used as a rule are nupercaine (Ciba) 1:1500 and procaine 10 per cent. In this series over 96 per cent. of cases were given nupercaine. . . . When ephedrine alone was used 37.7 per cent. of cases failed to maintain blood pressure. When the combination of ephedrine and pitressin was used 8–10 minutes before spinal puncture, 22.2 per cent. failed; and when used twice, i.e., repeated just before the incision, only 7.8 per cent. failed. These figures speak for themselves. The combined groups give 14.8 per cent. failures. . . .

". . . we made several other observations. Foremost among these was the widening out of the pulse pressure. . . . It is logical to suppose that an intravenous injection of saline or saline and glucose will help stabilize the volume of blood disturbed by the incision and trauma. . . . From the standpoint of the surgeon, Dr. A. I. Willinsky volunteered the observation that with pitressin the gastro-intestinal tract is still further contracted and is entirely kept out of the field of operation. Should we happen to give an overdose of the combination we find no alarming results. The systolic pressure climbs up gradually to about 40 mm. above the preoperative reading and gradually returns to normal. . . . Readings were taken about one or one and one-half hours after the patient was returned to his bed and almost all of the readings showed no marked drop, but either a good maintenance or a return to normal pressures. In hypertensive cases we administered the combination only once (Technique II), with no untoward results. . . . The ages of the patients in this series included both extremes, 14 years being the youngest and 81 + the oldest. . . .

"Finally we would plead with surgeons who use pitressin in repeated doses to prevent or cure postoperative distention, to use the drug only in combination with ephedrine." Bibliography—26 references.

J. C. M. C.

BEUTNER, R.: *Studies in the detoxification of procaine.* Current Researches in Anesth. & Analg. **19**: 132–140 (May–June) 1940.

"Procaine hydrochloride is generally considered a safe local anesthetic, since in many thousand of instances it is administered without the slightest disturbance. Unexpectedly and, perhaps surprisingly, accidents will happen at times. We are thus reminded that it is a poison which may elicit violent convulsions or collapse, if by chance a high concentration reaches the cerebral centers. Like all local anesthetics procaine is kept from resorption in the general circulation by the addition of a vasoconstrictor like adrenalin (epinephrine), but this again is a violent poison. Efforts have therefore been made in my laboratory . . . to find less dangerous detoxifying agents. . . .

"The aim of the first line of work undertaken was to find a more penetrating procaine preparation. It is known that the addition of sodium bicarbonate renders procaine hydrochloride more penetrating. I found that procaine base can be dissolved by means of carbon dioxide directly, thus avoiding completely the use of a hydrochloride. . . .

"Solutions of procaine, prepared by this method, were studied pharmacologically according to the method described by G. P. Miley and this writer —for gauging the convulsive power of local anesthetics. The essence of this method is to observe the incidence of convulsions following the injection of a procaine preparation. . . .

"With larger procaine doses, the solution containing carbon dioxide was somewhat more convulsant than the hy-

drochloride but the difference was, after all, not very considerable. . . .

"It seems, therefore, that when injected intramuscularly, then allowed slowly to pass into the blood stream, procaine is liberated to nearly the same extent whether combined with hydrochloric acid or with carbon dioxide. Quite a different result was obtained, however, when the local action of these two procaine solutions was studied. As a strictly local action, the anesthetic effect on the cornea of a rabbit was tested. It was found to be more extensive for procaine dissolved by carbon dioxide than for procaine hydrochloride. . . .

"G. P. Miley and this writer . . . have shown that calcium chloride allays procaine convulsions. In order to demonstrate this point, [a] . . . statistical method was used. The method consists in injecting a large number of guinea pigs with the same dose of procaine with or without various drugs. The incidence of convulsions is noted. Guinea pigs were selected for these tests since they survive these convulsions except after high doses, while rabbits almost invariably die after procaine convulsions. . . .

"As examples, the following details of the observations may be quoted: 100 mg./kg. of procaine hydrochloride gave convulsions in 84.2 per cent. of the injected guinea pigs (204 being injected, observations by Dr. Wastl; Beutner and Miley quoted 86.7 per cent. in 139 injections). When 25 mg./kg. of calcium chloride were injected, the incidence of the convulsions was only 50.3 per cent. (36 injections, observations by Dr. Wastl). When 50 mg. were added 25 per cent. of the animals had convulsions; when 100 mg. were added 14.2 per cent. of the animals had convulsions (observations by Dr. Wastl, 36 injections; Beutner and Miley quoted 14.6 per cent. in 48). When 200 mg. were added no convulsions were seen at all. . . .

"Beutner and Miley . . . had alalready found that this anticonvulsive action of calcium chloride is a strictly local one; it works in the described manner only if the local anesthetic and calcium chloride are mixed and injected simultaneously. . . .

"The nature of this local anticonvulsive effect of calcium chloride can be understood if we add both magnesium chloride and calcium chloride to procaine hydrochloride. One might assume that such a salt combination would be more effective than calcium chloride alone, especially since magnesium chloride is known for its depressing effect on the central nervous system. However, this assumption proves to be incorrect. Magnesium chloride counteracts the anticonvulsive effect of calcium chloride. . . .

"From all the observations described, it is evident that calcium chloride detoxifies procaine hydrochloride by rendering tissue membranes more impermeable, in this fashion, preventing a rapid diffusion of the poison and protecting the cerebral centers from convulsions. . . .

"In order to be certain of the value and correct functioning of the statistical method used with calcium chloride the anticonvulsive effect of epinephrine was studied by this method (experiments by H. Wastl). Indeed, it was found that a slight addition of epinephrine very markedly decreases the incidence of procaine convulsions. . . . Strange though it may seem, ephedrine, a well known vasoconstrictor, shows no such detoxification. . . .

"In a very thorough investigation, W. J. R. Camp showed that potassium chloride, or other potassium salts, injected in large doses, have an epinephrine-like action. One should expect, therefore, that potassium salts may also relieve procaine convulsions. Ex-

periments have shown that this is the case, although the effect is not very large. . . .

"A study of the calcium salts of organic acids seemed advisable because of the considerable irritation produced by intramuscular injection of calcium chloride. . . . In our experiments the irritant action of calcium chloride was distinctly noticeable. . . . It must be added, however, that such an inefficiency of calcium gluconate is observed only when it is added to and injected simultaneously with the local anesthetic. If calcium gluconate is injected separately it is not entirely inactive. . . .

"In an attempt to explain the slight anticonvulsive action of calcium gluconate on simultaneous injection it seemed reasonable to assume that the calcium content *per se* was not so important as perhaps the calcium ion content. . . . The conclusion is that calcium gluconate does not contain any calcium ions at all; obviously this is the reason why it completely fails to relieve procaine convulsions. . . .

"This absence of electric conductivity, or of ionization, of calcium gluconate is quite a rare and peculiar property. So far as known today no other calcium salt is completely non-ionized. The other organic calcium salts investigated so far are all ionized completely or nearly so. . . .

"Another extensive experimetal series was carried out, using butyn sulphate in the place of procaine as a local anesthetic. As is well known, butyn is a higher homologue of procaine, differing from it in possessing a butyl group in the place of the ethyl group of procaine and a propanol group in place of the ethanol. Accordingly butyn is much more toxic. It is convulsant in doses as low as 20 mg./kg.: 18 animals were injected; all had convulsions, yet survived. With doses as high as 50 mg. or more, all of the injected animals died, since their convulsions were extremely violent. Nevertheless calcium salts were seen to inhibit these violent butyn convulsions quite efficiently. . . .

"All the anticonvulsive agents mentioned so far act by rendering the tissue membranes or the brain centers less permeable. All these have no effect if injected separately or later. They are inactive after procaine has reached the brain. It is known that barbiturates and other centrally depressing drugs also check procaine convulsions. (Tatum and others.) However, this action, in contrast to that of calcium salts appears only if the barbiturate is administered 15 to 30 minutes before the local anesthetic. It was found that if pentobarbital or phenobarbital is mixed with procaine solutions and injected simultaneously, the incidence of expected convulsions is even higher than if procaine is given alone. . . . If the same amounts of these barbitals were injected half an hour earlier than the procaine, no convulsions appeared at all. . . .

"Another depressing drug was tested, calcium bromide. This was found to act exactly like calcium chloride. The same anticonvulsive action was seen which undoubtedly is due to its calcium content, while the bromine, in spite of depressing effect, plays no part.

"These observations show that the barbiturate or bromide has no effect on cell permeability. Its central depressing action is considerably slower than the central stimulating, or convulsant, action of the local anesthetics." Bibliography—5 references.

J. C. M. C.

E. FRIAS AND F. FERNANDEZ. *Postoperative Plate-like Atelectasis.* Current Researches in Anesth. & Analg. 19: 98–101 (March–April), 1940.

"Aside from infection of the bronchi, aside from massive and lobar