

Is human cerebrospinal fluid reabsorbed by lymph?

Lymph drainage therapy (LDT) and manual drainage of the central nervous system

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“The lymphatics are closely and universally connected with the spinal cord and all other nerves, long or short, universal or separate, and all drink from the waters of the brain.”

A.T. Still, *Philosophy of Osteopathy*, pg. 105.

“Possibly less is known of the lymphatics than any other division of the life-sustaining machinery of man.”

A.T. Still, *The Philosophy and Mechanical Principles of Osteopathy*, pg. 66.

These two quotes from the father of osteopathy still today remains so contemporary. The latest scientific reports agree that about half of cerebrospinal fluid (CSF) may be reabsorbed by the lymphatic circulation. That proportion can even be greater when the CSF pressure increases.^{24,48,86} But in spite of this new information, the relationship between lymphatic circulation and CSF still generates controversy among experts espousing their various theories.

This article describes some of the new concepts concerning the circulation between CSF, cerebral interstitial fluid (CIF) and lymph. It also will present some specific lymphatic techniques (Lymph Drainage Therapy) that can help facilitate the exchange of these fluids.

Cerebrospinal fluid (CSF) production

“...the cerebrospinal fluid is one of the highest known elements that are contained in the body...” A.T. Still, *The Philosophy and Mechanical Principles of Osteopathy*, pg. 44.

Scientists agree that production of CSF is done mainly by the highly vascularized choroid plexus. However, other experimentation found that the choroid plexus are responsible for only 60 to 85 percent of the total production of CSF.^{33,34,71} Some studies have shown that about 15 to 30 percent of CSF is produced in an extrachoroidal origin.⁷⁹ The capillary endothelium of the cerebral tissue is believed to be the major source of extrachoroidal CSF production.^{15,81,99,101}

Cerebrospinal fluid (CSF) absorption:

1) *Choroid Plexus:*

The choroid plexus may absorb about 1/10th of their own secretion.^{87,99} For that reason, the function of these structures has been compared to that of the proximal renal tubule.

2) *Arachnoid villi and granulations (pacchionian bodies: the venous side)*

In 1914, Weed made an important discovery when he showed that the arachnoid villi and granulations are the major source of CSF absorption.⁹⁷

Villi and granulations are covered by a epithelium with very tight junctions. On the apical cap of arachnoid cells, the dural coat is lacking, and the presence of open channels has been shown to connect the arachnoid bodies to the venous side. The exact role of the arachnoid villi and granulations in reabsorption of CSF is still unclear. Well limited channels up to 100 microns in diameter have been described at the apical cap of the arachnoid granulations and seem to be in continuity with the SAS.^{12,18,19,33,34,58,93} Pinocytosis or vesicles seem to be another possible mechanism of CSF transfer.¹⁹

We can already observe that a link between intracranial and extracranial veins exist. The cranium is made of

an inner and outer plate (lamina) of resistant compact bone with an intervening layer of light, spongy bone (the diploe). The diploe is covered by a network of veins (the diploic veins: anterior and posterior temporal diploic veins, frontal and occipital diploic veins) that receive venous drainage of the entire skull. Emissary veins are veins without valves that pass through the cranial bones to connect with the superficial extracranial veins, for example the superficial temporal vein. There is a connection between intracranial veins, diploic veins, emissary veins and extracranial veins (temporal, occipital, parietal).

Clinical studies also have shown that stimulation of lymphatic drainage also activates venous reabsorption⁸³ Specific manual lymphatic drainage techniques can specifically facilitate extracranial lymphatic circulation and are able to activate CSF/venous exchanges/lymphatic exchanges.

3) *The lymphatic side*

"...the lymphatics are almost the soul requisite of the body..." A.T. Still, *Philosophy of Osteopathy*, pg. 109.

Lymphatic vessels have been noted only in the dura, the pia mater,⁶⁸ the pituitary capsule, the orbit, the nasal mucosa, and the middle ear. To date, a lymphatic system has not been identified within the brain itself. However, some type of lymphatic-like drainage is necessary to evacuate the small amount of proteins of the central nervous system, which becomes particularly important in cases of edema, hemorrhage or infection.^{16,25} The significant presence of the lymphatic system to help the scavenger cells (macrophages and microglia) evacuate large proteins in extracranial connective tissue is lacking in the central nervous system.

In addition, the central nervous system requires fast pathways equivalent to the lymphatic system, for circulation of immunocompetent cells, which lead to lymphatic nodes and/or the spleen in order to activate a significant immunological response.^{31,32,63,101}

A) Lymphatic Drainage of the CSF: "Perineural Pathways"

By injecting Berlin Blue dye into a dog's subarachnoid space, Schwalbe, in 1869, made the first observation that the lymphatic pathways were the major means to absorb CSF.⁸⁷ Later, in 1872, Quincke theorized that the CSF can leave the subarachnoid spaces through small areas surrounding the nerve roots.⁸⁰

In 1875, Key and Retzius were the first to demonstrate the circulation through the arachnoid granulations into lymphatic vessels in the nasal mucosa, the frontal sinus and along cranial nerves using dye-colored gelatin.⁵⁷

Their model held until 1914 when Weeds, who judiciously used alternatively two solutions of a ferrous cyanide then acid, observed precipitation of blue crystals into the lateral ventricles of cats and rabbits. He concluded that the arachnoid villi were the dominant way for CSF to be reabsorbed.^{97,98} After reviewing Weed's work today, we know he observed that a certain amount of dye colored the course of cranial nerves and cervical lymphatics, but he concluded at the time that the lymphatics are an "accessory pathway" for CSF absorption. After that, the theory of central nervous system lymphatic drainage was slowly discarded.

Numerous published studies show that some constituents of the CSF in animals drain into cervical lymph nodes. Passage from the CSF to the deep cervical nodes occurs within 1mm in the rabbit,¹⁰³ and 30mm in the rat and guinea pig.^{6,11,59}

In 1968, Foldi was one of the first scientist to use ligation of the cervical lymphatics to provoke lymphostatic encephalopathy in dogs.^{31,40} The recent research by Boulton et al^{7,8} illustrates that about one half (48 percent) of the protein tracer injected in the lateral ventricles of sheep is transported into extracranial lymphatics.

Mistakes or imprecision in standard studies have minimized the role of lymph in CSF reabsorption. Courtice and Simmonds, in 1951, injected radio-labeled albumin and recovered about 5 percent in the cervical lymph nodes.^{29,89} They reported that 95 percent was reabsorbed by arachnoid villi. Actually, they recovered only 14 percent of all the radioactive substances. After correcting the calculations, their experiments showed that approximately 30 percent was reabsorbed in the cervical lymphatics.

After several experiments, Brinker et al showed that at least 50 percent of CSF is reabsorb through the lymphatics rather than arachnoid villi.¹⁷ The increase in CSF intraventricular pressure eventually will augment the amount of CSF drained by the lymphatics^{24,48,55,69,86} and amount of the fluid recovered seems to depend on the molecular weight.

However, strong scientific evidence of these findings in human subjects is still insufficient.²⁴ Smith showed that various tumors of the central nervous system (medulloblastoma, glioblastoma), can metastasize into the lymphatic system.⁹⁰ Ogilvy also observed gliomas spread to deep cervical lymph nodes.⁵²

In addition, clinical observations help us understand that some of the constituents of the CSF are reabsorbed in the periphery of the body. McComb observed that children with hydrocephalus develop nasal congestion, facial and periorbital edema when their cranial shunts develop an obstruction.⁷¹

1) Drainage through nasal lymphatics:

The historical experiment of Schwalbe using Berlin blue dye, showed some quantity of the marker passing along olfactory bundle nerve pathways. Numerous experiments with different species confirmed the existence of this pathway.^{9,10,11,23,31,37,55,59,66,67,71,72,87,88,97,103,105}

Jackson showed in 1979 that inflammatory blockage of nasal mucosa lymphatics can facilitate central nervous system retrograde viral infection.

Carbon particles and labeled proteins follow the olfactory tracts and pass through the cribriform plate (lamina cribrosa) to the nasal mucosa, the retropharyngeal lymph nodes and the angulus venosus at the base of the neck (internal jugular vein, subclavian vein, brachio-cephalic vein).

At the level of the fila olfactoria passing through the cribriform plate, the layer of dura and arachnoid fuses and becomes continuous with the one-layer thick perineurium. Perhaps 90 percent of radio-labeled particles follow this route in the rabbit.³⁰

The perineurium space seems to communicate freely with the loose interstitial tissue of the submucosa (passive escape pressure-dependent, no tight junctions). Pinnocytosis is another mechanism that has been proposed.⁵⁵

Adjacent lymphatic vessels can easily reabsorb constituents of the CSF and escape into the nasal mucosa. Intranasal and intraoral lymphatic drainage (including soft and hard palate, palatoglossal and palatopharyngeal arches, subglossal lymph circulation) can help activate this circulation.

2) Drainage through optic nerve pathways:

Numerous studies also identify the optic pathways as a route for the SAS to be reabsorbed from the central nervous system.^{5,11,35,0,69,71,88}

Markers injected in the SAS also have been shown to reach the retro-orbital connective tissue. Shen found some arachnoidal trabecular network at transitional areas at the end of the SAS and the posterior uveal/periorbital compartment.⁸⁸

Lymphatic drainage of the orbits and periorbital tissues to the temporal and parotidians lymph nodes helps activate this circulation.

3) Drainage through auditory pathways:

Some experimental animal studies have shown that constituents of the CSF also may drain via the perilymph then the fenestra rotunda, to the mucosa of the middle ear.³ The communication between SAS and the ear takes place through the cochlear duct.⁵⁹ Activation of lymph flow through drainage of the preauricular and post auricular

lymph nodes, external auditory meatus, and auricle of the ears also can be used clinically.

4) Other nerves pathways: trigeminal nerves, facial nerves and other cranial nerves.²

This circulation can be activated with extensive lymphatic drainage of the neck and face.

5) Spinal nerve root:

In 1928, Pigalew injected a tracer in the lumbar dural space and found it in the abdominal and pelvic lymphatics, including the pancreas, suprarenal glands and paraaortal lymph nodes. Brierley and Field¹⁴ detected Indian ink suspension in the lumbar and sacral nerve roots. Later a small quantity of this marker was observed in the lumbar para-aortic lymph nodes.⁵³

Lymphatic drainage of the spine is accessible following deep or superficial lymphatic pathways. Deep lymphatic drainage involves pathways through the intercostal nodes to the paraspinal nodes or through the quadratus lumborum. The superficial drainage of the spine follows three distinct lymph territories, or lymphotomes, that drain to the cervical, axillary or inguinal lymph nodes.

6) Direct dural pathway

Under high pathological pressure, the CSF can escape from the arachnoid barrier and be reabsorbed by the lymphatics of the dura mater.¹⁹

B. Lymphatic drainage of cerebral interstitial fluid (CIF): "Intravascular/perivascular pathways"

Passage from the brain to the deep cervical nodes takes place in 3 hours in the rabbit,¹⁰² 8 hours in cat and sheep.^{11,30}

Dubois-Ferriere first demonstrated the connections between the intraadventitial circulation and the cervical lymphatics.³⁶ These studies, which were followed by those of Kozma, Casley-Smith and others, showed that carbon particle markers injected in the cerebral cortex were detected in the adventitia of cerebral blood vessels both intra- and extra-cranially.^{12,20,21,22,56}

Virchow (1851) and Robin (1859) described spaces located inside the main cerebral blood vessels, located between the basement membrane of the glial limitans externally and the tunica media.^{38,94,95} These spaces have been described as perivascular or more appropriately intraadventitial.^{21,23,44,45,96,104}

Extra cerebral blood vessels present in the adventitia a circulation of minute vessels and nerves that is called the

“vasa-vasorum”: the vessels inside the vessel.^{51,77,85} Cerebral vessels after passing through the layer of dura mater have no vasa-vasorum in the adventitia²⁸ and their endothelial cells are joined by tight junctions.¹⁰⁴ However, the surface of the adventitia contains many circular openings measuring 1 to 3 microns (stomata), which connect with the intraadventitial spaces on one side and CSF on the other side.¹⁰⁴ A free communication between the perivascular pathways and SAS has also been described.^{60,82,98}

Two schools of thought exist concerning whether the delicate layer of pia mater coats the blood vessels when they enter the cerebral tissue. The possible continuity between the SAS and perivascular spaces is yet another subject of controversy.

Several investigators support the viewpoint that the pia mater follows the blood vessels in the SAS that enter the cerebral parenchyma.^{45,47,64,65,78,84,94,98,105} Zhang showed that intracortical arteries are coated at their source by a sheath of cells derived from the pia mater, while veins are covered incompletely by some pial cells.

Other studies concluded that the pia mater does not accompany the blood vessels in the cerebral tissue.^{20,21,22,23,26,37,40,41,42,43,44,54,65,101}

Foldi^{41,53,62} and his team ligated the cervical lymphatics of numerous animals. In his report, he stated that researchers noted lymphostatic hemangiopathy characterized by spaces in the blood vessels of the neck, edema fluid in the adventitia of intracranial/extracranial as well as intracerebral vessels (...)” those spaces being 6-10 times larger than usual.⁴⁴

Intraadventitial spaces, which follow the course of blood vessels, are present throughout the body. The fact they do not present valves and that retrograde lymph flow is possible, constitutes an alternate pathway, if needed, for lymph circulation. In the case of the CNS, these structures represent a natural escape for some of the constituents of the CIF in order to drain into lymphatic pathways.

In conclusion CSF and CIF may choose between two major pathways: the neurolymphatic pathways along perineurium of nerves, principally olfactory nerves, and hemangiolymphatic pathways, perivascular/intravascular pathways, along major arteries and veins.

Clinical applications: lymph drainage therapy

“We lay much stress on the uses of blood and the powers of the nerves, but have we any evidence that they are of more vital importance than the lymphatics?” A.T. Still, *The Philosophy and Mechanical Principles of Osteopathy*, pg. 65.

“...your patient had better save his life and money by

passing you by as a failure, until you are by knowledge qualified to deal with the lymphatics” A.T. Still, *Philosophy of Osteopathy*, pg. 105.

Lymphology has evolved as a new branch of medicine as medical science is only beginning to fully understand the role that lymph plays in the body. The first recorded use of gentle manual techniques to activate the lymphatic flow took place at the beginning of the 20th century. Osteopath F. P. Millard, a graduate of the Kirksville Osteopathic College, was the first practitioner to document specific techniques working on the lymphatic system.⁷⁵ Specific lymphatic techniques, like cranial techniques, were introduced in a second time, in the history of osteopathic manipulation.

Scientific descriptions of a lymphatic rhythm have been described in human,^{39,46,61,91,92} but very few practitioners are working with stimulating lymph circulation in a direct and specific manner in the same way we work with the CSF circulation. There is a whole new and very rich field of osteopathy to deepen and expand into.

Lymph Drainage Therapy is an original method of lymphatic drainage developed by French physician Bruno Chikly. The particularities of LDT are that it teaches practitioners how to manually attune to the 1) specific rhythm, 2) direction 3) depth and 4) quality of the lymph flow consistent with scientific discoveries.^{46,91,92}

1) Human lymphatic rhythm:

The main vessel of the lymphatic system (lymphatic collectors) consists of two or three layers of spiral muscles with specific contractions that are innervated by the sympathetic and parasympathetic system (49, 56, 73, 78, 81). Contrary to some views, the lymphatic system is not a passive system; lymph does not need to be pushed with our fingers like a tube of toothpaste. Obstruction on the way has to be removed, specific pressure and rhythm needs to be applied in synchrony with the lymphatic system. Even though one main lymphatic rhythm has been scientifically described in humans in practice two different lymphatic rhythms have been identified: the capillary and lymphangions rhythm, and a pre-lymphatic (connective tissue) rhythm.

2) Direction of the lymph flow:

Advanced LDT practitioners can assess and manually “map” the flow of the lymphatic circulation during sessions. This method consists of manually assessing the specific direction of lymphatic flow and finding areas of fluid retention, edemas or fibrosis. The mapping tools are very

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