SPINAL ANESTHETIC SOLUTION

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No Drawing. Application May 17, 1940,
Serial No. 335,700

7 Claims. (Cl. 187—52)

This invention relates to spinal anesthetic solutions, and has particular reference to spinal anesthetic solutions such as those described in Patent No. 1,888,934, issued November 23, 1932.

The history of spinal anesthesia indicates that the objectionable features thereof have been attributed by various observers to different causes as follows: 1, muscular relaxation with diminished negative intrathoracic pressure; 2, splanchnic dilation; 3, cerebral anemia, as a result of splanchnic dilation; 4, vasomotor paralysis and sudden absorption of Novocaine into the blood; 5, diffusion of the anesthetic into the medullary region; 6, vascular absorption of the anesthetic and its systemic effects; 7, anesthetization, anesthetic paralysis of the white rami, the sympathetic ganglion and post ganglionic fibres; 8, the slowing up of the heart, with imperceptible pulse, paralysis of the cardiac accelerator nerves through the sympathetic, often with resultant shock. To quote Babcock, the greatest American authority:

"If the lower eleven dorsal and the first three lumbar roots are completely blocked, every blood vessel in the body, from the vertex to the toes is completely relaxed; the heart rate falls to 40, 50 or 60; no pulse may be felt at the wrist; and while there may be a soft, faint pulse in the carotid with the completely relaxed vascular system and the partially relaxed muscular system, the blood lies in the dependent portions of the body as in a cadaver. The skin is pale, and incisions through non-dependent portions of the body are dry and bloodless.

I have observed during the past fifteen years by animal experiments and constant use of spinal anesthesia, evidence that there are other factors governing and controlling the reactions encountered in spinal anesthesia quite different than those cited above. I have since discovered that the objectionable features of spinal anesthesia hereinafter named were not brought about by the causative factors as hereinafore stated, but were due to a temporary systemic depletion of adrenalin. It was observed that the extent of depletion and the degree of dysfunction was in direct ratio to the severity, duration and extent of the anesthetic agent on their nerve supply. The solution disclosed in Patent No. 1,888,934 appeared to offer no answer to the difficulties above mentioned nor did it forecast the discovery and solution of the present application. Thus it was not known to inject suprarenin into the spinal fluid, nor that such injection, thereof could be effected without untoward results and with avoidance of the difficulties hereinafore stated.

nor was it known that the combination of suprarenin with the spinal anesthetic would result in an intensified anesthetic action that is greatly prolonged without increasing the amount of the spinal anesthetic, whereby the amount of suprarenin and of the spinal anesthetic used may be such as to adapt them for compatible action. It may be mentioned that suprarenin is a synthetic equivalent of the blood pressure controlling adrenalin and does not oxidize as readily as the latter.

One object of the invention therefore is to provide an improved spinal anesthetic solution having as a base a spinal narcotic comprising a suitable alkaline ester of an aromatic acid together with a secondary anesthetic constituting a general systemic pressor, combined with a common vehicle which serves to encapsulate the drugs for protection thereof and for a prolonged regulated action of the drugs to thus avoid untoward results while permitting a much larger mass of the drugs to be injected into the spinal fluid than would otherwise be feasible.

More particularly, my spinal anesthetic solution may have as a base an alkaline ester of an aromatic acid adapted for use as a spinal anesthetic agent, such as the monobutyric chloride of para-amino benzoyl - diethyl - amino - ethanol, commonly known as Novocaine or Procaine, and/or its p-butyramino benzoic acid dimethylaminoethanol generally known as Pontocaine, and/or alpha-butyloxycinchoninic acid diethyl-ethylene diamide, or Nupercaine, and/or Perca

caine.

By the secondary anesthetics I have reference to such as act as local vasoconstrictors and general systemic pressors, particularly suprarenin and/or ephedrin; preferably I use both so that the suprarenin shall maintain blood pressure, while the ephedrin serves to prolong the pressor and vasoconstrictor properties of the suprarenin and to overcome the toxic effects of adrenochrome which is being formed as an end result.

These latter anesthetics are combined with the spinal anesthetic and with the vehicle hereinafter described to provide a solution having such high viscosity as to be rather adhesive or tenacious and having the capacity of precipitating on contact with the spinal fluid to form a semi-permeable membrane or wall which permits only outward osmotic flow of the drugs encapsulated thereby, thus protecting the suprarenin against...
oxidation and allowing a gradual feeding of the drugs in their proper coefficient relationships to avoid untoward effects even though the injected mass of drugs is so substantial as to be prohibitive unless injected with my solution. The vehicle must naturally be ultimately absorbed by the body in order not to create any untoward effects.

In order that the broad significance of the invention may be clearly understood it will be necessary to discuss various anesthetic actions to which the invention relates. By desire to prevent the formation of adrenal alone in the spinal fluid, and hence to eliminate the poisonous effects of adrenaline to prevent the extreme depressor effects and extreme shock caused by the systemic absorption of adrenaline; and to supply to the body the active principle secreted by the medullary tissue of the chromaffin bodies to thus counterbalance within normal physiological limits the adrenal depletion here-tofore produced with spinal anesthesia as practiced generally and in accordance with Patent No. 1,888,934.

Oftentimes it is important that the solution shall also contain other drugs, as well as the drugs hereinbefore mentioned, and that the solution shall nevertheless encapsulate the same for a definite time and for causing a regulated supply of the drugs according to the viscosity, tenaciousness and predetermined solubility of the fortifying agent which produces the osmotic enclosing wall or membrane. Thus the outward osmosis of the ingredients is in all cases rendered interdependent, establishing a regulated pressor vasoconstrictor anesthetic stimulant coefficient.

In spinal anesthesia various anesthetics have been used for surgical operations below the costal margin, including stovaine, Procaine (Novocaine and Neocaine), Tucoalcine, Pontocaine, (also known as Panvical), Nupercaine (also Known as Percafine), metycacline, aminocaine, and durocaine, with the injection effected through the arachnoid membranes into the spinal fluid. The method described in Patent No. 1,888,934 overcame numerous undesirable effects which had heretofore been produced. Suprarenin with its heart stimulating action was well known, and an improved method for its administration intramuscularly is described in patent application, Serial No. 352,483, filed April 30, 1949, by me, according to which a great many difficulties and objectionable effects heretofore encountered are overcome. The method described in the patent application involved the combined molecular and bulk encapsulation of the anesthetics for the regulated, prolonged release of the drugs to the tissues after injection of greatly increased quantities of the drugs. Ephedrine is in many ways similar to suprarenin, causing a bronchial relaxation, a rise in blood pressure, hyperglycemia, inhibition of intestinal muscle and excitation of other smooth muscle. It also has a cologic effect, but is only about one-thousandth part as powerful as suprarenin. Its general pressor effects which last for about twenty minutes when injected into the tissues of the body are diminished when injected into the spinal fluid. On the other hand, it does not produce a secondary reaction as with oxidised adrenaline.

I found that by dissolving synthetic suprarenin in a viscous, tenacious solution having glue-like properties, that I could exclude the systemic oxygen from the synthetic suprarenin and prevent a rapid oxidation within the tissues. The encapsulation of the suprarenin with an alcohol soluble and the tenacious glue-like material afforded a molecular protection for the suprarenin against systemic oxidation in the body fluids or the tissues. I found that when the alcohol soluble glue-like material was mixed with the spinal fluid or other body fluids or sera precipitated, forming a semi-permeable osmotic membrane between the alcoholic suprarenin solution and the aqueous spinal fluid which further prevented the oxidation and deterioration of the suprarenin. The amount of the alcohol soluble glue-like substance in the solution, I found that I could control the pressor and vasoconstrictor properties of suprarenin from three to six hours when injected into the spinal fluid. I found that by substituting ethyl oxide for a part of the ethyl alcohol in the solution, I obtained a stronger more resistant semi-permeable osmotic membrane, which further delayed the elimination of the suprarenin and prolonged both its pressor and vasoconstrictor properties.

I found that by adding ephedrin to the suprarenin, I either prevented the formation of adrenalin or counteracted or prevented the toxicity and depressor and vasodilator effects of adrenergic. I found that various anesthetic drugs as procain, novon, procain hydrochloride, and propyl-amino-ethanol, p-butylinbenzoe acid dimethylaminoethanol, alpha-butoxyxininchronic acid diethylythylene, etc., could be added to the solution containing the suprarenin and/or ephedrin and could be stored in a pocket within the subarachnoid space or an intramuscular reservoir and be eliminated by and through the osmotic membrane together with and the suprarenin and/or ephedrin and the ratio of elimination of one depending upon the other.

I found that by adding a spinal anesthetic agent to the viscous solution containing the suprarenin and/or ephedrin, I intensified the anesthetic action of the drug and prolonged the duration of anesthesia two or three times without increasing the amount of the anesthetic agent. I found that the semi-permeable osmotic one-way membrane was instantaneously formed by precipitation or a chemical reaction by and between the viscous solution or vehicle and the spinal fluid; that the permeability and osmotic features could be increased or decreased by adding to or taking from the glue-like material or by adding to or taking from the ethyl oxide. I have fortified the material so that anesthesia with 20 mgs. of Pontocaine could be maintained for twelve to fourteen hours; that the pressor and vasoconstrictor properties of the suprarenin combination lasted for twenty to twenty-eight hours. This was accomplished experimentally but is not advised as both cases showed a severe adrenoxidase reaction.

I found that the semi-permeable osmotic one-way membrane prolonged and retarded the elimination of the anesthetic agent and the suprarenin and/or ephedrin from the solution or vehicle but did not delay the absorption time of the anesthetic by the sensory nerves or of the suprarenin by the tissues. It did not delay the elimination time of any of the ingredients. When Neocaine is used as an anesthetic agent, the viscosity of the solution controls the anesthetic action on the motor nerve trunks to such an extent that there may be no motor anesthesia (paralysis) or a partial motor anesthesia. The block of motor anesthesia is not observed with Pontocaine or
Nupercaine as these drugs attack the motor and sensory nerves alike. I found that there was a deficiency in the absorption and elimination of the suprarenin content and the anesthetic drug that intensified and prolonged the anesthetic and depressor value of both. I found that the toxicity of the suprarenin had been reduced more than six times; that the toxicity of the anesthetic agent had been reduced from two to six times depending upon the drug...0003 gm. suprarenin injected subcutaneously will cause a severe reaction instantaneously, causing cold clammy sweats, fulness in the head and extreme nervousness, described by the patient as a jittery feeling which passes away in a minute or two. This reaction is due to the sudden increase in the blood pressure.

The same amount pocketed in the subarachnoid space will give no reaction. .002 gm. or six times the amount of commercial adrenalin, injected into the muscles will produce no immediate or delayed perceptible reaction. Instead of the pressor effect disappearing in a minute or two, the pressor effect here is maintained from eighteen to twenty-four hours. Instead of the cold, clammy sweat, fullness in the head and the jittery feeling, the body temperature is raised from one to three degrees and maintained for from eighteen to thirty-six hours. There is a lack of perspiration and the patient feels warm and comfortable. There are no unpleasant head sensations or nervous reactions. With ephedrin I have used 300 to 400 mgs, without observing toxic reaction or shock. With this solution, I have used as much as 1500 mgs. (experimentally) without observing toxic effects, but this amount is not necessary.

I found that the blood pressure could be maintained at normal, above normal but not subnormal before, during and after the administration of the anesthetics and the suprarenin and/or ephedrin vehicle in the subarachnoid pocket or in the intramuscular reservoir. That the systolic blood pressure rose, the diastolic pressure remained normal or slightly decreased, that the pulse pressure increased, that in hypotension cases both the systolic and diastolic pressures assumed a normal ratio within a few minutes and maintained this ratio for the duration of the anesthetic; that hypertensive cases reacted to and within the normal limits and remained within or slightly above normal limits during the period of use. Experimentally I used a greater percentage of ethyl oxide in the solution and was able to keep the two solutions separated for over three months. I found that by using a too large percentage of ethyl oxide in the suprarenin-ephedrin anesthetic compound, I not only caused diffusion but I delayed absorption so that there was no anesthesia for several minutes and not insufficient anesthesia. I found that a 3% solution of ethyl oxide to be sufficient to prevent diffusion and not delay the absorption of the suprarenin-ephedrin anesthetic through the osmotic membrane. The beneficial action of ethyl oxide is due to the fact that it is nonmiscible with the water of the spinal fluid, is light in weight and absorbable by the human body.

I found that vasomotor paralysis due to the sudden absorption of Novocaine into the blood and vascular absorption of the anesthetic and its systemic effects were not causative factors of a drop in blood pressure.

I have found that by maintaining artificially a normal suprarenin-ephedrin reserve that the untoward symptoms attributed to the effects of spinal anesthesia are not observed. I have found in over six hundred cases that there is no diminished blood flow or progressive loss of vascular tone and acute cardiac failure or oxygen starvation of the heart or respiratory mechanism, pallor, cyanosis, dry bloodless wounds.

My spinal anesthetic solution will not mix with the spinal fluid until the anesthetic agent has been absorbed by the intradural nerve trunks and nerve roots. The spinal anesthetic solution has the additional characteristic that it is tenacious, viscous, and somewhat adherent, a further characteristic that it contains suprarenin and ephedrin that act as local vasoconstrictors and general systemic pressors. The suprarenin and ephedrin are so protected by the adhesive ingredients that they do not come in contact with the oxygen of the spinal fluid or the tissues and that they will not oxidize and deteriorate until after they have been absorbed into the system. It has the further characteristic that by contact with the spinal fluid either by a chemical reaction or precipitation there is a semi-permeable osmotic membrane formed between the anesthetic solution and the spinal fluid that further protects the anesthetic and the suprarenin from oxygen contact. Due to this semi-permeable membrane it has an additional character as seen in the alcohol solution that it will float in or on the spinal fluid not unlike a fat globule on water and as a result anesthesia can be produced higher or lower on the body surface as the operator desires by merely adjusting the position of the patient. Also, according to my improvements, a spinal anesthesia of the legs: 5 c.c. that contains suprarenin and/or ephedrin that will not oxidize in the solution or in the spinal fluid or the tissues for more than six hours and can be eliminated into the body fluids or tissues in sufficient quantities and at such a rate that it will maintain a normal physiological reserve of suprarenin in the blood and tissues. The solution is stable and sterile and may be kept for long periods of time as a ready-to-use solution without discoloration or deterioration. With Novocaine, instead of one hour or one and one-half hours of anesthesia, I am able to secure two and one-half to three hours, with the same amount of drug or one-half the amount. With Pontocaine, I obtained from four to six hours because of its non-diffusible properties. I have prepared it so that a definitive solution will bath and anesthetize the nerves to a fixed height in the spinal canal. Two c.c. will anesthetize the coccygeal nerves and produce perineal anesthesia; 3 c.c. to 4 c.c., depending on the height of the patient, will anesthetize the lumbar nerves and produce anesthesia to the tenth inter-
space and anesthesia to the umbilicus; 6 c. c. will anesthetize the nerves up to the sixth thoracic interspace and produce anesthesia to the costal margin. The viscosity and the semi-permeable membrane will permit osmosis of the anesthetic agent and the suprarenin in a definite ratio and in sufficient amounts to maintain blood pressure and prolong the anesthetic action. There is sufficient local vasoconstrictor action to intensify anesthesia. As a further check on the suprarenin anesthetic agent, the viscosity and osmotic action, I injected the solution into the muscles for duration of anesthesia and then gave Novocaine crystal dissolved in spinal fluid or Pontocaine dissolved in normal saline to recheck the suprarenin elimination and regulation to maintain a normal blood pressure; post-anesthetic taps were made, the solution aspirated and checked for the ratio of anesthetic content.

A table anesthetic solution can be produced by including therein a glue-like adhesive substance preferably in the nature of gliadin or maize in that has been treated with acetic acid which treatment increases the viscosity and glue-like properties and enables me to dilute the gliadin acetate in less alcohol. The gliadin acetate or maize acetate is insoluble in spinal fluid and precipitates on contact with the spinal fluid forming a semi-permeable one-way osmotic membrane between the spinal anesthetic solution and the spinal fluid. When I refer to gliadin or a solution of gliadin or maize, it will be understood that this includes the alcohol soluble protein found in wheat and corn. For the spinal anesthetic agent, I prefer to use Novocaine, monohydrochloride or para-amino benzoyl-diethy laminoethanol or Pontocaine, p-butylamino benzoic acid di-methylaminoethanol. However, like alkamine esters of aromatic acids adopted for use of spinal anesthesia as anesthetic agents may be employed, for example: Nupercaine, alpha-butyloxychino namic acid diethyl-ethylene diamide. When these latter drugs are used the pH of the solution must be increased sufficiently to hold the Pontocaine and Nupercaine in solution and prevent precipitation or precipitation. As an adrenalin substitute I prefer to use the synthetic suprarenin chloride as it is more stable and will withstand sterilization by heat better than will the glandular product. The ephedrin will not oxidize or break down under the ordinary heat that is used for sterilization. I prefer to use this to help prolong the pressor and vasoconstrictor properties of the suprarenin and to overcome the depressor and toxic reaction of adrenoxide, which is constantly being formed in the tissues as an end result.

In preparing the spinal anesthetic solution the proportions may be greatly varied depending upon the various conditions to be met but I prefer solutions in which monohydrochloride of para-amino benzoyl-diethy lamino-ethanol is of 5%, gliadin acetate 0.13%, ethyl alcohol 18%, ethyl oxide 3%, suprarenin 0.0057%, and ephedrin 0.5%, and a balance being distilled water. The alcohols are added to lower the specific gravity of the solution, the ethyl alcohol to hold the gliadin in solution, the ethyl oxide to prevent diffusion and strengthen the semi-permeable membrane. The increased glue-like properties obtained by using gliadin acetate offers a better molecular incapsulation for the suprarenin and prevent oxidation in the tissues.

A greater viscosity and a prolonged action may be obtained by adding ½ or 1% gelatin or 5% glucose, for instance, in the foregoing formula. The gelatin protects the suprarenin better than does the glucose. Good results have also been obtained with solutions prepared as follows:

- **Gliadin acetate**
  - 2
- **Ethyl alcohol**
  - 18 c. c.
- **Suprarenin hydrochloride**
  - 0.0057
- **Ephedrin**
  - 0.5
- **Distilled water sufficient to make **
  - 100 c. c.

According to the method of preparation, the gliadin acetate is dissolved in the ethyl alcohol making a mucilaginous solution having definite elastic adhesive properties; this and the suprarenin and ephedrin are thoroughly mixed and partially dissolved, small amounts of distilled water being added to complete the solution. The monohydrochloride of para-amino benzoyl-diethyl-amino-ethanol (Novocaine) is added to bring the total contents up to 100 c. c. The solution is acidified sufficiently to obtain a pH of 4.6, which is near the isoelectric point of the Novocaine; whereas for Pontocaine a pH of 6 is desirable and for Nupercaine a pH of 7. The solution is then placed in glass septic ampules containing 6 c. c. and immediately sealed. Maiz acetate may be used instead of gliadin acetate in the same quantities and prepared in the same way. The maize acetate has greater glue-like adhesive properties than gliadin acetate. On contact with the spinal fluid it produces a stronger membrane with less permeability. It is not ingested as readily by the spinal lymphatics as is the gliadin. It has greater protective powers for the suprarenin. I prefer to use the maize for intramuscular injection and the gliadin for intradural injection because the gliadin acetate will prevent oxidation of the suprarenin up to six hours which is sufficient for intradural work, whereas, I endeavor to create a depot action in the subarachnoid space for from fifteen to twenty-four hours. Instead of the monohydrochloride of para-amino benzoyl-diethyl-amino-ethanol I may use 500 mgs. of p-butylamino ethylamine (Novocaine) of preferably 300 mgs. of nypharan Pontocaine and increase the pH of the solution to 7.5.

The above solutions are prepared to float on the spinal fluid, that is, they are hypobaric and have a specific gravity of approximately 0.933. To prepare a hyperbaric solution that will gravitate to the dependent portions of the spinal canal and more readily bathe the sensory nerves, I add glucose to the above solution in sufficient quantities to make a solution with a specific gravity of 1.025. The glucose adds to the viscosity of the solution and prolongs anesthesia and with monohydrochloride of para-amino benzoyl-diethyl-amino-ethanol further decreases motor anesthesia. With this solution short operations may be performed on observing any appreciable motor anesthesia (paralysis). When the anesthetic is confined below the second lumbar vertebra there is no motor anesthesia.

In the formulas herein given dextrin may be substituted in place of gliadin acetate or maize acetate. The dextrin referred to is a water soluble corn derivative closely allied to dextrose or glucose. In an aqueous solution it forms a mucilage that retards the absorption of the vasoconstrictor and anesthetic drugs. It has a
high specific gravity and is desirable for use with hyperbaric solutions. When thus used, the
alcohols may be reduced from 3 to 5%; in some
cases 5% gelatin and 6% glucose may be added.
The dextrin may be substituted for gelatin and
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glucose to the extent of 5 gms. of either. In
genral, it is preferable to use dextrin, and/or gela-
tin and glucose or the very specific or hyperbaric
solutions, and the gelatin or maizin acetates, which
are alcohol soluble, for the light or hypobaric
solutions. Thus the specific gravity may vary
between 0.983 for the light solution and 1.295 for
the heavy solution.

It is important to note that so-called blank
solutions may be prepared containing suprarenin
and ephedrin in the viscous vehicle, with no anes-
thetic. These may be prepared in 6 c. c. ampules
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to permit the individual doctor to add thereino
his preferred anesthetic. In such cases, I prefer
to use a light solution as disclosed in the second
formula herein. 100 c. c. thereof may be divided
into ampules of 6 c. c. capacity into which there
may be dissolved 200 to 300 mgs. of Novocaine,
10 to 30 mgs. of Pontocaine, 10 to 15 mgs. of
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Nupercaine, 50 to 75 mgs. of stovaine, 150 to 250
mgs. of metycaine, or the same amount of amin-
ocaine.

The heavy blank solution is preferably pre-
pared with malzin acetate 1 gm., ethyl oxide 7.5
grams, dextrin 5 to 7 gms., suprarenin hydrochlo-
ride 0.097 gm., ephedrin hydrochloride 0.5 gm.,
and distilled water sufficient to make 100 c. c.
of the solution. Of course, the water soluble ve-
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hicle will not produce precipitation by contact
with the spinal fluid, and hence such retardation
of drug absorption as will occur will not be as
efficient or prolonged and will be due solely to
molecular encapsulation instead of being due to
both molecular and bulk encapsulation of the
drugs.

It will be understood that the above solutions
and their ingredients are submitted to illustrate
preferred embodiments of the invention, and not
in a limiting sense; and that various changes and
substitutions may be made therein by those
skilled in the art without departing from the
principles of the invention.

I claim:

1. A spinal anesthetic solution adapted to be
injected into the spinal fluid for prolonged,
regulated diffusion of the anesthetic, comprising
a spinal anesthetic, glidadin acetate adapted to
precipitate on contact with the spinal fluid and
being sufficient to encapsulate the anesthetic, ethyl
oxide non-miscible with said fluid and being suf-
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ficient to cooperate with said glidadin acetate
to encapsulate the anesthetic for a prolonged period
of time in the spinal fluid for a regulated release
of the anesthetic, ethyl alcohol in which said
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glidadin acetate is soluble and serving to control
the specific gravity of the vehicle, and water in
sufficient to cause precipitation of the glidadin
acetate outside of the spinal fluid.

2. As a new composition of matter, a spinal
anesthetic drug adapted to act in the spinal fluid
and being absorbable by the body, and an aque-
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ous vehicle for surrounding the drug to permit
a restricted controlled release of the drug to the
spinal fluid, including an alcohol soluble viscous
vegetable protein including one of a group con-
sisting of glidadin acetate and malzin acetate,
adapted to precipitate upon contact with the
spinal fluid and being sufficient for encapsu-
lizing the drug and being ultimately absorbable
by the body alcohol, and ethyl oxide non-miscible
20
with the spinal fluid and being sufficient in
amount to substantially enhance the encapsu-
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lation action.

3. As a new composition of matter, a liquid
spinal anesthetic drug including suprarenin hy-
drochloride adapted to act in the spinal fluid
and being absorbable therein, an alcohol soluble
acetate of a vegetable protein including one of a
group consisting of glidadin acetate and malzin
acetate adapted to precipitate upon contact with
the spinal fluid and being sufficient to sub-
stantially strengthen the encapsulating action of
the precipitate to thus form a semi-permeable casing
about the drug for releasing the drug at a regu-
lated prolonged rate while protecting the en-
cased drug from oxidation, ethyl alcohol, and
water insufficient to cause said precipitation prior
to contact with the spinal fluid.

4. As a new composition of matter, a spinal
anesthetic drug, alcohol soluble malzin acetate
adapted to precipitate upon contact with the
spinal fluid and being sufficient to encapsulate

the drug for a retarded release of the drug in
the spinal fluid, alcohol ethyl oxide non-miscible
with the spinal fluid and being sufficient to sub-
stantially strengthen the encapsulating action to
thus provide a semi-permeable mass about the
drug for a slow, uniform and prolonged release
of the drug, and water insufficient to cause said
precipitation prior to contact with the spinal fluid.

5. As a new composition of matter, a spinal
anesthetic drug, a vasoconstrictor drug for pro-
moting blood pressure which would otherwise
be reduced by the anesthetic, ethyl alcohol, wa-
ter, an alcohol soluble acetate of a vegetable pro-
tein absorbable by the body alcohol and water
insufficient to encapsulate the drugs by precipita-
tion upon contact with the spinal fluid, said vegetable
protein including one of a group consisting of glidadin
acetate and malzin acetate, and ethyl oxide non-
miscible with the spinal fluid and being suf-
cient to substantially strengthen the encapsulat-
ing action of the precipitate for a regulated pro-
longed release of the drugs in a controlled rela-
tion to each other.

6. As a new composition of matter, a spinal
anesthetic, a vasoconstrictor drug for promoting
blood pressure which would otherwise be reduced
by the anesthetic, glidadin acetate sufficient to en-
capsulate the drugs by precipitation upon con-
tact with the spinal fluid, and ethyl oxide non-
miscible with the spinal fluid and being sufficient
to substantially strengthen the encapsulating ac-
tion of the precipitate for a regulated prolonged
feed of the drugs in a controlled relation to each
other, alcohol sufficient to control the specific
gravity of the composition in the spinal fluid,
and water insufficient to cause said precipitation
prior to contact with the spinal fluid.

7. A new composition of matter for infection
into the spinal fluid, including:

Spinal anesthetic----------------------grams-- 5
Suprarenin hydrochloride..............do--------0.0057
Ephedrin-----------------------------do--------0.5
Glidadin acetate......................do--------0.13
Ethyl alcohol..............................c. c.------15
Ethyl oxide..............................c. c.------3
distilled water sufficient to make 100 c. c. of the

composition.

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