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AJNR Am J Neuroradiol 1982, 3 (2) 121-125

<http://www.ajnr.org/content/3/2/121>

This information is current as
of May 24, 2024.

Experimental Production of Arachnoiditis with Glove Powder Contamination during Myelography

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Adhesive spinal arachnoiditis is a rare condition of several causes, including complications of myelography. An experiment was conducted to study the effects of surgical glove powder contamination in the cerebrospinal fluid. The subarachnoid space of 45 rabbits was injected with either a suspension of powder from sterile surgical gloves, Pantopaque (iophendylate), or a combination of the two agents. Mild to severe arachnoiditis was produced in 10 of 17 animals injected with the combination of powder and Pantopaque. Only two of 16 rabbits injected with glove powder and one of nine with Pantopaque had more than minimal changes of arachnoiditis. Three rabbits (two injected with glove powder alone and one with both agents) died of meningitis within 1 week of the injection. The combination of glove powder and Pantopaque is synergistic in producing arachnoiditis. These results emphasize the importance of meticulous technique in myelography.

Several factors have been shown to cause arachnoiditis in man. Most patients with arachnoiditis have intervertebral disc disease and have undergone myelography and/or surgery [1-3]. Other etiologies include infection (tuberculous or pyogenic) [1, 3], nonsurgical trauma [2, 3], tumors [1-3], subarachnoid hemorrhages [1, 3], and intrathecal injections (spinal anesthetics, contrast material) [1-4]; some cases are idiopathic [1-3]. Adhesive spinal arachnoiditis is a rare but serious condition occurring after Pantopaque myelography in less than 1% of patients [1, 5]. In about half the patients, the onset of symptoms is within 1 year of the procedure [1].

While much has been written concerning the relation of positive contrast myelography to arachnoiditis, little attention has been given to the possible effects of contaminants that might be injected intrathecally [6-9]. We conducted an experiment in rabbits to study the potential production of arachnoiditis from surgical glove powder contamination injected into the cerebrospinal fluid (CSF).

Materials and Methods

Fifty-one young adult New Zealand white rabbits weighing 3.5-4.0 kg were anesthetized using intramuscular injections of ketamine (44 mg/kg) and xylazine (8 mg/kg). The suboccipital puncture site was clipped to remove the fur, then scrubbed with an antiseptic solution. The operator scrubbed his hands with the antiseptic solution, then performed the puncture without gloves. The method of suboccipital puncture is described by Kusumi and Plouffe [10]. After the subarachnoid space was entered, 0.1 ml of CSF was removed from each animal. The Pantopaque (iopendylate, Lafayette Pharmacal) was drawn up into a sterile syringe through a 5 μ m filter before it was injected directly into the subarachnoid space or before it was mixed with the starch glove powder (Biosorb, Arbrook Inc.). After injection, the rabbits were elevated into an upright position in order to manipulate Pantopaque, Biosorb, or a combination of these agents into the lumbar region.

Two experimental groups were evaluated: a high-dose group using 10 mg of starch and a low-dose group using 100 μ g of starch. The groups were divided as (1) controls (six

Received April 21, 1981; accepted after revision September 19, 1981.

This work was supported by a grant from Lafayette Pharmacal, Division of Alcon Labs., Inc.

Presented at the annual meeting of the American Society of Neuroradiology, Chicago, April 1981.

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AJNR 3:121-125, March/April 1982
 0195-6108/82/0302-0121 \$00.00
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animals, suboccipital puncture only; (2) high-dose experimental group (nine with Pantopaque, 10 with Biosorb, and 10 with Biosorb in filtered Pantopaque; and (3) low-dose experimental group (eight with Biosorb and eight with Biosorb in filtered Pantopaque) (table 1). The rabbits were sacrificed at 30 and 60 days (table 1), with an intravenous injection of Beuthanasia-D (Pentobarbital 390 mg and Phenytoin 50 mg/ml). The entire spinal cord and meninges were removed via laminectomy.

The specimens were placed in 10% buffered formalin. Hematoxylin and eosin (H and E) sections were prepared from the cervical, thoracic, and lumbar levels with the meninges kept intact.

The H and E sections were all examined without knowledge of which substance had been injected. The amount of cellular infiltration and/or fibrosis was graded from normal to marked inflammatory changes (Figs. 1-4). The slides were also examined under polarized light to identify the birefringence of starch particles [11].

TABLE 1

Group/Dose	No. Sacrificed at:		Died During Study	Meningitis During Study
	30 days	60 days		
Control, suboccipital puncture only (n = 6)	3	3	0	0
High dose:				
0.1 ml Pantopaque (n = 9)	5	4	0	0
10 mg Biosorb in 0.1 ml NaCl (n = 10)	3	4	3*	6
10 ml Biosorb in 0.1 ml Pantopaque (n = 10)	5	5	0	2
Low dose:				
100 µg Biosorb in 0.1 ml NaCl (n = 8)	4	4	0	0
100 µg Biosorb in 0.1 ml Pantopaque (n = 8)	4	3	1†	0

* Animals died 3, 7, and 27 days after injection.
 † Animal died 2 days after injection.

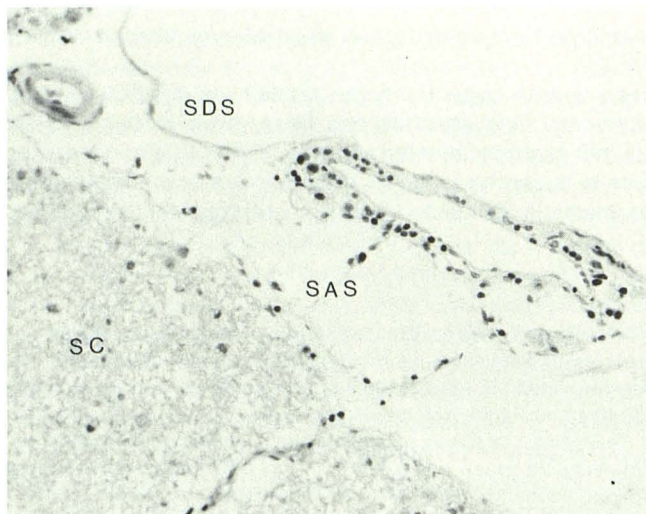


Fig. 1.—Minimal cellular infiltrate in subarachnoid space in animal injected with Biosorb and Pantopaque. Thoracic section. Sacrificed at 30 days. H and E, ×64 SC = spinal cord; SAS = subarachnoid space; SDS = subdural space.

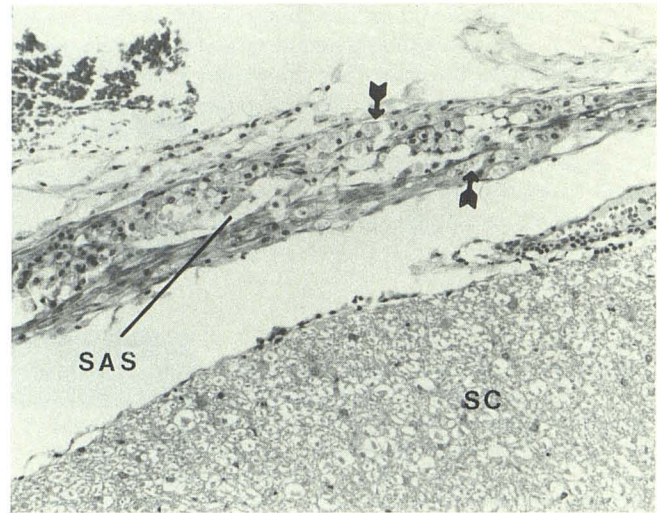
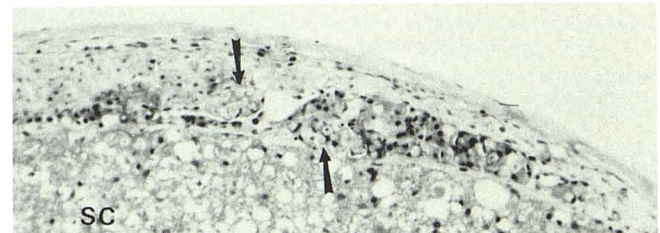
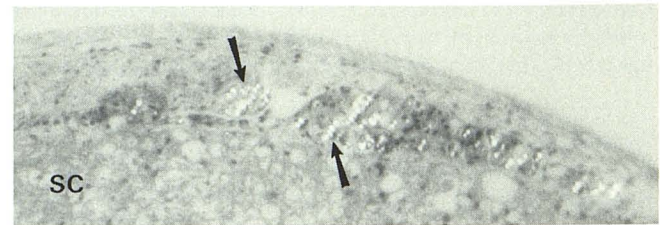


Fig. 2.—Moderate perivascular cellular reaction in subarachnoid space with localized aggregation of starch particles (arrows), inflammatory cells, and concomitant fibrosis. Lumbar section from animal injected with Biosorb and Pantopaque. Sacrificed at 30 days. H and E, ×40. SC = spinal cord; SAS = subarachnoid space.



A



B

Fig. 3.—A, Moderate mononuclear cellular reaction and starch particles (arrows) in meninges at lumbar level. Sacrificed at 30 days after injection with Biosorb and Pantopaque. H and E, ×40. B, Same section viewed with polarized light. Characteristic birefringence of starch particles (arrows). SC = spinal cord.

Results

Except for one rabbit that had a "bloody tap," the control animals demonstrated no significant subarachnoid reactions. This animal had perivascular meningeal and parenchymal cellular infiltrates consisting mostly of macrophages and lymphocytes. The reaction was most prominent in the leptomeninges of the lumbar spine.

In the high-dose group (fig. 5), eight of the 29 animals

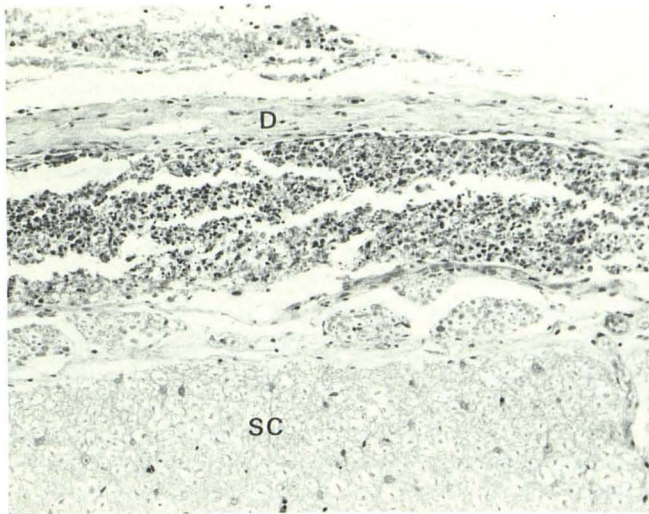


Fig. 4.—Marked subarachnoid infiltration with eosinophils and some mononuclear cells. Many cells with karyorrhectic nuclei. Lumbar section. H and E, $\times 40$. SC = spinal cord; D = dura mater.

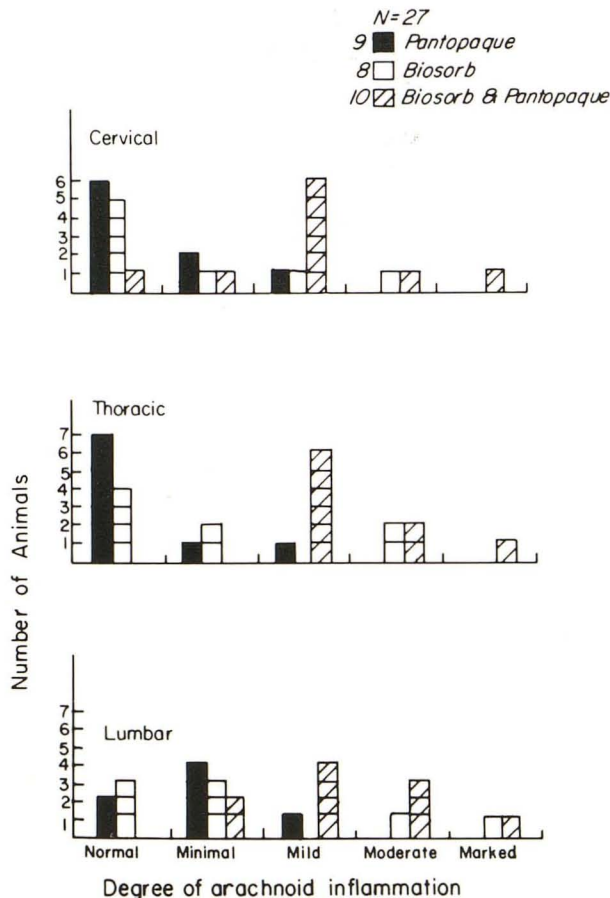


Fig. 5.—Combined data of high dose group sacrificed at 30 and 60 days.

developed signs of meningitis (hyperreflexia and hyperesthesia) within 24 hr of the injection; six had been injected with starch powder and the other two with starch powder and Pantopaque. Of these, three rabbits died (at 3, 7, and 27 days after the injection). Each had been injected with starch powder only and demonstrated minimal or mild cellular infiltrates in the leptomeninges. In the rabbit dying at 3 days the infiltrate in the leptomeninges contained eosinophils.

In the nine animals injected only with filtered Pantopaque two of five demonstrated minimal focal cellular infiltrates in the leptomeninges at 30 days. At 60 days, another two animals had minimal focal areas of fibrosis, one with and the other without evidence of cellular infiltration, and another rabbit had a mild inflammatory infiltrate at all levels examined. The inflammatory changes at 60 days tended to be more extensive in the leptomeninges of the lumbar spine. Of the total of 25 histologic sections examined in the nine rabbits injected with Pantopaque alone, 10 sections demonstrated only minimal or mild inflammation and the rest were normal.

In the 10 rabbits injected with the high dose of Biosorb alone, seven survived for examination at 30 and 60 days. One animal at each time had an intraparenchymal cellular infiltrate that was perivascular and perineuronal. The infiltrate varied from minimal to severe in different areas. Leptomeningeal fibrosis was identified at 60 days in another animal with moderate cellular infiltrates. Four animals had no abnormalities.

All of the 10 rabbits injected with 10 mg of Biosorb mixed with Pantopaque demonstrated inflammatory changes. In addition to the cellular infiltrates seen in other groups, localized aggregations of starch particles and inflammatory cells were identified in all five rabbits sacrificed at 30 days. Starch particles were identified by their characteristic birefringence under polarized light. In three of five rabbits sacrificed at 60 days, there was significant leptomeningeal fibrosis. All five had other changes similar to the animals sacrificed at 30 days.

The combined results of the high dose groups sacrificed at 30 and 60 days are shown in figure 5. The two animals that died less than 1 week after the injection are not included in the tabulated results.

The second experimental group was injected with 100 μ g of the starch powder either in sterile saline or in Pantopaque. Only one of eight animals injected with starch powder alone had inflammation in the meninges at either 30 or 60 days. Half of the eight animals injected with both starch powder and Pantopaque had leptomeningeal inflammation at 30 days and none at 60 days (fig. 6). One animal died 2 days after the injection, but had no evidence of meningeal inflammation.

The cellular reaction contained eosinophils in two of the animals (fig. 4). The reaction was focal with no evidence of parasitic infestation. One animal dying at 3 days had been injected with 10 mg of starch powder. The other animal was sacrificed 30 days after injection with 100 μ g of starch powder suspended in Pantopaque.

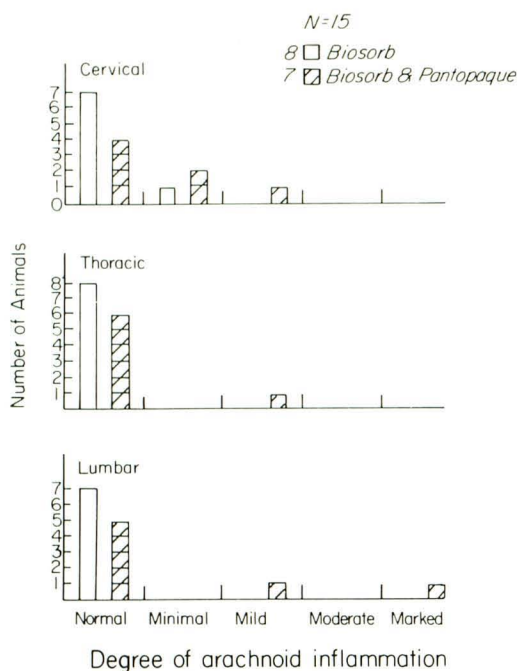


Fig. 6.—Combined data of low dose group sacrificed at 30 and 60 days.

Discussion

Symptomatic adhesive spinal arachnoiditis occurs in 1% or less of patients undergoing positive contrast myelography [1, 5]. Some authors believe there are many asymptomatic patients with arachnoiditis [1, 12–14]. In patients undergoing Pantopaque myelography, the incidence of clinical signs of arachnoiditis are greater in those having large amounts [5–6 ml] of Pantopaque remaining in the subarachnoid space [1, 2, 5, 13, 15]. Bergeron et al. [12] stated that arachnoidal reaction occurs “unfailingly” in the presence of retained Pantopaque.

Several authors [12, 16, 17] have described a potentiating effect of blood mixed with Pantopaque in producing earlier and more marked subarachnoid reaction. In the series of Shaw et al. [1], technical difficulties were encountered in performing myelography in 39% of the patients who developed arachnoiditis. Winkelman et al. [18] suggested that many cases of adhesive spinal arachnoiditis are due to breaks in myelographic technique.

In 1955, Wise [19] applied glove powder (talc or starch) to the exposed conus medullaris and cauda equina in dogs. Histologic examination up to 60 days later demonstrated granulomatous changes in the dura with an adherent arachnoid. The changes were more pronounced with talc than with starch. He concluded that glove powder left in an operative site may cause or contribute to postoperative arachnoiditis.

In postsurgical cases, Antopol was the first to report granulomata caused by the use of talc as a glove powder [19]. In 1947, Lee and Lehman [20] described a new glove powder derived from corn starch (Biosorb) which is

“essentially” nonirritating to tissues. Subsequent studies [19, 21–24] have shown that this starch glove powder can cause granulomata in the peritoneum when the powder is in “clumps” rather than finely dispersed [25].

In our experiment, eight of 45 animals developed hyperreflexia and hyperesthesias within 24 hr after the suboccipital injection. These signs were indicative of aseptic meningitis. Six of the animals had been injected with 10 mg of Biosorb and two with 10 mg of Biosorb suspended in Pantopaque.

All rabbits injected with 10 mg of Biosorb mixed with Pantopaque demonstrated inflammatory changes. In addition to the cellular infiltrates, localized aggregations of starch particles and inflammatory cells were identified in all five rabbits sacrificed at 30 days. In three of the five rabbits sacrificed at 60 days, there was significant leptomeningeal fibrosis.

The response to the intrathecal injection of starch glove powder may primarily be a nonspecific inflammatory reaction to a foreign substance. However, the eosinophilia in 6% (two of 36) of the animals injected with the starch glove powder (one injected with 100 μ g Biosorb in Pantopaque and the other injected with 10 mg of Biosorb) may indicate a hypersensitivity reaction [26] that could occur with very small amounts of the powder contaminating the cerebrospinal fluid. There have been several reports of delayed hypersensitivity to starch powder in humans [22] and in animals [27].

Using a scanning electron microscope, Seigel et al. [28] have shown that starch particles from surgical gloves can be introduced through a spinal needle if the stylet is inadvertently handled during myelography. Preliminary data using a Coulter Counter demonstrate that the mean number of starch particles injected into the low-dose group is only a factor of two to three greater than the average number of particles that can be injected through a spinal needle after handling the needle stylet with unwashed gloves. Further work would be necessary to show whether the dose used in this experiment would cause similar effects in primates.

This experiment demonstrates that either milligram or microgram quantities of starch glove powder injected into the subarachnoid space of rabbits can cause arachnoiditis. The effect of the starch glove powder mixed with Pantopaque is greater than with either substance injected separately.

While the incidence of symptomatic arachnoiditis after Pantopaque myelography is low, maintaining high standards of sterile technique to avoid the introduction of contaminants into the cerebrospinal fluid would very likely contribute to decreasing the morbidity of myelography. Such preventative measures as wiping the gloves with sterile water or saline and handling the spinal needle only by the hub would reduce the possibility of glove powder contamination.

ACKNOWLEDGMENTS

We thank Barry Newton of Lafayette Pharmacal for suggestions in the initial planning of this experiment; and Norma Jean Dempsey, Janet Hebert, and Robbe Sokolove for secretarial assistance.

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