

ALTERNATIVE PATHWAYS FOR DRAINAGE OF CEREBROSPINAL FLUID IN THE CANINE BRAIN

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ABSTRACT

Although the brain has no formal lymphatic system, a substantial quantity of cerebrospinal fluid (CSF) has nonetheless been shown to drain via cervical lymphatics. To pursue further the issue of alternative drainage pathways for CSF, we infused a solution of Ringer's lactate (RL) into the cisterna magna of the dog brain and monitored both the flow and concentration of total protein of cervical lymph. This maneuver promoted a nearly three-fold rise in intracranial pressure and was accompanied by a rise in cervical lymph flow and fall in its protein content. In addition, a profuse nasal discharge (11.4ml/hr) developed with a moderately high protein content of the rhinorrhea fluid (1.8g/dl), along with similar appearance times of Evans blue dye (instilled in the cisterna magna) in both cervical lymph and the rhinorrhea fluid (48-70 minutes after infusion).

These findings suggest alternative drainage pathways for CSF besides the arachnoid villi (Pacchionian bodies) including connections with lymphatics in the neck and along the olfactory nerve, and around the cribriform plate to the nasal submucosa, and with proptosis, perhaps also through the aqueous humor-canal of Schlemm and nasolacrimal duct.

The cerebrospinal fluid (CSF) has been widely studied but outstanding ques-

tions remain regarding its circulation and absorption. Bradbury et al. (1) demonstrated in rabbits that interstitial and perivascular channels drain brain interstitial fluid (ISF) to cervical lymphatics. These intracranial extracellular pathways function like lymphatic channels but are not lined by endothelium and have been termed "prelymphatics" (2).

Rhinorrhea develops in the canine (but not the rabbit; MWB Bradbury, personal communication) when intracranial pressure is raised by a fluid infusion into the cisterna magna (3,4). This nasal discharge in the canine is composed of CSF, ISF, and infusate plus plasma proteins that transude from cerebral capillaries and possibly other ill-defined constituents received along the drainage pathway. To elucidate this phenomenon further, we infused Ringer's lactate solution into the cisterna magna of dogs and examined the flow and protein composition of cervical lymph and fluid discharge from the nose.

MATERIALS AND METHODS

Eleven mongrel dogs (18-20kg) were anesthetized with I.V. sodium pentobarbital (25-28mg/kg). A cuffed endotracheal tube was inserted and connected to a Bird respirator.

Using sterile technique, the right and left cervical lymphatics were cannulated with fine polyethylene tubing (PE 50 or

60) two to four cm inferior to the retropharyngeal (i.e., deep cervical) lymph node. Lymph flow was measured by timed collection and samples of lymph were analyzed for total protein content by the biuret reaction (5) and compared with blood plasma and cerebrospinal fluid (CSF). Total protein in cisternal samples of CSF were measured by the Trichloroacetic acid method (6).

A #20F spinal needle was inserted into the cisterna magna with the dog lying on the right side. Ringer's lactate (RL) solution was administered intracisternally by gravity drip at a rate that averaged ~ 167ml/hr. At intervals, the RL infusion was stopped temporarily so that the cisternal pressure could be measured by manometry.

Cervical lymph and cisternal fluid were collected before and near the end of the infusion. Blood samples were obtained from the femoral vein at the beginning and end of each experiment. Nasal drainage was collected at timed intervals. Evans blue dye (T1824) (0.25ml) was injected into the cistern and its appearance time noted visually in cervical lymph and nasal drainage.

RESULTS (Table 1)

After a mean of 352ml of RL infusion into the cisterna magna over ~ 140 min-

utes, the cisternal pressure rose in six dogs from 15.2 (9.5-24.5) to 35.2 (18.5-42.0) cm of RL ($p < 0.05$). Orbital and conjunctival edema and proptosis developed in 9 of 11 dogs. Total protein in cisternal fluid fell from 0.04g/dl before infusion to 0.01g/dl after the infusion.

Right cervical lymph flow increased from 1.8 ± 1.4 ml/hr before cisternal infusion to a peak of 4.8 ± 3.4 ml/hr after infusion. Similarly, left cervical lymph flow increased from 1.4 ± 1.1 ml/hr to 2.5 ± 1.7 ml/hr. On the other hand, the total protein in right cervical lymph decreased in cisternal infusion from 2.2 ± 0.7 g/dl to 1.5 ± 1.6 g/dl and that in left cervical lymph from 1.8 ± 1.0 g/dl to 1.2 ± 0.8 g/dl. Blood plasma protein was unchanged (6.0 ± 0.2 to 5.8 ± 0.1 g/dl) over this interval.

After instillation of Evans blue into the cisterna magna, dye appeared in right cervical lymph within 46 minutes and left cervical lymph after 70 minutes. In two dogs in which nasal discharge was collected, and a mean volume of 270ml of RL had been infused into the cisterna magna, the mean rate of nasal discharge was 11.4ml/hr with a mean total protein content of 1.8g/dl. A profuse nasal discharge was noted in six other dogs and a moderate discharge in two more. The gross appearance time of Evans blue dye in the nasal effluent was 48 minutes.

Table 1

Findings Before and After Cisternal Infusion of Ringer's Lactate					
	Before Infusion	(n)	After Infusion	(n)	
CSF pressure in cisterna magna (cm RL)	15.2±7.2	(5)	35.2±13.9	(5)	
Flow (ml/hr)					
Right cervical lymph	1.8±1.4	(4)	4.8±3.4	(5)	
Left cervical lymph	1.4±1.1	(5)	2.5±1.7	(5)	
Rhinorrhea			11.4	(2)	
Total Protein (g/dl)					
Right cervical lymph	2.2±0.7	(5)	1.5±0.6	(4)	
Left cervical lymph	1.8±1.0	(3)	1.2±0.8	(4)	
Rhinorrhea	-		1.8	(2)	
CSF (mg/ml)	0.4±0.58	(8)	0.1±0.02	(3)	

COMMENT

Cervical lymph derives from several sources including the skin, subcutaneous tissue, and muscles of the head and neck and drains to regional local lymph nodes, thence to cervical lymphatics. It characteristically contains a substantial amount of protein that leaks from plasma (7). CSF, by contrast, normally contains only a minute amount of plasma protein which derives as an ultrafiltrate of plasma through tight blood endothelial junctions into brain interstitium, and also by secretion of the choroid plexus lining the cerebral ventricles (8).

After infusion, however, of a modest amount of crystalloid solution into the CSF, a notable rise in lymph flow occurs in cervical lymph accompanied by a fall in the lymph total protein content without significant change in the plasma protein level. These findings suggest an escape route for "protein-poor" intracranial CSF and cisternal infusate into cervical lymph to account for the rise in lymph flow and "dilution" of its protein content. This conclusion is supported by the appearance of Evans blue dye in cervical lymph after infusion into the cistern and the moderate to profuse drainage high in protein content from the nares, also colored with Evans blue dye after selective RL infusion into the cistern with nearly a three-fold rise in intracranial pressure.

These data suggest that alternative extracranial pathways exist in the canine for the escape of CSF with increased intracranial pressure. Although no discrete lymphatic pathways are identifiable in the brain, interstitial and perivascular spaces not lined by endothelium (termed "pre-lymphatics") and perineural lymphatics along cranial nerves may transport excess intracranial fluid to cervical lymphatics or interconnect with a rich lymphatic plexus adjacent to the cribriform plate and drain into nasal submucosa and the nasal cavity (1,9-11). Moreover, with severe proptosis, some CSF may seep into the anterior chamber of the eye and then escape via the canal of Schlemm and the nasolacrimal duct to contribute to rhinorrhea (12).

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