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Review of modern anesthetic agents, indications and contraindications

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A REVIEW OF MODERN ANESTHETIC AGENTS;
INDICATIONS AND CONTRAINDICATIONS.

Ray Meidinger.
A Review of Modern Anesthetic Agents,
Indications and Contraindications.

The presentation of a review of modern anesthetic agents would not be complete without a brief summary of the historical background of man's conquest of pain. Anesthesia and analgesia are a comparatively recent heritage of medical science. Yet, an attempt to alleviate pain presents a story of long, arduous labor on the part of the most persistent research minds of all ages, today, yesteryear, and century after century gone before, far back into the unwritten, unintelligible eras of mankind's earliest existence upon this earth.

Today, we accept the attitude that anesthesia has always existed and little is known of the daily tragedy of intense human sufferings due to operative procedures in past history. The daily scenes which occurred in the surgical amphitheaters of the past centuries were so gruesome and distressing that no one cared to recount them, much less put to print just what occurred.

Ancient, medieval and modern history furnish numerous examples of the use of drugs or other media which by some means of dulling consciousness, bring about partial or complete unconsciousness. The ancients produced a degree of surgical anesthesia by administering preparations of poppy, mandragora and certain varieties of hemp (1). Later surgeons obtunded sensations before operations by giving alcoholics, opiates, by producing syncope through phlebotomy or ischemia by arterial compression. (2) Muscular relaxation to facilitate the reduction of dislocations or other manipulations, was obtained by the use of alcoholics, re-
laxants, and emetics such as tartar emetic and tobacco enemas. (2)

At the close of the eighteenth century modern surgical anesthesia was foreshadowed by the following discoveries: of hydrogen in 1766 by Cavendish; of nitrogen in 1772 by Rutherford; and of Oxygen and Nitrous oxide in 1774 by Priestly. A big impetus to the discovery of general anesthesia came when Lavoisier in 1775 pointed out the importance of oxygen present in inspired air for the continuance of life. This directed the attention of many men to the constitutional effect of other gases when inhaled. Among these men was Humphrey Davy (2) who early inhaled nitrous oxide and noticed its anesthetic properties so that he wrote:

"As nitrous oxide in its extensive operation appears capable of destroying physical pain, it may probably be used to advantage during surgical operations in which no great effusion of blood takes place." (2).

Henry Hill Hickman, (2) a member of the Royal College of Surgeons in England was the first to render animals insensible to pain by inhaling gases in 1820 and 1823. Little attention was paid to his experiments at this time.

The anesthetic properties of ether fumes was well known in 1839 as revealed in current literature in describing the so called "ether frolics." Yet, ether was not used in surgery till 1842 when Crawford W. Long of Georgia successfully used it in a surgical operation. General anesthesia developed rapidly after that time. (2)

Horace Wells of Hartford Connecticut extracted teeth under nitrous oxide in 1844. William T.G. Morton a dentist and medical student, following the advise of his preceptor Charles Jackson, experimented with ether, and gave the first successful public de-
A demonstration of surgical anesthesia in the Massachusetts General Hospital, October 16, 1846. In 1847 Sir James Y. Simpson of Edinburgh, (3) after experimenting on himself and friends introduced chloroform or terchloride of formyl, as it was then known, as an anesthetic.

From 1842 to 1847 two powerful, successful anesthetic agents were given to the world which were put into general use. Yet, as has always been the case, the medical profession reacted to the use of anesthetics in its usual stereotyped fashion and opposition to its use was made on all sides. It is interesting to note that when Simpson (3) carried the use of Chloroform and ether into the practise of obstetrics physicians condemned its use as unphysiological to alleviate the pain of child birth. The clergy condemned the use of anesthesia as contrary to the teachings of the bible itself; for it was written "that in sorrow shall she bring forth" (4) Simpson (2) met these superstitions and religious objections ingeniously and pointed out that God himself had introduced anesthesia in surgery and obstetrics since He had caused a "deep sleep to fall on Adam," when he excised the rib that gave birth to Eve.

Surgical anesthesia is the term suggested by our own physician-poet Dr. Oliver Wendell Holmes (1) to indicate the absence of sensation deliberately produced by a suitable agent. Even though the patient is unconscious of sensation, harmful impressions may register in the cerebral and spinal centers as shown by changes in blood pressure and other reactions, hence Crile (5), has proposed the term "Anosci-Association or Anociation. Anociation is a term for a psychic and sensory anesthesia, so perfect that noxious or harmful impressions are prevented from reaching the brain. This is a more modern concept.
Ether, Chloroform and nitrous oxide were practically the only anesthetic agents used up till very recent times. However, other anesthetic agents and methods were known. Among the more important contributions was the isolation of coacain, the alkaloid of coca leaves, by Goedèke (6) in 1855. Cocain was introduced as a local anesthetic agent in 1884 by Carl Koller (7) who used it in ophthalmology. The introduction of the hypodermic syringe in 1858 (7) with the previous isolation of cocain made it possible for the development of regional anesthesia which is taking such an important place in anesthesia today.

The modern regime and concept of anesthesia has presented a number of agents both for inhalation and for the production of anesthesia by other methods than that of inhalation such as intravenous, rectal, oral, intratracheal insufflation, intradural, sacral and thru infiltration with the hypodermic needle. There is a tendency to use combinations of agents such as the gases-nitrous oxide, oxygen and ether also ethylene and oxygen. The introduction and employment of new drugs as the barbiturates, sodium amytal, luminal, nembutal, pronocot and avertin or tribromethonal. Yet, with all of the new drugs, agents etc. introduced the old agents are still used but by either new methods of administration or in combination with other agents. Ether, the oldest anesthetic agent used still plays the most important role in anesthesia today.

"ETHER" (ethyl oxide, \((C_2H_5)_2O\)) is a very volatile inflammable, explosive liquid, with a rather disagreeable pungent odor. Ether was first discovered by Valerius Cordus (1) in 1540 who named the product "Oleum Vitriolidulce."

The anesthetic and analgesic powers of ether is probably
brought about thru entering into a loose physiochemical combinat-
on with vitally important lipoids in the cells of the central
nervous system, so changing the constituents as to arrest the power
of reception and conduction. (8).

Ether stimulates the respiratory mucosa to increase secretions.
The respiratory center in the medulla is first stimulated causing
rapid, full respirations, followed by depression with slow shallow
breathing. The heart is stimulated and accelerated. There is a
slight early rise in blood pressure, later followed by vasodéla-
tion, slow full pulse and finally gradual fall in blood pressure
with a terminal rapid weak pulse. In toxic doses, unless there
is a serious cardiac disease, respiratory arrest precedes that of
the heart. Large doses cause hemolysis and capillary hemorrhage
into the stomach with black or coffee-ground vomit. Parenchym-
atous changes occur in the liver and kidneys, the excretion of
urine and nitrogen is diminished. The urinary chlorides are in-
creased, and albumin, sugar, cylindroids, casts, excess of leu-
kocytes and acetone are often found in the urine after profound
etherization.

Ether is eliminated thru the lungs, kidneys, skin and gastro
intestinal tract. It is largely eliminated within two hours fol-
lowing etherization but may require two or three days to complely
eliminate it.

The open drop method is apparently the most popular and safe-
st method of etherization in use today. In this method, due to the
low concentration of ether fumes, the blood remains well oxygenated
thruout. The use of the open drop method in the hands of an ex-
perienced anesthesist is not unpleasant to the patient and carries
the least danger.

The open drop method is the most fool proof and most easily controlled method. Yet, it cannot be employed in all operations and other methods must be employed. The induction stage of ether-ization is usually very stormy with most patients when used alone so that these two objections must be avoided.

The excitement stage during induction is being avoided by premedication with morphine, pantopan or the barbiturates. Induction is also made more pleasant by preliminary induction with nitrous oxide-oxygen or ethylene-oxygen then switching to ether to continue the anesthesia. Much of the post operative distress is alleviated by giving inhalations of 95% oxygen with 5% carbon dioxide to stimulate breathing and to wash out the ether from the tissues. (5).

There are various gas machines produced today to administer ether in vapor form with oxygen in known concentration. This is a closed method of administration which provides a rebreathing bag. The closed method reduces the amount of ether needed and if properly controlled produces a more even narcosis. This method may also increase the injurious effects of the anesthetic especially if an acute infection of the respiratory tract is present or if rebreathing is carried too far. Other methods of administering air, oxygen or ether gases emregnated with ether vapor may be done by; the mouth thru suitable tubes, the pharynx thru a nasal inhaler or a tube introduced thru the nostrils or mouth, by the trachea or by the rectum with the ether-oil anesthesia. Intratracheal anesthesia or intratracheal insufflation is one of the
more important advancements in ether anesthesia.

Intratracheal insufflation was first introduced by Meltzer and Auer in 1909 (9) and made popular by Magill (10), of London who perfected the method. Intratracheal insufflation is the name given to a method by means of which a mixture of air and ether is driven deep into the large bronchi. The mixture is propelled by external pressure of from 15-20 mm. of water thru a tube inserted into the trachea by means of a direct laryngoscope. The introduction of the laryngoscope is made possible by previous induction with ether by the open drop method or thru the use of nitrous oxide-oxygen with the addition of ether.

The aim of intratracheal anesthesia is to provide a free airway for respiration over which the anesthetist has perfect control. The overflow of gases prevents the invasion of foreign material from the pharynx into the larynx during intra-oral operations. The apparatus for giving the anesthesia can be arranged free of the field of operation and need not impede the surgeon or interfere with his aseptic technic. The precise control of intrathoracic pressure makes intratracheal insufflation the method of choice for surgical procedures within the thorax. It is also of value in operations about the head where it is necessary to move the head about from one position to another. (9).

Rectal ether anesthesia was introduced by Pirqoff in 1847 who proved that ether vapor was absorbed rapidly in the rectum to produce anesthesia. Ether vapor alone produced too much irritation to be used and as a method was discarded. Gwathmey (11) in 1913 introduced oil-ether colonic anesthesia based upon the rate of evaporation of ether from an oily mixture.
According to Gwathmey (11) in the administration of this anesthesia two distinct processes take place. The first is the physical separation of the ether from the oil, the second, the physiologic absorption of the liberated ether vapor. The dissolution of the mixture in the colon is at a constant rate and the total vapor liberated is limited by the amount of ether used. From a mixture containing six ounces of ether, the ether is absorbed at the rate of two ounces per hour; this produces the required saturation of the blood for anesthesia. The constant elimination by way of the lungs prevents the cumulative effect which may occur in the inhalation methods. In this type of anesthesia there is a marked amnesia and analgesia following the stage of anesthesia sometimes lasting for as long as eight hours.

Advantages in the use of oil-ether rectal anesthesia are: (12) It is controllable, as the ether can be washed out at any time. The prolonged analgesic properties of colonic ether make it possible to carry out extended operative procedures. Psychic trauma is absent, amnesia marked and the stage of excitement eliminated.

The disadvantages are: It does not give complete muscular relaxation. It is a complicated and time consuming method which requires the cooperation of the patient for its administration and a competent person to watch the patient before and after the operation to prevent the swallowing of the tongue.

Ether is the most toxic of all anesthetic agents with the exception of chloroform. (13) Post operative nausea and vomiting leading to dehydration and intoxication are often serious. It is a serious irritant to the respiratory mucosa and after etherization two per cent of all patients have some form of pulmonary compli-
eration; four per cent after abdominal operations and eight per cent after upper abdominal operations. (14) Infections of the upper air passages find easy access to the lung in etherization. However, because of its small margin of danger and its simplicity of administration it is the safest anesthetic in the hands of the physician who has not the time to devote to the study of anesthesia. Ether still remains our foremost anesthetic in uncomplicated cases because of its muscle relaxing qualities.

Ether is contraindicated in acute upper respiratory infections. It is unwise in pulmonary tuberculosis, renal disease, diabetes, acidosis, ophthalmia and brain operations in general. It is less adapted though frequently used for infants, young children and in the aged. (13)

"CHLOROFORM", our most toxic anesthetic agent is still used throughout the world and entirely so in the tropics (15), and on the battle field. Chloroform is also used to a great extent in obstetrics. Chloroform was discovered by Samuel Guthrie (2) of Sacketts Harbor, N. Y., in 1831. Its anesthetic properties were proven by Sir James Y. Simpson in 1847. (3).

Contrasted with ether, chloroform is six times more powerful, is less bulky and non inflammable. It has a sweetish, rather pleasant odor; acts more rapidly and agreeable; does not cause pharyngeal or bronchial irritation or nausea. There is no objectionable odor to the secretions following its use. The depressant effects of chloroform on the brain is $3 - 3\frac{1}{2}$ times as great as that of ether, and its power to arrest respirations is 3 times as great. The depressant action on the heart is about 25-30 times as great
as that of ether.

Toxic symptoms produced by chloroform develop with great suddenness as contrasted with ether. Death occurs thru an arrest of respiration or thru sudden cardiac collapse. Chloroform produces serious post anesthetic results of edema, fat infiltration, multiple hemorrhage, necrosis of the central portion of the liver lobule and parenchymatous changes in other organs.

There are few indications for the use of chloroform due to its known toxic effects and it should not be used where ether agents could be used. Chloroform is always preferred by the patient, for it causes less irritation and less feeling of suffocation. It is often preferred by the surgeon because it induces anesthesia sooner and less is required, it also produces more complete muscular relaxation and is preferred by some obstetricians in doing certain manipulations such as a version. In the tropics anesthesia with ether may be difficult to induce owing to its rapid evaporation, so that in these cases chloroform may be necessary. In operations where the cautery is used and a general anesthesia is indicated chloroform may be used rather than ether or ethylene due to their explosive and inflammable nature. (19)

Chloroform should not be used in serious heart disease, in shock, acidosis, cyanosis anasaica, status lymphaticus or diabetes. (13).

"NITROUS OXIDE" (N₂O) a colorless odorless gas was discovered by Joseph Priestly (2) in 1772. It was used as an anesthetic agent for the extraction of teeth in 1844 by Horace Wells. Its modern use of administration with oxygen was demonstrated by Andrews in 1868. (2) The gas is supplied in steel cylinders compressed into a liquid so that one ounce of the liquid produces three and one third gallons of gas.
Nitrous oxide supports combustion outside the body, (16) for if a glowing splinter of wood is held in it, it bursts into flame exactly as if it were immersed in oxygen. In the tissues of the body, however, nitrous oxide behaves in the same way as any indifferent gas, such as hydrogen or nitrogen; that is, the tissues exposed to it suffer from asphyxia owing to the oxygen of the air being excluded. Animals die after inhaling nitrous oxide in almost the same time as after hydrogen or nitrogen, and at death the spectrum of the blood shows no oxyhemoglobin to be present, the tissues having used up all the available oxygen. Nitrous oxide, therefore, does not support combustion in the animal body, the nitrogen is not split off from the oxygen at body temperature as it is when the oxide is exposed to high temperatures outside of the body. However Nitrous oxide has a special effect on the central nervous system.

Nitrous oxide depresses the brain by virtue of its molecular form just as chloroform and ether does. (16) When the pure gas is inhaled it produces anesthesia in from thirty to sixty seconds with cyanosis and asphyxia. If a mixture of nitrous oxide and oxygen is administered there must be at least 80-90 per cent concentration of nitrous oxide to produce satisfactory anesthesia. With this mixture a degree of anoxemia is always present. (16) Death occurs not from the direct action of the nitrous oxide on the respiratory centre, but from the lack of oxygen to this particular centre. (16)

A transient two-three minute nitrous oxide anesthesia is the safest general anesthesia known today. Nitrous oxide-oxygen mixture given for moderately prolonged operations has little toxic
effect when administered by a skilled anesthetist. Prolonged anesthesia may be followed by acidosis and evidence of parenchymatous damage, such as nausea, vomiting, headache and depression which may last several days. However, in the hands of a skilled anesthetist it is a safe anesthetic agent but is not satisfactory for all operations.

Complete muscular relaxation is hard to attain and thus precludes its use in many operations and manipulations. In modern anesthesia Nitrous oxide is used for preliminary induction where ether is later used. This avoids the preliminary disagreeable effects of ether. Local or regional anesthesia is reinforced by light nitrous oxide-oxygen anesthesia producing a desirable anesthesia. Nitrous oxide is also used with various basal anesthetic agents such as the barbiturates and avertin. (13)

The use of nitrous oxide is contraindicated in patients who have a feeble, obstructed or crippled respiratory mechanism for the gas apparatus imposes an undue and added strain on the respiratory mechanism. Its use is contraindicated in arteriosclerosis, aneurysm or vascular hypertension. In the very young, senility, hemiplegia and operations on the brain are contraindications for its use. Acute or Chronic diseases of the lungs such as pulmonary tuberculosis and pneumonia are definite contraindications to its use. (13)

"ETHYLENE" (C₂H₄) is a colorless gas with a peculiar phosphorous like odor, produced by the dehydration of ethyl alcohol. Thomas Nunnely (14) a surgeon of Leads was the first one to experiment with ethylene when he produced anesthesia by the administration of ethylene and chlorine in 1829. Nunnely was not satisfied with the results obtained and its use was not thought of until
recent times. In 1918 Arno B. Luckheart (17) began experimenting with ethylene and in 1923 introduced it as an anesthetic agent in human practise. For anesthetic purposes ethylene is administered with oxygen. Its action seems to be intermediate between nitrous oxide and ether. It resembles nitrous oxide as to its manner of administration and rapidity of induction and recovery. It resembles ether as to the depth of anesthesia and muscle relaxing qualities. Ethylene has a wider anesthetic zone, is more easily managed and causes less cyanosis than nitrous oxide.

From the pharmacological standpoint, ethylene-oxygen anesthesia is interesting in that a satisfactory degree of suppression of consciousness and of the reflexes can be produced with scarcely any effects upon other functions. Respirations are slightly depressed, being slow, regular and somewhat shallow as in normal sleep. The pulse may be slightly slowed and the blood pressure show a reduction of 10-15 mm of mercury. (17) The skin is dry, pink and warm with no signs of cyanosis. The mucous membranes are not irritated and the secretions of mucous or saliva is not increased. The blood is bright red, there being probably a combination between ethylene and hemoglobin, however the blood changes are practically nil. (18) The gas is practically entirely eliminated thru the lungs which occurs quite rapidly following its withdrawal. Lethal effects of ethylene are produced by respiratory paralysis. 100% ethylene kills very rapidly, much more rapidly than 100% nitrous oxide. (16).

Ethylene anesthesia permits the administration of much higher concentrations of oxygen than in nitrous oxide anesthesia. Ethylene anesthesia induction is usually begun with a 20% oxygen - 80%
ethylene mixture. The anesthesia is usually carried along with a 50% mixture so that anoxemia does not exist with this type of anesthesia.

From the foregoing discussion it would appear that ethylene-oxygen anesthesia is the perfect anesthesia, yet, it has its objections, and disadvantages. The main objection to the use of ethylene is its highly explosive (19) quality. The gas may be ignited by a cautery, open flame, sparking commutator, electric fan or by the static spark. Ethylene is not explosive in less than 5% mixture with air. 5-10% mixtures are explosive, higher percentages are inflammable but not explosive. With oxygen, ethylene is violently explosive, however at mixtures above 60% it ignites but does not explode. Ethylene has about the same density as air and may drift for a considerable distance and ignite. Ethylene subjected to high pressure with oxygen may explode spontaneously. (19)

The advantages of ethylene-oxygen anesthesia apparently outnumber the disadvantages. The gas is quick in action and not unpleasant to take. Recovery is rapid and produces very little nausea or vomiting, dangers to the respiratory tract and postoperative complications are minimized. The explosive hazard of ethylene-oxygen mixture may be eliminated by proper wiring of the machine, table and patient to prevent the production of a spark. By keeping the humidity of the operating room above 56° by means of steam from radiator humidifiers or from the sterilizing room near the operating room, inflammability is done away with. (19)

There seems to be few contra-indications to the use of ethylene-oxygen anesthesia except that certain patients are refractory to this anesthesia and produces little anesthetic effect. Ethylene-oxygen anesthesia is preferable to Nitrous oxide in all fields and
particularly useful in operations on the thyroid, in patients with diabetes, nephritis and other conditions in which cyanosis and acidosis is to be avoided. (21)

Ether, Chloroform, Nitrous oxide and ethylene are the principal agents given in inhalation anesthesia today. Acetylene and ethyl Chloride are also used but are much inferior to the other agents and are not recommended by many surgeons. Ethyl Chloride is a powerful but dangerous anesthetic agent, producing anesthesia in one minute (14). Its margin of safety is too small to permit its use and its toxic results are greater than chloroform. Induction with ethyl chloride is sometimes used switching to ether to carry the anesthesia. Ethyl Chloride is still popularly used for local anesthesia due to its volatility.

"REGIONAL ANESTHESIA" is meant that form of anesthetization accomplished by the injection or application of some local anesthetic agent into or upon a local part. Regional anesthesia may be produced by field block, which consists in creating an encircling wall of anesthesia by infiltrating the tissues in definite planes around the operative field, by nerve block which consists in making injections of a local anesthetic agent in close proximity to the nerve or nerves whose conductivity it is desired to cut off, thru infiltrating the operative field directly and by direct application of the agent to mucous membranes, conjunctiva etc.

There have been many local anesthetic agents produced and used with varying success. (6) The first agent used was cocaine, the alkaloid of erythroxylon coca. Cocaine was introduced as a local anesthetic in 1884 by Carl Koller (7) who used it in ophthalmology.
Cocaine is a powerful local anesthetic agent yet, a dangerous habit forming drug. In the early days of local anesthesia with cocaine, a number of fatalities occurred from its use. These have become less frequent with increasing experience of the margin of safety within which it can be used, but nothing can alter the fact that cocaine is a highly toxic substance and habit forming. These defects have prompted the search for less dangerous substitutes. In the search for substances to replace cocaine, several hundred local anesthetics have been introduced, but only a few have been widely used.

Some of the important local anesthetic agents used as substitutes for cocaine are butyn, alpyin, tropocaine, stovain, novocain or procain, tutocain, eucain and beta-eucain. Benzocain, butesine picrate, orthoform, anesthesin and chlorbutanol are also substitutes but are slightly soluble in water and therefore have limited uses. (22).

Tropacocaine is a natural alkaloid found in Java coca leaves. It is a benzoic ester of a base, pseudotropine. The other substitutes are synthetic products of similar structural formula to cocaine in that all the compounds contain a benzoyl group. (22). The benzoyl group appears to be the narcotizing radical. Cocaine and eucaine resemble one another structurally in that both possess the grouping $\text{C}_6\text{H}_5\text{COO} - \text{CH}_2\text{CH}_2\text{-CH}_2\text{-NH}_2$, procaine and butyn possess the grouping $\text{NH}_2\text{C}_6\text{H}_4\cdot\text{COO}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{NH}_2$, and stovain and alpyin possess the grouping $\text{C}_6\text{H}_5\text{COO}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{NH}_2$. These compounds are all alkaline esters of aromatic acids and derivatives of benzyl alcohol ($\text{C}_6\text{H}_5\text{CH}_2\text{-OH}$) which has local anesthetic properties.
A comparison of the toxicity of the more popular local anesthetic agents including cocaine is given in the following graph (Fig. I.) by Drs. Hooper and Becker. (23).

<table>
<thead>
<tr>
<th></th>
<th>Butyn</th>
<th>Alypin</th>
<th>Cocaine</th>
<th>Tropocaine</th>
<th>Apothesine</th>
<th>Beta Eucaine</th>
<th>Stovain</th>
<th>Novocain</th>
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<td>mgms</td>
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<td>10</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
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<td>70</td>
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**Fig. I. Local anesthesia toxicity (23)**

Novocain (Procain), as seen from this comparison (Fig. I.), is the least toxic substance known for local anesthesia. Watery solutions up to ten percent have little irritating or toxic effect upon the tissues. It may be sterilized and resterilized by boiling, without marked effect upon its anesthetic properties. Cocaine decomposes when heated. In an adult over 500 c.c. of a one percent solution may be injected subcutaneously without evident toxic effect. For local infiltration anesthesia ½, 1 or 2 percent isotonic solutions in saline or Ringer's solution are used and are not toxic. The addition of epinephrin in the strength of 1:60,000 to 1:100,000 or 3 to 5 minims to each 30 c.c. doubles the intensity and quadruples the duration of anesthesia. Novocaine is also used on denuded surfaces or serous surfaces but not upon mucous surfaces for it is a feeble and uneffective surface anesthesia as compared with cocaine or butyn.
Today, local anesthesia is used very extensively not only for minor surgery but also in many major operations so that local anesthesia is a rival for inhalation anesthesia. The technique of local infiltration, field block and nerve root block has been well worked out and is an important addition to modern anesthetic methods. The most important advancement in local anesthesia is the spinal nerve root block or spinal anesthesia. Spinal anesthesia employs all the principles of local anesthesia but on a larger scale.

Spinal anesthesia, lumbar anesthesia, rachianesthesia or more accurately rhizanesthesia may be briefly defined as an extensive regional nerve block without loss of consciousness, affected by injecting an anesthetic solution into the subarachnoid space of the spinal canal. In no other way can so extensive an analgesia be produced with so small an amount of drug.

The first to attempt spinal anesthesia was Corning (24) of New York in 1885. The first anesthesia was effected by injecting a solution of cocaine between the spines of the vertebra. Quincke (6) did the first spinal puncture. Following this Bier (6) of Germany purposely produced anesthesia on himself and six assistants by the use of 1 c.c. of a two percent solution of cocaine injected into the spinal canal. After Bier's experiments many surgeons attempted to use this new type of anesthesia but many fatalities resulted due to the indiscriminate use of cocaine and improper technique of injection so that the method was soon discarded.

Spinal anesthesia was again used following the discovery of Novocain in 1904 which is seven to ten times less toxic (Fig. I.) than cocaine. There was a sudden impetus to the use of spinal anesthesia at this time. Many surgeons used this type of anesthe-
sia on every patient without much regard for technique of admin-
istration or dosage. Again many fatalities resulted so that the
method was discarded. There was another awakening just prior to
the world war, which interest waned. Recently, within the last
ten or twelve years spinal anesthesia has come to stay. It has
become a topic for scientific discussion and the subject has taken
a conspicuous position in the minds of hundreds of surgeons. The
subject has been debated pro and con in hospital staff rooms and
its advocates are as rapid in its favor as its opponents are the
reverse. There have been some surgeons who have used spinal anes-
thesia routinely since 1904 with good results, among these surgeons
are Maccock (14) (16) and Boyd. Each of these surgeons have pre-
formed over 20,000 operations under this method with few fatalities.

When a local anesthetic agent is injected into the cavity of
the spinal arachnoid it affects the nerve roots with which it comes
in contact by narcotizing them. The most marked effect is upon
the sensory roots in the immediate region of injection (22). How-
ever, the anterior motor roots and sympathetic fibers are also af-
fected.

The posterior roots are affected by the loss of pain, tactile,
temperature and muscle sense in the involved segments. The widest
and most intense effect is upon the pain or protopathic sense.
The anterior roots are affected by loss of voluntary movement, par-
alysis, muscular relaxation, and absence of superficial and deep
reflexes. The sympathetic fibers (white rami communicantes run-
ing in the anterior roots) are affected by causing a vaso motor
palsy, varying with the number of rami affected. When all the
white rami from the second dorsal to the second lumbar are blocked
there is complete vasomotor relaxation of the entire body. If
the head and shoulders are raised with complete vasomotor palsy,
the patient becomes pulseless and unconscious from cerebral anemia.
(25).

Contractions of the heart become slower and weaker from the
interruption of cardio-augmentor nerves, diminished vis a tergo
and unopposed action of the inhibiting vagus. The corresponding
drop in blood pressure may vary from 0 to 70 mm. of mercury depend-
ing on the height of anesthesia. (26).

Respirations are quiet, slow, of small amplitude and largely
diaphragmatic from paralysis of the abdominal and thoracic muscles.
(26).

There is an increase in peristalsis, strong gastric and intes-
tinal contractions occur with relaxation and incontinence of the
anal sphincters. This effect is due to the block of the inhibitor
nerves while peristaltic stimulation continues unopposed thru the
vagi. Transient nausea and vomiting are produced from 5 to 15
minutes following the injection of the anesthesia and corresponds
with the maximal drop in blood pressure. (25).

Urinary secretion is temporarily reduced from the fall in
blood pressure. The skin is dry, warm and in marked fall in blood
pressure, pallid but not cyanotic. The uterus in labor continues
active forcible contractions and hemorrhage during labor and abor-
tion is reduced.

The intensity and duration of analgesia varies directly with
the dose and concentration in the spinal fluid. (14) The nerve
roots first reached by the anesthesia are affected most intensely
and for the longest time. Therefore the injection should be opposite
the nerve-roots supplying the operative field.

The height of analgesia from a given dose of a local anesthetic injected through a definite interspace will vary according to the specific gravity of the solution used, the force of the injection, the amount of fluid withdrawn, and the decompression of the dura. (27) (14) A heavy 10 per cent solution of Novocain injected through the fourth lumbar interspace rarely induces anesthesia above the lumbar segments. (27). By dilution, so that a 4 per cent solution is injected the mid lumbar region is reached. By decreasing the specific gravity below that of cerebro spinal fluid, as when 10 per cent alcohol is added, the area of anesthesia is higher. Forcible injection, the bulk of injection, and the amount of fluid previously withdrawn greatly influence the height of anesthesia.

There has been much discussion and disagreement concerning the diffusibility of spinal anesthetic agents upwards in the spinal canal and causing death thru affecting the vital centers. Gastron Labat (6) states: "The assumption that the anesthetic agent diffused to the brain and is the cause of respiratory failure is based on neither chemical or laboratory findings but is due to cerebral anemia due to vaso motor paralysis. Circulation of the spinal fluid from cranial cavity to the spine and out to the venous system at nearly all levels is also a factor against upward diffusion." Pitkin (27) has also proven that solutions remain at the site of injection by taping the spinal canal with needles at various intervals afterwards. Pitkin (27) also found that unless an excessive dose has been used, the drug becomes fixed, preventing further diffusion in the first ten minutes following injection.
Death, in spinal anesthesia, is caused from respiratory and cardiac collapse. Spinal anesthesia produces respiratory failure in two ways, thru a paralysis of the motor nerves of respiration or thru a paralysis of the vaso motor nerves of the splanchnic area which results in a loss of blood pressure followed by a myocardial and medullary ischemia (25) (26).

Most of the surgeons who have used spinal anesthesia agree that novocain crystals, dissolved in spinal fluid is the safest agent to use. It is agreed that ephedrine and epinephrine should be given to counteract the alarming drop in blood pressure. Post operative headaches, paralysis and other complications appear to be due to improper technique in introducing the spinal anesthetic agent or to improper management of the patient while under the influence of the agent. The indications and contra indications for spinal anesthesia is greatly disputed.

Pitkin (27) states that spinal anesthesia is adapted to all classes of cases. Be the blood pressure high or low, the patient old or young, fat or thin, cardiac, nephritic, alcoholic or addict. This statement concerns anesthesia for operations below the es- stal margin. Many other surgeons do not agree that spinal anesthesia fits all cases and are of the opinion that there are rather definite indications and contra indications for its use.

Contraindications are; hypotension, a systolic pressure under 100, extreme shock, hemorrhage with exsanguination, obesity, myocardial degeneration, aortitis and obstructive coronary disease, asthenis starvation, exhaustion, advanced senility extreme cachexia, advanced sepsis with cyanosis or a moribund state. Other contra-
indications are a lack of trained assistants to watch the patient. A critical or unfavorable community or a neurotic patient who may attribute to the unconventional anesthetic any real or imagined symptoms that may develop later. Definite contraindications are inflammatory processes and infection at the site of injection, and involvement of the cerebro spinal system by tumor, syphilis or meningitis.

Advantages for spinal anesthesia are; 1. It removes the dread so many patients have of going to sleep. 2. Freedom from post operative nausea and vomiting and strain on the incision. 3. Better relaxation of the abdominal wall and the elimination of the tendency of the bowels to protrude especially in emergency abdominal work. 4. It is the anesthesia par excellence for patients with pulmonary tuberculosis and in intestinal obstruction. 5. Minimal general toxemia with absence of respiratory, hepatic, or renal irritation or stimulation. 6. Relaxation of sphincters, desirable in rectal operations. 7. Fall in blood-pressure reducing hemorrhage and protective in arteriosclerosis, aneurysm, and certain other cardio-vascular diseases. 8. It is not a lipoid solvent and is therefore desirable to use in the presence of auricular clot, as in mitral stenosis. 9. There is no pre or post operative excitement or delirium and progressive shock of operation is antidated by rise in blood-pressure as the anesthesia passes off.
Spinal anesthesia has come to stay and no doubt has a very useful place in anesthetic methods used today. Spinal anesthesia is being made more safe as its actions and results are being better understood. However, spinal anesthesia does not offer a safe method for general use on all patients. It has its limitations and requires selection of cases and careful, skilled technique of administration and care. Once the drug is injected into the spinal canal it cannot be recalled and nothing can prevent the drug from acting. Babcock (14) summarizes spinal anesthesia in a statement; "It is a very personal method strongly appealing to the temperament of certain operators equally unadopted to others." This statement may apply to other agents as well.

Some twenty years following the introduction of general anesthetic agents the attention of investigators of anesthesia was drawn by the introduction of Chloral hydrate by L'Heritier (28). It was shown that chloral hydrate produced effects similar to other anesthetic agents in that it produced unconsciousness and sleep. As a result of this attention many valuable drugs have been added to therapeutics as soporifics or narcotics. Important among these new drugs are the derivatives of barbituric acid which are used to a great extent in modern anesthesia.

"BARBITURATES". There have been many derivatives of barbituric acid produced and used with varying success. The effectiveness of the derivative seems to be increased with the length and complexity of the side chain and with the addition of the halogens. A comparison of these derivatives is best given in a presentation of the structural formula of these compounds along with the derivation of barbituric acid.
Urea

Malonyl

Barbituric acid. (Malonyl urea).

Veronal (Diethyl Malonyl Urea).

Amytal (Iso amyl ethyl Malonyl Urea).

Alional (Iso. Allyl propyl Malonyl Urea).

Ipral (Calcium ethyl iso propyl malonyl urea).

Neonal (N. Butyl ethyl malonyl urea)

Luminal (Phenyl ethyl malonyl urea).
The most popular barbiturate used today is amytal and its soluble salt sodium amytal. Pronacton is also used with success. To Zerfor and Mc Callum (13) of Indianapolis is generally given the credit for popularizing sodium amytal. They in turn give credit to Fredet and Perlis as the first to induce general anesthesia in man with compounds of the barbituric acid series. The preparation which they used was somnifene (di-ethyl allyl barbiturate).

Sodium Amytal may be used in doses of 3 to 9 grains per mouth as a sedative or from 6 to 35 grains given intravenously for anesthesia. Sodium amytal given intravenously is given in the form of a ten per cent solution in distilled water. The solution is injected at a rate not to exceed 1 c.c. per minute, preferably slower.(29)

After about 3 c.c. of sodium amytal solution has been given intravenously usually the patient will drop off to sleep. Induction of anesthesia is very pleasant with no excitement stage. Usually unconsciousness will come on suddenly after the injection of from 7 to 9 c.c. of the amytal solution. Rarely more than 15 c.c. is required for surgical anesthesia (29) If larger doses 15-22 c.c. are given relaxation is more complete but the patient has a very long period of unconsciousness post-operatively.
In anesthesia with sodium amytal the sleep at first is quiet and peaceful but later changes to typical snoring. The pupils are normal or slightly contracted. The gag reflex is present unless very large doses are given. The knee jerks are absent. Respirations are slightly shallower and increased in rate. Blood pressure in a normal case usually drops 20 to 30 mm. of mercury during injection and rises to normal within 30 minutes. The maximum anesthesia is obtained in about 15 minutes and is frequently maintained for at least two or three hours. The length of time required to return to consciousness varies with the dose given. With from 7 - 12 grains the patient can usually be aroused an hour or so following operation. With from 15 to 22 grains, he sleeps 72 hours (29) with large doses before consciousness returns. With the return to consciousness there is no nausea or vomiting. There may be considerable restlessness which necessitates the constant attention of a nurse until full consciousness is regained.

The advantages of this type of anesthesia are:

1. The ease of its administration from the patient's point of view; it is pleasant and there is no excitation period.

2. There is no post operative vomiting.

3. It produces no irritation of the respiratory passages and no kidney irritation.

4. It greatly facilitates the administration of nitrous oxide, ethylene and ether, if these are necessary, without added risk to the patient, and the amount of these anesthetics is greatly reduced.

5. Sodium amytal - greatly lessens the toxicity of the local anesthetics, procaine and cocaine (30) It is a valuable adjunct.
in preparing patients for spinal anesthesia and local infiltrations.

The disadvantages of this anesthesia are:

1. A hyperesthetic condition of the skin may develop in some cases, which is not even wholly obliterated with the spinal anesthesia.

2. The long period of time required for the patient to become conscious. During this recovery from the anesthesia the patient is often restless and irresponsive and requires constant, attentive nursing to prevent bodily injury or injury to the operative site.

3. Inability of the patient to properly raise mucus.

4. There is an objectionable fall in blood pressure which may persist for some time.

5. It is very difficult to gauge the proper dose. There is a greater variation in the amount of sodium amytal required to produce anesthesia than in inhalation anesthesia.

6. Once the drug is injected there is no effective way to stop or neutralize any overdose. Ephedrine in 3/8 grain. and caffeine sodium benzoate in doses of 7.5 to 10 grains with the use of carbon dioxide and oxygen may overcome an overdose.

John S Lundy (31) states that barbiturates serve best when used as preliminary medication with the idea of reducing the amount of anesthetic which will then be required in order to produce anesthesia, relaxation and quiet respirations without anoxemia. This appears to be the general opinion concerning the use of barbiturates. That it should not be used as a general anesthetic, because when it is increased to these limits, death has taken place in several instances due to respiratory failure (32). (Philip D. Amadon).

Sodium Amytal and other derivatives of barbituric acid are best
used as basal anesthetic agents. It is adapted to individuals who are too excitable to be prepared with morphine-atropine medication. It also finds a great use in obstetrics where a sedative dose can be given to carry the patient along with less pain and discomfort.

The barbiturates have the property of causing obliteration of the memory to painful stimuli and in this way eliminates much of the psychic shock of surgical procedures.

One of the most recent, useful anesthetic agents produced is avertin. It is one of the most promising drugs of the newer anesthetic agents. Yet, like the barbiturates avertin will produce surgical anesthesia but is used principally as a basal anesthetic.

"AVERTIN", or tribrom-ethanol, was first used in Germany, as an anesthetic by Eichholtz, in 1927. Since that time, avertin has been used in many thousands of cases in Germany and in other countries.

Tribrom-ethanol is a white crystalline substance, soluble in water at 104°F. (40°C). up to 3.5 per cent. It must be protected from light and air. It is made into solution in amylene hydrate, 1 c.c. of which contains 1 gm. of the drug. The amylene hydrate dissolves tribrom-ethanol in high concentration, and is itself readily soluble in water. This product is called "Avertin".

There is danger of the avertin fluid being decomposed especially by heating the solution to over 104°F. when it decomposes into debromacetaldehyde and hydrobromic acid, which are highly irritating to the bowel. This may be avoided by testing with a solution of Congo red. The color will turn to blue or violet of the solution has decomposed.
Avertin should be administered in a 3 per cent solution as a retention enema, the dose depending upon the age, weight and general health of the patient. Children tolerate the drug better than adults and the aged less than those in middle life. According to weight, the dose varies from 70 to 110 mgms. per kilo (35). The poor risks, the feeble and aged need a much smaller dose than the healthy young adult.

Within a few minutes after injection of the drug the patient usually goes into a profound sleep, from which he cannot be aroused. There is no excitement while under the influence of avertn. Within fifteen minutes muscular action ceases and the muscles of the jaw and tongue relax. At this point, the anesthetist inserts an airway to avoid respiratory difficulty from swallowing the tongue. In large doses avertn, causes a slowing of the respirations and a drop in blood pressure from 5 to 10 mm. of mercury.

The duration of anesthesia varies. In a series of 500 cases O. Sohildbach (35) states that anesthesia usually lasts from 2-3 hours and that the sleep is deepest about 20 minutes after induction and maintains itself at this level for about one hour. Waking occurs in the same uneventful manner as the induction.

It is estimated that 80 per cent of the drug is absorbed in the first twenty minutes, and 95 per cent in two hours (33). Excretion is accomplished by the kidneys after detoxication in the liver by a combination with glycuronic acid. (33).

The general opinion is that avertn should be used as a basal anesthesia only and not to produce surgical anesthesia.

Its disadvantages are:

1. Its wide variations in susceptibility.

2. Withdrawal is impractical and anesthesia cannot be lightened.
3. There is danger of the avertin fluid being decomposed especially by heating the solution to over 104 degrees Fahrenheit.

4. There is danger of respiratory and circulatory depression.

Its advantages are:

1. Ease of which the anesthesia can be given and the absence of an excitement stage.

2. Better relaxation is possible with the lighter anesthetics.

3. There is a moderately long post operative sleep and reduction of postanesthetic nausea and vomiting.

Avertin is contraindicated in diseases of the kidneys, liver or rectum, serious hypertension cachexia and shock. (35)

Avertin is indicated especially for nervous, excitable adults and children, as well as mental patients. Its greatest sphere of usefulness is in operations about the head and neck, where great care must be taken that the blood does not run down the trachea and cause asphyxia. It is also particularly indicated in operations on the brain or spinal cord (31) In obstetrics and gynecology it has a distinct value (31).

This discussion includes practically all of the popular, useful, anesthetic agents in use today as given in the current literature. There are other agents and methods used but they have not merited popular use. All the anesthetic agents named are useful in their place. They all have their objections and advantages.

The advantages and disadvantages of the anesthetic agents and methods are realized by the leaders of medicine and surgery today. They realize the seriousness of carrying a living being to that level of insensibility which, in many respects, simulates death. They also recognize that the anesthesia is, in most instances as
important as the operation. The surgeon is no longer willing to have their patients merely rendered insensible to pain by means of ether in order that he may operate with confidence and freedom. They insist upon choosing the agent or combination of agents and method best suited to the individual surgical case, thus preventing accidents of anesthesia and rendering the patients recovery and convalescence as uneventful as possible.

"CONCLUSIONS".

1. General anesthesia was born of pure empiricism.

2. Crawford W. Long was the first to produce and use a general anesthesia (1842).

3. Wells, Jackson, Merton and Simpson were early pioneers in the use of anesthesia and deserve credit for helping to introduce and popularize anesthesia.

4. Ether, despite its many objections, is yet the most popular anesthetic agent used and probably the safest considering the use of general anesthetic agents today.

"The harmlessness of an anesthetic agent is considered to stand in direct ratio to its ease of control rendering the patient unconscious to operative pain and to the ability to regulate or stop its action at will, depending upon the patient's condition. The only anesthetic agent so far known which possesses such properties to an appreciable extent is the inhalation anesthetic "ether".

5. There are many new methods introduced for the administration of ether, each desirable for particular operations, but no one method adapted for routine use in all surgical cases.
6. Chloroform anesthesia is pleasant and unirritating but is toxic and has a high mortality rate when compared with most of the other drugs. Chloroform is suitable only when better methods are unavailable or cannot be used.

7. Brief Nitrous oxide anesthesia is the safest anesthesia. It is used to advantage in minor surgery and dentistry.

8. Nitrous Oxide-Oxygen anesthesia is superficial and is used to supplement other anesthetic agents such as the barbiturates, avertin, local and spinal anesthesia.

9. Ethylene Oxygen is a desirable, safe anesthesia but is not used as much as it might be due to its inflammable property. The hazards of ethylene anesthesia may be greatly eliminated by proper precautions and is more desirable for anesthesia than nitrous oxide in all fields of use.

10. Ethyl Chloride as an inhalation anesthesia should not be used. Its usefulness remains as a local anesthetic agent.

11. Local anesthesia provides a method whereby many operations may be done without subjecting the patient to the hazards of a general anesthetic agent.

12. Novocain is the least toxic of all local anesthetic agents. Yet, it does not displace all the other local anesthetic agents.

13. Spinal anesthesia is becoming more popular and safer as its action is better understood. Its use requires special technique and care. The high mortality is due to its indiscriminate use and lack of selection of cases. Spinal anesthesia is dangerous to use above the diaphragm.

14. The barbiturates should not be given with the idea of producing surgical anesthesia. They are best used as premedication for
other anesthetic agents such as nitrous oxide, ethylene, ether and local anesthesia.

15. Avertin should be used as a basal anesthetic.
Avertin is used with considerable success in neuro surgery and in plastic surgery about the head.

16. Anesthetic agents should be given by a trained anesthetist who is thoroughly familiar with the action of the various agents.

17. The popularity and use of the various modern anesthetic agents is best presented by noting the methods and the frequency in which the various agents are used in some of the hospitals and clinics today.
The records of the University Hospital and The Mayo Clinic are given as representative.
Table I.

Agents, combination of agents, and methods used in anesthesia, in the Mayo Clinic in recent years. (36). \textit{Percent of cases.}

<table>
<thead>
<tr>
<th>Agent of Method</th>
<th>1930</th>
<th>1929</th>
<th>1928</th>
<th>1927</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local Anesthetic agents (spinal included)</td>
<td>37.2</td>
<td>36.2</td>
<td>40.36</td>
<td>40.2</td>
</tr>
<tr>
<td>Local and Ether (spinal included)</td>
<td>0.11</td>
<td>0.18</td>
<td>0.26</td>
<td>0.3</td>
</tr>
<tr>
<td>Local and gases (spinal included)</td>
<td>10.6</td>
<td>8.0</td>
<td>9.96</td>
<td>11.3</td>
</tr>
<tr>
<td>Spinal (used alone)</td>
<td>9.3</td>
<td>4.59</td>
<td>1.19</td>
<td>0.4</td>
</tr>
<tr>
<td>Ether (used alone)</td>
<td>7.09</td>
<td>15.2</td>
<td>16.75</td>
<td>19.6</td>
</tr>
<tr>
<td>Gases (with or without ether)</td>
<td>30.6</td>
<td>31.0</td>
<td>30.13</td>
<td>26.9</td>
</tr>
<tr>
<td>Ethyl Chloride by Inhalation</td>
<td>0.01</td>
<td>0.27</td>
<td>0.26</td>
<td>0.08</td>
</tr>
<tr>
<td>O1-Ether Colonic</td>
<td>0.005</td>
<td>0.57</td>
<td>0.58</td>
<td>0.6</td>
</tr>
<tr>
<td>Chloroform</td>
<td></td>
<td></td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Barbiturates</td>
<td>0.11</td>
<td>1.27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tribromethyl alcohol</td>
<td>0.091</td>
<td>0.009</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table II.

Special Anesthetic Agents and Methods used in The Mayo Clinic in 1930, 1929 (36)

<table>
<thead>
<tr>
<th>Agent</th>
<th>1930 number</th>
<th>1929 number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional block</td>
<td>4740</td>
<td>3213</td>
</tr>
<tr>
<td>Barbiturates (intravenously)</td>
<td>505</td>
<td>617</td>
</tr>
<tr>
<td>Barbiturates (by rectum)</td>
<td>23</td>
<td>20</td>
</tr>
<tr>
<td>Tribromethyl Alcohol</td>
<td>47</td>
<td>14</td>
</tr>
<tr>
<td>Tribromethyl alcohol and Barbiturates</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Intratracheal Anesthesia</td>
<td>300</td>
<td>120</td>
</tr>
<tr>
<td>Intrapharyngeal anesthesia</td>
<td>45</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>5662</td>
<td>4002</td>
</tr>
</tbody>
</table>
Table III.

Agents of Special Interest used in anesthesia.

<table>
<thead>
<tr>
<th>Agent</th>
<th>1930</th>
<th>1929</th>
<th>1928</th>
<th>1927</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local, including Spinal</td>
<td>58.4</td>
<td>49.9</td>
<td>51.6</td>
<td>52.2</td>
</tr>
<tr>
<td>Ether</td>
<td>37.6</td>
<td>43.6</td>
<td>44.6</td>
<td>45.9</td>
</tr>
<tr>
<td>Ethylene</td>
<td>26.3</td>
<td>27.2</td>
<td>30.9</td>
<td>33.5</td>
</tr>
<tr>
<td>Nitrous Oxide</td>
<td>37.3</td>
<td>34.0</td>
<td>27.9</td>
<td>18.9</td>
</tr>
<tr>
<td>Carbon Dioxide</td>
<td>43.7</td>
<td>39.4</td>
<td>32.5</td>
<td>25.0</td>
</tr>
<tr>
<td>Ethyl Chloride</td>
<td>0.15</td>
<td>0.71</td>
<td>0.73</td>
<td>0.34</td>
</tr>
<tr>
<td>Acetylene</td>
<td>0.06</td>
<td>0.22</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Barbiturates</td>
<td>2.71</td>
<td>2.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tribromethyl Alcohol</td>
<td>0.23</td>
<td>0.06</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table IV.

Agents used in The University Hospital

<table>
<thead>
<tr>
<th>Agents of Method</th>
<th>1931</th>
<th>1929</th>
<th>1928</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ether</td>
<td>540</td>
<td>822</td>
<td>1093</td>
</tr>
<tr>
<td>Gas</td>
<td>154</td>
<td>125</td>
<td>115</td>
</tr>
<tr>
<td>Condal</td>
<td>56</td>
<td>18</td>
<td>35</td>
</tr>
<tr>
<td>Sacral</td>
<td>18</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>Spinal</td>
<td>386</td>
<td>118</td>
<td>1</td>
</tr>
<tr>
<td>Rectal</td>
<td>16</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Local</td>
<td>700</td>
<td>666</td>
<td>469</td>
</tr>
<tr>
<td>Chloroform</td>
<td>11</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Ethyl Chloride</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Records of anesthesia beyond 1928 are not complete so that they may be presented. However, the anesthetic agents and methods for various months during the year could be obtained and are given.

Table V.

<table>
<thead>
<tr>
<th>Agent of Method</th>
<th>February 1925</th>
<th>February 1920</th>
</tr>
</thead>
<tbody>
<tr>
<td>General (Ether)</td>
<td>90</td>
<td>94</td>
</tr>
<tr>
<td>Local</td>
<td>47</td>
<td>15</td>
</tr>
<tr>
<td>Candal</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Gas</td>
<td>7</td>
<td>0</td>
</tr>
</tbody>
</table>

In the way of summary it is seen that man has done much towards the conquest of pain in recent years but there is much left to be done. The physiological action of anesthetic agents is not well understood. A more thorough knowledge of this action would lead to the production of safer agents and methods. The anesthetic agent effects the cells in the central nervous system in such a way so that conduction and reception is impaired or done away with. This action is reversible, if not death ensues.

Pain, at one and the same time, is man's most kindly friend and his most malign enemy. Pain is our best friend, because it warns us of disease; and takes us to the physician for relief. Pain is our basest enemy, because, if unassuaged, it plunges us into the gloomiest depths, even into dissolution and death. High or low, rich or poor, strong or weak, unmitigated pain levels us all, and its control would confer on mankind the most euphrosyne joy.
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