An Experimental Evaluation of the Effects of Subarachnoid Injection of Phenol-Pantopaque in Cats

A Histological Study*

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This study was undertaken in an attempt to explain certain puzzling phenomena observed in the clinical use of injections of phenol. We had noted the incongruity of relief of subjective pain without diminution of sensibilities of pain and touch as tested for in the usual neurological examination. Others observing this phenomenon had hypothesized this was the result of selective destruction of the smaller fibers but histological verification of this hypothesis has not appeared in the literature. Furthermore, we sought an answer as to why, in spite of a uniform procedure, the results of injections of phenol often were unpredictable and, even more disturbing, why there often would be an early recurrence of pain or spasticity after what appeared initially to be a successful injection.

Satisfactory human material for this study was not available from our clinical series as the conditions treated were chronic and patients either died at home or in most instances are still alive. The few cases available for pathological study were unsuitable for evaluating the histological changes wrought by the phenol, as the condition treated might well of itself have brought about the changes observed in the spinal cord or roots.

Method

Twenty-nine adult cats, weighing 2–2.5 kg., were operated upon following anesthetization with intraperitoneal Nembutal.† A lumbar laminectomy was performed and the material to be tested was injected by direct visualization into the subarachnoidal space. Materials for testing were prepared by dissolving phenol crystals in Pantopaque in strengths of 1:10, 1:15, and 1:20. Each animal to be tested was injected with 1/10 cc. of the solution and so positioned as to layer this material onto the right-sided roots of the cauda equina. Controls consisted of 3 cats injected subarachnoidally with absolute alcohol and positioned head-down, 3 cats with surgical posterior rhizotomy, 1 cat subjected to a sham procedure with isolation but not section of a posterior root, and 2 cats injected with Pantopaque alone. The effects of phenol on “gamma” hypertonicity were studied by layering 1:10 phenol-Pantopaque against the cervical roots in 3 cats rendered decerebrate by an intercollicular section. Injected animals were kept in the experimental position for at least 1 hour to allow for full reaction of the phenol with the nerve roots.

Chronic animals were observed daily for motor and sensory changes. Those selected for histological study were anesthetized on the 7th to 10th postoperative day and perfused with 15 per cent formalin. The brain and spinal cord were preserved in fresh 15 per cent formalin (changed frequently) for 2 to 5 months. Frozen serial sections of the spinal cord and roots were cut at 15 and 25 µm in transverse, sagittal, and horizontal planes, stained using the Nauta-Gygax technique and examined microscopically. The patterns of degeneration were plotted on drawings of transverse, sagittal, and horizontal spinal-cord sections and photomicrographis were taken of representative fields of degeneration.

Observations

Physical. Immediately following injection of 1:10 and 1:15 solutions of phenol around the cauda equina there appeared a rhythmic twitching and jerking of the right hind limb. This movement was more marked with the stronger (1:10) solution and usually lasted 5 to 10 min. It is likely this movement caused some undesired dispersion of the phenol-Pantopaque solution and might account for some of the histological findings to be described below.

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There was little difference in the reactions of the phenol-treated as compared to the control cats when they were challenged during the postoperative period with such noxious stimuli as pin prick, firm periosteal pressure, and intracutaneous injection of histamine.

Motor deficit was obvious in the cats treated with 1:10 phenol. There were weakness and hypotonia in both hind limbs, more marked on the "down" or right side, and the patella and ankle reflexes were diminished to absent. The placing reflex was absent in the lower limbs. All motor deficit cleared by the 7th postoperative day. Animals treated with 1:15 phenol showed similar but less severe deficit. One cat of this group, however, was weak in all limbs and had no stretch reflexes for several days after the injection. Another cat showed weakness and an absent placing reflex only in the right hind limb. In both of these latter cats the deficit disappeared by the 7th postoperative day. There was no demonstrable motor deficit in the cats injected with 1:20 phenol-Pantopaque. In 3 decerebrate cats the 1:10 phenol-Pantopaque caused an obvious diminution in the extensor rigidity of the forelimbs. This was less noticeable after 30-45 min. and the full measure of rigidity had returned some 4 hours after the injections.

Histological. It was apparent on examining the silver-stained sections of the spinal cord and roots that greater destruction had been wrought by the more concentrated solution (1:10) and the damage was, as expected, more severe on the dependent side. Somewhat unexpected, however, was the capricious manner in which the phenol had acted. The various concentrations of phenol appeared to differ more in a quantitative than a qualitative manner in their action of selective destruction of fibers. Thus, in any section taken from the lumbar or sacral cord evidence of degeneration in all fiber-size groups was present and yet, in the same section, there were intact small and large fibers adjacent to the degenerated fibers (Figs. 1 and 2).

A similar distribution of degenerated fibers was seen with all concentrations of phenol tested (Figs. 3 and 4). The majority of the degenerated fibers entered the posterior columns through the dorsal and medial margins, although a few small fibers were seen coursing through the zona spongiosa to fields of preterminal degeneration which were present in the substantia gelatinosa and nucleus proprius. Degenerated axones of various sizes could be followed to zones of degenerated preterminal elements located in sensory, internuncial, and motor groups of cells of the ipsilateral sacral and lumbar spinal cord. Other degenerated fibers were observed to pass to the opposite side of the cord. In more rostral sections degenerated fibers were found in the fasciculi gracilis and proprius.

Degenerated axones in the proximal dorsal root were more abundant in the periphery of this structure, as though the action of the phenol was in part dependent on a surface phenomenon (Figs. 5 and 6). The alcohol-injected controls showed a more profuse degeneration of axones (Fig. 7) than did the cats injected with 1:10 phenol (Fig. 1). Again, fibers of all sizes were involved but with alcohol there was profuse degeneration as any given root-entry zone would show almost total destruction. The pattern of terminal distribution of the degenerated fibers in the ipsilateral cord at the level of the injection and at more rostral levels was similar to that described for the phenol-injected animals (Fig. 8).

Sections of the cord at the level of a surgical posterior rhizotomy revealed degeneration of all but a few fibers at the root-entry zone. The few intact fibers likely represent fibers entering from adjacent levels. There was a pronounced increase in the number of degenerated small fibers seen in the tract of Lissauer in the surgical-rhizotomy group (Fig. 9) when compared to the phenol-injected cats (Fig. 10). The intact tract of Lissauer on the side contralateral to the surgical rhizotomy is shown in Fig. 11. The dorsal roots and root-entry zones of the control animals with the sham operation or injection of Pantopaque showed no evidence of axonal degeneration.