but could not make a new lasting memory trace of a picture shown to them. Since the reticular formation in the brainstem is the presumed locus of action of the anesthetic agents used at that level of anesthesia, and since eye centering is also thought to be a function of the reticular formation, the authors hypothesized that the reticular formation also had an important role in making new memory traces. Further, Abt, Essman, and Jarvick studied the effects of ether inhalation on mice 0–24 minutes after they had been given a single-electric-shock conditioning trial. The ether, if administered within the first 8 minutes after the shock, appeared to make the mice behave as if they had retrograde amnesia for the shock. Each of these studies demonstrates that the inhalation anesthetic agents have some action on new memory formation.

Cherkin and Harroun, in a recent review of anesthesia and the memory processes, analyze the factors contributing to amnesia for the events occurring during surgical operations. Sensory stimuli perceived during the operation in the form of pain, noise, or emotionally charged conversation, as well as the type and level of anesthesia, and the premedication, all influence the patient's memory of the procedure.

Perhaps careful studies of amnestic function in the postanesthetic period will reveal a greater incidence of memory defects, and will shed some light on this important subject and on the etiology of transient global amnesia.

REFERENCES


Progressive Changes in the Concentration of Ethyl Alcohol in the Human and Canine Subarachnoid Spaces

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One difficulty inherent in the use of subarachnoid alcohol block to treat intractable pain of terminal cancers is that the debilitated patient must be held in an unnatural, uncomfortable position for a protracted time. The conventionally recommended time for absolute immobility of the patient, 45 to 60 minutes, seems to have been based on experience only, not on quantitative data. In the present study the changes in the concentration of alcohol in the subarachnoid space with time have been investigated in an attempt to determine how soon after the instillation of alcohol the position of the patient can be changed without danger of complications from further spread of the neurelytic effect of the alcohol.
Material and Methods

Clinical Study: Thirteen subarachnoid alcohol blocks were achieved in eight patients with intractable pain from terminal cancer. The nature of the study was explained and consent was obtained from each patient. The patients were placed in a ventrally flexed, 45-degree semiprone position in which the target spinal segments were brought to the peak of the spinal convexity. Following subarachnoid puncture with a 20-gauge, 7-cm needle, 0.3 ml per segment (total as much as 1.2 ml; average 0.75 ml) of absolute ethyl alcohol was instilled at a rate of 0.2 ml/min. At scheduled times (fig. 1) two to seven 20-μl samples of cerebrospinal fluid (CSF) were withdrawn into 50-μl microsyringes inserted into the hub of the spinal needle. Care was taken to remove only the minimal amount of CSF needed, in order to prevent excessive loss of CSF.

In one patient additional CSF samples were taken through a second needle placed 1.0 cm ipsilateral to the other on the side of the block, parallel to the first needle. In each of three other patients, a CSF sample was withdrawn after 20 minutes in the semiprone position. Immediately thereafter, these patients were turned prone and another sample was taken. During the positional change the sampling site was always kept higher than the rest of the spinal segments. The intervals between the last two samplings ranged from 2 to 3 minutes.

Animal Study: Eighteen mongrel dogs, weighing 6.5 to 14.5 kg, were anesthetized with secobarbital sodium, 30 mg/kg iv. Each dog was placed, with a thick pillow underneath the abdomen, in a maximally flexed prone position, with the target spinal segment at the peak of the spinal curvature. Spinal
puncture was made in the lumbar region with a 20-gauge needle. Observation of the outflow of CSF permitted adjustment of the position of the needle tip so that it lay barely in the subarachnoid space. Absolute ethyl alcohol, 0.03 ml/kg, was instilled at a rate of 0.2 ml/min. Four to eight CSF samples per animal were withdrawn at scheduled times (fig. 2).

**Analysis of CSF for Alcohol:** CSF samples were analyzed for alcohol content by gas chromatography. The unit used was a Shimazu GC-3AF (Shimazu Seisakusho Ltd., Kyoto, Japan) with a hydrogen-flame ionization detector. The chromatographic column, a stainless steel tube 200 cm long and 4.0 mm ID, was packed with Chromosorb 60/80 mesh coated with polyethylene glycol 1,000, 25 per cent by weight. The flow rates of the carrier gases, nitrogen and hydrogen, were 50 and 40 ml/min, respectively. Column, oven, and detector temperatures were 100, 120, and 150 C, respectively. The internal standard used was 0.2 per cent n-propanol. The samples were so diluted that the concentrations measured were between 0.01 and 0.5 per cent. Under these conditions, accuracy was at least 98.5 per cent and results were reproducible to within 1.0 to 2.0 per cent of the indicated values. Concentration was expressed as per cent in volume of CSF.

**Results**

**Clinical Study:** The results of the clinical study are shown in figure 1. At zero time after completion of the instillation, mean alcohol concentration in the CSF was 25.6 per cent. It declined rapidly to levels as low as 3.1 per cent after 10 minutes. Thereafter, the rate of decline became much slower. After 30 minutes the alcohol concentration was 0.9 per
TABLE 1. Comparison of CSF Samples Taken through Two Needles 1.0 cm Apart in the Same Spinal Interspace of a Patient

<table>
<thead>
<tr>
<th>Position of Needle</th>
<th>Alcohol Concentration (Per Cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5 Min</td>
</tr>
<tr>
<td>Midline</td>
<td>2.51</td>
</tr>
<tr>
<td>Off-midline</td>
<td>—</td>
</tr>
</tbody>
</table>

TABLE 2. Effect of Positional Change on Subarachnoid Alcohol Concentrations

<table>
<thead>
<tr>
<th>Concentration (Per Cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Semi prone</td>
</tr>
<tr>
<td>Prone</td>
</tr>
<tr>
<td>Patient A</td>
</tr>
<tr>
<td>Patient B</td>
</tr>
<tr>
<td>Patient C</td>
</tr>
</tbody>
</table>

cent, and after 60 minutes, 0.2 per cent. The scatter of the concentrations was considerable for the first 5 minutes, but thereafter the values clustered closely together. The changes in concentration seemed to result in two separate exponential curves, with the bend occurring about 13 minutes after instillation.

Table 1 shows the results obtained from the patient from whom CSF samples were taken simultaneously through two needles placed 1.0 cm apart in the same spinal interspace. Ten and 20 minutes after the instillation all CSF samples withdrawn through the two needles had concentrations of less than 2.0 per cent. Table 2 shows the concentrations of alcohol in CSF samples withdrawn from three patients before and immediately after the positional change from semi-prone to prone. None of the samples taken after the positional changes had a higher concentration than the preceding sample.

Animal Experiments: The results of the animal study were essentially the same as those of the clinical study (fig. 2). The rate of decline of the alcohol concentration was only slightly different, 39.3 per cent at zero time, 4.3 per cent after 10 minutes, 1.1 per cent after 30 minutes, and 0.2 per cent after 60 minutes. The bend of the composite curve occurred about 10 minutes after instillation.

DISCUSSION

In the present series of patients, in whom the rate of instillation was very slow, uptake by nerve tissue seems most likely to have been the cause of the initial rapid disappearance of alcohol. Several reports1-4 of concentration changes of local anesthetics in the subarachnoid space are also in agreement, in that the primary mechanism of the initial rapid decline was found to be uptake by nerve tissue. The data of Koster, Shapiro and Leikensohn,3 describing procaine's behavior in the subarachnoid space, when rearranged on the semilog coordinates, closely resemble our human and animal data. Although there are distinct differences between experiments using local anesthetics and alcohol, it appears that the disappearances of these substances from CSF follow similar patterns. The contributions of other mechanisms (dilution due to turbulence, vascular absorption, vascular pulsation, convection, diffusion, etc.) to the nature of the curve have not been quantified.

To determine how soon after instillation the patient's position can safely be changed, the minimal concentrations of alcohol at which nerve fibers sustain irreversible changes must be known. These, however, have not been determined definitively. Adriani5,6 states that in the subarachnoid space 30 per cent alcohol temporarily destroys the sensory fibers but not the motor fibers, and that 8 per cent causes only a reversible sensory block. Pitkin7 added 10 per cent alcohol to reduce the specific gravity of the procaine solution used for spinal anesthesia, apparently without untoward effects. Under clinical conditions similar to ours, Stern8 estimated the alcohol concentration immediately after the completion of instillation to be 20-25 per cent of the concentration injected (cf. 25.6 per cent in the present human study). Therefore, it seems permissible to assume tentatively that the highest alcohol concentration that will produce only transient effects when it comes into contact with the nerve roots should lie in the range of 2-3 per cent (25 per cent of 8-10).

In the present clinical study the time necessary for the mean concentration to fall to 3 per cent was about 10 minutes. However, the CSF was not necessarily sampled where the
alcohol concentrations were the highest in these patients, because of the 45-degree semi-prone position used. In one patient the alcohol concentrations at the tips of two needles placed 1.0 cm apart in the same spinal interspace approximated each other and were less than 2.0 per cent within 10 minutes of instillation. Furthermore, to test the above suggestion, the positions of the last three patients were changed from semi-prone to prone 20 minutes after the instillation. In none of these patients was the alcohol concentration of the last sample (0.59, 1.39, and 0.37 per cent) higher than that of the preceding one (1.01, 2.52, and 0.48 per cent). Therefore, the CSF at the relevant spinal segments seemed to be homogeneous with regard to alcohol concentration 10 minutes after instillation and fairly isobaric with CSF at other segments. It appears unlikely that CSF containing less than 3 per cent alcohol causes irreversible changes to nerve roots, even if it is displaced in toto during positional change. In the three patients described above there were no untoward side-effects after positional change.

In the animal study the dogs were placed prone, so that sampling of CSF from areas with the highest alcohol concentrations was possible. Despite the fact that the dogs were given twice as much alcohol per kg body weight, the rate of decrease in mean alcohol concentration was only slightly slower than that in the human subjects, reaching 3 per cent approximately 15 minutes after instillation. This rapid decrease in the dog may be attributable to the anatomic features of this species; if uptake by nerve tissue is the major determinant of the changes in concentration, alcohol instilled in the canine subarachnoid space, packed more fully with spinal cord and nerve fibers, should disappear faster than the same amount instilled into the human subarachnoid space.

CONCLUSION

In both human subjects and dogs the concentrations of alcohol instilled into the subarachnoid space declined along a composite curve which seemed to consist of two separate exponential curves, initially rising to a peak at 10 minutes and later flat. If necessary, the position of a patient who has received a subarachnoid alcohol block may be changed safely 20 minutes, and probably even 15 minutes, after instillation, provided that the amount instilled has not exceeded 1.0 ml. After 15 and 20 minutes the mean alcohol concentrations will have decreased to 1.6 and 1.3 per cent, respectively; the upper limit of 2 SD is about 3 per cent or less, which seems unlikely to cause irreversible damage to nerve roots.

ADDENDUM

Since completion of this study nine additional subarachnoid alcohol blocks have been done in seven other patients. Between 15 and 20 minutes after instillation, all of these patients were turned from semi-prone to other positions which they preferred. There were no complications attributable to this "premature" positional change.

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