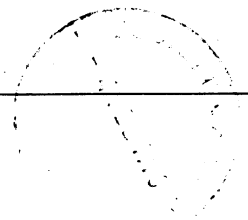

Section of Anæsthetics

President R Bryce-Smith DM

Meeting 3 October 1975

President's Address

The Enigmas of Spinal Analgesia

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I have chosen the subject of spinal analgesia not only because it fascinates me, but because I sense a reawakening of interest in this form of pain relief. In the United Kingdom, spinal analgesia has passed through many troughs and peaks of popularity. By now, most of these are historical, although the reverberations of the Woolley and Roe case can still be felt. To me it seems quite unfair and illogical that the technique suffered such a devastating setback in general acceptance as a result of this most unfortunate incident. Perhaps a similar accident today might be viewed more calmly – at least it should be, if consideration is given to the hazards of hepatitis following halothane, renal damage after methoxyflurane, malignant hyperpyrexia invoked possibly by several agents, not to mention electrocution from sophisticated monitoring devices. But these risks are taken, presumably because it is thought that the advantages outweigh the disadvantages. Might not this be the case also in spinal analgesia? Such a viewpoint has been expressed by many reputable anæsthetists and I would merely wish to suggest that we might reexamine some of the problems.

If one leaves out the immediate complications of hypotension, respiratory failure and inadvertent total spinal block, one is concerned essentially with neurological complications. Of these, the effects on the cranial nerves would seem to fall into a separate category. The causes may be difficult to determine precisely in the case of some nerves, although there would seem to be a reasonable explanation for VI nerve palsies (Bryce-Smith & Macintosh 1951), even if alternative theories have been proposed. With the exception of I and X, all the cranial nerves are reported as having been involved, but fortunately recovery can be confidently expected. Thus these complications, as well as headache, while troublesome to the patient whilst they exist, are not of grave significance. I would prefer to devote my attention to the more serious consequences of spinal analgesia – those in which the patient suffers permanent neurological damage, for it is these that have aroused most emotion and medico-legal attention. Further, they are the least understood complications and hence those that engender most fear. The most valuable review of these misadventures has been by Greene (1961) and it is doubtful if even today we know their causation. However we may be encouraged that Greene found the frequency of such complications to be probably less now than in the preceding fifty years.

The pathological findings associated with neurological complications are due to involvement of the meninges or the nerve tissue itself. In the majority of cases both elements exist but one type is usually predominant. Arachnoiditis is likely to be more pronounced in that portion of the subarachnoid space in which the highest concentration of local anæsthetic was present and thus the cauda equina is most frequently involved. This type is chronic in onset and development, with a tendency to progress. Alternatively, the meningeal involvement may be an inflammatory response, either septic or aseptic, both acute in onset, although the aseptic variety tends to become chronic and produces results similar to chronic arachnoiditis.

When nerve tissue is primarily involved, meningeal reactions are minimal and the histological picture is one of acute myelopathy with destruction of myelin in nerve roots or the cord. The onset of symptoms is immediate, the neurological deficit complete but nonprogressive.

Direct trauma with a needle is unlikely to occur in the region of the cauda equina since the nerves are free-lying. But it may occur in the lumbar

region where the nerves are relatively tethered as they leave the dura at the intervertebral foramina and when a needle is introduced too far laterally, usually causing immediate paraesthesia. The result is a radiculitis involving a specific nerve root. The cord is only involved if the puncture is made above the level of the second lumbar vertebra and is rarely followed by an arachnoiditis unless there is a hæmorrhage causing in effect an aseptic meningitis. But the introduction of a needle or knife lateral to the midline is effectively that sophisticated neurosurgical operation of rhizolysis, while damage to the substance of the cord bears a remarkable similarity to percutaneous (Lipton 1968) or even surgical cordotomy, myelotomy or even commisurotomy.

The factors that have been invoked at one time or another make an impressive list. Infection speaks for itself and can be attributed to faulty technique and will therefore be the anæsthetist's total responsibility. Extenuating circumstances there may be, but even if they exist, they cannot exonerate. Even a diagnostic lumbar puncture must not be performed unless the operator can be completely certain of the absolute sterility of his technique, his apparatus and the drugs used.

The nature of any solution introduced into the subarachnoid space has always been suspect. But even if the risk of infected material can be ignored – and the quality control of our manufacturers is now so careful – there remain other possibilities over which there is rather less rigid control but which may play an important part. These include chemical irritation of the nerve roots or meninges, mechanical damage by the inherent physical properties of the solution and contamination of the solution, either deliberate or inadvertent.

When amylocaine hydrochloride (Stovaine) was one of the standard solutions used for spinal analgesia, two preparations existed. One, Barker's solution made hyperbaric by the addition of 5% glucose remained of value until the late 1940s. In many ways it behaved and was used in a similar fashion to more modern drugs. The specific gravity was 1025 and the duration of the effect about one hour. There was perhaps a somewhat high incidence of post-anæsthetic difficulty with micturition, usually treated with small doses of an acetylcholine preparation to encourage the contraction of the atonic smooth muscle of the bladder, but long-term neurological disturbances were unusual.

On the other hand, Chaput's solution, containing 10% amylocaine and 10% sodium chloride, had a specific gravity of 1080 – vastly heavier than anything that might be used today. The incidence of cauda equina lesions was considerable and it soon went out of fashion. But what was the factor that caused this damage? It is not unreasonable to imagine that such a heavy solution might fall with great rapidity and thus form a bolus of injected material at the lower end of the dural sac. If this were so, then, the tonicity of this preparation might well adversely affect the osmotic balance of nerve tissue with which it came into contact. Equally, the concentration of amylocaine, already higher than in Barker's solution, would be far greater around the nerve roots and one might therefore infer the possibility of chemical irritation.

But there is no proof that either really occurred and we must bear in mind that sterility at that time, both in terms of the manufacturers' control and the anæsthetist's technique, left much to be desired by current standards. So perhaps we should reintroduce infection as yet a third possibility. It is, however, pertinent to remember that amylocaine itself had a well-recognized liability to cause tissue damage, to such an extent that its use for infiltration was forbidden because extensive sloughing following such application was far from unknown. Why then should it have been considered less damaging when in contact with the more delicate nerve tissue?

But to confuse the picture further, barbotage was a standard procedure for extending the area of analgesia. Reference today to techniques for treating chronic pain problems, particularly those of cancer, include barbotage (Lloyd *et al.* 1972). True, Lloyd recommends the withdrawal and reintroduction of 20 ml of cerebrospinal fluid, without the addition of any local analgesic agent. It is suggested that the relief of pain, or more crudely, interference with neurological mechanisms, is due to local asphyxia from a pressure effect, for at post-mortem, there is histological evidence of peripheral demyelination.

While thinking on these lines, I would also refer to the technique of irrigating the subarachnoid space with saline. Originally this was done with hypothermic normal saline at 0°C and the results were almost certainly due to the hyperosmolarity of the saline at this temperature (Hitchcock 1967). Equal results are obtained by the use of normothermic saline in a 12% concentration (Hitchcock & Prandini 1973). What price then Chaput's solution which had an equivalent concentration of nearly 20%? Again, urinary incontinence and complete cauda equina lesions have been reported following this technique, although it may be considered a reasonable price to pay for the relief of unbearable pain.

Neurolytic agents used specifically for creating nerve damage and thus interfering with painful impulses were also possible contaminants of spinal solutions. Of these, phenol (Maher 1955) and alcohol (Russell 1936), were also commonly used to sterilize the outside of ampoules. Whether the interpretation of events in the Woolley and Roe case (Cope 1954) was accurate or not is

irrelevant, but it resulted in an investigation which led to the recognition of minute cracks occurring in glass ampoules through which sterilizing solutions on the outside could pass and virtually replace the local analgesic on the inside. Surely these cracks did not occur in glass ampoules only in the late 1940s and early 1950s? It is reasonable to assume that they may have been present since the very introduction of this form of packaging. If this were so, then many accidents might have been, not 'idiopathic' but simple contamination with one or other of the sterilizing agents entering in this fashion.

Other contaminants must also be considered. These are the ones deliberately introduced, for example chlorocresol as a bacteriostatic agent and again an agent recommended for neurolysis (Maher 1963). Gliadin was also used once upon a time in Duracaine (a procaine preparation) with the object of 'holding' the local analgesic solution in contact with the nerve tissue for as long as possible. Fortunately the risks of this addition were soon recognized but this was perhaps a lesson which had not been learnt when Efocaine was introduced as a means of causing long-term nerve block. The results of this preparation were frequently distressing to the patient and also to the anæsthetist, particularly our American colleagues, who suffered the consequences of the most punitive medicolegal actions.

It will now be recognized that comparison is being made between what was common practice in the not-so-distant past in the conduct of normal, spinal analgesia and what is deliberately practised today to produce long-term pain relief with the specific aim of causing nerve damage.

It is thus possible to recognize from the list of possible causes of complications culled from previous publications (Greene 1961, Lund 1971) many common factors between the techniques for treating chronic pain and the possible causes of spinal complications. Of these, the most obvious are: alcohol, phenol, chlorocresol, rhizolysis or cutting of nerve roots with a needle, hypertonic saline for alteration of osmolarity, and barbotage (Table 1).

Provided these possibilities are recognized, and if contamination and infection can be excluded, the list of likely causes of spinal complications begins to shrink to a gratifying extent. There is little evidence that the drugs used for spinal analgesia today are responsible for direct chemical irritation of nerve tissue, nor damage from an abnormal hydrogen ion concentration. The latter is part of the manufacturers' quality control and with the exception of cinchocaine which undergoes precipitation at a pH of 6.5, an adjustment to normal pH is possible without detriment to the sterilization and storage of the local analgesic solutions.

Table 1

Possible causes of complications following spinal analgesia

Contamination	Deliberate: Glucose SODIUM CHLORIDE Strychnine GLIADIN CHLOROCRESOL ALCOHOL Inadvertent: PHENOL ALCOHOL
Mechanical damage (needle)	SPECIFIC NERVE SPINAL CORD Hæmorrhage in cord
Vascular	Hæmatoma (intra- or extra-dural) Spinal artery syndrome
Chemical irritation	Spinal solutions Contaminants
HYPERTONICITY	Saline Glucose
BARBOTAGE	
pH	
Infection	

Causes in capital letters are common factors in techniques for the control of chronic pain

Thus we are left with the possibilities of vascular complications, many of which, if not completely avoidable, can be minimized by careful technique: and the awakening of preexisting and perhaps dormant central nervous system disease which is always quoted as a possibility – even though no properly documented instances have been found in which a post-spinal complication could be ascribed to this cause (Macintosh & Lee 1973).

I would therefore leave this aspect of spinal analgesia, hoping that I may have persuaded you that the dreaded neurological complications are little more than spectres to which we can ascribe a name and which should be viewed in a proper perspective. They may occur, but with no greater frequency than the other unexplained accidents of anæsthesia. Thus they should never be regarded as adequate reasons for withholding a form of pain relief which has undoubted merits and advantages in a variety of circumstances. Spinal analgesia is not just a relic from the past, suitable only for adverse circumstances (Boulton 1967).

But even if we can dispose of a number of enigmas with such comparative ease, the unexpected behaviour of the occasional spinal block still needs an explanation: and in seeking one, it may be helpful to review factors in the behaviour of cerebrospinal fluid which are not normally considered part of the anæsthetist's practical knowledge.

Cerebrospinal fluid is produced by the choroid plexuses in the brain and passes through the various chambers to enter the subarachnoid space through the foramina of Luschka and Magendie. A circulation of fluid is maintained which flows caudad round the cord, posterior to

the dentate ligament which ends at about the level of L1, and then ascends anteriorly towards the brain. But it must be admitted that the mechanism for propelling the CSF in what has been termed the third circulation – the other two being blood and lymph – is far from clear (Milhorat 1975). Absorption takes place through the various venous plexuses; if they are obstructed a rise in CSF pressure results. A rise in intracranial pressure in response to a volume addition has an effect similar to a compression of the venous outflow tract, with consequent decrease of flow and elevation of intravascular pressure proximal to the obstruction. A pressure-volume curve can be drawn from these facts, which are the result of an interaction between the elastic properties of the spinal dural sac and the resistance of the vascular bed to compression and distension (Lofgren 1975). Since normally there is a regular production of cerebrospinal fluid at a rate of about 0.5 ml/min, it is clear that a rise in venous pressure from any cause will obstruct the flow of CSF and will also appreciably affect the CSF pressure. In fact, cerebrospinal fluid and venous pressures are always closely related whereas arterial pressure is of little significance. Under normal conditions if the rates of formation and absorption are equal, then the cerebrospinal fluid pressure would be equal to the average capillary hydrostatic pressure, less the capillary osmotic pressure (Ryder *et al.* 1953).

The addition of fluid to the cerebrospinal fluid compartment leads to a sharp, transient rise in pressure followed by an immediate displacement of some of the blood volume contained in the distensible, craniospinal vascular bed. Naturally this depends on the degree of distensibility and the volume of cerebral and systemic vascular pools so that there may be considerable CSF volume changes with relatively small pressure changes. The reverse is true when fluid is withdrawn.

Glucose appears to be actively transported across the blood-CSF barrier but the rate at which this occurs is difficult to determine (Ruch & Fulton 1960). It is well appreciated that the intravenous injection of hypertonic glucose has the effect of withdrawing fluid from the cerebrospinal fluid in order to restore osmolarity. So in the reverse fashion, does the deposition of hypertonic solutions into the cerebrospinal fluid tend to withdraw fluid from the vascular bed into the cerebrospinal fluid, thus increasing its volume and pressure. Since the site of injection in spinal analgesia is in the lumbar region, a pressure gradient will be created in a cephalad direction, thus greatly increasing the return flow of fluid to the cerebral circulation (Marx & Orkin 1965).

Although the blood-brain barrier appears to be remarkably impermeable to large molecules, it has been found that the total protein content of CSF is significantly raised in preeclamptic women at term (Merrit & Fremont-Smith 1938). They suggest that the specific gravity of CSF is determined by the protein concentration and in particular, the albumin fraction. The protein content of the lumbar CSF is in any case higher than elsewhere, but the implication is that the specific gravity of the CSF might be unduly high in some circumstances. More recently though, it has been suggested that glucose is the significant factor in determining specific gravity (Davis & King 1954). Marx & Orkin found that the alterations in serum proteins associated with pregnancy were not necessarily present in the CSF of parturients and decided that the altered response to spinal analgesic drugs during pregnancy could not be explained on the basis of alterations in CSF proteins or protein binding of the local analgesic drug. However, they did see a lower specific gravity in pregnant women at term than in nonpregnant women, but did not consider that the differences were statistically significant. But the figures given which show these insignificant 'total' protein changes between 'normal' CSF and the CSF of pregnant women, show a difference in the globulin fraction. Even if albumin is responsible for determining the specific gravity, and this is indeed doubtful, it is globulin which determines the viscosity of cerebrospinal fluid. By calculation, the differences quoted would be sufficient to cause a rise in viscosity from 1006 to 1100 centipoises (cP). It is reasonably certain that this particular feature was not considered and conceivably this change in protein, although apparently small, may be sufficient to alter the behaviour of a spinal drug.

It is unlikely that this is the sole explanation for such strange behaviour of spinal solutions as is sometimes encountered. Indeed it is necessary to consider the other factors which have already been mentioned. Theoretically at least, the following facts must be borne in mind:

(1) Glucose is actively transmitted across the blood-brain barrier and this implies that the addition of glucose in the form of a spinal analgesic solution might provoke an immediate, active response.
(2) Volume changes are related to pressure changes which in turn affect the CSF flow. As pointed out, this involves the return in a cephalad direction of CSF anterior to the dentate ligament. A vigorous injection, with consequent high pressure changes, would cause a higher distribution of local analgesic than might otherwise be expected.
(3) If glucose is largely responsible for determining the specific gravity of cerebrospinal fluid, the addition of 1–2 ml of 5% glucose, still more 7.5%

glucose, in the form of a spinal solution, would create a totally abnormal situation. This would clearly depend on the speed and facility with which mixing or diffusion took place. Normally it would be slow, but vigorous injection of the spinal solution could create at least a local situation in which the specific gravity of the CSF and injected solution would be almost indistinguishable.

(4) Not only may the CSF glucose be altered extrinsically by the injection of a heavy, local analgesic solution, but the change could be intrinsic by physiological or pathological changes which raise the blood sugar. Obvious examples are pregnancy on the one hand and diabetes on the other.

(5) There is some evidence that the volume of cerebrospinal fluid at term is considerably less than normal. This is believed to be due to the venous engorgement in the extradural space (Assali & Prystowsky 1950), an hypothesis supported by the pressure-volume curve determinations by Lofgren. On the other hand, Greene (1958) is doubtful whether the volume does vary appreciably, but that fluid retention occurs towards term is not questioned. This can be demonstrated by pre- and post-delivery urinary output charts (Bryce-Smith & Williams 1955) even if these bear no direct relationship to cerebrospinal fluid volumes.

We are left then with a number of established facts which could alter either the specific gravity or the viscosity of the cerebrospinal fluid. Experimentally, either can be altered without affecting the other. How significant any alteration may be, still depends on how one looks at the problem. For example, if the specific gravity of CSF is raised by an intrinsically high glucose level, then an apparently hyperbaric solution more closely approaches an isobaric preparation and will not follow the expected rules of gravity control. Theoretically too, a rise in the viscosity of the cerebrospinal fluid might have the same effect since movement through the more 'sticky' solution would be slower. The reverse is clearly also true and all these possibilities would be exaggerated by the simple mechanics of the turbulence created at the time of injection. At such times it may be necessary to forget that normally the circulation of cerebrospinal fluid is relatively slow and that diffusion, if one understands by this term the intermingling of different molecules, requires several hours to cover a few centimetres.

If one believes that alterations in specific gravity are of paramount significance, then it is as well to know what effect the injection of a standard local analgesic solution will be. This has been looked at in two ways. First, by depositing 1 ml of heavy spinal solution into 30 ml mock cerebrospinal fluid – the understood volume of CSF within a total spinal run. The immediate effect in the case of prilocaine and cinchocaine (both containing 5% dextrose) was a rise in specific gravity to 1012 and with lignocaine (containing 7.5% dextrose) to 1015. Within a minute samples taken from the same site showed that the specific gravity had fallen to 1006 with each drug: surprisingly little difference between the preparations, but the experiment was crude and it served to show a local effect which was soon dissipated by gravity, mixing, turbulence and other factors.

Since the effect was so local and since in many instances, true mixing is only likely to occur in the inferior portion of the dural sac, the different spinal solutions were mixed completely with 5 ml of CSF which had an initial specific gravity of 1004. In the case of lignocaine the final specific gravity was 1015, and in the case of prilocaine and cinchocaine, it was 1010.

Paradoxically, then, one may argue that the solution containing more glucose will lead to a smaller specific gravity differential than will the lighter solutions. In consequence it may also be necessary to consider to what extent glucose causes distribution of the local analgesic and how much it behaves as an independent agent altering the specific gravity of the cerebrospinal fluid.

Nevertheless, in spite of raising such doubts, there is ample reason for believing that in the majority of instances, the difference between the specific gravity of cerebrospinal fluid and the injected local solution will be of overriding importance. Again, since the influence of specific gravity is so clear-cut, and has only been questioned in minor detail, the other factors to which I have already made passing reference have received scant attention.

My own interest in this subject was aroused a few years ago when difficulty was experienced in obtaining either the well-tried and understood cinchocaine, popular in this country if virtually banned in the USA, or indeed any acceptable substitute, for spinal analgesia. Our attention turned to lignocaine spinal, a 5% solution in 7.5% glucose, which has a specific gravity of about 1035. Certainly this is heavier than the cinchocaine solution to which we had become accustomed, but such preparations are widely used in Scandinavia, in the USA and in India.

We were greatly surprised, therefore, to have several patients in whom the solution appeared to sink with astonishing rapidity. Far greater concern was felt when the drug travelled cephalad in patients in the lateral position. Granted that this was seen on three occasions in women with wide buttocks: the effective spinal run was therefore equivalent to several degrees of head-

down tilt – a hazard publicized as long ago as 1943 (Mushin 1943). This seemed sufficient reason to consider other factors which might play a part – particularly factors which might vary with the physiological state of the patient. The viscosity of the cerebrospinal fluid seemed the most promising since, in simple terms, one could imagine that during periods of water retention the cerebrospinal fluid might become diluted and the viscosity less. In times of dehydration, which need only be quite shortlived, as for example during the preoperative starvation of a patient, the reverse should be the case. The first difficulty was to establish the normal value. 'Documenta Geigy' gave a figure of 1020 cP, but it appeared that this stemmed from a book published in 1919 (Levinson 1919), again quoting another author. Eventually the original source was traced and it was discovered that this figure was derived from post-morten specimens: four hydrocephalics, three of whom had died at birth and the fourth subject, an old man who had died of a cerebral tumour (Polyani 1911). Since the source of the cerebrospinal fluid was suspect, a revised standard would obviously be required.

We obtained fresh samples of CSF from apparently normal, healthy adults and determined the viscosity using an Ostwald viscosimeter. Determinations were made on 12 subjects and gave a mean value of 1006 cP (compare Geigy's 1020–1027) (Table 2).

The specific gravity of these samples was measured with a refractometer and gave a mean value of 1004.5. By dividing the centipoise value by the specific gravity, an alternative unit, the centistoke, is obtained. This proved to be of more than academic interest since early publications often failed to quote the unit of viscosity. Table 3 gives a comparison of these values in different solutions.

Having ascertained the normal value for viscosity of cerebrospinal fluid, various 'mock' solutions were prepared of a differing viscosity but keeping the specific gravity constant. This was achieved by dissolving a small quantity of a highly viscous agent, such as gelatin, in a large volume of saline to give solutions of what might be loosely termed low, medium and high viscosity. Fortunately normal saline was found to have a viscosity of 1006 cP, the figure found to be the normal for cerebrospinal fluid. Two other solutions were prepared, one with a viscosity of 1077 cP and the second 1133 cP, values on either side of the estimated 1100 cP which should have been given by Marx & Orkin's patients.

Table 2

Viscosity of CSF in healthy adults (mean values)

	Viscosity (cP)
Male ($n=6$)	1009 (± 0.005)
Female ($n=6$)	1003 (± 0.004)
Mean (male and female)	1006 (± 0.004)

Table 3

Viscosity and molecular weight of various solutions

	Viscosity		*Molecular weight*
	cP	*cSt*	
Lignocaine	0.94	0.908	234
Prilocaine	0.95	0.929	257
Cinchocaine	0.86	0.839	344
Cerebrospinal fluid	1006.0	1.001	

cP, centipoise cSt, centistokes

Using these three artificial solutions in a glass spinal column, different local analgesic solutions coloured with fluorescein, were injected and studied. The results of the preliminary investigation when the spinal solution was injected in a manner comparable to the performance of a clinical, spinal anæsthetic, were so bizarre that no meaningful interpretation could be applied. It was clear that mechanical currents, temperature changes, dilution and miscibility of the solution affected the distribution and already it was obvious that a number of other physical factors apart from viscosity and specific gravity were involved. In an attempt to unravel some of these factors, a second series of tests were performed using a Hamilton syringe, whereby one drop of uniform size of the test agent could be dropped on to the surface of the cerebrospinal fluid from a uniform height and the rate of fall within the spinal canal measured over a 20 cm run. A minimum of 12 runs for each local analgesic preparation in the 3 different mock spinal solutions were carried out. The results were plotted as graphs, indicating the rate of fall of the test preparation.

Allowing for a few abnormal readings, quite clear patterns emerged. Figure 1 gives a comparison between three preparations in a mock cerebrospinal fluid of 1006 cP. Here the cinchocaine took some 15 seconds longer than 5% glucose to fall 20 cm. The difference does not appear to be very remarkable although it is in fact 16% slower and suggests that cinchocaine itself exerts some effect. Incidentally, an almost identical graph was obtained with prilocaine spinal, although lignocaine, with 7.5% glucose, fell 27% faster than cinchocaine. It can be seen that the rate of fall over the first 10 cm was not appreciably different. This finding applied to all tests carried out with different drugs and solutions of different viscosities. Thus one might reasonably claim that, when spinal analgesia is performed at L2–3 in the sitting patient, specific gravity differences or changes in viscosity of the cerebrospinal fluid are of no practical significance. The spinal solution will reach the bottom of the dural sac in about 30 seconds, provided no abnormal injection technique is used.

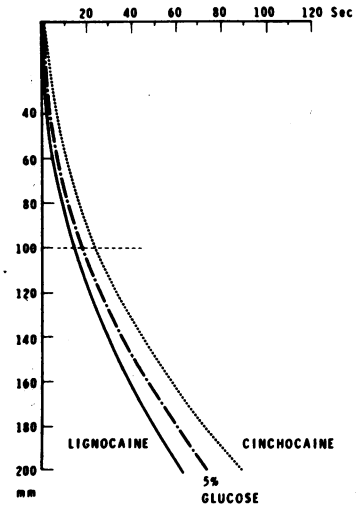

Fig 1 *Comparison of three agents falling 200 mm through CSF of normal viscosity (1006 cP) and specific gravity*

Alterations in the viscosity of the mock cerebrospinal fluid solutions produced somewhat unexpected results. Thus cinchocaine was significantly slower in the medium solution (1077 cP) (Fig 2) but fell as rapidly in the highly viscous solution (1133 cP) as in saline (1006 cP). On the other hand, prilocaine was slower in the most viscous solution and faster in the medium solution than in saline, although the differences were not very pronounced. Lignocaine behaved with no significant differences in any solution although any change tended to be slower in the more viscous solutions. One must presume that the greater specific gravity had an overriding effect.

Similarly, 5% glucose alone gave identical results in the three solutions, confirming the earlier statement that the local analgesic itself has some effect, presumably due to the inherent nature of the drug in terms of molecular weight, miscibility or solubility. It should be noted that as the molecular weight of glucose is 180 and that of the local analgesic agents considerably greater, molecular configuration could also play a part.

It was observed that the paradoxical results in the more viscous cerebrospinal fluid solutions occurred when the test solution remained as a discrete bolus. In other words, mixing had not taken place, possibly due to an alteration in solubility or surface tension.

It would appear that the speed of distribution is greatest with lignocaine but this must not necessarily be confused with speed of action. The two are not synonymous and in clinical practice it was found that prilocaine 'worked' far more quickly than either of the other agents. Under the experimental conditions there was little difference in the speed of distribution over a short distance, and thus similar conditions applied to all drugs and the property of prilocaine to work quickly is therefore most noticeable (Fisher & Bryce-Smith 1971). On the other hand, in a high spinal performed in the lateral position, the more rapid distribution of lignocaine should be obvious.

Yet if the viscosity experiments were not entirely convincing, and indeed were to some extent paradoxical, other observations made at the same time were interesting. The local analgesic solution usually tended to fall in the manner of an inverted cone, with areas of the most deeply coloured solution making the most rapid progress. Reinforcement of this advancing cone took place in the central area. The appearance was of dilution occurring at the periphery – a very reasonable proposition – until a state of equilibrium was reached with the surrounding liquid. Unless reinforcement occurred, the cone tended to lose its impetus and become stationary. This could be interpreted as a temperature effect, since, as in clinical practice, the injected solution was at room temperature. Thus local analgesic solution injected would take a variable time, according to volume, to become warmed to body temperature. The effect of temperature on specific gravity has been well understood and, in his accounts of hypobaric spinal techniques, Etherington Wilson (1935) stressed the importance of warming the light solution of cinchocaine. But there will be an obvious difference in the time taken to raise 15–20 ml of solution from room to body temperature (as in the so-called hypobaric technique) and 1–2 ml of heavy solution. The

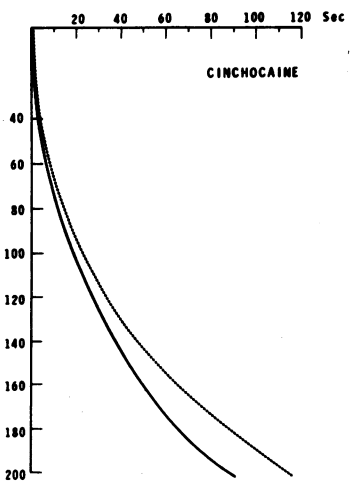

Fig 2 *Comparison of rate of fall of cinchocaine through CSF solutions of different viscosity:* —— *1006 cP,* ····· *1077 cP*

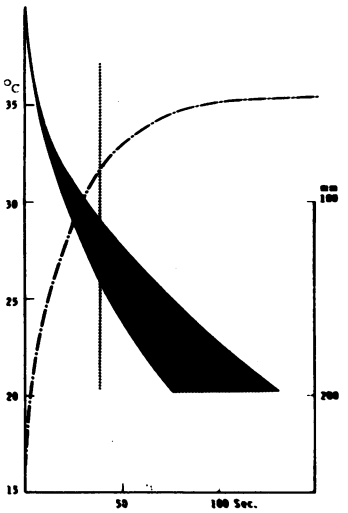

Fig 3 *Comparison of temperature and viscosity scatter. .—.—.— change in temperature of 1 ml of solution at 16°C placed in a water bath at 37°C. Shaded area indicates scatter of results in viscosity experiment with prilocaine in CSF with viscosity of 1133 cP. Scatter widens after 40 seconds (vertical line)*

time taken for 1 ml of solution injected at room temperature to reach 37°C is of the order of two and a half minutes. This time scale was established by placing 1 ml of cooled solution in a thin-walled plastic envelope which also contained a thermocouple; this was then plunged into a water bath thermostatically controlled at 37°C. As the temperature rose, a clock was started at 16°C, the lowest temperature considered likely as an acceptable room temperature. Readings were taken at intervals until the temperature of the local solution had approximated to that of the water bath. Even this is a very poor guide since such a simple experiment takes no account of many additional factors.

These temperature experiments did show one point of interest. Body temperature was reached, not in a simple linear fashion, but as a curve which tended to flatten after 40–50 seconds. No appreciable differences were found in the time curves of different agents. A series of almost identical curves resulted, showing an initial sharp rise in temperature followed by a much slower rise for the last degree or two.

Looking again at our viscosity measurements, it was seen that the readings taken within the first 40 seconds were reasonable. Thereafter the results gave a much wider scatter. The two time scales match and it would therefore not be unreasonable to suggest that as the injected solution warms to near body temperature, the physical characteristics are changed, leading to a slower rate of fall as both the effects of viscosity and the specific gravity differences become less (Fig 3).

To recapitulate: specific gravity is of the utmost importance in determining the behaviour of a spinal solution. However, in some circumstances the specific gravity of the CSF may be abnormally high due to the presence of glucose. Added glucose in the local analgesic solution, when injected vigorously, can paradoxically reduce the specific gravity differential between the cerebrospinal fluid and the injected solution. When the viscosity of the cerebrospinal fluid is also raised, this may slow down the gravitational movement of the injected solution, particularly in a spinal run of more than 10 cm, making it subject to the flow of cerebrospinal fluid. If at the same time there were alterations in the pressure/volume relationship – and these are inevitable – the usually sluggish upward return flow of CSF anterior to the dentate ligament would be greatly increased: and this effect would be further augmented whenever the spinal vascular bed was distended.

It is not beyond the bounds of possibility that where these factors come together, as in pregnancy at term, an abnormally high distribution can occur when certain drugs are used for producing spinal analgesia. I can offer no proof that this is the case, but at least one may propose a logical explanation for this final enigma.

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