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THE USE OF THE BARBITAL COMPOUNDS
IN PRODUCING ANALGESIA AND AMNESIA IN LABOR

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The Lord God said unto Eve, "I will greatly multiply thy sorrow and thy conception; in sorrow thou shalt bring forth children." Genesis 3:16

Many a God-fearing man has held this to mean that any attempt to ease the suffering of the child-bearing mother would be a direct violation of the Lord's decree. Even though the interpretation of this phrase has formed a great barrier to the advancement of the practice of relieving labor pains, attempts to achieve this beneficent goal have been made at various times throughout the ages. Interpretation of ancient Egyptian hieroglyphics reveals that crude methods were employed in striving to attain such an end. During the Renaissance it was thought that by brewing certain drugs and allowing the vapors to permeate the air, relief was obtained, even if largely through the suggestability of the patient.

In more recent times (1847) Sir James Young Simpson of Edinburgh first used an anesthetic for this purpose. During the early years, ether was employed in obstetrics both as an analgetic and anesthetic.

In 1880, Klekowitsch of St. Petersburg, and in 1881, Winchel of Dresden first used nitrous oxide in labor. Somewhat later, Webster and Lynch (111) and others popularized the use of nitrous oxide anesthesia and analgesia in American obstetrics.

At the turn of the nineteenth century, Kroenig, Gauss (45), and Steinbuchel (113), popularized the morphine-scopolamine "twilight sleep".

The ether-oil rectal technic, now known as the Gwathmey method, followed the experimental work in 1913 of George B. Wallace of the then New York University and Bellevue Medical College. Davis (29) and Gwathmey (50, 51) applied the results of Wallace's work to clinical practice in the Lying-In Hospital of New York, and for the next few years this became a most popular method of obstetrical analgesia in this country.

In 1904, Fischer and Dilthey discovered barbituric acid and compounded some early derivatives. It was several years later, however, before these compounds were first used in the obstetrical field. During 1921-1923 Bardet and v. Cleisz (19) developed the clinical use of Somnifen (diethyl-barbituric acid and allyl-isopropyl barbituric acid) in obstetrics in France. I.C. Hirst (14) and others were the first clinicians who thoughtfully studied the actions of the barbiturates in obstetrics in this country. They worked with

sodium amytal and reported their results in 30 cases in 1929. Vogt and Kautz (62) also reported on the obstetrical use of pernocton in 1929. Robbins et al (92) used sodium amytal intravenously and reported favorable results in 100 cases in 1929. Moorehead and Mussey (82) were probably the first to use sodium amytal orally for this purpose.

With the advent of anesthesia and analgesia in labor, there has raged a continual verbal warfare between the advocates for such alleviation and their adversaries, who oppose such practice in general. Furthermore, as the number and variety of drugs and methods have increased, each individual drug and method has gained its champion as well as its adversary, until the literature is overflowing with pro and con discussion.

At present, every patient who comes to the obstetrician for his services insists upon being reassured that her delivery will be painless. She wishes to go to sleep with the first pain and wake with the baby in her arms, and she is sure from reading the various accounts in current literature, that this is not only possible, but it is her rightful privilege.

Particularly has this been true since the introduction of the barbituric acid derivatives. Immature

intimations as to the success of these products have been avidly seized upon by the public. Several of the current women's magazines make each new obstetric analgesia the object of the most fervent discussion, proclaiming it a panacea for women's suffering. After reading such literature the patient feels that the physician who is not able to guarantee such alleviation is not up to date in his views and practice. Thus the physician, in order to maintain his practice, must adopt some such method. The manner of sensationalizing which started thirty years ago in the propaganda of "twilight sleep", and which repeated itself in the case of Gwathmey anesthesia and pernocton, is now busied with the newer forms, amytal, nembutal, and every other new barbiturate that is manufactured.

Since this paper deals chiefly with the use of the barbituric acid derivatives, a brief consideration of the pharmacology of these drugs is in order.

Much as regards action, use, toxicity, excretion, and dosage is still to be learned about these compounds, but as their applicability is so widespread, extensive research in this field is continually in progress.

Of the ever increasing number of these derivatives, we may say that in general the action of all is essentially similar. The chief differences lie in the variation in duration of action and variation in toxicity, both of which are largely dependent on the

rate of excretion and/or destruction of the drug in the body (17). Thus they differ in dosage and somewhat in breadth of therapeutic zone ($\frac{\text{fatal dose}}{\text{therapeutic dose}}$) (101).

The barbitol compounds are chiefly sedative and hypnotic in action, although slightly analgesic (23). Localization of action is chiefly in the central nervous system, Keezer and Keezer (23) believing that small doses affect the diencephalon. Koppany (23) reports that large doses are found to be equally concentrated in every portion of the central nervous system. At any rate, the threshold for pain stimuli is increased, but obstetrical patients show an unconscious registration to painful stimuli.

In small doses, the barbiturates produce a natural depression of respirations, in that they cause sleep. In large doses, the respiratory center is directly depressed. The basal metabolic rate is not significantly changed, although it may be slightly lowered because body activity is reduced in sleep. Temperature falls slightly. With rapid injection there is a temporary fall in blood pressure because of vasodilatation and slight direct cardiac effect. There is little change in circulation or pulse. Variation of opinion exists regarding the blood sugar level after administration of barbiturates. Coagulation time of blood is shortened in cats and pigeons. Ordinary doses have no signi-

ficant effect on the liver. Depression of smooth muscle activity occurs but the uterus is not affected even by full analgetic dosage, and uterine response to pituitary remains normal (101). Motility of the gastro-intestinal tract is reduced, resulting in a decrease of nausea and vomiting. The calcium content in the blood is lessened due to depression of respirations and increase in carbon-dioxide tension. Decreased urinary output results from the fall in blood pressure.

The response to the barbiturates is highly variable in different individuals, hence each case must be considered by itself when dosages are prescribed, and a patient should be tested early in her pregnancy for a possible idiosyncrasy. Body weight must be considered, but not that due to excess fat. Temperament is also a factor, the thin nervous woman needing larger doses than the opposite type of person. A fear of impending events in an expectant mother will necessitate a larger dose. Then, of course, physical condition may limit dosage; the toxic patient with liver damage will have a reduced power of elimination for the drug. Hyperthyroids will need larger amounts (17).

This variable response to the barbiturates is one of the disadvantages in their use. Often, also, the hypnotic effect is preceded by considerable excitement, inebriation, and even delirium, hence the patient must

be attended at all times. There may also be a skin reaction, which may last two or three days.

Acute poisoning is fairly common, sometimes from over-susceptibility, but generally from overdosage (e.g., in the therapeutic use of the larger doses in connection with anesthesia especially by vein.) Acute poisoning is manifested by coma, sometimes with preceding excitement; marked drop in blood pressure; depression or even paralysis of respirations; fall in temperature; greatly diminished reflexes; possibly asphyxial convulsions and mydriasis; and lung disorders--atalectasis, pulmonary edema, or pneumonia may result. Treatment of this poisoning consists of evacuation of the drug by stomach tube if possible (emetics are less effective because of the depression of the medullary centers); keeping the patient warm; administration of caffeine or strychnine or use of artificial respirations. In severe cases picrotoxin has proved effective (dosage 3 mgm. intravenously and repeated in thirty minutes in smaller doses).

Excretion of the barbiturates takes place almost exclusively in the urine, although pentobarbital sodium is destroyed chiefly in the liver. The total amount recovered from urine and the speed of excretion vary

greatly, and these differences are largely responsible for the varying duration of action of the individual barbiturates. Quantitative excretion in urine of these drugs is as follows: barbital 75%; dial 30%; phenobarbital 10-40%, pernocton 5-30%; and a very small amount of pentobarbital sodium. Amytal and neonal cannot be recovered from urine, nor does the urine contain any depressing decomposition products. Barbital is excreted slowly, and traces have been found after nine days; phenobarbital is also slowly excreted; but pentobarbital and pernocton are excreted very rapidly, hence the shorter duration of action.

Pentobarbital sodium is probably considered the most desirable of the barbiturates for obstetrical use because it has 5.5 times the efficiency of barbital, 2.7 times the safety ($\frac{\text{efficiency}}{\text{toxicity}}$), and $\frac{1}{9}$ the duration of action, although it is 2 times as toxic (14).

Following is a table from Sollman (101) in which nine of the more commonly used barbital compounds are listed in order of increasing toxicity. The column to the right of the list gives the comparative therapeutic breadth ($\frac{\text{fatal dose}}{\text{therapeutic dose}}$) of the compounds; #1 representing the lowest therapeutic breadth, and #9 the greatest. The last column compares the premedication efficiency in relation to nitrous oxide anesthesia;

#1 representing the lowest efficiency, etc. Since many of the methods of obstetrical amnesia rely upon the use of nitrous oxide during the perineal stage, we feel that the last column is of some significance.

Barbital	-----	3	-----	2
Phanadorn	-----	7	-----	6
Nembutal	-----	5	-----	7
Dial	-----	9	-----	8
Phenobarbital	-----	2	-----	4
Amytal	-----	8	-----	3
Pernocton	-----	4	-----	1
Pentobarbital	-----	6	-----	9
Ipral	-----	1	-----	5

Before entering into more specific discussion of the use of these various drugs, let us first consider the condition which we are attempting to ease.

There are three well recognized subdivisions of the pains of labor. The first pains felt by the patient are caused by contraction of the fundal fibers, and these are occasionally severe enough to call for relief. They are of a cramp-like nature and are usually vaguely localized in the lower abdomen. Some of these may be due to the process of thinning out of the lower uterine segment, resulting from fundal contractions. These pains often continue for hours, and occasionally for

days before effective labor begins.

The second type of pains, which appear when effective labor starts, are more pronounced, and are due to effacement and dilatation of the cervix and upper birth canal. These pains are of a distressing nature, and are felt in the back as well as in the lower abdomen, and may continue for hours. By the time they have reached their maximum intensity, the patient's morale is often entirely shattered by the suffering she has undergone. It is at this time that the misery of labor often reaches its climax.

The third type of pains are those derived from the stretching and tearing of the sensitive structures when the presenting part is descending through the lower birth canal. These pains are described by those who have suffered them without anesthesia as a sensation of being torn apart. The supreme anguish comes when the fetal head slips over the perineum (28).

In most clinics, it is the practice to give some type of inhalation anesthesia, such as nitrous oxide, ethylene, and/or ether, during these last stages of agony. Such complementary anesthesia is frequently started just before the patient is draped for delivery (14). However, the methods of analgesia and amnesia to be discussed below are designed to render the patient

oblivious to all pains from the beginning of effective labor until after the final agonies of delivery.

In studying such methods of analgesia and amnesia, it is evident that no routine method is applicable to every individual case (91). It is necessary to know each patient's physical condition and know her psychologically and emotionally. Findley (40) finds that in general, the Nordic type of patient will be suitable for a regime that would be altogether unsatisfactory for the Latin type. The obstetrician, thus knowing his patient, must also know the action of the drugs being used, the mechanism of labor, and the progress each patient is making (56).

Thus, since no routine regime is applicable to each individual patient, it is to be hoped that by study of the numerous methods described in the literature, a fairly accurate conception of the relative advantages, and more particularly, the disadvantages, of those methods can be determined. Then by correlating such conceptions with the characteristics of each separate patient, we may work out the form or forms of analgesia most applicable to one's own circumstances.

In reviewing the literature on the use of the barbital compounds, we find that not only are many different members of this group used, but that they are used in

combination with many other hypnotics and sedatives. Thus considering the various number of barbital compounds used, the various other drugs with which they are combined, the various routes of administration, and the wide variation in dosage, it is readily seen what a diversified number of plans or regimes of treatment are evolved. Each has its champion.

There is little value in discussing in detail each of the regimes. In spite of their apparent dissimilarity most of them can be grouped into a few general types, each of which embraces its general characteristics. Furthermore, it is conceded that most of these methods are good in the hands of the skilled user. It has been stated that the ease or comfort of the parturient is determined to a great extent by the first visit to her obstetrician; i.e., by the state of mind which he is able to leave with her during this first interview. This would tend to show that whatever the method used in obtaining analgesia and amnesia in labor, the success will lie in the skill of the accoucheur and his ability to instill confidence in the patient.

This is not the entire story, however. Over and above the factors just mentioned, there is still considerable actual physical pain, variable in different women. There is no doubt but that certain of these

drugs or drug combinations act more efficiently in either abolishing the pain sensibility, or producing forgetfulness so that this pain is not remembered.

From the various reports in the literature it is difficult to comparatively evaluate these methods because of varying criteria used by different workers. However, in the following pages we shall enumerate what we feel to be the important specifications of an ideal method of producing analgesia and amnesia. Then we shall describe in some detail a few of the methods most widely used at present time, and try to evaluate them according to our ideal standard. Finally we shall present a chart of several groups of cases, attempting to compare results in regard to some of the important effects.

Of the numerous specifications stated for an ideal regime of analgesia and amnesia, most of them can be grouped in the following:

1. The degree of amnesia and analgesia must be sufficient.
2. It must be harmless to the mother, and not produce complications.
3. It must be harmless to the baby.
4. It must not delay labor.?
5. It must not increase operative frequency?

6. It must be simple, and reliable in the hands of the general practitioner.

Now to examine a few of the methods.

In reviewing the recent literature, it is found that pentobarbital sodium, or nembutal, has the most advocates, and the majority of these men prefer to combine it with some other drug, such as scopolamine or paraldehyde. Hence, in our first regime we shall consider the use of nembutal and scopolamine.

It is known that during labor the action of the digestive system is somewhat inhibited, and that any great amount of food taken just before or after the onset of labor probably acts as a barrier to efficient and rapid absorption of the barbiturate when given by mouth. Thus the patient should be cautioned to eat frequent but small meals when the onset of labor is imminent.

Various obstetricians, using the nembutal-scopolamine regime, differ in opinion as to when the first dose should be administered. Some use as indication the patient's own subjective reaction to pain; some the duration and frequency of contractions (106); some the stage of dilatation of the cervix; and others the fact that the cervix is showing progressive changes in effacement and/or dilatation. Toland and Dugger (106) say

that the drugs must be given as early as possible after labor is definitely established, and that it is a mistake to wait until the woman is suffering violent pain. Randall (56) of the Mayo Clinic agrees with this, stating that the successful use of pentobarbital sodium depends, in a large part, on keeping the analgesia a little ahead of the patient's requirements. If analgesia is started late, or the initial dose is insufficient, it is frequently found that one does not "catch up" with the patient and does not obtain a satisfactory analgesia. Others, (56) however, maintain that giving the drugs early in labor definitely impedes the progress.

There has been some difference of opinion as to the dosage of the barbiturate. Formerly it was thought that to obtain the best amnesia and analgesia, a fairly small initial dosage should be given. Irving (58) and his associates recommended giving an initial dose of 6 grains of nembutal by mouth as soon as labor was established, followed in 45 minutes by 1/150 grain scopolamine hydrobromide subcutaneously (in women under 160 pounds). Supplementary doses of 1-3 grains of nembutal were given at intervals of not less than 3 hours, providing the dosage did not exceed 15 grains. More recent workers (106, 40), claim that a higher initial dose of nembutal ($7\frac{1}{2}$ -9 grains in patient under 160 pounds), with scopolamine given simultaneously, results

in less restlessness and gives a higher percentage of complete amnesia. At any rate, the dosage most commonly used is between $4\frac{1}{2}$ and 9 grains of nembutal, depending on the patient's weight, accompanied by a single dose of scopolamine, ranging from $1/200$ to $1/100$ grains. In a few clinics, the patient is carried entirely on scopolamine, after the initial dose of nembutal. The patient will usually be restless during actual uterine contractions, but the restlessness should subside when contractions are over; restlessness between contractions is the usual indication for additional dosage of nembutal (14, 40, 106).

The patient receiving pentobarbital sodium should be isolated from everyone but an attendant, and should be in a darkened, quiet room. In some clinics the patient is placed in a crib where her activity need not be restricted, for she will be unable to harm herself by falling out of bed (106). Others feel that a low bed, preferably pushed against the wall, is sufficient. In any case, a special attendant, thoroughly familiar with handling such patients, must be on hand constantly. This attendant is a most important part of the regime. She must be instructed not to handle, disturb, or physically restrain the patient unless absolutely necessary. Rectal examinations must be reduced to the

minimum. In keeping the patient on the bed, it has been found advisable for the attendant to block the patient's escape by placing the body in the patient's path, rather than actually restraining her manually. Restraint will cause marked restlessness and struggling on the patient's part, even though sufficient dosage of nembutal has been given.

In this manner, the patient is carried until she is ready to be draped for delivery, at which time many obstetricians wish to start inhalation anesthesia. This latter is continued, in varying degrees by different men, until after the delivery of the baby.

Now to see how well this regime fulfills the ideal requirements.

As regards amnesia and analgesia, this is reported as varying from 60-93% complete amnesia, 7-24% partial amnesia, and 3-10% failures (14). The failures which have been recorded are ascribed to one of the following reasons: (1) insufficient dosage, due to starting the drug too late in the course of labor, or because of poor absorption due to a full stomach; (2) because of pains or fear so severe that there was not enough blood throughout the splanchnic area to carry on normal absorption; (3) because the nervous system was naturally "resistant" to this particular drug.

In regard to the safety of the mother, it must be

admitted that there is frequently a rather high incidence of restlessness and excitement. Montgomery (79) states that in many such cases, aseptic technic is impossible, thus exposing the mother to the possibility of infection. However, there is no record of increased morbidity or mortality as a result of puerperal infection.

Galloway et al (44) in a series of 1,415 cases receiving nembutal and scopolamine, made a special study in regard to maternal and fetal morbidity and mortality. In comparing a large series of cases not receiving the nembutal and scopolamine with the above cases, they show that maternal morbidity, as judged by the standard of the American College of Surgeons, was slightly less in those receiving the drugs.

Of course, most workers are agreed that this method is contraindicated in patients who are poor anesthetic risks; who have acute liver damage or heart disease; or show any pulmonary or upper respiratory pathology (14). The recent work of Montgomery (40) in analyzing the maternal death rate in Philadelphia, gave a very important part to errors in judgment in selection of patients, as well as errors in technic.

In regard to the incidence of cervical lacerations, some believe them to be decreased under this regime, while others say there is no change. It has been sug-

gested by the former that the patient has been allowed to advance well into the second stage of labor without conscious pain, and thus has not had the inherent urge to "push down" before the cervix was completely dilated.

There is also much controversy as to whether post partem hemorrhage is increased, decreased, or remains the same, when this program is used. Those who ardently maintain that hemorrhage is decreased, describe the uterus as a bundle of muscle which must have a period of rest following a contraction, so that the end-products of muscular contraction (i.e., carbon dioxide and lactic acid) may be removed. Therefore, the patient who has received no sedation may "maul" her own uterus by aberrant abdominal muscle contractions, which continually stimulate the uterine musculature, and allow no time for rest. Finally after delivery, the muscle groups are in such a state of fatigue relaxation (14) that they cannot sufficiently retract and contract to produce adequate hemostasis.

The question of post delivery sleep has also been argued pro and con. Some believe that the post-delivery sleep, which varies from 6-12 hours after this delivery, is beneficial to the patient; others believe it detrimental and try to awaken the patient within a few hours after delivery.

Most of the reports indicate that the majority of the infants show no reaction to the drug, but mention an occasional sleepy baby (14). Irving and his associates (58) summarize, "Neither pentobarbital, sodium amytal, scopolamine, rectal ether, nor paraldehyde, could be held responsible for the symptoms of asphyxia that were encountered in some of the newborn infants. It is our belief that the untoward effects of analgesia may well be explained by nitrous oxide-oxygen mixture above the 85:15 level, producing a degree of fetal asphyxia dependent upon the duration of the exposure and size of the infant."

Galloway (44) states that a large percentage of the newborn show a moderate degree of somnolence, flaccidity and bradycardia, but does not consider these as fetal morbidity since these conditions have not led to an increase in fetal mortality.

Thus as regards the second and third of the requirements, it is doubtful whether the regime is entirely harmless to the baby and mother, although in comparison with other programs designed to produce the same effect, this one rates favorably.

In regard to the fourth requirement, the consensus of opinion is that labor is usually accelerated. In 576 labors, Danforth and Danforth (26) found that in

primiparae, the first stage of labor was shortened by an average of 2.5 hours over patients not receiving nembutal. The reasons for this are not definitely known. It appears that the drug does not act upon the propulsive powers, but rather hastens dilatation of the cervix. Some maintain (14) that there is a relaxing activity on the cervical musculature and the perineal floor. Still others maintain that there is a relaxation of the voluntary abdominal muscles, which at the time of uterine contraction in parturients who have received no sedation, are usually unconsciously contracted, thus preventing the uterine contractions from fully expending themselves in cervical dilatation.

In most of the reports on this subject, the operative incidence is markedly increased. "Prophylactic" forceps or outlet forceps deliveries are particularly increased, probably due to the patient's lack of coordination which is required for the expulsive effort necessary to complete the delivery. In many clinics, outlet forceps has become almost a routine method.

As to being reliable in the hands of the general practitioner, it must be stated that this is far from true. Such methods should be attempted only by the

experienced obstetrician, and then only in hospitals with facilities for handling such patients, and attendants experienced in this line. The majority believe that this method is contraindicated in home obstetrics.

It is evident that the most unsatisfactory effect of the nembutal -scopolamine program is the marked restlessness and frequent excitement of the patient. It seems to follow, then, that the barbiturate alone or in combination with scopolamine, produce amnesia, but little or no analgesia. The failure to produce analgesia results in varying degrees of restlessness ranging from marked excitability to violent resistance, none of which is remembered by the patient after labor. To eliminate the difficulty and danger of excitation to the mother, and still conserve the beneficial effects of the barbiturates in producing satisfactory amnesia, Douglass (32), Colvin and Bartholomew (21), Rosenfield and Davidoff (93), and others used paraldehyde as an analgesic, in combination with a barbiturate.

This method has given excellent results in the hands of those well versed in its use, but it, too, has objectionable features. Because of the disagreeable taste and odor of the paraldehyde, most men have felt that it should be administered rectally, and it is this feature that proves objectionable to so many

obstetricians. The objections raised to rectal medication are: (1) difficulty in placing the drug above the presenting part; (2) tendency of the patient to expel the medication; (3) comparatively slow and variable absorption time, probably due to depleted circulation of the lower bowel by the encroaching head; (4) inadvisability of doing rectal examinations following rectal medication.

Many schemes have been devised by which the paraldehyde can be given orally. Probably the most satisfactory of these is the method of Douglass et al (32) in which the odor and taste of paraldehyde is masked by combining the drug with propylene glycol, alcohol, and syrup of acacia, and administering the preparation chilled. Douglass states that in practice, the paraldehyde has been so satisfactorily disguised as to offer no problem in administration by mouth. 80% of his patients stated that it was an entirely new tasting medicine and not unpleasant. 20% complained of bitterness, sweetness, or a slight burning sensation. Thus it seems plausible that this method of giving the paraldehyde could satisfactorily be used in the following regime.

There have been numerous procedures described for the administration of barbiturates and paraldehyde rectally, the chief differences being in when and how

much of the drug to give. Representative of the current method is the following as used by Rosenfield and Davidhoff (93, 94) in their practice since 1932.

As soon as labor is definitely established, following routine preparation and enema, the patient is given $4\frac{1}{2}$ grains nembutal by mouth, followed in 15 minutes by 3 grains more. In 15-20 minutes after the second dose of nembutal, the patient is turned on her left side and given a rectal instillation of 6 drams paraldehyde in $1\frac{1}{2}$ ounces olive oil.

The mixture must be injected high in the rectum above the presenting part in order to avoid expulsion. This can be done by using a 3-ounce aseptic glass syringe with a plunger, and attached to a #20 F. rectal tube. The mixture is injected quickly between pains, and a pad is held against the anus for 10 minutes thereafter. A small amount of air in the syringe aids in completely emptying the contents into the rectum.

The patient drops into a deep sleep a few minutes after the injection of the paraldehyde. This sleep lasts from 3-12 hours, depending on the susceptibility of the patient. The average patient will show signs of awakening 4-6 hours after administration. At this time a rectal examination is done, and if it is evident

that several hours of labor are required for delivery, $1\frac{1}{2}$ -3 grains of nembutal are given by mouth or by rectum. Usually if the nembutal is placed in a capsule on the patient's tongue and a small quantity of water dropped in the mouth, the patient will swallow the water and capsule. 2-4 drams of paraldehyde may also be given at this time, and repeated as necessary.

In most cases, the initial dosage is sufficient to carry the patient to the stage where inhalation anesthesia is begun. When the presenting part appears on the perineum and crowns, the patient is carried to completion of delivery by inhalations of oxygen-nitrous oxide during contractions.

By this program, complete amnesia ranged from 64-95%, partial amnesia from 6-20%, and failures 0-16%. The factors contributing to failures were: (1) too rapid progress after administration of medication; (2) prolonged labor, with failure to administer subsequent dosage; (3) expulsion of injection; (4) inability to coordinate administration of drugs; (5) "immunity", or idiosyncrasy to drugs; (6) administration of medication too late in the course of labor.

In addition to amnesia, a large percentage of the cases reported obtained satisfactory analgesia (93,94), considering the absence of restlessness as a criterion of this condition.

Under this form of analgesia, most patients slept soundly and quietly through labor, and moved only occasionally with pains. The most restless of them were not delirious or noisy.

Colvin and Bartholomew (21) found that not only was the incidence of excitement and restlessness decreased by this method, but that patients did not resist inhalation anesthesia during expulsion, as was the case when a barbiturate and scopolamine were used. They also noted that the duration of administration of nitrous oxide-oxygen was considerably less in these patients.

On the whole, the results reported from this regime as regards amnesia and analgesia, appear to be more satisfactory than those of the nembutal-scopolamine method.

As regards fetal and maternal mortality, there were no cases attributable to the medication. There was no increase in the incidence of perineal or cervical lacerations (21, 93, 94, 22). Fetal apnea was reported in a wide range of variability, Irving et al reporting that 50% of the babies required some form of resuscitation, while Douglass and Payton (32) reported that all of the babies in their series cried spontaneously.

As regards delay in labor, Douglass and Payton, and Rosenfield and Davidhoff noted a temporary decrease in intensity and frequency of contractions, lasting from 30 minutes to 1 hour following medication, but stated that regular, more intense normal contractions followed, so that actually the length of labor was not increased.

As in the nembutal-scopolamine method, most of the babies were delivered by "prophylactic" forceps, hence there was an increase in operative deliveries. Douglass and Payton state that the expulsive efforts of the mother were not abolished; Colvin and Bartholomew feel that most of the deliveries could be satisfactorily done without the aid of outlet forceps.

As to the simplicity of this method, it appears that the factor of rectal medication would make it somewhat more difficult than the previous method. Many of its advocates say that because of the absence of delirium and marked excitability, a special attendant is not required to watch the patient, but merely someone to prevent the patient from rolling off of the bed. Colvin and Bartholomew even suggest this regime for routine use in suitable home deliveries. Most men, however, feel that the method requires hospitalization, and agree that the obstetrician should be well trained in its use.

Another regime employed in a few clinics (14, 70) is a modified Gwathmey technic, in which pentobarbital sodium is used instead of magnesium sulphate. Highly satisfactory results as regards amnesia and analgesia and low incidence of operative deliveries have been reported.

Of the numerous other regimes employed in present practice, sigmodal given rectally (37, 39), barbiturate compounds with ether in oil, rectally (107, 58), and certain barbiturate compounds intravenously (67, 109, 1) have given good results in the hands of those experienced in their use.

In examining the literature on the use of the barbiturate compounds in producing amnesia and analgesia in labor, we hoped to be able to chart results obtained by the various methods, in order to show a comparison of their values, as regards the more important features. The attempt has not been very successful, however, because so many of the reports have failed to give specific figures on their results. Furthermore, the criteria of successful results have been so variable in different clinics, that features considered as excellent in one clinic would be classed as only fair in another.

The features which we attempted to compare were:

- (1) degree of amnesia; (2) total duration of labor;
- (3) the percentage of patients showing excitement and restlessness (we consider this roughly to be the reciprocal of the degree of analgesia); (4) the percentage of babies apneic at birth; (5) the percentage of mothers having postpartem hemorrhage; (6) the incidence of spontaneous deliveries, low forceps, mid forceps, and other types of operative deliveries;
- (7) the fetal and maternal mortality.

It was found that some of the most promising series reported the degree of amnesia as excellent, good, or fair, etc., with no specific interpretation as to what was meant by these adjectives. The series that we have compared are graded as complete amnesia, partial amnesia, or failures, complete amnesia meaning that nothing was remembered from the time the medication took effect until after delivery; partial amnesia meaning that only isolated "islands of memory" were recalled; and failure meaning that a considerable portion of the experience was remembered. There was also a wide variation in interpretation of excitement and restlessness.

Fetal apnea was designed in our chart to mean the "sleepy" babies that required some means of resuscitation, but here again there was great breadth of interpretation.

In comparing postpartem hemorrhage, comparatively few reports stated their criterion for this condition.

The type of delivery was given in nearly all cases, but considering the fact that many clinics almost routinely used "prophylactic" forceps, it is doubtful if the comparison of "total duration of labor" averages has much significance.

In attempting a comparison of figures on maternal and fetal mortality, it was found that in almost every series where these occurred, they were attributed to some cause other than the medication producing amnesia and analgesia. Therefore, in our chart these figures have been entirely omitted.

Thus we have been forced to omit many of the reports in which apparently excellent results were obtained, but it is hoped that those included will give some indication as to the comparative success in some of the various methods.

One of the most significant pieces of work reported in this field, and included in our chart, is that of Irving and his associates (58). Investigating

the value of the various present day methods, they conducted 160 labors using the sodium amytal-scopolamine regime, and seven groups of 100 patients each using, (1) pentobarbital sodium and scopolamine; (2) sodium amytal and rectal ether; (3) pentobarbital sodium and rectal ether; (4) pernocton; (5) pentobarbital sodium and paraldehyde, rectally; (6) pantopon and scopolamine; (7) pantopon and rectal ether. During the expulsive stage, nitrous oxide-oxygen anesthesia was given all patients, ether being added on rare occasions when required.

In this total series of 860 cases, particular attention was paid to asphyxia and respiratory depression of the newborn, excitement of the mother, amnesia produced, operative incidence, length of labor, blood loss of mother, and pulse, blood pressure and respiration of the mother during, and for one hour after, labor.

A few other series have been reported sufficiently adequately to be included in the chart.

Following the chart are explanatory notes giving dosage and references.

			Degree of Amnesia			Total Duration of Labor		Undesirable Effects				Type of Delivery			
			Complete %	Partial %	Failure %	Primiparae Hrs.	Multiparae Hrs.	Excite- ment %	Restless- ness %	Fetal Apnea %	Postpartum Hemorrhage %	Spon- taneous %	Low Forcep %	Mid Forcep %	Other Operative Deliveries %
1.	Daichman et al Sodium amytal orally	60 cases	28.3			17.3	11.6	5	28.3	13	0	71.6	18.3	8.3	1.8
2.	Scapecello Sodium amytal and luminal orally	39 cases	62	25	13	13.5		8	15	2					
3.	Emmert and Goldschmidt Sigmodal rectally	125 cases	77	19	4	15	10.6	32	6.6	22.2	2.4				
4.	Tritsch and Brown Dial intravenously	60 cases	3.3	5	91.6	16.8		90	13.3	1.6		90	3.3		6.7
5.	Irving et al Pernocton intravenously	100 cases	42	43	15	14.3	8.5	15		47	10 over 300cc.	73	27		
6.	Lewis and Hamilton Sodium amytal intravenously	76 cases	83	17	0	16	9	6	58	8	0	73	18		9
7.	Irving et al Pentobarbital sodium and scopolamine	100 cases	86	14	0	14.5	9.5	17		37	3	70	30		
8.	Averett Pentobarbital sodium and scopolamine	160 cases	69	26	5					5	0.6	16	74	7.5	2.5
9.	Tritsch and Brown Sodium allurate and scopolamine	25 cases	68	20	12	13.3		20	56	16		80	16		6
10.	Daichman et al Sodium amytal and scopolamine	53 cases	67.9			17.5	9.2	5.7	39.6	5.7	0	53	41	3.7	2.3
11.	Bauer et al Pentobarbital sodium and scopolamine	100 cases	69	10	21			6	42	14	4	77	18	4	1
12.	Irving et al Sodium amytal and scopolamine	160 cases	80	20	0	14.7	12.7	17		39	12 over 300cc.	71	29		
13.	Rucker Sodium amytal and scopolamine	150 cases	96	4	0					14	.6				
14.	Colvin and Bartholomew Sodium amytal orally and paraldehyde rectally	100 cases	82	16	2	16.2	9.5	2	4	9	3	81	9	7	3
15.	Rosenfield and Davidhoff Nembutal orally and paraldehyde rectally	50 cases	94	6	0				8	10		0	88	10	2
16.	Irving et al Pentobarbital orally and paraldehyde rectally	100 cases	64	20	16	17.2	10	24		50	3 over 300cc.	63	37		
17.	Conn and Vant Nembutal orally and paraldehyde rectally	103 cases	92												
18.	Tritsch and Brown Sodium amytal orally and ether-oil rectally	25 cases	40	36	24	15.7		4	68	16		92	8		
19.	Tritsch and Brown Barb-eth-oil rectally	25 cases	84	8	8	14.5		8	48	24	8	76	20		4
20.	Irving et al Sodium amytal orally and ether rectally	100 cases	72	25	3	16.2	9.5	5		41	15 over 300cc.	63	37		
21.	Irving et al Pentobarbital orally and ether rectally	100 cases	66	28	6	19	13.2	4		47	5 over 300cc.	58	42		
22.	Daichman et al Sodium amytal orally and morphine	91 cases	50.5			17	11		2.2	8.7	1.1	55	26		19
23.	Tritsch and Brown Sodium amytal orally and morphine	25 cases	28	32	40	16.3		0	64	16		76	20		4
24.	Tritsch and Brown Sodium allurate orally and pantopon	25 cases	75	25	0			2	13	36		84	12		4
25.	Olson and van Ess Pernocton intravenously and morphine	53 cases	39	34	27	23.6	13.3	10		15.6		22	75		3
26.	Irving et al Pantopon and scopolamine	100 cases	18	67	25	17.6	12.5	4		67	25 over 300cc.	54	46		

1. Sodium amytal orally, grains 6-15. (Ref. 24)
2. Sodium amytal grains 6, orally, and luminal grains 6, orally. Additional dosage if necessary. Ether during perineal stage. (Ref. 99)
3. Sigmodal 10cc. rectally after labor definitely established. Repeat 5cc. if necessary. (Ref. 38, 39)
4. Dial 2cc. (grains 3) intravenously. Dose repeated if necessary. (Ref. 107)
5. Pernocton (10% aqueous solution) 1cc. per 30 lbs. weight intravenously. Additional dosage if necessary. Nitrous oxide-oxygen during expulsion. (Ref. 58)
6. Sodium amytal grains $7\frac{1}{2}$ intravenously. Follow by grains 5- $7\frac{1}{2}$ intramuscularly if necessary. Nitrous oxide or ether during expulsion. (Ref. 67)
7. Pentobarbital sodium grains $4\frac{1}{2}$ -6, orally, and scopolamine hydrobromide grains 1/100-1/150. Additional dosage of both if necessary. Nitrous oxide-oxygen during expulsive stage. (Ref. 58)
8. Pentobarbital sodium grains 6 and scopolamine hydrobromide grains 1/100. Additional dosage of both as necessary. Nitrous oxide-oxygen during expulsion. (Ref. 2)
9. Sodium allurate grains 9 orally, and scopolamine grains 1/400-1/100. (Ref. 107)

10. Sodium amytal grains 9 orally, and scopolamine grains 1/150. Additional dosage as necessary. (Ref. 24)
11. Pentobarbital sodium grains 6 orally, and scopolamine grains 1/150. Additional dosage as necessary. (Ref. 77)
12. Sodium amytal grains 9-12 orally, and scopolamine grains 1/150. Repeat amytal if necessary. Nitrous oxide-oxygen during second stage. (Ref. 58)
13. Sodium amytal grains 18 orally, and hyoscine grains 1/200. Additional dosage as necessary. Nitrous oxide or ether during expulsion. (Ref. 95)
14. Sodium amytal grains 3-6 orally, and paraldehyde drams 6-8 rectally. Nitrous oxide-ether during perineal stage. (Ref. 21)
15. Pentobarbital sodium grains $7\frac{1}{2}$ or sodium amytal grains 6 orally, and paraldehyde drams 4-6 rectally. Nitrous oxide and ether during perineal stage. (Ref. 93)
16. Pentobarbital orally and paraldehyde rectally. Nitrous oxide-oxygen during expulsion. (Ref. 58)
17. Pentobarbital sodium grains 6 orally and paraldehyde drams 6-8 in olive oil, rectally. Pentobarbital sodium in additional dosage if necessary. (Ref. 22)
18. Sodium amytal grains 6-9 orally, and ether ounces $1\frac{1}{2}$ in oil, and quinine sulphate grains 20, rectally. (Ref. 107)

19. Ethyl barbituric acid grains 8, N-butylethyl barbituric acid grains 5, quinine grains 20, ether ounces $2\frac{1}{2}$, mineral oil ounces $1\frac{1}{4}$; all given rectally. (Ref. 107)
20. Sodium amytal grains 9-12 orally, and rectal ether. Nitrous oxide-oxygen during expulsion. (Ref. 58)
21. Pentobarbital sodium grains $4\frac{1}{2}$ -6 orally, and rectal ether. Nitrous oxide-oxygen during expulsion. (Ref. 58)
22. Sodium amytal grains 9 orally, and morphine grains $1/6$. (Ref. 25)
23. Sodium amytal grains 6-9 orally, and morphine grains $1/8$ - $1/6$. Dose repeated as necessary. (Ref. 107)
24. Sodium allurate grains 9 orally, and pantopon grains 1-6. Dose repeated if necessary. (Ref. 107)
25. Pernocton 1cc. per $12\frac{1}{2}$ kilo. weight intravenously, preceded by morphine grains $1/6$ in primiparae in first stage of labor. Pernocton repeated in smaller doses as necessary. Nitrous oxide and ether during expulsion. (Ref. 109)
26. Pantopon grains $1/3$ and scopolamine grains $1/150$. Additional dosage as necessary. Nitrous oxide-oxygen during expulsion. (Ref. 58)

27. Gwathmey technic using pantopon instead of morphine. Nitrous oxide-oxygen during expulsion.
(Ref. 58)

CONCLUSIONS

1. The ideal method of producing amnesia and analgesia has not been found, but various new methods and combinations are continually being tried in hope of finding the ideal.
2. The majority of obstetricians have no routine method, but use more than one type of sedation as indicated by the type and condition of the patient.
3. Several of the different methods give almost equally satisfactory results in the hands of the obstetricians skilled in their use.
4. Of the barbiturates, pentobarbital sodium, either alone or in combination with other drugs, seems to have the greatest number of advocates.
5. Labor, when conducted under the influence of these drugs, should be supervised by the obstetrician having a thorough knowledge of the use of such drugs.
6. Regardless of the regime used, a great part of the success depends upon the degree to which the patient's confidence has been gained, and the serenity and hopefulness instilled in the patient's mind by her accoucheur.

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