort to the use of antidotes, but in treatment for overdosage of pentothal sodium we would recommend first, oxygen; second, metrazol intravenously; and third, picrotoxin. For respiratory failure, the use of a resuscitator with 100 percent oxygen is recommended. When stronger drugs are employed, as basal anesthetics, overdosage is not uncommon, but this is not the case with pentothal sodium, which seems to have a greater margin of safety".

To date, few cases have been encountered to whom Weinstein and Light (41) would hesitate to administer rectal pentothal sodium. However, they consider the following as contraindications to its use: 1) severe involvement of the trachea, edema of glottis, and mediastinum, 2) any other condition in which there is dangerous heart impairment with decompensation, and 3) any of the severe primary anemias.

PERSONALLY CONDUCTED CASE REPORTS

I have been fortunate in having the opportunity to administer sodium pentothal personally under the direction of Miss Delores Broughton, R.N.A., at the Immanuel Hospital here in Omaha. I have only three cases but even with this small number, I believe I have been able to more thoroughly understand the manner in which this drug works.

Case Number One was Mr. D. R., a young man of 16 years, who entered the hospital for an open reduction of the styloid process of the left ulna and repair of the annular ligament of the same arm. His story was that he had fractured his left arm thirteen days prior to entry, at which time the arm was splinted by his local doctor; he was sent to Omaha for further treatment. Upon physical examination, he was found to be in good physical condition, weighing one hundred fifty-five pounds. The only positive findings were the fractured forearm and multiple erythematous papules over the skin of the face and forehead. His blood pressure at this time, the night before surgery, was 125/68, pulse 72, and respirations 18. He was prepared with a soapsuds enema and nembutal gr. one-half the night before surgery. He rested well that night, and thirty minutes before surgery was given

three grams of sodium pentothal dissolved in one ounce of distilled water per rectum, and gr. 1/150 atropine sulphate per hypo. His blood pressure at this time was 125/82, pulse 84, and respirations 18. These readings remained unchanged, and good relaxation was obtained. There was no excitement stage and induction was very smooth. Upon returning to his room, his pulse rose four to twelve beats per minute, but soon returned to eighty. He became somewhat restless two hours after surgery, was nauseated and vomited small amounts of green fluid. This restlessness persisted through the afternoon, as did his partial stuporous condition. The night after surgery, he slept well after he was given morphine gr. one-quarter per hypo and nembutal gr. one-half by mouth. The next day he felt good and ate well. The following day he was dismissed.

Case Number Two was Mr. E. M., a laborer of 59 years and weighing one hundred and seventy pounds, who came to the hospital six months after he had fallen from a scaffold, complaining of persistant weak and painful right knee. Examination disclosed an internal derangement of cartilage of the right knee and chronic degenerative arthritis. His blood pressure on admission was 145/90, pulse 84, and respirations 24. He was prepared, as was the first case, with a soapsuds

enema and nembutal gr. one-half the night before surgery. Fifty minutes before his going to the operating room, he received morphine sulphate gr. 1/8 and atropine sulphate gr. 1/150; and thirty minutes prior to surgery, he was given three and one-half grams of sodium pentothal in one ounce of distilled water per rectum. He entered the operating room not completely asleep and was given nitrous oxide and ether by machine, only very small amounts of which were necessary. The patient was completely relaxed, and an arthrotomy was performed. His color remained good, and no excitement stage was noticeable. His blood pressure remained at 145/90 throughout, the pulse stayed at 96, and respirations dropped from 24 to 18 during the operation. After operation, his pulse rose to 100, respirations to 20, with no appreciable change in blood pressure. He awoke one hour and ten minutes after the administration of the sodium pentothal only to go back to sleep, and he continued to sleep in long intervals throughout the day. The night after operation, he was given morphine gr. 1/6. He expressed no complaints on this day, and only those referable to the surgery on the days that followed.

Case Number Three was Mrs. G. F., a 31-year old housewife weighing one hundred and thirty-five pounds,

who entered the hospital complaining of pain in the region of the coccyx for the past three months. After examination, a diagnosis of coccydynia was made. On entry, her blood pressure was 130/80, pulse 86, and respirations 20. Her preoperative care consisted of a soapsuds enema and nembutal gr. one-half the night before surgery, and 2.5 grams of sodium pentothal in one ounce of distilled water per rectum and atropine gr. 1/150 per hypo thirty minutes prior to surgery. The coccyx and lower end of the sacrum were excised and the peroneal floor repaired. Only small amounts of ether (open drop technique) was required for complete anesthesia. The blood pressure, again in this case, remained unchanged as did the heart rate, with a depression of respiratory rate to 18 per minute. The patient responded three hours after surgery. During this time, there was a rise in pulse to 120 and in respirations to 24, the pulse returning to 72 two hours postoperatively, at which time she was given morphine gr. 1/6 for pain. The respirations returned to 18 later in the day. There was no appreciable change in blood pressure at any time. The patient received nembutal gr. one-half that evening, having given no complaints during that day or the days that followed which were referable to the anesthetic.

Although conclusions can not be drawn from this small number of cases, the conclusions made by workers in this field are seen to hold true here. As Thomas (32) states, respiration is rarely depressed, blood pressure is not appreciably affected, and elimination of the drug is rapid. The stage of excitement is eliminated in most cases, there is no apprehension or disagreeable memory of the operation, the postoperative awakening period is fairly rapid, and certainly, as he states, the technique of administration is simple.

It may be noted here that a soapsuds enema was used in the preoperative preparation of these three patients. This is not the method found to be the most effective by Weinstein and Adams (46), who prescribe a plain water enema the night before surgery. The change in technique seemed, however, to give rise to very little, if any, difference in results.

COMPARISON OF ETHER AND AVERTIN WITH SODIUM PENTOTHAL VIA THE RECTAL ROUTE

Sodium pentothal produces anesthesia with muscular relaxation as does ether without nearing the danger zone, and as compared with avertin allows less psychomotor agitation during the operation and the awakening period.

Ether exerts a less toxic action than avertin, while sodium pentothal evidently exerts a less toxic action than does ether.

As far as the stability of the preparation is concerned, sodium pentothal is undoubtedly the most stable of the three, ether being next in having the disadvantage of being so very volatile, and avertin the least since it so readily decomposes into poisonous products.

The duration of anesthesia is less than that of ether but probably about the same as that of avertin in the case of sodium pentothal. Avertin and sodium pentothal have the advantage over ether in that they cause a more rapid induction, and perhaps even the unpleasant sensations of ether during the initial period is eliminated. Avertin is less irritating upon the mucosa of the large bowel, while sodium pentothal is still less irritating than avertin.

Avertin is less toxic on the liver but more toxic upon the kidneys through which it is eliminated, but sodium pentothal is now thought to be non-toxic on both these organs. The awakening with avertin is much slower than with ether; however, it is frequently associated with psychomotor disturbances, which are supposedly less with sodium pentothal.

Convenience to the anesthetist and less chance of error are afforded by sodium pentothal than by either of the other two preparations, since it is stable and requires no testing before it is given, nor does it need be followed by extensive flushing of the bowel postoperative, as is the case with ether.

Another distinct advantage of sodium pentothal as a basal anesthetic is that it can be dissolved in such a very small amount of water that even the largest dose need not exceed the volume of one or one and one-half fluid ounces, which is a much smaller volume than that necessary in the case of ether or avertin. This naturally increases the chance of the patient's retaining the drug.

INDICATIONS FOR ETHER, AVERTIN, AND SODIUM PENTOTHAL PER RECTUM

While it is possible to produce surgical anesthesia with ether for most extra-abdominal operations, one must never attempt to produce deep anesthesia, because there is considerable danger of overdosage. It is, of course, understood that it should be used when spinal, peripheral, and inhalation anesthesia prove inadequate and the use of avertin is contraindicated or sodium pentothal is not available.

The most frequent indications for rectal anesthesia are:

In surgery of the nervous system, brain and cord, ether has been preferred to avertin due to the motor agitation, completing the sub-anesthesia with local infiltration. This has been found by most authors to be inadvisable with avertin. Against ether is the greater frequency of capillary hemorrhage, but sodium pentothal can now be used with little of these dangers.

In the surgery of the ear, nose, and throat, rectal anesthesia is indicated and should be used more extensively than it is (11). Here, ether is preferable to avertin and sodium pentothal, because one does not have a loss of pharyngeal and laryngeal reflexes as is frequently seen with avertin. This is important

because it avoids the danger of aspiration into the trachea of saliva or blood from the pharynx.

The same holds true for oral surgery, plastic surgery, and other operations on the face, which have a definite indication for rectal anesthesia by one of the above-mentioned substances.

However, Gordon (14) prefers sodium pentothal for thyroid surgery; the indications are less frequent because most surgeons prefer regional anesthesia or gas. If local anesthesia is used, however, sodium pentothal is the basal anesthetic of choice.

For thoracic surgery, ether and avertin are of equal value, but in abdominal surgery, avertin and sodium pentothal are almost exclusively indicated as a basal anesthetic, while ether is inadvisable due to the distension of the colon which produces marked embarrassment for the surgeon (36). In orthopedic surgery, all three substances are frequently indicated, probably the best relaxation of long muscles being afforded by sodium pentothal.

In the aged and in those with hypertension, it is more advisable to use avertin than ether; in cachectic individuals with hypotension, there is less danger with ether than avertin, while sodium pentothal can be used in either case.

Among the most discussed indications for avertin are operations upon the biliary tract due to the fact that, according to some authors, its action upon the liver is minimal, while according to others it offers considerable danger. Sodium pentothal is used with no danger of furthering the liver damage.

In renal surgery, it certainly is inadvisable to use avertin, because it is eliminated through the kidneys and frequently leaves signs of local irritation (albuminuria), but sodium pentothal may be used without hazard.

CONCLUSIONS

First, it should be emphasized to the reader that we are dealing with two time-honored drugs, avertin and ether, together with one, sodium pentothal, which is so new that it has yet to establish its own advantages and disadvantages. Considering the few thousand cases reported on the use of sodium pentothal rectally, one finds himself viewing its advantages quite strongly and, in doing so, may blind himself to the developments yet to show themselves which may be on the less agreeable side of the picture. With this in mind, I believe the following conclusions may be drawn:

Sodium pentothal apparently is the least toxic of the drugs discussed herein. Its dosage is more accurately calculated than that of ether and is as accurate as that of avertin. There is no danger of its decomposing to poisonous products. It is less depressing to respiration and has little effect upon pulse and blood pressure.

Conclusion 1: Sodium pentothal presents itself today as being a safer drug than ether and avertin when used rectally as a basal anesthetic.

Excellent relaxation has been reported in all cases studied in which sodium pentothal has been given

rectally. Relaxation with sodium pentothal per rectum has been described as being as good as, if not better than, that achieved with avertin and ether. Preparation of the mixture to be instilled into the rectum is very simple in the case of sodium pentothal, requiring a minimum of apparatus as compared with that of ether and avertin. A much smaller volume of sodium pentothal is administered than is the case with avertin and ether.

Conclusion 2: Sodium pentothal presents a convenience to the surgeon in that good relaxation is obtained; to the anesthetist in that its preparation is speedy, simple and requires very little apparatus; and to the patient since he is required to retain a much smaller volume within his rectum. Also, of added economical significance is the fact that sodium pentothal is relatively inexpensive.

The present conception is that sodium pentothal is not detoxified by the liver or excreted by the kidneys, and, if it is, causes no damage to these organs regardless of whether damage is present prior to its administration. It is non-inflammable, thus lending itself to surgery requiring the use of the cautery or Bovie knife. It has been used with great success with local and spinal anesthesia, without causing undue

hemorrhage, motor excitability, lowering of blood pressure or excessive depression of respiration, as has been seen with avertin and ether per rectum. It is said to work synergistically with cyclopropane, ethylene, and sodium pentothal intravenously. This allows it to be used to greater advantage in neck, thoracic, orthopedic, and brain surgery. It produces no lesions in the bowel nor does it give rise to undue distension when administered rectally, as has been seen with ether and oil, thus lending itself very well to abdominal surgery.

Conclusion 3: Sodium pentothal per rectum seems to have a greater adaptability than ether or avertin per rectum, and with few contraindications.

Since there has been so little work performed under sodium pentothal as a basal anesthetic, it goes almost without saying that until further work is completed, the results must be deferred until a sufficient test of this drug has been allowed.

Conclusion 4: Although today sodium pentothal seems to offer many advantages over avertin and ether in oil, considerably more must yet be unfolded which may prove or disprove the conclusions drawn here. It seems to be the use of the drug rectally which bears watching for further development and final conclusions.

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