The Primary Respiratory Mechanism

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Introduction

William Garner Sutherland[1] proposed the primary respiratory mechanism (PRM) that unites the fundamental physiology, cellular metabolism, of the most distant regions of the human body into a coordinated holism. Magoun[2(p.34)] summarized this aspect of the PRM as the "dynamic metabolic interchange in every cell (of the body) with each phase of (its) action." Sutherland, following the methods of Still, based his hypothesis upon a rigorous study of anatomy. He proposed an extremely subtle mechanism that is particularly difficult to prove, or from the perspective of the nulhypothesis, to disprove. Although much research has been performed to elucidate the proposed components of the PRM, the underlying mechanism remains undefined.

Unproven hypotheses may be lent credibility by corroborative experiences. To any physician who has employed Sutherland's methods to treat a patient, or to any patient who has benefited from such treatment, there is corroboration beyond doubt. Such anecdotal evidence, however, is insufficient for individuals who demand rigorous scientific documentation.

Early in the history of osteopathic education, A. T. Still was purported to have felt that anatomy was the one subject an osteopath ought need to know. Later he stated that the student of osteopathy must know, in addition, physiology and chemistry.[3(pg. xvi)] Consequently, Sutherland, who was an early student of Still's, developed his ideas from the perspective of applied anatomy,[4(p.5)] for at the time, the science of anatomy was significantly more developed than the sciences of physiology and biochemistry.

Physiology and biochemistry are now highly advanced and it is appropriate that we now look into these disciplines for evidence that corroborates Sutherland's hypothesis. If the proposed mechanism of Cranial Osteopathy is congruent with scientifically established phenomena, it must be accorded a higher level of credibility. Additionally, the recognition of a body of scientifically validated material will assist future research into Sutherland's discovery.

Over the years, many authors have commented upon the similarity of the Traube-Hering (TH) oscillation (Figure 1) to the cranial rhythmic impulse (CRI), the palpable manifestation of the PRM.[5-9] The Traube-Hering oscillation was initially recognized in 1865 when Traube[10] reported the measurement of a fluctuation in pulse pressure with the frequency of respiration that persisted after respiration had been arrested. In, 1869, Hering[11] confirmed Traube's discovery. Several years later, in 1876, Mayer[12] identified a similar, but slower rate, oscillation. Collectively, these phenomena are now known as the Traube-Hering-Mayer (THM) oscillation.[13] Components of the THM have been measured in association with blood pressure,[10,13-19] heart rate,[13,19,20] cardiac contractility,[21] pulmonary blood flow,[22] cerebral blood flow and movement of the cerebrospinal fluid,[23-25] and peripheral blood flow including venous volume and body temperature regulation.[13,17,19,26] These oscillations are the result of a complex interaction between the sympathetic and parasympathetic components of the autonomic nervous system and renin-angiotensin upon the cardiovascular system, and they are an integral aspect of homeostasis.[17]

Neural activity producing and coordinating the THM oscillation emanates from the floor of the fourth ventricle in the nucleus of the tractus solitarius (NTS). There are lateral pressor areas in the NTS responsible for vasoconstriction, and medial depressor areas responsible for vasodilatation. These areas within the NTS exhibit inherent automaticity.[26] The vagus, cranial nerve X, arises from the medulla immediately adjacent to the NTS and contributes to the THM oscillation through its cardio-inhibitory efferent fibers. A complex interrelationship of tonic activities, reflecting phasic input from the brainstem and the humoral effect of renin-angiotensin, gives rise to the THM oscillation.

Recognizing that Sutherland's proposal is a masterpiece of insight, we

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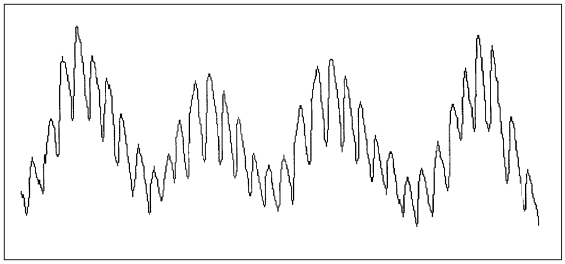
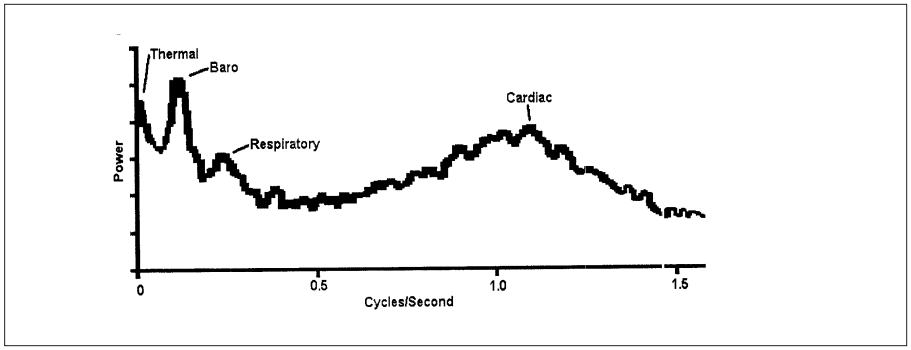


PRM Figure 1: Four Traube-Hering oscillations, in a thirty-second recording of fluctuations in blood flow velocity (heart rate 70 bpm, Traube-Hering rate 8 cpm) measured with laser-Doppler flowmetry,

are still confronted by the question of how it works. Sutherland [4(p.13)] described the PRM as consisting of four features. The first feature is the fluctuation of the cerebrospinal fluid (CSF). The second is the reciprocal tension membrane, which is the dura mater that acts to balance the system by uniting its boney components. The third is the motility of the central nervous system (CNS), and the forth is the articular mobility of the cranial bones and of the sacrum between the ilia (later authors have separated this last feature into two components). It is the first and third components of Sutherland's mechanism that may be considered in the context of the THM. In the following paper, I will attempt to explain the CRI and the PRM, which are discussed in the context of the THM oscillation and related physiology and biochemistry.



PRM Figure 2: Power spectrum analysis (Fourier, Transform) of blood flow velocity demonstrating distinct frequency peaks at 1 cpm (Mayer, thermal oscillation, CRI slow tide, 0.01 Hz), 6 cpm (Traube-Hering, baroreflex oscillation, CRI fast tide, 0. 1 Hz), 15 cpm (respiratory oscillation, 0.25 Hz) and 66 cpm (heart rate, 1. 1 Hz)

The rate of the CRI

The CRI has a traditionally agreed upon rate of 10 to 14 cycles per minute.[2,27-30] Using various methods, many researchers have measured the CRI on human subjects[5,9,28,31-36] and animals.[37,38] In these studies, rates have been reported for the CRI of between 3 and 14 cycles/min.

Becker[27] stated that the CRI consists of two components, a "fast tide" (8-12 cpm) and a "slow tide" (0.6 cpm). Frymann,[5] using a pressure transducer applied to the head to monitor the CRI and a plethysmograph applied to the finger or arm, noted that cranial motion recordings coincided with appendicular volume changes. The plethysmograph also demonstrated "long slow cycles from 50 to 60 seconds" duration which were thought not to be related to cranial changes. Upledger,[35] using plethysmography to monitor the CRI, identified "a frequency of 9-11 cpm" and an "even slower frequency of 1-2 cpm".

The fast Fourier transform spectral analysis of blood flow velocity (Figure 2) reveals three significant peaks at frequencies below the peak for heart rate. These are, from highest to lowest frequency, representative of respiration, Traube-Hering, and Mayer oscillations. The Traube-Hering component demonstrates a frequency range from 5 to 10 cycles per minute and is associated with baroreflex activity.[17-19,39,40,41] Because the response time for the parasympathetic nervous system is shorter than that of the sympathetic nervous system, only the parasympathetic system reacts rapidly enough to directly mediate Traube-Hering activity above 6 cpm (0.09-0.17 Hz).[18,19]

The Mayer component of the THM oscillation demonstrates a frequency range from 0.5 to 2.5 cycles per minute (0.008 to 0.04 Hz),[17-19,26,39,40] and is associated with thermal regulation.[17,26,42,43] The sympathetic and parasympathetic nervous systems are both directly responsible for the modulation of cardiovascular fluctuations in the range of the Mayer low frequency oscillation. This component of the THM oscillation is further regulated by activity of the renin-angiotensin system.[18,19]

Using laser-Doppler blood velocity flowmetry, we have shown that the Traube-Hering component of the oscillation is simultaneous with the fast tide of the CRI.[9] We measured the ratio at 2:1 between Traube-Hering and CRI, which indicates a slower rate (3-7 cpm) for the CRI than has been reported in most osteopathic literature. This rate is, however, consistent with the rate for the palpated CRI measured by Norton.[36]

Lockwood and Degenhardt[44] further analyzed Frymann's data and demonstrated cycle to cycle variability that bears striking resemblance to frequency modulation demonstrated in the laser-Doppler blood velocity flowmetry measurements of the THM.[9]

Frymann,[2 (p. 322)] referring to her landmark studies measuring the CRI, is quoted as follows: "The cranium is not only an elastic rather than a rigid container, but appears to at least at times involve itself in at least three distinct oscillatory motions. First, an oscillation having the same period as the breathing of the subject. Next, an oscillation having a period of five or six seconds, independent of the breathing cycle, i.e., the former normally does not occur as a harmonic of the latter. Lastly, a very slow cycle from one to several minutes duration. There is little doubt that the second of the distinct oscillations is the Sutherland wave . . ." Thus, it is logi-

cal to argue of the THM oscillation that the Traube-Hering oscillation is the "Sutherland wave", or "fast tide", of the CRI and that the Mayer oscillation is Becker's "slow tide".

A whole-body phenomenon

The CRI and the THM oscillation share the quality of being demonstrable throughout the body. The CRI is palpable in all areas of the body.[2,5,6,29-31] The THM oscillation effects all tissues of the body through their impact upon the entire circulatory system. They have been measured simultaneously in the right index finger, right second toe, and pinna of the right ear.[41]

It is important to note that although the THM is discernable throughout the body, it does not consistently affect all areas measured simultaneously.[41] This property may explain the difficulties experienced when two examiners have attempted to concomitantly palpate the CRI.[45]

The relationship between the CRI and pulmonary respiration

Pulmonary respiration is recognized as closely associated with, yet independent of, the CRI.[1,2,5,6,29,30,46,47] Respiratory cooperation of the patient is often employed in association with cranial treatment.[1,2,27,48-51] Cranial manipulation has been said to effect respiration,[47,51] and spontaneous deep sighing respiration has been reported coincidental with the therapeutic end point.[29] Fourier analysis of the THM shows that the low frequency oscillations, Mayer, Traube-Hering and respiration, are distinctly separate components.[13,18,19,39,52] The Mayer and Traube-Hering components, however, are closely linked to, and may be modulated by, pulmonary respiration through the phenomenon of frequency entrainment.[53,54] Entrainment occurs when two systems are oscillating at close frequency, one to the other. The dominant frequency will force the second oscillation to assume, in synchrony, the same frequency as the dominant input.[17,26,55-57] MacPartland[8] has suggested further that entrainment might play a significant role in cranial treatment, for example CV-4, directed at modification of the CRI.

Fluctuation of the cerebrospinal fluid and motion of the central nervous system

The first and third features of the PRM, the fluctuation of the CSF and the inherent mobiIity of the CNS, are readily explained in the context of the THM oscillation. Sutherland stated: "According to my present hypothesis . . . the brain involuntarily and rhythmically moves within the skull. This involuntary rhythmical movement involves dilation and contraction of the ventricles, during respiratory periods. The ventricle dilation and contraction in turn effects cerebrospinal fluid circulatory activity; and the circulatory activity effects movement of the arachnoid and dural membranes; and through the special reciprocal tension membrane. . . effects mobility of the basilar articulations."[1(p.51-52)] . . . "The hypothesis does not include dilation nor contraction of the spinal canal. The spinal canal merely moves upward and downward. . . The cerebrospinal fluid throughout the vertebral column fluctuates by way of the arachnoid membrane; the membrane being hung from above, with only one attachment, and that at the sacrum."[1(p.52-53)]

Motion of the brain[58] and CSF,[58-59] in synchrony with the cardiac cycle, has been demonstrated utilizing magnetic resonance velocity imaging. The images show that, during cardiac systole, there is a net inflow of blood into the brain, causing it to expand in volume and move in a complex fashion. Because of the lesser mobility of the skull, this volume change causes the central portion of the brain and the brainstem to be displaced in a caudal direction. The CSF in the lateral ventricles of the cerebral cortex moves medially into the third ventricle. The CSF in the third ventricle moves in a caudal direction into the fourth ventricle to allow for CSF oscillation the fourth ventricle acts as a "mixing chamber". An amount of CSF equal to the volume change of the brain, displaced from the ventricles and intracranial subarachnoid space into the spinal canal, moves through the spinal subarachnoid space in a caudal direction, thereby increasing pressure in the dural sac surrounding the spinal cord. During diastole, because of the lower intracranial pressure, there is recoil of the caudal displacement of the brain, and the CSF motion reverses direction. For this to occur effectively, the system must demonstrate capacitance. The spinal dural sac acts as the required capacitor.

As blood flow velocity and pressure has been demonstrated to fluctuate at the frequency of the Traube-Hering oscillation, so too, using ultrasound, volume oscillations at the rate of Traube-Hering waves have been measured in the brains of conscious healthy humans.[60] In patients with normal pressure hydrocephalus, intracranial pressure, measured via a catheter inserted into the lumbar subarachnoid space, showed pressure fluctuations at the same frequencies as the THM oscillation.[25] The Traube-Hering component has been labeled the C waves and demonstrates an amplitude from barely discernible to 20 mm. Hg. Lower frequency waves, at the frequency of Mayer waves, with an amplitude as great as 50 mm Hg are identified as B waves. Thus, it may be presumed that the motion of the brain and the CSF, in synchrony

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with the cardiac cycle, continues in similar fashion at the rate of the Traube-Hering oscillation.

Utilizing exposure times that were too slow to assess cardiac and Traube-Hering synchronous motions, computerized tomography has been employed to observe movement of the lateral and third ventricles in the normal brain. It was shown that the brain, rostral to the foramen of Monro, demonstrates a complex rolling peristaltic motion with a rate (26 sec to several minutes in duration) in the range of the B waves or the Mayer component of the THM.[61]

The pulsating brain, can therefore, be considered to act as a pump, energized, at least in part, by the volumetric fluctuations of circulating blood and CSF. As the intracranial blood volume increases, within the skull CSF moves through the ventricular system and is displaced into the extracranial subarachnoid space, increasing the amount of CSF in the spinal dural sac capacitor. As intracranial blood volume decreases, the tension of the spinal dural sac facilitates the return of CSF into the skull, Thus, synchronous with, and, at least partially because of the THM oscillation, the CSF may well be described as "ebbing and flowing".

The primary respiratory mechanism

The PRM is described as the driving force associated with the activity of cellular metabolism.[1,2,30] Magoun[2(p.34)] specifically states: "By this means every cell in the body receives not only the inspired oxygen but also the nutrition, the enzymes, the hormones and whatever else contributes to high level wellness. Included in this internal respiration is the elimination of waste metabolites through the proper emunctories."

The THM oscillation is intimately involved in the regulation of peripheral blood flow and, consequently, tissue perfusion. Circulatory and body core temperature homeostasis is a result of the THM oscillation.[13,17,19,26] A hypothetical explanation for the PRM, therefore, can be devised by employing our understanding of the THM oscillation.

Heart rate, blood pressure and blood flow velocity fluctuates at the THM frequencies. Thus, the peripheral vascular system is entirely under the influence of the THM oscillation.[10,13,17-26,39-43] Cellular respiration is dependant upon effective tissue perfusion, a manifestation of the peripheral circulation. A model for the PRM can consequently be constructed based upon the physiology of peripheral circulation. It is appropriate, therefore, to consider how each component of the system, the arterial resistance vessels, the capillary bed interface with the interstitium, cellular respiration, the lymphatic return, and the venous capacitor and return, contributes to the function of the PRM.

The arterial resistance vessels: The arterial system is the active location of blood pressure modulation. This occurs to a great extent through baroreflex control of arterial vasomotor tone. The Traube-Hering oscillation is a direct manifestation of baroreflex activity.[13,19,62,63] Stretch receptors in the arch of the aorta, at the bifurcation of the brachiocephalic artery, in the common carotid arteries, and in the carotid sinuses continuously monitor systemic arterial pressure. Sensory neurons transmit information regarding the status of the blood pressure (increasing or decreasing) to the NTS in the floor of the fourth ventricle. Neural activity producing the THM oscillation emanates from the NTS. Within the spinal cord, myelinated vasoconstrictor fibers under the control of the NTS, descend to the thoracolumbar sympathetic ganglia. From there unmyelinated post-ganglionic fibers carry vasoconstrictor activity to the periphery. The pressor and depressor areas of the NTS exhibit inherent automaticity.[39] Even though oscillating sympathetic activity demonstrates frequency content from just above O.o cpm (0 Hz) to heart rate, 60-180 cpm (1-3 Hz) in humans, the arterial vasculature responds to modulation of sympathetic stimuli as low-pass filters with significant gain only to frequencies below 9 cpm (~0.15 Hz).[64] This response of rhythmic tonic activity, reflecting phasic input from the brainstem, gives rise to the THM oscillation of blood flow velocity and pressure.[14]

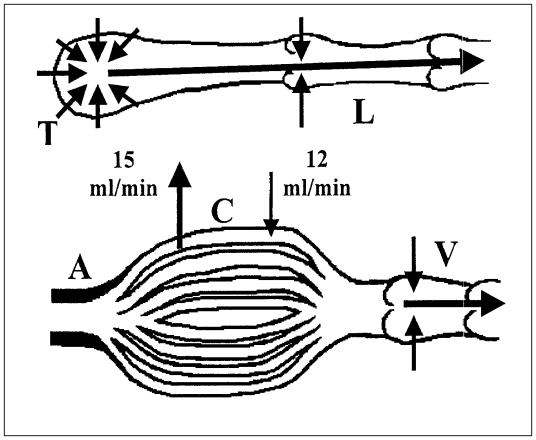
The capillary bed interface with the interstitium: Capillary, and consequently cellular, perfusion is determined by interplay between central regulation and local requirements. Blood flow, through the peripheral tissues demonstrates periods of underperfusion alternating with increased perfusion, such that there is flow through individual capillaries that satisfies local metabolic tissue demands. The variation in tissue perfusion has been demonstrated to occur in discrete locations, in groups from 10 to 15 capillaries. The control of this local fluctuation in blood flow velocity is, therefore, presumed to be at the level of the supply arterioles.[65]

Local blood flow oscillations occur independently, at the 7-10 cpm frequency; however, these oscillations are probably coordinated by the central Traube-Hering oscillation through entrainment of frequency.[17,26,55-57] Thus, although regulated by local tissue requirements, the oscillating arteriolar vasomotion is synchronized by the NTS.

Arteriolar motion drives fluid into the interstitium by physical activity. Periodic changes in arteriolar diameter implicit to vasomotor activity, when combined with the length of the active vessel, produces an equivalent displacement of the tissue mass and its fluid.[66,67] Additionally, in the cap-

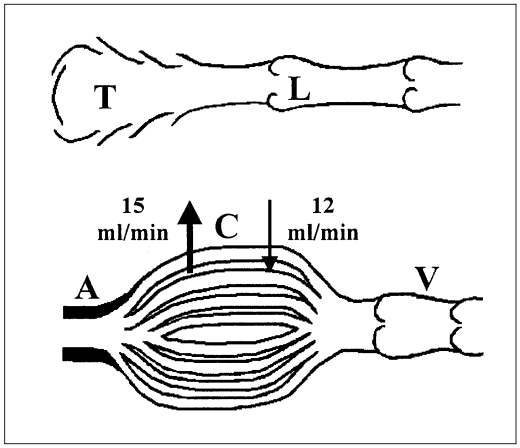
Forces moving fluid out of the vascular compartment:	
Mean capillary pressure	17.0 mm Hg
Mean negative interstitial pressure	7.0 mm Hg
Interstitial fluid colloid osmotic pressure	4.5 mm Hg
Total outward pressure	28.5 mm Hg
Forces drawing fluid into the vascular compartment:	
Total colloid osmotic pressure	28.0 mm Hg
The summation of these forces results in a net outward force of:	0.5 mm Hg

PRM Figure 3: Starling's equilibrium: The direction and rate of transfer between plasma in the capillaries and fluid in the interstitial matrix depends upon; the hydrostatic pressure on each side of the capillary wall, the osmotic pressure of protein in the plasma and in the interstitial fluid, and the properties of the capillary wall as a filtering membrane. The hydrostatic pressure varies as a manifestation of the THM oscillation.

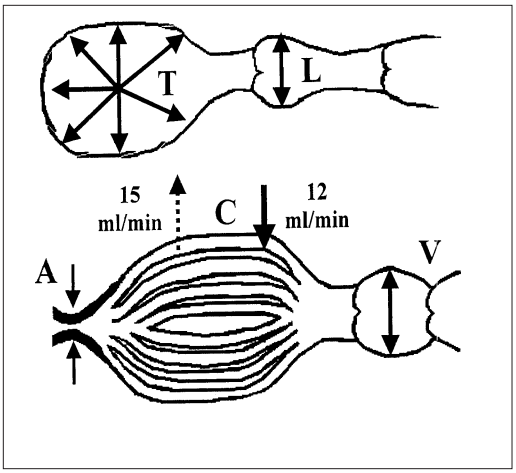


PRM Figure 6: As arterioles dilate, increased blood flow results in increased intracapillary hematocrit and pressure. Consequently interstitial pressure increases, compressing the lymphatic and venous vasculature thereby driving lymph and blood centrally.

PRM Figure 4: The vascular system and the interstitial matrix; arteriole (A), capillary bed (C), venule (V), terminal lymphatic (T), lymphangion (L). Starling's equilibrium requires that for every 15 ml of fluid that enters the interstitial matrix from 12 to 13.5 ml returns to the arteriovenous system, leaving 1.5 to 3 ml to be returned centrally via the lymphatics.



PRM Figure 5: With arteriolar constriction, intracapillary hematocrit and pressure, and consequently interstitial pressure, decreases to approximate venular pressure. This enhances fluid return into the capillaries and also results in distension of the lymphatic vasculature and venules.



illary beds, local contractile responses to distension have been demonstrated in some tissues.[14(p.127)]

This oscillation also has significant effects upon Starling's equilibrium (Figures 3 and 4). Arteriolar vasomotion causes capillary hematocrit changes in such a way that during periods of vasodilatation, with increased blood flow velocity, there is increased local hematocrit and, therefore, increased transcapillary pressure gradients (Figure 5). During the alternate vasoconstrictive phase, the hematocrit decreases, and intracapillary pressure drops to the level of adjacent venules facilitating reabsorption from the interstitium (Figure 6).[65]

Cellular respiration: Oscillating "oxygen availability waves" in the central nervous system have been recognized for years in both animals[68-71] and humans.[72-75] Following these studies, it has been shown that cortical metabolism oscillates at a mean rate of 9.58 cpm.[76] This was demonstrated by reflectance spectrophotometry of the cortical cytochrome oxidase redox state. Associated local fluctuations in blood volume were

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shown to occur. These data suggest that the cyclic increases in cortical oxidative metabolism represent the primary local oscillatory process, followed by reflex hemodynamic changes that effect local tissue perfusion, and in this specific study, intracranial blood volume. Although this process does not occur synchronously throughout the brain, it is not unreasonable to conclude that the relatively close frequencies of the cytochrome oxidase redox state and the Traube-Hering oscillation also allows the two processes to become entrained, thus linking local and central control of tissue perfusion.[17,26,55-57]

The work on cytochrome oxidase redox state and associated arterial vasomotion was published several years before the recognition of the vasomotor effect of nitric oxide (NO). Among other sites, NO is generated in arteriolar walls by endothelial nitric oxide synthase. The generation and release of NO occurs as the result of shear forces exerted by the flow of the blood against the vessel wall. As vasoconstriction increases the shear forces, NO release results in vasodilatation. NO is also released into the interstitial space where it enters the cell, binds to and reversibly inhibits mitochondrial cytochrome oxidase, with resultant reduction of cellular oxygen consumption. The NO-mediated inhibition of cellular oxygen consumption may be modulated in part by the redox state of cytochrome oxidase in the mitochondria.[77] It is also of interest to note that NO has been demonstrated to act as a mediator of the baroreflex in the NTS.[78]

The lymphatic return: Sutherland noted an asso1ciation between the PRM and lymphatic circulation. "Compression was applied around the head with the intent to limit all basilar activity. The experiment resulted in an immediate change of the movement of the diaphragmatic respiratory mechanism, as well as an indication of a change throughout the systemic lymph channels; the indication in the lymph activity being greater in its manifestation than the author has thus been able to secure through the application of the lymphatic pump method."[1(P.55)]

As blood flows through the capillaries, fluid filters out into the interstitial space. In a resting adult, approximately 15 ml/min (Figure 4) leaves the vascular space and 12 to 13.5 ml/min (or 80-90%) returns. This results in 1.5 to 3 ml/min, or 2 to 4 L/24 hr, carrying 80-200 gm of protein that remains in the interstitium and, therefore, must be removed by the lymphatic system each day.[79(p.5)]

Effective lymphatic drainage necessitates the efficient movement of fluid through the interstitial space. As much as 99.9% of interstitial fluid exists in a gel-like state. Proteoglycan filaments form weak cross links with each other, with collagen fibers, and with protein molecules to give the interstitium its gel-like consistency. Consequently, fluid does not flow freely through the interstitial space.[79(p.6)] The interstitial gel, however, demonstrates elasticity.[79(p.15)] An oscillation of this gel matrix with a more fluid sol state in synchrony with the PRM has been proposed.[80] Tissue fluid pressure is a determinant of fluid transfer between the blood and tissue spaces and between tissue spaces and terminal lymph vessels.[79(p.16)] It is probable that Traube-Hering mediated pressure changes induce fluid movement through the interstitial matrix.

The key requirement for lymphatic filling is a volume change of the terminal lymphatic. (Figure 4) The cells of the terminal lymph vessels are arranged in an overlapping-shingle fashion that allows interstitial fluid to enter the vessel. Due to the presence of one-way valves within the proximal lymphatic vessels, volume increases in the end lymphatics can occur only when fluid traverses the interstitium and crosses the lymphatic endothelium. The hydrostatic pressure in the end lymphatic vessels is presumed to be similar to that in the interstitial fluid, with transient differences between the two compartments being quickly equilibrated.[79(p.62)] Negative interstitial pressure (-7 mm Hg) of Starling's equilibrium (Figure 3) causes the interstitial fluid to be pulled into the terminal lymphatic vessels. The negative interstitial pressure is maintained by removal of protein from the interstitium by the lymphatics.[79(p.19)] Additionally, intermittent motion in the tissues associated with the Traube-Hering-mediated arteriolar vasomotion causes pulses of fluid to move into the terminal lymphatics.[79(p.7)] The Traube-Hering-driven fluctuating intracapillary pressure and hematocrit further adds to this mechanism.

Once the terminal lymphatic becomes filled to capacity, the overlapping cells approximate one another, augmented by the drop in interstitial pressure from arteriolar vasomotion and fluctuating intracapillary pressure and hematocrit (Figure 5). This prevents fluid return to the interstitial space.

Lymph is propelled centrally by Traube-Hering-induced movement of surrounding tissues and by contraction of the lymphatic endothelial cells (Figure 6). Vascular distension may be the stimulus that releases prostaglandin H_2 and thromboxane that act as mediators in lymphatic vasomotion.[81,82] Lymph endothelial cells contain actin or actomyosin filaments that are capable of causing the cell to contract.[79(p.25)] Lymph vessels have been shown to demonstrate spontaneous contractions varying from 1 to 30 cycles per minute.[79,83-91] Olszewski[84] reported spontaneous lymphatic vascular contractility at a rate of 1 to 9 (ave. 4) cycles per minute that was independent of arterial pulse rate, respiration, and body movements.

Lymphatic vessels proximal to the terminal lymphatic consist of a series of individual units, lymphangions (Figure 4). A lymphangion is that portion of a lymphatic vessel between two adjacent one-way valves. The presence of valves in the lymphatic vessels and the low resistance along this pathway, insures that any volume decrease of the end lymphatics must occur because of the displacement of fluid centrally.[79(p.58)] Each lymphangion is also capable of spontaneous independent contractility. The pacemaker for contraction appears to be located in the lymphangion wall just proximal to the valve.[85] Although lymphangions may contract randomly, they function more efficiently when contracting synchronously. Lymphatic vessels tend to develop synchronous activity easily.[71] Again, Traube-Hering-driven entrainment probably insures optimal efficiency of this aspect of the mechanism.

The venous capacitor and return: Of the fluid entering the interstitial space from the capillary bed, 10 to 20% returns to the general circulation via the lymphatic system, but the majority, 80 to 90%, re-enters the capillary bed and exits the region via the venous system.

The venules (Figure 4) are of relatively greater diameter, with thinner muscular walIs, than arterioles. They are innervated by the sympathetic nervous system. Their walls can contract and relax, thereby contributing greatly to capacitance of the vascular system and the regulation of tissue perfusion, [14(p.111),72] and providing a physical mechanism for the observed frequency modulation of the THM waveforms.[9,52] The venules (post-capillary resistance vessels) help to regulate capillary hydrostatic pressure and thereby effect fluid exchange in the capillaries.[14(p.118)] As precapillary arterioles constrict, there is a resultant intracapillary hematocrit decrease and a drop in intracapillary pressure to the level of adjacent venules facilitating reabsorption from the interstitium.[65] It is probable that post-capillary resistance control lies in the larger venules up to 300 micrometers in diameter.[14(p.127)]

The thin walled veins act as a capacitance system, holding up to 80% of systemic blood.[14(p.150)] Reflex changes in sympathetic tone affect the caliber of the veins and, thereby, the size of the venous capacitor as well as, to some degree, the compliance of their walls.14(p.124) Resultant changes in the venous capacitance will impact both the nature (selection of coupled frequencies) and the degree (magnitude of the coupling) to which frequency modulation contributes to changing the THM waveform and any associated systems.

As the vascular system fluctuates with the Traube-Hering oscillation and, in concert with arterial resistance, the venous capacitor is contracting slowly and regularly.[13,19,92] This fluctuation facilitates fluid movement through the interstitium. It facilitates lymphatic circulation, and it facilitates the return of venous blood to the heart. Vasomotion resulting from the Traube-Hering oscillation accounts for the negative interstitial pressure of Starling's equilibrium. (Figure 3) General anesthesia and certain drugs (calcium channel blockers) disrupt the Traube-Hering oscillation. This results in the development of peripheral edema.[65]

Up to this point we have considered most everything in the context of the Traube-Hering oscillation. The venous system is, however, intimately involved in thermal regulation. Thermal regulation is under control of the sympathetic and parasympathetic components of the autonomic nervous system in concert with renin-angiotensin.[17,26,42,43] It is a manifestation of the Mayer oscillation, the frequency 0.5 to 2.4 cpm (0.008 to 0.04 Hz,[17-19,26,39,40]), and irregularity of which bears a striking similarity to Becker's "slow tide."[27] It consists of a controlled shifting of blood between the compliant splanchnic veins, that typically contain up to 30% of blood volume, and the cutaneous veins.[93]

Conclusion

Comparison of CRI measurements and descriptions of the PRM from the osteopathic literature with along current information about the THM oscillation demonstrates much more than coincidental similarity. It is proposed that there is sufficient evidence to conclude that the Traube-Hering, baroreflex, oscillation is the Sutherland wave, or "fast tide" of the CRI, and that the Mayer, thermal reflex, oscillation is the "slow tide" of the CRI described by Becker. It follows therefore that the PRM can be logically explained in the context of the THM oscillation and associated physiology and biochemistry. Utilizing the THM to understand the PRM offers a holistic model. It unites the CNS with every cell in the body through the sympathetic and parasympathetic branches of the autonomic nervous system and the cardiovascular system.

The floor of the fourth ventricle provides the frequencies, 5.4-10.2 cpm (0.09-0.17 Hz. fast tide) and 0.5-2.4 cpm (0.008-0.04 Hz, slow tide). The THM oscillation synchronized with the metabolic requirements of individual brain cells provides, at least in part, for motion of the CNS that, in turn, drives the circulation of the CSF.

The PRM, however, must include more than just an oscillation of the CNS. It is a total body phenomenon, and is proposed to occur as follows. The heart, under the central influence of the brainstem, beats with a rhythm, the frequency of which fluctuates at the component frequencies of the THM. It pumps blood that arrives in ***all*** of the capillary beds in the body via arteries and arterioles whose walls are contracting at those same frequen- ➔

cies. Blood pressure, capillary blood flow rate, capillary hematocrit, and venous capacitance are all oscillating at these frequencies.

The THM oscillation is less constrained as the blood passes through the capillaries and enters the venous system than in the thicker walled arterial system. The capacitance of these thin walled vessels allows for significantly greater volume fluctuations with proportionate displacement of adjacent structures. The arteriolar and venular vasomotion and blood pressure and hematocrit fluctuation that results from the THM oscillation aids in the distribution, and mixing of extravascular fluids and facilitates, mechanically, the passage of fluid through capillary and lymphatic walls.

Locally, the metabolism of the individual cell, regulated by the respiratory activity of its mitochondria, is oscillating independently, with essentially the same frequency as the Traube-Hering component of the THM. Cellular respiration regulates local arteriolar tone. Oscillating hematocrit and blood flow velocity, in turn results in oscillating shear forces effecting the vascular epithelium with resultant modulation of NO synthesis. Increasing NO liberation results in local vasodilatation and inhibition of mitochondrial activity.

Capillary hematocrit, and consequently Starling's equilibrium, fluctuates under this influence. Cellular metabolic exchange occurs within the interstitial gel medium. Fluid, that will not move as freely through this gel as it can in a purely liquid medium, is pumped in and out of the intravascular compartment and through the interstitium by the oscillating pressures. The central THM blood flow and pressure oscillations act to entrain the local metabolically-induced oscillations.

Fluid, proteins and particulate matter, not returned to the arteriovenous system are removed from the interstitium via the lymphatics. End lymphatic filling and fluid transport through subsequent lymphangions is subject to spontaneous vascular contractility. Again, efficiency of the system is enhanced through entrainment by the central THM oscillation.

Fluid returned to the capillaries is transported back to the heart through the thin walled veins. The capacitance of the veins permits variable sequestration of blood in the periphery. Oscillation of the venous system at the rate of the Traube-Hering oscillation facilitates efficiency of blood return to the heart. Oscillation at the Mayer frequency, specifically between the splanchnic and cutaneous veins, maintains body core temperature.

The coordinating effect upon the lymphatic and venous systems by the Traube-Hering mediated oscillation might be looked upon as a "peripheral heart" functioning to efficiently return lymph and blood to the heart. The beating of the heart (70 beats per min) and that of the Traube-Hering "peripheral heart" (8 cycles per min) can be seen in Figure 1.

Thus, local and central control mechanisms act synergistically to satisfy the metabolic demands of the peripheral tissues. Locally, the activity of the musculature of the vascular bed is modified and integrated by changes in the composition of the extracellular fluid. Neural control is exercised via specialized sensory endings of peripheral afferent cells within the integrative centers of the central nervous system. Response occurs to varying levels of oxygen, carbon dioxide and hydrogen ion concentration and temperature of the blood and extracellular fluid. Or as Magoun proposed of the PRM, the THM oscillation facilitates "dynamic metabolic interchange in every cell, with each phase of action."

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