HYDROGEN ION CONCENTRATION OF THE SPINAL FLUID AND ITS RELATION TO SPINAL ANESTHETIC FAILURES *

ELLIS N. COHEN, M.D., AND RALPH T. KNIGHT, M.D.

Minneapolis, Minnesota

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CULLEN (1) reported that 99 per cent of failures to obtain spinal anesthesia after introduction of the analgesic drug can be ascribed to failure to introduce all or part of the analgesic substance into the subarachnoid space. He further stated that in rare individuals analgesia cannot be secured even after repeated injections and suggests that the hydrogen ion concentration of their spinal fluid is such that precipitation of the drug as a base is not effected, and the drug is incapable of inducing analgesia. Heard (2) suggested that the hydrogen ion concentration of spinal fluid may hold the secret of spinal anesthetic failure after seemingly perfect injection. Although both authors take into account the possibility of nonprecipitation of the anesthetic base causing failure of analgesia, neither considers an extreme alkalinity of the spinal fluid as a possible cause of spinal anesthetic failure. Heard stated that increasing alkalinity potentiates analgesia. This is true only until that hydrogen ion concentration is reached where gross precipitation of the alkaloid base occurs, and at or beyond that point spinal failure may also occur. We are reporting 2 cases of spinal anesthetic failure in which extreme alkalinity of spinal fluid was present.

Case 1. H. T., white male age 20, was to be operated for marsupialization of a pilonidal cyst. The patient appeared in excellent physical condition. Procaine, 150 mg., was selected as the anesthetic agent and injected in 3 cc. of a 5 per cent solution of glucose which was injected between the fourth and fifth lumbar vertebrae. At the end of twenty minutes anesthesia had not appeared. It was thought advantageous to use another agent, and 15 mg. of pontocaine in 3 cc. of 5 per cent glucose solution was injected between the third and fourth lumbar vertebrae. Another fifteen minutes elapsed, and still spinal anesthesia did not develop. The patient was put to sleep with pentothal, and the operation satisfactorily carried out under this anesthesia. Although the surgical procedure required fifty minutes, the patient gave no evidence of late development of spinal anesthesia, and full dosage of pentothal was required to maintain relaxation. At the termination of the operation, a third lumbar puncture was performed for diagnosis and 10 cc. of spinal fluid removed and sent to the

* From the Division of Anesthesiology, University of Minnesota Hospitals, Minneapolis, Minnesota.

laboratory. On recovery of consciousness the patient was again tested for any evidence of spinal anesthesia, and none was present. The laboratory report that afternoon showed the spinal fluid to be within normal limits, except for extreme alkalinity: the pH was 8.35.*

Wound healing was uneventful, but the patient had several complaints after the anesthesia. On the first postoperative day he complained of backache, headache and an aching numbness of both lower extremities. The latter extended anteriorly to the groin and posteriorly to about the level of the third lumbar vertebra. He was given symptomatic treatment, but his complaints persisted. On the third postoperative day another lumbar tap was performed. The intradural pressure was found to be very low, and flow of spinal fluid could be obtained only by jugular pressure and by having the patient strain. A sample was removed for the laboratory, and 25 cc. of 5 per cent glucose solution then injected intrathecally. He complained of increased pain in his back and legs upon injection, but obtained some relief of his headache almost immediately. In addition, it was hoped that by adding the 5 per cent glucose intrathecally, it would lower the spinal fluid pH and aid in washing away any of the precipitated alkaloid base which might be present and causing nerve irritation. The following day, although the headache had recurred somewhat, the pain in his legs had lessened considerably. Next day the patient was much improved and continued on to an uneventful and rapid recovery. He was discharged fourteen days postoperatively.

The laboratory reports were as follows: on the operative day the spinal fluid was normal; pH determination was not valid. On the third postoperative day the pH of the spinal fluid was 7.91; the cell count was 11 per cm.

Case 2. R. H., white male, age 35, was to be operated on for removal of a loose cartilage of the knee. His general physical condition was excellent, but on questioning, he volunteered the information that two years previously he was operated on for reduction of a dislocation of the same knee joint. A spinal anesthetic (agent unknown) was given at that time, but after fifteen minutes anesthesia did not develop, and general anesthesia was substituted. Our selection was pontocaine 10 mg. combined with 1 cc. of 10 per cent glucose solution and 50 mg. of ephedrine (Whitacre's 1-1-1 technic). This was given between the third and fourth lumbar vertebrae. Some degree of anesthesia developed within ten minutes, and a sensory level determined by pin prick was found to be above the umbilicus. When a towel clip was put into the region of the knee the patient complained that he felt pain. Operation was delayed for an additional fifteen minutes, and although the anesthesia progressed slightly, it was still not complete enough for surgery. The patient was put to sleep with pentothal and anesthesia maintained as light as possible. General anesthesia was carried on for twenty minutes, and then it was found that the spinal anesthetic was adequate by itself. The surgical procedure required fifty minutes and the spinal anesthetic was unsupplemented for the remaining thirty minutes. As the last few stitches were being put in, however, the patient began to complain of return of sensation, and by the time he had returned to his room, no sensory level remained. Since our pontocaine-ephedrine-glucose spinal anesthesia had been providing adequate anesthesia for three to four hours, and in this case there was both a delay in onset of adequate anesthesia (forty-five min-

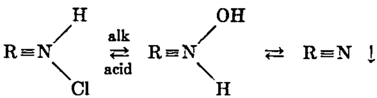
* This figure obviously is in error. Test tube was covered with cotton plug only.

utes) and a very transient effect (thirty minutes), it was decided to check the spinal fluid pH.

The laboratory reports were as follows: the spinal fluid was normal, but the pH was 7.80; the blood pH was 7.45.

The normal hydrogen ion concentration of spinal fluid is slightly higher than that of blood. Both Pitkin (3) and Vehrs (4) gave its pH as 7.6. Adriani (5) gave its pH as 7.35, and Kolmer (6) reported a range of 7.35 to 7.40. Heard (2) called attention to the fact that while the textbooks do not emphasize much variation in pH, considerable differences do occur from patient to patient. The alkalinity of spinal fluid is caused mainly by the bicarbonates of sodium and potassium. Carbonic acid and sodium bicarbonate form the most important and abundant buffer pair. Drawn spinal fluid usually increases in alkalinity because carbon dioxide is lost (5). Levinson (7) reported that the hydrogen ion concentration of spinal fluid decreases steadily on standing. He found the pH of 177 spinal fluids to range between 7.4 and 7.6 with 2 cases showing a pH of 7.7. Samples, however, on standing open to the air or with just a cotton plug, rapidly increased in alkalinity. The pH rose from 7.4 to 7.6 at the end of one hour; to 7.9 in two hours; and to 8.0 in five hours. Samples filled to the top of the test tube and tightly stoppered with paraffin showed little loss of carbon dioxide even after twelve to twenty-four hours. In collecting our samples we adhered to the technic of drawing spinal fluid with a syringe and then injecting the fluid through the long spinal needle under a few cubic centimeters of mineral oil in the test tube. The mineral oil layered well on top of the spinal fluid, and with these samples tightly corked with rubber stoppers, little carbon dioxide was lost.

Spinal anesthetic agents are marketed as the hydrochloride or the acid salt. The anesthetic salt is water soluble and has little or no affinity for nerve tissue. When the salt is injected into the weakly alkaline spinal fluid, a gradual precipitation of the alkaloid anesthetic base takes place, thus liberating the active agent.



(anesthetic salt) (anesthetic base)

The anesthetic base is insoluble in water, but soluble in lipoid and has a marked affinity for nerve tissue. Gros (8) called attention to the fact that in the case of local anesthetics, the addition of alkali to the solution potentiates the anesthesia, but that the solution must not be so alkaline that the base is actually precipiated. Adriani (5) stated that alkalinized solutions potentiate action six to seven times, but that

in solutions of high pH, action is decreased since free base is precipitated. To provide maximum anesthesia, the anesthetic base must be either in a true or a colloidal solution. In this state the largest area of free surface is provided, and positively charged ions of the anesthetic base are strongly adsorbed by the nerve fibers. If gross flocculation or precipitation occurs, the amount of free surface which is active diminishes, fewer ions remain in solution, and anesthetic effectiveness diminishes (9).

It would thus seem that extreme alkalinity of the spinal fluid might precipitate the anesthetic agent as the alkaloid base and cause a failure of anesthesia. In our 2 reported cases of spinal anesthetic failure the hydrogen ion concentration of the spinal fluid in both instances was on the highly alkaline side. We, therefore, decided to determine the upper pH limits above which the common anesthetic agents would precipitate when mixed with solutions of cerebrospinal fluid. The following standard anesthetic solutions were prepared and are the ones most frequently used at our hospital.

1. Procaine—50 mg. per cubic centimeter of 5 per cent glucose solution.
2. Nupercaine—1 mg. per 1.5 cubic centimeter of 0.5 per cent saline solution (Jones solution).
3. Pontocaine—5 mg. per cubic centimeter of 5 per cent glucose solution.
4. Pontocaine 1–1–1 with 3.3 mg. per cubic centimeter of 3.3 per cent glucose and 16.6 mg. of ephedrine per cubic centimeter.
5. Metycaine—30 mg. per cubic centimeter of Ringer's solution.

Using a Beckman photoelectric pH meter we measured the pH of these solutions and found them all to be on the acid side.

1. Procaine solution—pH 5.35.
2. Nupercaine solution—pH 6.02.
3. Pontocaine solution—pH 3.33.
4. Pontocaine 1–1–1 solution—pH 5.30.
5. Metycaine solution—pH 3.99.

These mixtures of anesthetic agent were then mixed with normal spinal fluid in the ratio of two parts spinal fluid to one part of agent mixture. It was felt that this ratio would grossly correspond to the amount of spinal agent which contacted each cubic centimeter of spinal fluid as the agent was first introduced. The actual figure would necessarily vary with each individual case and with each technic. According to Maxson (10), 8 cc. of liquid fills the subarachnoid space from the sacral region to the sixth thoracic vertebra. Since we usually use about 3 cc. of medium, this ratio of agent mixture to spinal fluid seemed about right. The spinal fluids used in this experiment were from three

normal individuals, and the resultant pH of the mixed spinal fluids was 7.47. After mixing our anesthetic agents with the spinal fluid, the resultant pH was determined. All were on the slightly alkaline side, but at that pH range no gross flocculation or precipitation was present in any of the tubes.

1. Procaine mixed with spinal fluid—pH 7.20.
2. Nupercaine mixed with spinal fluid—pH 7.40.
3. Pontocaine mixed with spinal fluid—pH 7.22.
4. Pontocaine 1–1–1 mixed with spinal fluid—pH 7.36.
5. Metycaine mixed with spinal fluid precipitated—pH 7.15.

These solutions of anesthetic agent in spinal fluid were then titrated with 0.05 Normal sodium hydroxide until the first persistent cloudiness appeared. The end point in all cases appeared quite sharp. The range of precipitation was found to be as follows:

1. Procaine mixed with spinal fluid precipitated—pH 9.40.
2. Nupercaine mixed with spinal fluid precipitated—pH 8.35.
3. Pontocaine mixed with spinal fluid precipitated—pH 8.10.
4. Pontocaine 1–1–1 mixed with spinal fluid ppt.—pH 8.10.
5. Metycaine mixed with spinal fluid—pH 8.05.

To prove that our spinal anesthetic agents were the substances precipitated by titration with dilute sodium hydroxide and not the protein present in spinal fluid, a further experiment was carried out. Large amounts of sodium hydroxide were titrated into several samples of spinal fluid, and even though the pH rose to 12.60, no visible precipitation occurred. We can, therefore, assume that the spinal fluid protein itself is relatively stable in extreme alkaline solution, as would be expected.

The essential laboratory findings are tabulated in table 1.

TABLE 1

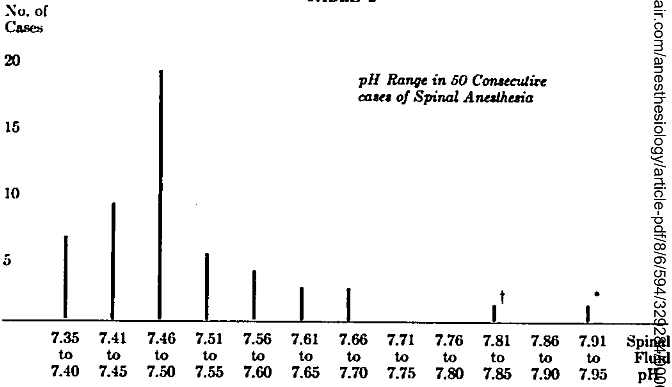
	pH in Aqueous of Saline Solution	pH Mixed with Spinal Fluid	Precipitated in Spinal Fluid at pH
Procaine	5.35	7.20	9.40
Nupercaine	6.02	7.40	8.35
Pontocaine	3.33	7.22	8.10
Pontocaine (1–1–1)	5.30	7.36	8.10
Metycaine	3.99	7.15	8.05

It would thus appear that as the pH of the spinal fluid rises slightly past pH 8, many of the common spinal anesthetic agents precipitate and become ineffective analgesic agents for intrathecal use. This would suggest a possible explanation for the failure of anesthesia in our 2 reported cases. In the first case there was complete failure of anesthesia, and the spinal fluid pH was found to be on the extremely

alkaline side, pH = 7.91. In our second case the anesthesia was both delayed and fleeting. In this case the pH was also very alkaline, pH = 7.80. Thus in these patients the ranges of precipitation, and anesthetic failure are closely approached.

To complete our series we collected and analyzed spinal fluids from over 50 consecutive cases. These specimens were taken preoperatively, and in all of the cases the spinal anesthesia was successful. The pH ranged from 7.35 to 7.70. It will be noted in table 2 that in both of our 2 cases of spinal anesthetic failure, the hydrogen ion concentration apparently was well outside the normal range.

TABLE 2



* Spinal Anesthetic Failure—Case 1. † Spinal Anesthetic Failure—Case 2.

In summary, we suggest that high alkalinity of spinal fluid is an occasional finding in certain patients, and may be the cause of spinal anesthetic failure when other possibilities have been ruled out. In addition, our first mentioned case poses the possibility that it may actually be harmful to the patient to inject certain agents if high alkalinity is present. If the spinal anesthetic agent grossly precipitates out, the insoluble crystals of anesthetic base may be the cause of nerve tissue irritation. In time it may be found desirable to predetermine the hydrogen ion concentration of the spinal fluid before selecting or even using any agent intrathecally. A simplified method of determining pH of spinal fluid in the operating room would be most helpful.

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MEETING OF THE SOUTHEASTERN SECTION OF THE AMERICAN SOCIETY OF ANESTHESIOLOGISTS

JUNG HOTEL, NEW ORLEANS, LOUISIANA

February 16, 17, and 18, 1948

PROGRAM

Monday, February 16, 1948. 7:30 a.m.

Clinics: Touro Infirmary, Baptist Hospital, Charity Hospital and Foundation Hospital.

1:00 p.m. to 2:00 p.m.—Registration—Charity Hospital Auditorium.

2:00 p.m.—Auditorium—Ansel Caine, M.D., presiding. (Papers will be limited to 20 minutes. Discussion, 3 minutes.)

1. Anesthesia for Thoraco Lumbar Surgery. Sam Clark, M.D., Louisville, Ky.
2. Resuscitation of the Heart. Frank Faust, M.D., New Orleans, La. Wilmer Baker and Associates.
3. Clinical Studies on Amidone as an Analgesic Agent. Benjamin Robbins, M.D., Nashville, Tenn.
4. Demerol Scopolamine Analgesia in Labor. John M. Brown, M.D., and Perry Volpitto, M.D., Augusta, Ga.
5. Management of Anesthesia for Thoracic Surgery. A. J. Ochsner, M.D., and George B. Grant, M.D., New Orleans, La.

5:30 p.m. to 7:00 p.m.—Cocktails—Jung Hotel.

7:30 p.m.—Banquet—Jung Hotel. Charles McCuskey, presiding.

1. The Hospital Administrator Looks at Anesthesiology. O. P. Daly, Director, Charity Hospital.
2. Thoracic Surgery and Its Role in the Development of Modern Anesthesiology. Alton Ochsner, M.D., New Orleans, La.

Tuesday, February 17, 1948. 9:00 a.m.

Charity Hospital Auditorium—Perry Volpitto, M.D., presiding. (Papers limited to 20 minutes.)

1. Further Studies with Jet Injection as a New Method of Subcutaneous Administration of Drugs and Local Anesthetics. Robert A. Hingson, M.D., Memphis, Tenn.
2. Nupercaine-Glucose-Spinal Anesthesia—Results of 5,000 Clinical Administrations. D. A. Roman, M.D., and John Adriani, M.D., New Orleans, La.
3. Further Studies on Intravenous Procaine. Stevens J. Martin, M.D., Hartford, Conn.

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