# Physiology of spinal anesthesia

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# THE PHYSIOLOGY OF SPINAL ANESTHESIA

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# THE PHYSIOLOGY OF SPINAL ANESTHESIA

Spinal anesthesia has emerged from the dangerous period in which it was considered necessary merely to inject a solution of a local anesthetic within the spinal dura and then to operate with little further attention to the patient. The need for a very precise technique and for the constant supervision of the anesthetized patient is now recognised. The physiologic changes due to the blocking of the spinal rami are now evident. Methods for localising the block to designated segments of the spine have been developed. The control of the duration and the intensity of the analgesic is possible within limits. The pain of operation may be abolished with or without complete loss of tactile sense and of muscular contraction.

The important influences of point of injection, of dosage, of force and rapidity of injection, of bulk, rapidity of diffusion, concentration and specific gravity of the solution used, and of preceding decompression of the dura have become evident. Patients unsuited for spinal anesthesia are now carefully weeded out or especially fortified. Antidotal measures efficient to prevent circulatory failure and asphyxia have been standardised. Measures for producing an associated unconsciousness are available.

Spinal anesthesia offers to the operating surgeon the stimulus of a highly technical method directly under his control. He may assume the personal responsibility for the suc-

cess and safety of the analgesia and in a large measure control its location, duration and degree.  If during the operation, the onus cannot be thrust upon the assistant; the blame rests upon the operator.  Or should the surgeon prefer, the injection may be given and the patient's condition supervised by a specially trained anesthetist.

With properly induced spinal anesthesia the operator finds the patient in ideal condition for the operation. There is complete freedom from pain or other sensation in the operative field; the tissues are absolutely relaxed, greatly facilitating operative manipulation; the intestines are contracted and do not protrude from the abdominal incision; the anal sphincters are open and the expression of flatus or other content of the lower bowel is strongly stimulated.  Upon the parenchemytous cells of the body the effect of the few centigrams of drug used is inconspicuous.  The brain, liver, kidneys, lungs are particularly free from toxic action due to the anesthetic.  In no other way can such profound and so extensive an anesthesia be produced by so small a dose of drug and with so little general toxicity.  With no other method does the depressing action of the anesthetic appear in the early stage of the operation when the patient can best withstand it.  The shock from the operation as it proceeds is, in part at least, antidoted by the rising blood pressure as the blocked sympathetic rami regain their function.  With the technical improvements now available, no other anesthetic of

Equal range leaves so few sequelae. Usually sensation returns without other symptoms. Ably used it is much quicker, simpler, less painful in induction, gives more uniform and dependable anesthesia and produces better relaxation than caudal or sacral anesthesia.

If a well performed operation brings a sensation of satisfaction, how much greater the achievement if it has been accomplished with comfort and relative safety to the patient and with the utmost facility to the operator. But spinal anesthesia has compensating disadvantages. It requires an accurate and precise technique for uniform results. A lack of skill in the administration is more obvious than with the use of ether; ignorance in using the method or lack of supervision during the period of analgesia may cost the patient his life. A death under chloroform or nitrous oxide often may be blamed upon the drug, but the mortality with spinal anesthesia usually is to be blamed upon the surgeon. Spinal anesthesia therefore necessitates a degree of skill and a working knowledge of the physiologic action of the method. It is a very personal method strongly appealing to the temperaments of many operators, but equally unadapted to others. It has a very wide field of usefulness and has supreme advantages for certain types of operation, but it is to be rigidly excluded from a limited class of patients. Perhaps with no other anesthetic are the indications or contraindications more clearly evident. (1)

SELECTION OF PATIENTS:  It is axiomatic that no one anesthetic
is suitable in all cases requiring surgical therapy.  The
induction of anesthesia, or better analgesia, should be based
upon a number of factors.  The anesthetic agent and type of
anesthesia employed should be made to conform to the patient's
condition and the condition demanding surgery.  In some cases
spinal anesthesia is the only type of anesthetic to be employed.
In many cases it is the best type of anesthesia, and in all
cases where it is indicated it can be made safe and effective.
Rarely, in the emotionally unstable and neurotic it cannot be
utilised, not because of its lack of analgesia but because of
the psychic relations of the patient.  It follows that the
indications for the use of spinal anesthesiaare determined
by the surgical indications, by the site of operative inter-
vention, by the age and debility of the patient, by the meta-
bolic conditions of the patient (nephritis, diabetes), or by
pulmonary and cardiac conditions (tuberculosis, bronchitis, etc.)
where inhalation is contraindicated.

Of all the forms or types of anesthesia it causes the
least metabolic and protoplasmic disturbances.  Primarily it
does not lead to pulmonary complications, uremia, or gastro-
intestinal complications.  It is par excellance the anesthetic
of choice in all surgical affectations of the lower abdomen,
including there intestinal obstruction and peritonitis, and
pathology of the vagina, perineum and rectum, and the lower

extremities.  Complete consciousness (radicular induction

without interruption to medullary conduction) is very desirable

in case the surgeon need make any unexpected decision and have

it accepted by the patient.

INDICATIONS FOR USE OF SPINAL ANESTHESIA:  For all surgery

below the diaphragm with certain exceptions as listed below.

a)  Cases in which a general anesthetic is dangerous, i.e.

the aged, the debilitated, and those patients with heart,

kidney, liver, lung and endocrine diseases.

b)  Cases with high blood pressure are difficult problems

for all anesthesias.  They can be subjected to spinal anes-

thesia if there is no definite evidence of cardiac weakness.

c)  Cases showing signs of renal dysfunction such as

high blood urea or albumin or cast in the urine.  Ether causes

definite destruction of renal tissue.  Even patients who have

gas anesthesia occasionally have albumin and casts in the

urine after operation.

d)  Intestinal obstruction of all types.

e)  Any case with an acute upper respiratory infection.

f)  Emergency operations, when there has been insufficient

time for the routine complete preparation of the patient.

CONTRAINDICATIONS:  Although the contraindications for spinal

anesthesia are exceptionally few, they are definite and cannot

be disregarded.  In former days the occasional death that was

reported due to spinal anesthesia was probably not due to the

anesthetic as such but rather to an unwise selection of patient,

the drug, the dosage or the technique employed.

The contraindications to the employment of spinal anesthesia are:

a)  Any marked involvement of the cerebrospinal nervous system, such as brain tumor, cord tumor, intracrainal or intraspinal hemorrhage, syphilis or meningitis.  Any case of turbid spinal fluid, though no other pathology is found, is included under this head.

b)  Any mechanical obstruction or limitation of the respiratory space, as from large pleural effusions or intra-thoracic growths.  Tuberculosis except in later stages with bilateral involvement are not included.

c)  Cases of hypotension from any cause are poor operative risks, especially if there is cyanosis, decompensation or the like.

d)  Grave ichteric subjects with lithiasic or cancerous pancreas are easily shocked with any form of anesthesia.

e)  Extremely depressed patients or those in a state of severe traumatic shock, whose vital centers are already functioning with great difficulty, do not well stand any sudden alterations in vasomotor tone.

f)  Septicemic cases with positive blood cultures should never be anesthetised with spinal anesthesia.  The puncture would eliminate the proctective barrier between the infected blood and the nerve centers.

g)  Patients with extreme myocardial degeneration and

an unstable circulatory system, passive congestion, etc., do not react to a sudden vasomotor change.

h) Suppuration at the site to be punctured or any other condition preventing thorough preparation of the area through which the spinal needle is to pass is a definite contra-indication for spinal anesthesia.

Spinal anesthesia in cases where the operation is below the umbilicus is relatively safe for all except those with involvement of the cerebrospinal nervous structures. Operations in the upper abdomen, especially on the stomach and duodenum, is dangerous unless every precaution is taken to control the drop in blood pressure. (2)

PHENOMENA ACCOMPANYING SPINAL ANESTHESIA: (3)(4)(5)

Spinal anesthesia is that form of local anesthesia with which certain areas of the body can be anesthetised by placing the anesthetising drug in direct contact with the nerve roots whose fibres supply those areas. "When the anesthetic is introduced into the subarachnoid space it is being placed into the spinal fluid which bathes exposed nerve roots, whose histological structures are slightly different from the peripheral nerve fibres in that, within the spinal canal the nerve roots are not covered by the epi-neurium or connective-tissue nerve sheath present in all extradural nerves. Consequently, the anesthetic is instan-taneously attracted and rapidly combines with these nerve roots much as a blotter absorbs ink, with resultant instan-

taneous anesthesia of the region supplied by them. The grey
substance of the spinal cord is not affected by the drug
because of its protective white sheath and because of the
greater affinity of the drug for the exposed nerve roots,
especially the sensory nerve roots. The anterior or motor
roots receive less of the drug for two reasons: first, be-
cause they are less suseptible from the physico-chemical
standpoint, and secondly, they receive a less concentrated
solution of the injection and are partially separated from it by
the interarachnoid trabeculas. This then explains why we may
have complete anesthesia of the lower limbs of the patient,
yet he is able to move his legs". The calculated dose of the
drug is given in the beginning and then cannot be changed.
If the anesthesia is incomplete it cannot be increased ex-
cept by repeating the injection, if an overdose is given it
will exert its toxic effect until eliminated.   (6)

"Experiments with dyes have led to the conclusion that
the drug will penetrate only the outer membrane of the cord
while it deeply impregnates the nerve roots, cauda equina and
the nerves for about 2 cms. beyond their exit from the inter-
vertebral foramina. Where it meets the nerve tissue in full
concentration, it penetrates quickly and deeply. That which
subsequently diffuses through the spinal fluid produces a
nerve block which varies in depth in direct proportion to
its concentration. It is excreted finally with the spinal
fluid into the lymphatics, entering the venous circulation

where it loses its activity.

"Excluding the type of patient and the nature of the operation one can attribute variations to these.

Variant Factors:

a)   The drug--the amount injected and the solvents used.

b)   The point at which it is injected.

c)   The force of injection.

d)   The rate of secretion, excretion and circulation of the spinal fluid is each individual patient.

e)   The position of the patient during and after the injection.

"When the drug is placed in contact with a nerve root it will either completely or partially block the fibres of that root.  Some fibres are more resistant to the drug than others and require, therefore, greater concentrations of the drug to block them.  They are blocked in the following order:

a)   The fibres which carry pain and temperature sensations from the skin and viscera.  These, besides being very poorly localised, have a low sensibility threshold which requires strong stimuli.

b)   Those fibres which discriminate touch and temperature, which arise from the skin and are sensitive to weak stimuli.

c)   The fibres which carry impulses of pressure or movement from muscles, tendons and joints.

d)   The fibres which carry impulses to the skeletal

muscles.

e) The sympathetic nerve fibres, which receive stimuli from the viscera and send out, among others, impulses which regulate the vasomotor system". (7)

With spinal anesthesia, therefore, the loss of the sense of pain is the most complete and lasting. These fibres have the widest areas of distribution. Nerve fibres causing vaso-dilatation are the least completely and permanently effected. These have the smallest areas of distribution. To summarize, we may say that with spinal anesthesia there is first loss of the sense of pain, then tactile sense, then motor sense, then of muscle power and finally of vasomotor control. As the de-pressant action of the drug wears off conduction through the nerve fibres gradually returns to normal and these lost functions return in the reverse order.

THE NERVOUS CONTROL OF THE BLOOD VESSELS: "If in the human being vasomotor paralysis is confined to the lower part of the body, the displacement of the blood into the periphery causes a demonstrable decrease in the blood pressurs, which, according to experience, however, is not fatal. (8)

"From the second thoracic to the second lumbar segment there are present sympathetic nerve fibres which emerge from the anterior root by way of the white rami communicantes and join the abdominal and thoracic sympathetic chain of pregang-liated fibres. These fibres carry vasoconstrictor impulses which keep the great splanchnic bed of blood vessels in a

state of constant contraction. In the thoracic region they carry impulses which accelerate the heart beat in apposition to the impulses of the vagus, which tend to slow the heart beat. If all of these fibres are cut in the experimental animal, there is at once noted a tremenduous dilatation of the blood vessels of the splanchnic bed, causing a pallor of the peripheral tissues with a marked drop in blood pressure. The heart is also slowed due to unopposed action of the vagus.

"In the human being the introduction of novocain into the spinal canal may result in a relaxation of all the splanchnic blood vessels with a profound drop of blood pressure, The circulation is also slowed." (9)

"Our knowledge of the nervous control of the blood vessels dated from the discovery, by Claude Bernard, that nerve fibers maintain them in a state of tonic constriction. Bernard showed that if, in the rabbit, the cervical sympathetic on one side be divided, the vessels in the corresponding ear dilate. Vessels come into prominence which were previously invisible, and on account of the greater flow of blood thus produced, the ear on the side of the section becomes warmer than the normal ear. If the head end of the divided sympathetic nerve be stimulated, all the vessels of the ear contract, and the ear becomes colder than that of the other side. The fact that the dilatation of the vessels is produced by section of the cervical sympathetic and lasts for a considerable time after any irritant effect of the section must have passed off, shows that the ear vessels are continually under the in-

fluence of tonic constrictor impulses arising in the central nervous system and proceeding to them along the nerve fibres of the cervical sympathetic.

"The paralysis of the ear vessels, though lessening the resistance to the flow of blood there, effects too small a vascular area to have any marked influence of the general arterial pressure. If the spinal cord be divided on a level with the origin of the first dorsal nerve, or higher, a wide area is effected and the blood pressure sinks considerably. In the dog it may fall from 120 mm. Hg. to 40 or 50 mm. Hg. The heart after the section beats more rapidly than before, so that the fall of pressure must be ascribed to a change effecting the blood vessels and lowering the resistance to the flow of blood. Since a maximal effect of the blood pressure is produced by section of the cord at this level, one may conclude that the tonic constrictor impulses to all the vessels of the body pass through this segment of the cord before leaving it to be distributed to the arterial walls.

"The source of these impulses may be made out by studying the effect of sections through different levels of the nervous system. Division of the cord at, or below, the second lumbar nerve causes no effect of the blood pressure. On making a section above the first lumbar nerve, the effect produced increases progressively until the first dorsal roots are reached, where it is maximal; stimulation of the lower end of the cut dorsal cord causes widespread vascular cons-

triction and a large rise of blood pressure. Section of the crura cerebri, of of the brain stem at the upper border of the fourth ventricle, leaves the pressure uneffected. Destruction of a small region of the medulla situated on each side of the middle line in the neighborhool of the facial nucleus, i.e. in the forward prolongation of the lateral columns, after they have given off their fibres to the decussating pyramids, causes an immediate and maximal lowering of the blood pressure.

"We must therefore conclude that all the vessels in the body are kept in a state of tomic contraction by impulses arising in this portion of the medulla oblongata, travelling down the cord as far as the dorsal region, and then passing out of the cord by the dorsal and upper lumbar nerves. This conclusion is confirmed by the fact that, whereas stimulation of the anterior roots of the cervical, lower lumbar and sacral nerves has no influence on the blood pressure, a rise of arterial pressure can be obtained by stimulating any of the anterior roots from the first or second dorsal to the second or third lumbar. The same effect is produced by stimulation of the white rami communicantes from these roots to the sympathetic system, by excitation of the sympathetic system itself, or of the splanchnic nerve." (10)

We have previously stated the order in which the various nerve tracts are effected by the anesthetic. The above transcript from "Starling" points out the relationship which may, and in all probability does, take place in some degree depend-

ing on the nature and amount of drug used with one of the vital
constituents, namely the blood vascular system. "It is to be
remembered that fixation of the anesthetic solution by the
nerve lipoids occurs rapidly and unless special factors are
brought into play the amount of diffusion of a few cubic
centimeters of the solution reinjected after withdrawal of
that amount of cerebrospinal fluid will always be quite
constant. The withdrawal of a greater amount of cerebro-
spinal fluid is an important modifying factor in determining
the level of anesthesia. If the amount of fluid reinjected
be kept constant, the greater the quantity withdrawn the
greater will be the diffusion and, therefore, the higher
the level of anesthesia. This is in accordance with the
well known physical law that the diffusion of liquids under
pressure is inversely proportional to the pressure. The
diminution of the cerebro-spinal pressure caused by withdraw-
ing a breater quantity of fluid causes greater diffusion of
the reinjected fluid. It was recognized in a general way
by those advocates of spinal anesthesia who advised against
the withdrawal of cerebro-spinal fluid, because of the pos-
sibility of the reinjected anesthetic solution reaching
vital medullary centers." (11)

Ever since the first spinal anesthetic was given and
the danger of vaso-motor collapse was recognised attempts
have been made to thwart it. These are almost as numerous
and varied as the articles written on the subject and range

from use of a variety of drugs and technique to means of
counteracting the process once it has begun. Ziegner offers
a plausible alleviation by stating, "Vaso-motor collapse in
operations on the lower half of the body may be prevented
by having the patient sit up until the vaso-motor sign is
positive, the reflexes are lost and mobility of the lower
segments has begun to disappear." (12)

The problem, however, is probably best handled by the
operator working from his own experience and keeping in mind
the physiological considerations of the region involved.

Vaso-motor collapse is best recognised by "sudden fall
in blood pressure followed by nausea, which if not relieved
will lead to vomiting, pallor of the skin, a feeling of com-
pression about the chest, thirst, air-hunger, cold sweats, and
a slowing of the pulse and respirations. With a complete
collapse in which the whole splanchnic nervous system is blocked
and the blood has collected in the great splanchnic pool, the
blood pressure may fall to zero. The function of the liver,
kidneys and the other organs may be greatly diminished. The
patient may become unconscious with cessation of the heart
beat. In such cases, if respirations are maintained and the
heart is not allowed to stop, a fall of blood pressure to zero
at the wrist is well born and the patient none the worse because
of it. With proper treatment the blood pressure may be grad-
ually restored, the vital organs returned to normal function,
and consciousness regained. There remains little if any

damage because of this transient paralysis. (13)

RESPIRATORY AND CIRCULATORY PHENOMONA

"Respiratory paralysis is the usual cause of immediate death from spinal anesthesia. Three mechanisms, or combinations of these, may be involved:

1. Direct action of the medullary respiratory centers by diffusion of the drug to the fourth ventricle in paralytic concentrations. The observations of Koster and Kasman, and of Johnson and Henderson, Who demonstrated experimentally that excessively high concentrations are required to bring about this effect, indicate that this type can probably be excluded from serious consideration. (14)(15)

2. Ascending block of the intercostal and phrenic nerves. This type of paralysis is unquestionably preventable and is secondary either to (a) ignorance of, or inexperience in, the technical aspects of the procedure, or to (b) unsuccessful attempts to produce a selective sensory nerve block of the neck and upper thoracic regions.

3. Insufficient nutrient flow of blood through the central respiratory mechanism secondary to cardio-vascular depression. Cardio-vascular depression in some degree is attendant on every intradural block involving the upper part of the abdomen and the thorax. Since the integrity of the respiratory center depends of the maintenance of adequate volume flow of sufficiently oxygenated blood, the obvious inference is that the latter mechanism is responsible for the

majority of cases of respiratory failure. We shall attempt
to demonstrate that the maintenance of an adequate volume flow
of well oxygenated blood is difficult if nerve impulses are
prevented from reaching a majority of the costal muscles by a
high thoracic block.

"A study of the factors concerned in the disturbance of
circulation may furnish some evidence as to the possible
means of prevention of respiratory failure.

"Nearly all authors have stressed paralysis of the splanch-
nic nerves, with a subsequent pooling of the blood in the
abdominal region, as the principal, if not the only, factor
involved in the circulatory depression. Experimental ober-
vations of the dog do not substantiate this view, as bilateral
splanchnotomy does not produce the characteristic fall of blood
pressure. Kremer and Wright have recently observed that
bilateral section of the splanchnic nerves of the cat produces
a fall in mean blood pressure of only from 0 to 15 per cent.
Furthermore, they found little or no change in venous pressure
although the vascular contracted bowel and blanched uterus
indicate that all of the "lost" blood is not in the splanch-
nis region. (16)

"Skeletal muscle tone is essential for the maintenance of
a stable capillary and venous bed. Loss of this tone accomp-
anies any intradural block. Undoubtedly the splanchnic area
is not the only region in which one can expect an enlarged
capillary bed. Plethysmographic records made in this labor-

atory indicate a considerable increase in leg volume of dogs under spinal anesthesia.

"It is of relatively little practical importance whether paralysis of the splanchnic nerves, the vasoconstrictor nerves to the skin and other vessels of the trunk and extremities or loss of skeletal muscle tone is the principal or contributory factor to the circulatory depression. All will admit that a marked decrease in the peripheral resistance to blood flow occurs in the region involved in the block.

"Significant, however, is the fact that a sensory and motor block of the tenth dorsal segment, which produces an increased capillary bed over a considerable portion of the body, is usually attended only with a moderate alteration in blood pressure. Rarely a marked drop in pressure may be due to a motor paralysis higher than is indicated by sensory examination. Apparently vasoconstriction in other parts of the body or an increased cardiac output can occur as a compensatory measure. Furthermore, adequate oxygenation of blood and normal thoracic activity occurs, since there is no respiratory involvement.

"Grave cardiovascular changes occur, as a rule, only in blocks that involve the chest. As the thorax is implicated, two important factors enter into consideration: (1) additional paralysis of the vasoconstrictor fibers and (2) intercostal nerve paralysis.

"While the first factor has been elaborated by writers

on the subject, little attention has been directed to the consequence of partial or complete loss of costal respiration when superimposed on a vascular incompetence involving two thirds of the body. Clinicians see patients who suffer no outstanding ill effects from a diminution in minute volume respiration, particularly if this is of short duration. This may explain why the diminished respiratory exchange occurring during spinal anesthesia has been minimised. The conditions that exist during spinal anesthesia deviate markedly from the normal. The increased vascular bed secondary to the afore-mentioned factors means low blood pressure, diminished minute volume flow of blood and poor oxygenation of tissues. The integrity of the medullary centers and heart is dependent on an adequate supply of oxygen. The additional anoxemia accompanying partial or complete thoracic paralysis may spell disaster.

"That the oxygen needs of the body are not adequately met, owing to a reduced volume flow of blood and a decreased gaseous exchange in the lungs proportional to the lowered thoracic excursion, is the contention that constitutes the main thesis of the present communication." (17)

In 1912, Gray and Parsons published a clinical study in which they stressed the intimate relationship existing between the fall in blood pressure and the costal paralysis. Their conclusions--"The main fall is due to the thoracic paralysis, which is not compensated for by overaction of the

diaphragm, and consequently the aspiration action of the thorax is diminished"--being at variance with the view of some physiologists concerning the mechanical movement of venous blood by variations in intrathoracic pressure, has not been generally accepted. We believe that their observation was essentially correct. Whether or not we accept their conclusions as to the mechanism involved, the fact remains that a partial or total loss of costal respiration diminishes gaseous interchange. (18)

"Isengerger and Lundy, in personal communication to the authors, observed that artificial respiration accomplished by alternate inflation and deflation of the lungs, with positive and negative intra pulmonary pressure would maintain a nearly normal blood pressure in dogs after complete paralysis of the spinal cord produced by large doses (2,500 mg.) of procaine hydrochloride intradurally. This observation indicates that the heart will remain competant in spite of the decreased peripheral resistance provided fairly normal thoracic activity and pulmonary interchange occurs. This method offers a means of study of the relative importance of the respiratory and cardiovascular factors with shich we are concerned under the conditions existing in high spinal block. (19)

The great fall of blood pressure observed after section of the cervical cord is not permanent. After a short time (as determined by animal experimentation), the pressure begins to rise, and if the animal be kept alive, may attain a height equal to that found in normal animals. Refering

again to Starling we find that if "the spinal cord (of such an animal) be destroyed, the blood pressure sinks practically to zero, because the animal has been, so to speak, bled into its own dilated blood vessels." Here again we see some divergence of opinion. "In addition to the chief vasomotor centre in the medulla, there is a series of subsidiary centers in the spinal cord, centers which we may probably locate in the portions of grey matter situated in the lateral horns of the cord and giving origin to the fibres which go to make up the white rami communicantes. By means of these spinal centres a certain degree of adaptation of the blood supply to the various parts of the trunk is possible. The important co-ordination between the state of the blood vessels and the condition of the central pump, the heart is however wanting, since the blood vessels are now cut off from the cardiac centers, and from that part of the central nervous system which receives the afferent impulses carried by the vagi."

Further experimentation in this same field has shown that the "spinal centers, like the chief vasomotor centre, are susceptible to changes in the composition of the blood supplied to them. If an animal be kept alive by means of gentle artificial respiration after division of the cord just below the medulla, the blood pressure soon resumes a normal level. If artificial respiration be now discontinued the asphyxia excites the centres of the cord, and the pressure

rises. Conversely, if the artificial ventilation be made excessive (acapnia), the blood pressure repidly falls, but is speedily restored if ventilation, at the same excessive rate, be carried on with air containing 5 per cent. carbon dioxide, or with expired air. After destruction of the spinal cord, these effects disappear. The spinal centres are also excited by lack of oxygen. There is a difference between the sensibility of the spinal centres to these substances as compared with the medullary centers. Here, as in the medulla, the common factor is probably increased H-ion concentration, the excitation threshold for the medullary centres being lower than that of the spinal centers". (*10)

The local spinal centers are connected with the medullary vasomotor center on each side by tracts of nerve fibres which descend in the lateral columns of the cord. (20)

"In spinal anesthesia a slight respiratory depression may occur without any degree of respiratory paralysis. This is not true respiratory parlaysis due to the drug but is the result of lessened bulbar function due to anemia plus cessation of abdominal breathing. This shallow breathing with frequent intervals of deep sighs readily clears up as the pallor, insomnia and other symptoms of a lowered blood pressure are relieved.

"When the patient's respirations slow gradually the cause is paralysis of the phrenic nerve and not of the respiratory centre. With neocaine or similar novocaine products, fortun-

ately, it is almost impossible to paralyze the upper cervical nerves when the drug is injected below the twelfth dorsal vertebra. This is because these nerves, which are very resistant to the action of the drug, are bathed in an extremely dilute anesthetic solution.

"True respiratory failure is due to a high anesthesia and it will vary with the height and concentration of the anesthetic, the vitality of the patient and the vigilance of the operator. When the roots of the cervical nerves leading to the diaphragm are involved, true respiratory failure begins; the unaided diaphragmatic breathing may cease so that the tidal air cannot be moved. This condition may be overlooked until far advanced. The patient may still be able to move the lips and tongue but be unable to talk. Cyanosis and unconsciousness may develop and the heart stop beating unless artificial respiration is begun. This is the important complication of high anesthesias and may prove fatal unless the operator understands what is happening and is prepared to combat it. If he is careful and vigilant, respiratory failure need not be feared." (21)

ANESTHETIC AGENTS:

It has been stated elsewhere in this paper that the successful anesthetic depends upon a wise and careful selection of patients who are adaptable to the type of anesthesia used. The patient selected, it now becomes necessary to choose a suitable anesthetic agent. Needless to say, a perfect anes-

thetic has not yet been found and while one anesthetist gets
most successful use from one, another finds a different one
to b his choice. It will, therefore, be necessary to list
a few of those in most common usage at present and also a
few considerations in favor of or against the anesthetic.

SPINOCAIN: Pitkin, George P., who is one of the fore-
most authorities in the field of spinal anesthesia has at-
tempted to produce an anesthetic in which the specific gravity,
diffusibility, and anesthetic property could in a measure be
controllable. In an article published by him in 1929 in the
British Medical Journal he states, "To prevent diffusion" of
the anesthetic throughout the subarachnoid space "we employed
many viscous agents, some of which had been advocated before.
But by the use of a solution of starch paste, we were enabled
to prevent dissemination for forty minutes. This solution,
even in sealed ampoules, could only be used when fresh. It
would ferment, precipitate, and become unstable within six to
eight weeks. Later we discovered that gliadin (the mucilaginous
content of wheat starch) was the substance that really produced
the viscid properties desired. This is relatively insoluble,
being soluble only in certain alcoholic solutions. If the
alcoholic content is increased or diminished it will precip-
itate out of the solution in crystalline masses. From gliadin
we were able to produce a jelly-like gelatinous substance
that we chose to call amyloprolamin, which was stable, soluble,
prevented dissemination for over two hours, or until the anes-

thetic drug was spent.

"To further check the action of the solution within the subarachnoid space and to determine whether a definite and fixed volume could be maintained throughout the duration of the anesthesia, to prove that dissemination would not occur in a cephalic direction, we colored the solution with methylene blue and tapped human spines from twenty minutes to one hour after the original injection. We obtained no colored solution from the sixth or seventh thoracic interspace. Its action was further checked by adding stains to the solution, injecting it into the dural sac of dogs, and noting the stained regions of the dord and arachnoid in necropsy specimens."

"To enable us to carry out our technique with as few manipulations as possible, and to place at our disposal solutions that could be controlled within the subarachnoid space, we devised the ephedrine-novocain solution, and the light and heavy spinocain." The latter two refere to a comparison of the specific gravity of the spinocain with that of spinal fluid. (22)

Spinocain has been found by many to be very useful but its complexity detracts from its adaptability in the hands of a novice. By far the greater majority of operators prefer a simpler drug. Of these we find novocain to be the one most widely accepted.

NOVOCAIN: or procaine hydrochloride (procain), occurs as small colorless crystals or as a white, crystalline powder. It is odorless and is stable in air. One gram is soluble in

0.6 c.c. of water and to a lesser extent in alcohol, chloroform and ether. It is incompatible with alkaloid precipitants.

"Procain exerts a paralysing action on all nerve tissue with which it comes in contact in sufficient concentration; this may vary from 0.1 to 0.2 percent. under diffenent circumstances. Systemic symptoms consist in nervousness and weakness with tremors, nausea and dizzyness, followed in severe poisoning by great weakness of the heart and respiration, and even asphyctic convulsions and death.

"Procain is very rapidly absorbed, both when applied to mucous membranes and when injected. That which reaches the blood stream is soon destroyed in the liver, very little if any being excreted. The rapid destruction explains the large doses which can be borne without danger if slowly administered.

"Procain is not irritating even in strong solution, its only marked topical action being paralysis of nerve tissue. Its effect is exerted on the sensory structures in smaller dose than on the motor. The blood vessels are usually slightly dilated, but marked hyperemia may occur. Recovery from the anesthesia is quite rapid.

"The symptoms of poisoning are not characteristic, consisting in weakness and faintness with nausea and pallor, weak pulse and failing respiration. It is not easy to state the toxic dose, as the effects vary so markedly with the manner of injection. The danger of severe poisoning bears a much closer relation to the rate of absorption than to the

total dose. Thus, concentrated solutions, from which absorption is rapid, are much more dangerous than dilute, and intravenous." (23)

"Novocain hydrochloride is the anesthetic agent employed in connection with the technique used by the majority of operators in regional anesthesia. Novocain is a German product. Salts of identical chemical formula are prepared in different countries under various names: procain, in America; syncain, scurocain, neocain, etc., in France. All of them are used with equal advantage, provided the particular brand selected is pure and sterile. The drug may be either in the anhydrous or crystalline form provided it is put up in special ampules. Solution is made by filling the ampule with the patient's cerebrospinal fluid. No other solvent is used and nothing else added to the novocain. The dose injected represents 1 centigram of novocain for each 15 pounds of body weight of the patient. The dose may be varied to suit the needs of the operator.

"The fall in blood pressure being the principal drawback of the method, it is customary to inject, some times before or immediately after the spinal injection, a stimulant which controls to a certain extent the circulatory condition, and serves to check at the same time the deleterious effects of the drug itself or of any impurities it may accidentally contain. Good results are obtained with the following stimulant, put up in 2.0 c.c. ampules:

| | |
|---|---|
| Caffein | 0.25 gm. |
| Spartein sulphate | 0.05 " |
| Sodium benzoate | 0.30 " |
| Strychnine sulphate | 0.001" |
| Distilled water q.s. | 2.0 c.c. |

"The solution must be neutral. It is injected subcut-
aneously when used as a preventitive and in the treatment of
light symptoms, such as pallor of the face and cold sweat.
It is injected in the subarachnoid space, in the case of total
respiratory failure, before any attempt is made to restore
breathing by artificial respiration." (24)

More will be said later in connection with synergistic
drugs to be used with procain and its derivitives.

PANTOCAIN: This is a relatively new product in the field
of spinal anesthetics, and at this writing is being used in
a manner of trial in several hospitals and clinics throughout
the country including the University of Nebraska Hospital, Omaha.
The drug has been found to be thermolabile, decomposing if ex-
posed to high temperatures of prolonged boiling. It is slightly
heavier than spinal fluid.

"The pharmacological action of pantocain has been
studied from the following three points of view, namely,
its toxicity, its optimal dose, and the duration of the effect
of the drug. When used intravenously it requires at least
six times the intraspinal dose to produce the lethal effect.
The duration of the effect of the drug lasts about 2 to 3
times as long as procain. In comparison with nupercain it
is just as effective dose for dose but enjoys the position of

being 3 to 4 times less toxic.  It has so far been found to be no more toxic than procain, and some observers have found it to produce a smaller average drop in blood pressure."  (25)

The following are a few drugs which have in the past been tried but for reasons such as those listed below have gained disrepute and been discarded.

STOVAINE:  Stovaine at one time in the history of spinal anesthetics was quite popular.  It was found to be too irritating when placed into the tissues and cases of meningitis have been reported from its use.  It decomposes by boiling and thus subjects the patient to rather toxic effects.

APOSTHESINE:  This drug was also popular at about the same time as was stovaine.  It was found to have no property of selection of nerve tissue, and was often severely toxic. Its action is slow and elimination also slow and often causes some pain in injection especially if injected fast.

TROPACOCAINE:  Tropacocaine was found also to be somewhat irritating when placed in the tissues.  It is very effective and absorption is rapid.  Absorption is so rapid as to be one of the drawbacks for its use, producing a toxic reaction in the form of central excitement and convulsions followed by rather wide spread paralysis often fatal due to respiratory and vasomotor paralysis.  (23)

NUPERCAINE:  This drug unlike those mentioned above is a derivitive of quinine.  It was found to have the essential properties of a good spinal anesthetic with one exception, it

is extremely toxic.  It is about five times as toxic as cocaine
when injected into the tissues and otherwise produces about the
same general vasomotor reactions.  (26)(27)

EPHEDRINE:  "Large amounts of ephedrine have been prepared
and it has been found that the basic substance isolated from
the Chinese drug Ma Huang, (which dates back some 5,100 years)
variously identified as Ephedra vulgaris Rich. var. helvetica
Hk. et Thoms and Ephedra equisetina, Bge., consist chiefly
of ephedrine together with about 20% of its isomer pseudo-
ephedrine.  These two alkaloids were found to be mutally con-
vertable by boiling with hydrochloric acid and in other ways,
and have the empirical formula $C_{10} H_{15} O N$.

The chemical structure of ephedrine, and its isomer,
has been studied by many workers.  It shows a close relation-
ship in chemical structure to epinephrine, to which it has
been found to have similar, and in some respects superior
physiological effects."

Pure ephedrine has been found to be actively alkaline in
reaction and combines readily with acids to form salts of
ephedrine.

Ephedrine hydrochloride, the salt which is most commonly
used for its synergistic property in conjunction with spinal
anesthesia occurs in a pure state as prismatic meedles; m.p.
$216^{\circ}$ C., $(a)D^{22} - 32.5^{\circ}$.  Easily soluble in alcohol and water.
Its aqueous solution is stable at boiling temperature.  (28)

INTRA SPINAL INJECTION OF STIMULANTS:

Bloch and Hertz have "witnessed the whole range of acute reactions to spinal anesthesia in their over 1000 (1921) applications of this form of anesthesia. They are usually combated by subcutaneous injections of stimulants, but the action of this is so slow that they now, in grave cases, inject about 20 cg. of caffein directly into the spinal cavity, as for the anesthesia itself. In four cases described, this resusitated the patients almost at once after complete arrest of the respiration. It is mentioned that one of the patients did not have a headache afterward. Experimental research seems to indicate that the caffein under these circumstances acts only as a stimulant for the centers of the medulla oblongata". (29)

"The outstanding effects of ephedrine are due to stimulation of the sympathetic nervous system and are qualitatively identical with those of epinephrine. As these effects are essentially the same in isolated organs or after destruction of the central nervous system, the drug acts peripherally like epinephrine, and is a true "sympathomimetic amine". In addition, it stimulates the central nervous system and depresses the heart, but these effects are ordinarily elicited only by toxic doses.

"Rise of blood pressure following intravenous injection of ephedrine was first observed in rabbits in 1917. A single intravenous injection of from 1 to 10 mg. per kilo. often

raises the pressure of an anesthetised animal by 100 or more
millimeters of mercury and maintains this rise for at least
15 to 25 minutes. The rise in blood pressure does not strict-
ly depend on the quantity of ephedrine given. Equally import-
ant factors are the kind of anesthetic and the condition of
the animal prior to its administration. Under pheno-barbital
it seems to rise higher than under morphine. With ether
anesthesia a primary rise may be followed by a fall with
recovery. The initial level of blood pressure has a bearing
on the response. If the blood pressure is very low, there
is observed a less striking rise, and sometimes the blood
pressure even falls after small doses. By repeated intraven-
ous injestions of the same dose of 1 or more mg. per kilo,
the first one is most effective in raising and sustaining
the blood pressure. Subsequent injections become more and more
ineffective not only in duration but also in the degree of
pressure elevation.

"The rise in blood pressure produced by ephedrine is
due to simultaneous vasoconstriction and cardiac stimulation,
produced by stimulation of the corresponding sympathetic
fibres.

"The action of ephedrine on the mamalian heart in situ
is essentially similar to that of stimulation of the accelerator
nerve--an increase in rate and amplitude of contractions. If
the vagi are intact, the heart may be slowed reflexly as
pressure rises, though amplitude of contraction is increased.

After section of the vagi, or after atropine, ephedrine always
accelerates the heart rate. It was found that ephedrine stim-
ulates the stellate ganglions as well as the sympathetic endings
or myoneural junctions in the heart, an action that is appar-
ently not shared by the closely related amines epinephrine
and tyramine, which stimulate only the endings or myoneural
junction.

"Further proof of the myoneural property of ephedrine
is demonstrated in its action on the denervated ciliary muscle,
on the bronchial muscle after treatment with physostigmine,
and upon isolated intestine.

"Secretion, including the maxillary, gastric and lymph,
are accelerated to a small extent in intravenous injections
of ephedrine." (30)(31)

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