

## INTRAVENOUS DEMEROL-SCOPOLAMINE AMNESIA DURING LABOR \* †

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### INTRODUCTION

DEMEROL or isonipecaine has been employed in obstetrics during parturition by many individuals (1-10) since its preparation by Eisleb and Schaumann in 1939 (11). The numerous technics and the various dosages that have been recommended by these investigators are reflected in the varied and often conflicting results which have been reported. The ambiguity of the available literature has induced a study of this agent in a series of closely observed obstetrical patients at the University Hospital.

A technic which previously had been described by a member of our department (12) was selected to be used throughout this study. It was adapted to the use of demerol instead of pentobarbital since the latter is not a true analgesic agent. Thus, the modification assured the parturient woman of, first, a degree of amnesia and, second, the maximum amount of pain relief which could be derived from an individualized dosage of demerol administered symptomatically to a point of moderate sedation by the intravenous route.

### METHOD

Demerol hydrochloride and scopolamine hydrobromide were procured in ampules to assure sterility for intravenous administration. A fresh stock solution was prepared for each patient by diluting 100 mg. (2 cc.) of demerol hydrochloride, 0.64 mg. or 1/100 grain (1 cc.) of scopolamine hydrobromide, and 7 cc. of sterile distilled water in a 10 cc. syringe equipped with a 26 or 27 gauge hypodermic needle. Each cubic centimeter of this solution, after thorough mixing, contained 10 mg. of demerol hydrochloride and 0.064 mg. (1/1,000 grain) of scopolamine hydrobromide. The exact amount of drugs (fig. 1) administered

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† Demerol, a brand of isonipecaine, was supplied for this study by the Winthrop Chemical Co., Inc.

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to a patient at any time was readily computed from a simple scale. (Hereafter, to avoid confusion, the dosage of these drugs will be expressed in cubic centimeters of the prepared solution.)

The onset of true labor in any normal primipara or multipara, i.e., labor pains of forty seconds' duration and occurring regularly at five-minute intervals or less, was the only indication necessary for the first administration of the demerol and scopolamine.

#### DILUTIONS OF DEMEROL AND SCOPOLAMINE

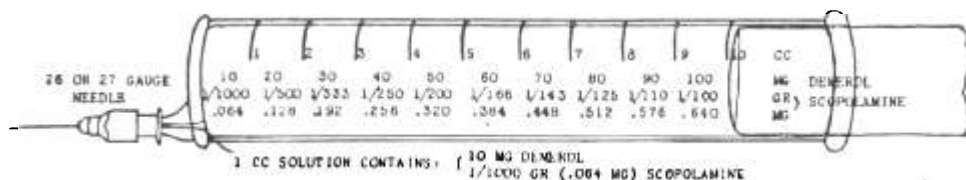


FIG. 1. Amounts of drugs administered at any time using stock solution.

A venipuncture was performed, usually in the antecubital fossa, and the administration of the prepared solution was begun immediately. The injection proceeded at a rate of 1 cc. per minute or slower, depending on the reaction of the patient. Whenever signs of nausea, vomiting, or any untoward circulatory reaction appeared, the injection was slowed or stopped altogether for a few minutes. When these symptoms had subsided, the administration again was begun and continued even more cautiously until the desired amounts of the drugs had been given.

The solution was given until the patient (1) began to talk incoherently, (2) showed signs of falling asleep between pains, and (3) exhibited only a slight amount of restlessness with each pain. At this point the injection was stopped and the needle was withdrawn. The initial dosage for patients who had received no previous drugs (fig. 2) was usually 8 to 10 cc. of the solution (average of 8.6 cc. in the series), and the initial dosage for patients who had previously received central nervous system depressant drugs, such as opiates and barbiturates, was usually 5 to 7 cc. of the solution (average of 6.1 cc. in the series).

A patient, after sedation by the initial injection, was observed at all times by a competent nurse in the labor room. She called the anesthesiologist and the obstetrician whenever the labor seemed to be progressing at a rapid rate or whenever the patient was almost ready for delivery; she called the anesthesiologist whenever the patient seemed to show excessive restlessness, coherency of speech, and apprehension between pains or excessive excitement with each pain. These signs served to indicate when it was time to administer the next dosage of the prepared solution. Occasionally, however, a primipara whose cervix was fully dilated and who was "bearing down" with each pain, or a multipara who was having severe pains and making rapid progress, showed more restlessness at this time. This usually could not be in-

terpreted to mean that the dosage was inadequate. Even momentary recognition of the physician and requests for more pain-relieving agent were encountered. In these cases it was necessary to observe extreme caution. Provided the initial sedation seemed adequate and the interval since it was given was short, amnesia of the episode was likely to occur without a supplementary amount of drugs.

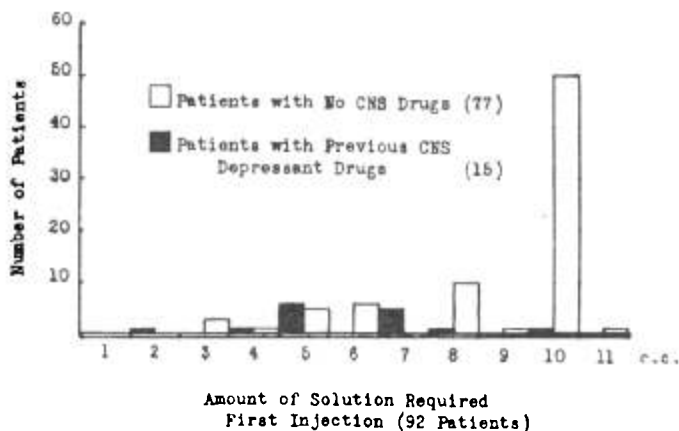


FIG. 2. First intravenous administration of demerol-scopolamine solution to 92 patients. Seven patients who were delivered by cesarean section and one patient who had an internal version and extraction of the fetus, all of whom received an inhalation anesthetic subsequently, are excluded.

The second intravenous injection of demerol and scopolamine (fig. 3) was required from two to four hours after the initial administration (average interval three hours). The amount of drugs required for patients who had previously received only a dose of demerol and scopolamine and those who had previously received central nervous system depressant drugs was about the same, probably because the effect of the central nervous system depressant drugs had worn off. The dosage for patients who had been given only demerol and scopolamine previously was usually 3 to 5 cc. of the solution (average of 4.3 cc. in the series), and for patients who had previously been given opiates or barbiturates was usually 3 to 5 cc. (average of 3.9 cc. in the series).

Multiparae usually required one or two intravenous injections of these drugs before the termination of labor; however, many primiparae required a third administration usually three to five hours after the second (average of four hours in the series). Here again, undue excitement with each pain; restlessness, alertness, and coherency between pains; and the lapse of time since the last injection served as criteria for the administration. The dosage of the third injection was usually 2 to 4 cc. (average of 3.3 cc.) for patients who had received no medication other than demerol and scopolamine, and was usually 2 to 3 cc. (average of 2.5 cc.) for patients who had previously been given central nervous system depressant drugs (fig. 4).

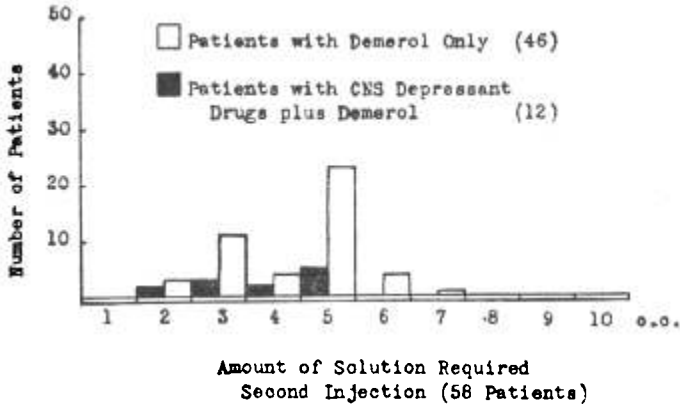


FIG. 3. Second intravenous administration of demerol-scopolamine solution to 58 patients (63.0 per cent of the original 92 patients whose administrations of the solution are shown graphically).

Six patients (6.5 per cent) required a fourth injection, and 2 patients (2.1 per cent) required a fifth injection, each of these occurring in long and difficult labors. The average dosage for both groups of patients for the fourth and fifth injections was 1.5 cc. of solution. It was apparent that the interval between the need for additional amounts grew longer with each injection, and that the amount of drugs necessary to produce the desired effect each time was roughly one-half that of the preceding dosage.

All episiotomies were performed under local anesthesia with procaine and repaired under cyclopropane anesthesia. Forceps were applied under cyclopropane anesthesia.

The 7 patients who were delivered by cesarean section and whose case histories are included in this report received 5 cc. of the prepared

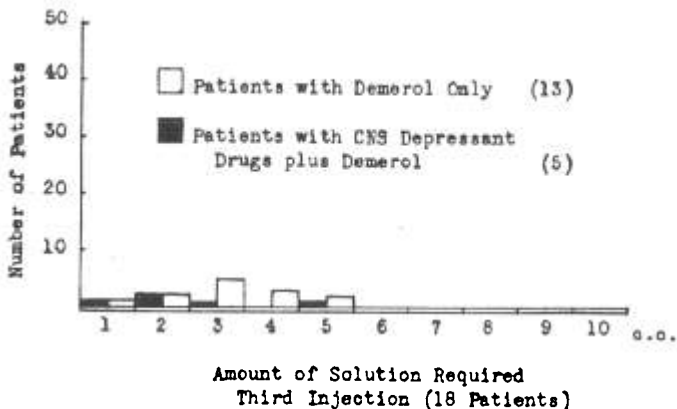


FIG. 4. Third intravenous administration of demerol-scopolamine solution to 18 patients (19.5 per cent of the original 92 patients whose administrations of the solution are shown graphically).

solution, intravenously, fifteen to twenty-five minutes before the induction of upper first plane of surgical anesthesia with cyclopropane.

### RESULTS

The technic as described has been employed in a series of approximately 250 private and staff obstetrical patients over a period of one year. One hundred unselected case histories comprise the material for this report. Ninety-five of these were consecutive deliveries and 5 were private cases in which cesarean section was performed under anesthesia administered by a member of the Department. Intravenous demerol and scopolamine were employed as preanesthetic medication in each of these. Both white and colored patients were observed, with ages ranging from 14 years to 39 years. Fifty-nine were primiparae and 41 were multiparae; 101 infants were delivered from 99 different mothers. One set of twins was delivered, and one mother had two labors during the study.

The presentation of the fetus in each patient was recorded upon the initial examination. The distribution is shown in table 1.

TABLE 1  
PRESENTATION OF THE FETUS (100 DELIVERIES)

Presenting Part	Number
Occiput	92
Breech	6
Face	2
Transverse	1
Total	101 (One set of twins)

Methods of delivery of the 95 patients are recorded in table 2. Five private patients who had cesarean section whose deliveries occurred at various times throughout the year, and whose histories are included because of their having received demerol and scopolamine as preanesthetic medication, are excluded.

TABLE 2  
METHOD OF DELIVERY (95 CONSECUTIVE PATIENTS)

Type	No.	%
Spontaneous Delivery	86	89.4
Low Forceps	5	5.2
Mid Forceps	1	1.1
High Forceps	1	1.1
Cesarean Section*	2	2.1
Int. Version and Extraction	1	1.1
Total (1 set of twins)	96	100%

\* Cephalopelvic disproportion after trial labor, 1 case; previous cesarean section, 1 case.

The progress of labor was interesting. No appreciable alteration of the course during the first stage was noted with the exception that the patient frequently slept between pains and showed varying degrees of motor activity with each pain. The second stage was characterized by hard, prolonged uterine contractions with adequate relaxation and rest between each pain. The charts frequently contained the notation that the second stage was “unusually rapid.”

A significant observation was that the patients, as a whole, were not as irrational as those who had received other forms of amnesia during labor. They were fairly quiet, easily aroused by calling their names, cooperative to a great extent, and did not require the close nursing care and restraint which frequently had been necessary in the labor room during the latter part of the second stage of labor. The third stage was not prolonged nor was an excessive amount of bleeding noted in any case. The uterus contracted down firmly in each instance following the routine postpartum manual massage and oxytocic drugs. The average times required for completion of labor in both primiparae and multiparae are shown in the 92 patients who completed labor without general anesthesia and operative intervention (table 3).

TABLE 3  
PROGRESS OF LABOR (92 PATIENTS)

	Primipara	Multipara
1st Stage	10 hr., 24 min.	7 hr., 42 min.
2nd Stage	1 hr., 42 min.	54 min.
3rd Stage	9 min.	7 min.
Total	12 hr., 15 min.	8 hr., 43 min.

Maternal and infant mortality—morbidity records were kept on all patients. There were no maternal deaths. All mothers were in good or excellent condition following delivery with the exception of one who had a severe anemia throughout pregnancy. She was given 2,000 cc. of blood during her period of convalescence in the hospital. Infant mortality figures showed one stillbirth in this series. The mother had been treated with pitocin in a rural area following a forty-eight-hour

TABLE 4  
INFANT MORTALITY AND MORBIDITY (101 PATIENTS)

Condition of Fetus	Demerol Alone	Demerol plus Other CNS Depressant Drugs	Total
Spontaneous Respiration	75	15	90
Apneic	3	7	10
Dead at Birth	1	—	1
Total	79	22	101

labor prior to admission, and the baby was in dire distress when admitted. Infant morbidity is tabulated in table 4.

The apneic infants were classified according to whether or not resuscitative measures were necessary (Torpin endotracheal insufflation technic) and on the basis of the drugs which the mother had received during parturition (table 5).

TABLE 5  
APNEA OF THE NEWBORN (101 PATIENTS)

	Demerol Alone	Demerol plus Other CNS Depressant Drugs	Total
Required No Resuscitation	1	3	4
Required Resuscitation	2	4	6
Total	3	7	10

The degree of amnesia was recorded from subjective examination. Each patient was questioned from twenty-four to forty-eight hours after delivery about events and persons which might have impressed the patient while she was under the influence of the demerol-scopolamine solution. A tabulation of this showed the amnesia to be satisfactory in 85.9 per cent of the patients and unsatisfactory in 14.1 per cent of the patients whose labor terminated without anesthesia and operative intervention (table 6).

TABLE 6  
AMNESIA DURING LABOR (92 PATIENTS)

Degree of Amnesia	Number	Per Cent
Excellent (remembered nothing)	49	53.3
Good (remembered isolated instances or persons)	30	32.6
Fair (spotty)	12	13.0
Poor (remembered labor)	1	1.1

The analgesic properties of demerol were assessed under four headings from objective observation of the patient during labor (table 7). Such factors as the strength of the uterine contractions, the progress of the labor, the patient's response to the labor pains, and the patient's apparent threshold for pain were taken into consideration when evaluating this relief of pain.

TABLE 7  
ANALGESIA DURING LABOR (92 PATIENTS)

Degree of Analgesia	Number	Per Cent
Excellent (showed no evidence of pain)	2	2.2
Good (showed marked relief from pain)	41	44.5
Fair (showed some relief from pain)	31	33.7
Poor (showed no appreciable relief from pain)	18	19.6

The intravenous administration of these agents produced significant side reactions. Thirst, dryness of the mouth and pharynx and occasional tachycardia commonly occurred and were attributed to the use of scopolamine. Other symptoms were noted, however, in 11 patients (11 per cent) and may be classified in order of their occurrence (table 8).

TABLE 8  
SIDE EFFECTS ENCOUNTERED (100 PATIENTS)  
11 Patients (11%)

Symptom	No. of Observations
Nausea	6
Vomiting	5
Slowing of Labor (temporary)	3
Excitement	3
Profuse Sweating	2
Dizziness	1

Postpartum obstetrical complications such as mastitis and sepsis of the episiotomy site were noted, but were in no way attributable to the intravenous injection of the demerol-scopolamine.

COMMENT

The administration of demerol and scopolamine during parturition has been studied in a series of cases. The use of this combination of agents is justified because the entire regime depends on the utilization of these two drugs for their pharmacologic actions during delivery. Scopolamine hydrobromide is an amnesic agent; demerol hydrochloride is a new synthetic coal tar analgetic. One hundred milligrams of demerol intravenously is reported to have the analgesic effectiveness of 10 mg. of morphine (13).

The intravenous route by which these drugs were administered is desirable. Roby and Schumann have used the subcutaneous and intramuscular routes. They reported (14) that, in several instances, failures were attributed to inadequate absorption from the site of injection, lack of receiving the routine administrations, or inadequate time for the absorption to occur before delivery. Probably the intravenous route involves a greater percentage of side effects than does either of the above routes yet, in our experience, these were of a minor nature and a temporary slowing or interruption of the injection upon the appearance of such symptoms is sufficient. One general surgery patient (not included in this report) showed a hypotensive state characterized by pallor, hyperhydrosis, disturbed vasomotor phenomena and tachycardia following the intravenous injection of demerol. The edema of uvula and epiglottis that Steinberg reported (15) has not been observed.

The effect of demerol on the uterus is controversial. It produces a distinct spasmolytic effect on smooth muscle tissues throughout the body in most instances by one of two mechanisms (16), yet Abreu and



Woodbury (17) observed no effect upon the uterus which is between three months and eight months pregnant. Yonkman, Noth, and Hecht (18) have observed an inconsistent activation of the flaccid uterus and a more pronounced relaxation of the tonic type of uterus. This work supports the previous findings of Gruber, Hart, and Gruber (19). It is our observation that the tonic uterus frequently relaxes well between pains and terminates labor more rapidly in these cases. It seems that the second stage may be somewhat shortened owing to an increase in the cooperation of the patient and the forceful, rhythmic relaxation and contraction of the uterine musculature.

The potentiation of barbiturate medullary depression by demerol has been reported (20). In a similar manner, it was suspected that patients who had received a previous dosage of morphine might require a smaller subsequent dosage of demerol. This was found to be true, especially at the first intravenous injection of the demerol-scopolamine mixture. By the time the patient was ready for the second injection of demerol, the effects of the previous depressant drugs had worn off and the amounts of demerol necessary for sedation in both groups of patients approximated the same figure. It is at the time of the initial injection of demerol or with the simultaneous administration of barbiturates, morphine and demerol that a medullary depression of the fetus can occur which later is responsible for an apneic infant at birth. Thus, it is our belief that the simultaneous administration of the barbiturates or morphine with demerol may prove to be dangerous and, furthermore, that the dosage of demerol be "individualized" by using the intravenous route in preference to "routine" administration by subcutaneous or intramuscular routes. Our evidence is found in the wide range of intravenous dosages necessary to produce the same symptomatic effect in this series of patients, and in the fact that patients with previous central nervous system depressant drugs require only one-half the usual amount of demerol initially.

Schumann (21) uses demerol and scopolamine as preanesthetic medication whenever cesarean section is indicated. The 2 patients in our series who had cesarean section, one internal version—extraction, and the additional 5 patients included in this report who had cesarean section, received these agents intravenously before operation. A dosage of 50 mg. of demerol and 1/200 grain of scopolamine hydrobromide (5 cc. of the prepared solution) was administered fifteen to twenty-five minutes before induction to upper first plane of surgical anesthesia with cyclopropane. In each individual the induction was rapid, smooth, and easily accomplished. A significant reduction in the amount of cyclopropane necessary to perform the indicated surgical procedure was apparent as a result of this preliminary medication. The incidence of resuscitation of the newborn did not seem to be materially increased, so this procedure is still employed at the University Hospital by our Department.

## SUMMARY AND CONCLUSIONS

A method is presented which utilized demerol hydrochloride and scopolamine hydrobromide intravenously during parturition.

The primary effect of this combination of agents was the production of adequate amnesia in a high percentage of the patients studied.

Demerol as employed in this regime produced a sufficient degree of analgesia to reduce the restlessness of the mother markedly during labor, but not a sufficient amount of analgesia consistently to abolish pain entirely.

The incidence of apnea neonatorum was low.

The previous or simultaneous administration of barbiturates or morphine with demerol resulted in a greater incidence of apnea of the newborn. It was necessary to reduce the amount of demerol administered under such circumstances.

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