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What is Myalgic Encephalomyelitis? ***

Unfortunately, the majority of physicians in the UK, Europe and North America, not to mention the rest of the world, have a poor and sometimes distorted idea of what Myalgic Encephalomyelitis represents. One of the several fallacies is that M.E. is just another name for Chronic Fatigue Syndrome (CFS). It is not and never has been. M.E. is a biphasic epidemic and sporadic enteroviral infectious disease. Up to 1955 and the introduction of Jonas Salk's polio immunization M.E. tended to occur in the same location and at the same time as polio epidemics. In epidemic form, both Polio and M.E. tend to peak in the north temperate hemisphere during the period of July to November, with a last small blip around Christmas when families tend to get together.

CFS is a syndrome based upon a series of symptoms that are common to hundreds of different, often serious diseases and diagnostic of none. CFS can also represent multiple different pathologies or diseases in the same person. At times, CFS may be related to undiagnosed genetic illnesses. Many physicians assume patients with multiple symptoms and no easily observable pathologies are actually hysterical, anxiety neurosis or depressive patients. They employ the term CFS in place of making the unwelcome diagnosis of hysteria or psychiatric disease. The term CFS should not be utilized, as in the minds of most physicians it is a disparaging term, and in the minds of many physicians, a term belittling to the patient.

Understanding M.E. is relatively simple. However, understanding M.E. was much simpler sixty years ago. Prior to 1954, if the patient fell ill with M.E. their illness would have been called: **Missed Polio.**

Missed polio was a diagnosis given prior to 1955, when the patients fell ill during a Poliomyelitis epidemic and were left disabled, weak, often in pain and with cognitive difficulties, but were not paralyzed.

The term Myalgic Encephalomyelitis was a name developed to describe the disabling chronic injury sustained by the nurses and physicians of the Royal Free Hospital in London England in 1955. This epidemic was part of the combined epidemic of paralytic and missed poliomyelitis which struck across England and London that year. This was also the same year that the first major successful paralytic polio immunization, the incredibly effective Jonah Salk immunization, began to be distributed in the United States of America.

The Salk immunization solved the problem of flaccid paralysis and death caused by the three known polioviruses but in 1955 Salk and colleagues didn't realize there were some hundred other dangerous enteroviruses which existed but had not yet been discovered. These missing links to the puzzle of acute and chronic enterovirus illness were not included in these Salk and later Sabin polio immunizations. Unknown to them, some of these other dangerous enteroviruses also caused

flaccid paralysis and several caused what they referred to as missed polio, what we know since the 1950s as myalgic encephalomyelitis. Many of these other disease causing enteroviruses are very similar in genetic structure to the then known polio-enteroviruses. Many differ, one from the other, by less than 5% of their genomic (genetic blueprint) structure. There are at least six or more enteroviruses causing paralytic or flaccid paralysis and I assume that one day they will all be included in the polio immunization. These relatively new enteroviruses appear to be on the ascendant.

In addition to **Myalgic Encephalomyelitis**, a partial list of **enteroviral provoked diseases** includes:

1. Poliomyelitis
2. Non polio-virus flaccid paralysis *
3. Meningitis*
4. Aseptic meningitis*
5. Epidemic pleurodynia, (also known as Bornholm disease, Devil's Grip) *
6. Hand, foot and mouth disease*
7. Type one diabetes, pancreatitis*
8. Peri-carditis and congestive heart failure*
9. Pneumonia and gastroenteritis viral deaths in the new-born
10. Haemorrhagic conjunctivitis (Apollo disease)
11. Bornholm disease, (a.k.a. epidemic pleurodynia, epidemic myalgia, devil's grip)
12. Type 1 diabetes mellitus *

**In my experience those marked with an Asterisk have at times been associated with M.E.*

Certain of the above disease spectrums have several things in common:

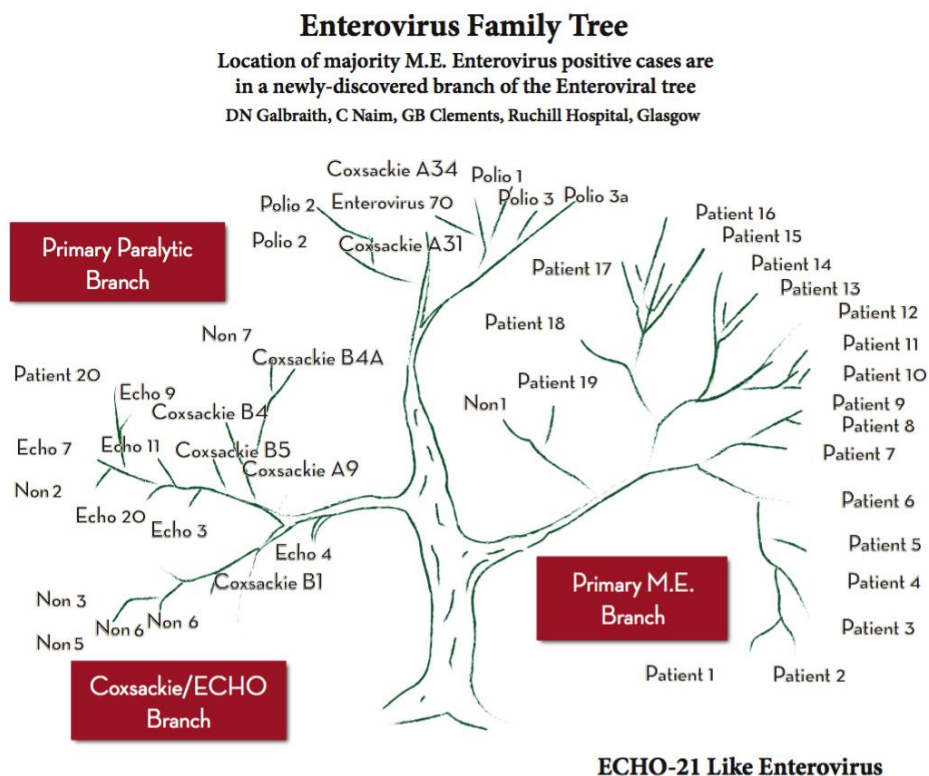
1. Where known, the shortest incubation period is 3-5 days, (short incubation allows epidemic spread)
2. A few: e.g. paralytic polio and M.E. are biphasic with early minor symptoms followed by severe chronic illness,
3. As in polio, the majority of those infected don't fall ill but tend to become immune for life,
4. Some are infected, show no signs of illness but become carriers, infecting other people,
5. Some fall ill for a few days or weeks and then recover,
6. Some fall ill, improve and get better only to have recurrent chronic illness, sometimes years later,
7. Some fall ill and remain chronically ill and disabled, and among adults, often for life,
8. Some die and, according to Dr. Ivar Wickman, some patients are identified as other illnesses including:
 - a. Landry's paralysis (both ascending and descending Guillain-Barré syndrome)
 - b. Chronic pain syndromes and
 - c. Patients with cognitive difficulties.

The enteroviruses causing paralytic polio or flaccid paralysis are typical of this class of viruses. Less than 5% of patients who fell ill with poliomyelitis were paralyzed or died. When M.E. patients die, they tend to be diagnosed as having had other cause such as encephalitis or an abrupt cardiac death. One of the pathologic vascular injuries given in this description of M.E. patients was found in M.E. patients who died during the 1934 Los Angeles epidemic.

There is also a major forgotten tragedy associated with the Salk and Sabin polio immunizations. These immunizations were so rapidly successful in preventing paralytic poliomyelitis that immediately after its release the number of cases of deaths and paralysis caused by the three known polioviruses ceased almost overnight in much of the western world. Nobody realized the number and extent of these some 100 different but similar enteroviruses in 1955 or the pathologies they continue to cause. Within ten years of the release of these immunizations, probably as many as 50,000 enteroviral researchers around the world were dismissed or their funding removed. Almost none of these enteroviral experts were left to work on the largely unknown enteroviruses causing M.E. and the other severe enteroviral diseases. I have no doubt 100,000 deaths or more occur every year around the world due to these enteroviruses. I have no doubt 100,000 cases of chronically disabling Myalgic Encephalomyelitis occur around the world every year.

The Invisible Disease: The tragedy persists today. There is yet no curative treatment or immunization for M.E. or any of these enteroviral illnesses. Other than for the three polioviruses, there are no preventive immunizations. Because M.E. so rarely kills, it has become an almost invisible disease. Yet several enteroviral infections in their most severe form result in various chronic disabilities and some in paralysis and death, in addition to causing a tremendous economic burden to the state. There is no doubt that enteroviruses cause M.E. To date, the only viruses recovered consistently in any epidemic of myalgic encephalomyelitis disease have been enteroviruses. This is the virus family we recovered in Canada during the 1984 North American pan-epidemic that struck Lake Tahoe, North Carolina, Montreal, and across Ontario and in all subsequent M.E. patients where a viral cause was found.

The following table represents some of the significant number of enteroviruses from this group of M.E. patients. There is no reason to believe that these 20 cases from my patients represent a complete list. These were all recovered from my Canadian and USA patients. It is obvious, as in Poliomyelitis where more than 6 different enteroviruses (not just the accepted three included in the Salk and Sabin immunizations) cause flaccid poliomyelitis, there are several enteroviruses which cause Myalgic Encephalomyelitis. This tree graph demonstrates as many as 20 or more enteroviruses, which can cause M.E. The following tree-map, of the numerous enteroviruses associated with M.E., was prepared from my patients by Drs. Carron Nairn, Daniel Galbraith and CG Clements, then at Ruchill Hospital, Glasgow during the period 1984-1992.



To understand Myalgic Encephalomyelitis it is easier to describe the pathology of both polio and M.E. diseases together since they are so similar in terms of their pathophysiology.

If you think physicians know so little about Myalgic Encephalomyelitis, it is also amazing how little physicians today know about paralytic poliomyelitis. So consider the following a brief refresher course on both illnesses, and as mentioned previously, both caused by several very similar enteroviruses. The enteroviruses that cause all of these illnesses, including poliomyelitis and Myalgic Encephalomyelitis, are 95% identical in terms of the genomic (genetic) structure. Let us start with **Paralytic Poliomyelitis**.

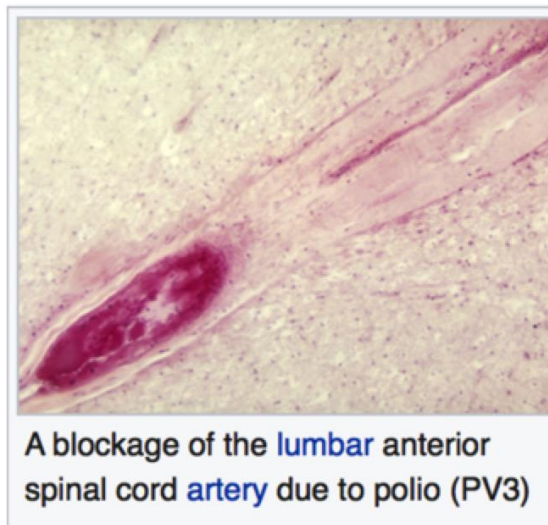
Poliomyelitis: is a fulminant enteroviral vasculitis, which injures the anterior horn cells and the small arteries nourishing the anterior horn cells. This vasculitis can attack the entire body but particularly the central nervous system, (brain, brain stem and spinal cord) but primarily the three polioviruses attack **(a)** the brain stem and **(b)** the anterior spinal cord that provides essential nerve conduction to the muscles. The anterior horn cells are the motor neuron nuclei that supply the muscles with their electrical ability to contract and relax and to allow all normal movement, including breathing. The **anterior horn cells** act very much like an electrical terminal in a house electric circuit.

The Accepted Theory: It is generally accepted that paralytic poliomyelitis is caused by at least three different enteroviruses attaching to polio-enteroviral receptors in the neurons of the anterior horn cell nuclei and destroying that neuron, causing neuronophagia and paralysis. Most of these findings were from animal studies and the question may well be asked, were they primarily looking at the anterior horn cells in a follow-the-leader fashion of many researchers. This of course is a very presumptuous statement. Dr. Van Wart and Dr. Marinacci stated that a few researchers, including themselves, also noted cuffing around the arterioles leading to the anterior horn cells in both paralytic polio and in M.E. patients. According to them, end-arteriole clotting leading to the anterior and posterior horn cells also existed in both M.E. and paralytic polio. The difference was the degree and severity of vascular and anterior horn cell injury. Individuals are still being paralyzed and still dying from both polio and non-polio enteroviruses. Autopsy material should be re-examined while we still have time to be verify whether these accepted truths are the only truths in the cellular causes of pathology.

The following is an alternative theory that might be considered.

The Site of Injury: The following Wikipedia photomicrograph is one of the two vascular injuries seen routinely in both paralytic poliomyelitis and myalgic encephalomyelitis. Polioviruses and other enteroviruses cause (a) an obstruction and (b) cuffing of blood vessels and (c) neuronophagia of the anterior horn cell nerve nuclei in the spinal cord as you see in the following micrograph. Obviously the entire area will be bathed in enteroviruses.

If the blood arterioles going to the anterior horn cell are blocked by inflammatory lymphocytes, no blood, no nutrients, and no oxygen arrive to the anterior horn cell. The anterior horn cell then shrivels and dies. If sufficient anterior horn cells are killed, the patient will be paralyzed. Depending upon the severity and locations of the obstruction, the individual can **(a)** escape visible injury and symptoms, **(b)** be weakened, **(c)** be temporally paralyzed, **(d)** be permanently paralyzed, **(e)** die or escape illness entirely and possibly become immune for life. The following micrograph is a photograph of the arteriole blocked due to the polio-virus type 3, (also referred to as Leon polio strain). In paralytic polio there are considerable numbers of such injuries. This lesion also occurs in M.E. but in most, but not all cases there are probably too few injuries to cause death and paralysis. You can easily see the red inflammatory blood clot within the arteriole to the lower left.



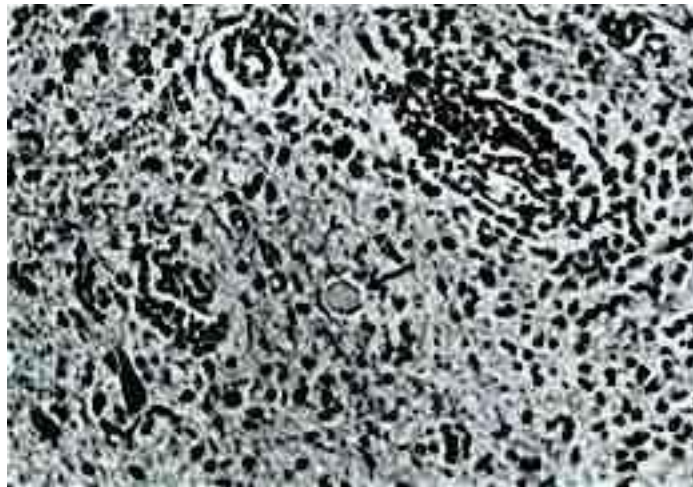
Circa 1940, Sabin autopsied monkeys to determine the cause of "non-paralytic" polio. First, there was no question that perivascular cuffing was evidence of an acute inflammatory response and thereby caused marked internal damage to the spinal cord as well as to brainstem neurons. Personal communication to B Byron Hyde from Dr. Richard Bruno

There is no doubt that both cuffing and arteriole obstruction occurs in both M.E. and CFS. The following are two microscopic slides illustrating both cuffing and arteriole inflammation in the presence of dead Anterior Horn Cells in paralytic polio. From these slides alone it is irrational to consider that paralytic polio was only an injury of the anterior horn cells. Both polio and Myalgic Encephalomyelitis are vasculitic conditions. The only significant difference between the two anatomically is the proclivity of where each of the two groups of enteroviruses causes most damage. The several (4+) enterovirus groups causing flaccid paralysis attack primarily from the brain stem down through the spinal cord. The 20-plus enteroviral groups observed by Galbraith and Nain in our M.E. patients, attack primarily above the brain stem. Ivar Wickman's work, following the 1905 paralytic polio epidemic in the Stockholm area, prompts the reasonable belief that polio epidemics were not simply epidemics of one enterovirus but a mixed bag of enteroviruses, a shot-gun blast of enteroviruses causing multiple types of injuries. This is more convincing when one observes that both polio and Myalgic Encephalomyelitis occurred in the same epidemics at the same time and the same place up to 1955, specifically in Los Angeles County Hospital, Akureyri Iceland and Royal Free Hospital.

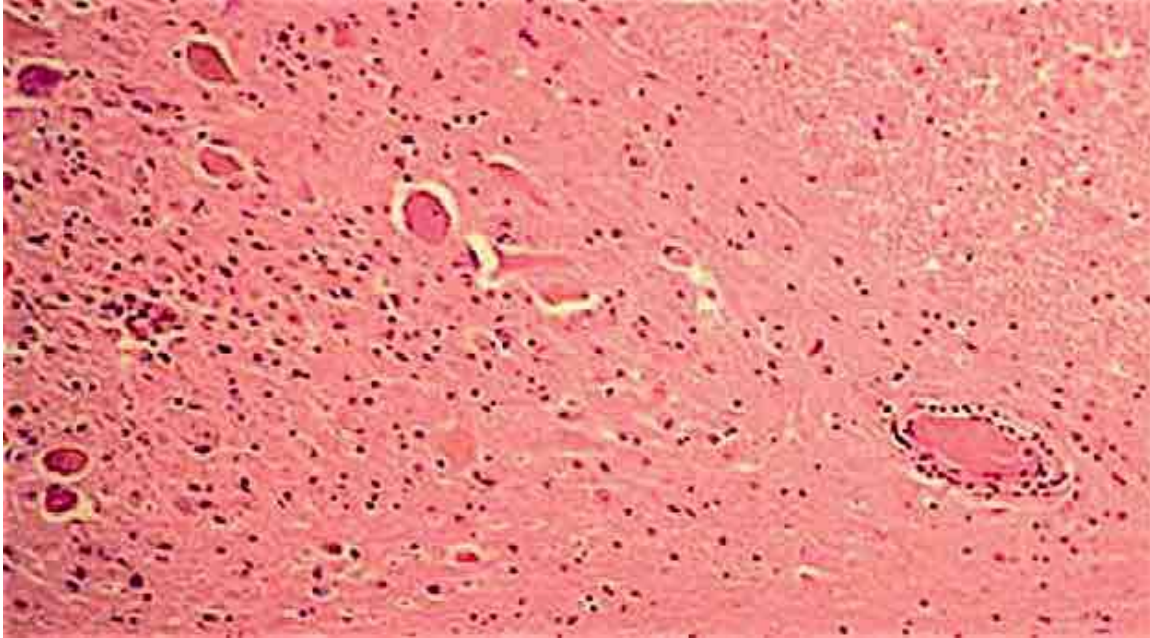
The following two microscopic views of paralytic polio spinal cord tissue demonstrate both vasculitis of arterioles with (a) inflammation and (b) cuffing of arterioles occurred in the same patients who died of paralytic poliomyelitis. I have placed the first historic black and white slide below:



The anterior horn cell is in the centre of the slide with a black arrow and the pathological arterioles are at 9, 11 & 1 O'clock of the anterior horn cell.



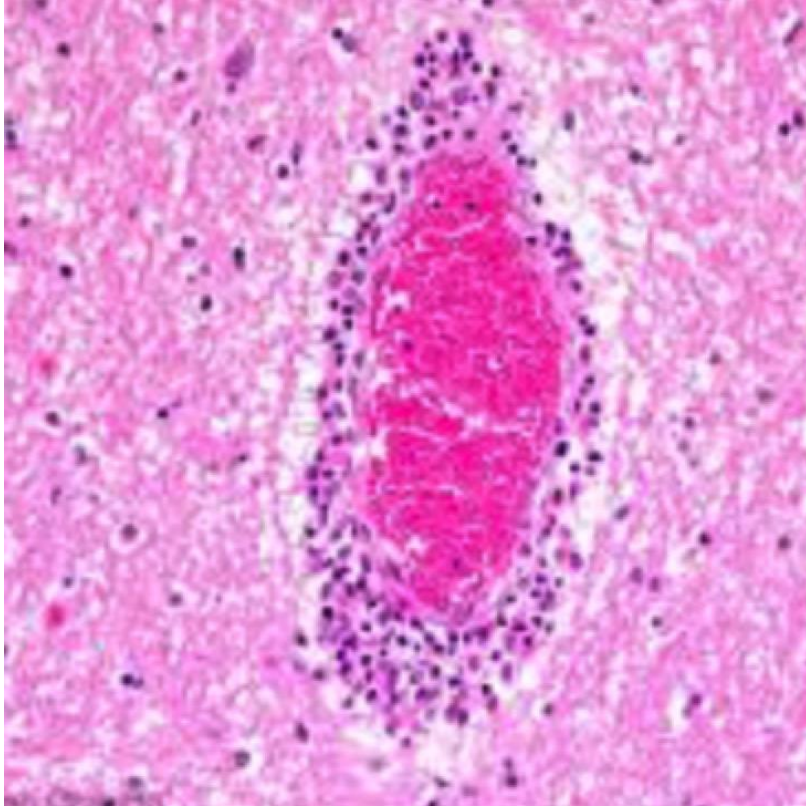
Sir W. Russell Brain in his 1940 textbook, Diseases of the Nervous System, page 445, gave the above microscopic view of both neuronophagia (death) of the anterior horn cell associated with both inflammatory infiltration and cuffing of the blood arterioles supplying the anterior horn cell (indicated with an arrow) in the same microscopic field.



Microscopic views of several dead anterior horn cells in left side and cuffing of arteriole in the lower right in paralytic polio patient.

The second microscopic slide above, in colour, shows multiple anterior horn cell deaths (approximately 6 solid red neurons with a white halo to the left) and one larger arteriole on the right with a ring of round cells cuffing the artery.

Myalgic Encephalomyelitis: Vascular Cuffing is one of the two arteriole injuries in both (a) Poliomyelitis and (b) Myalgic Encephalomyelitis. “Cuffing” is the second type of vascular injury seen in the three polio viruses and I assume in the several M.E. provoking enteroviruses. Since few M.E. patients die, there has been little research on anatomical cause since the work by Dr. Van Wart. This vascular pathology is equivalent to a valve regulating blood flow to the anterior horn cells. Instead of the arteriole being blocked, it is “cuffed” with a necklace of round cells or lymphocytes around the outside of the blood vessel wall or epithelium. This is not new information. This vascular injury was first published by the neurologist Doctor Alberto Marinacci and neuro-pathologist Dr. Van Wart, following the combined Poliomyelitis and Myalgic Encephalomyelitis epidemic at the Los Angeles County Hospital in 1934, where a few M.E. patients died. There is good reason to believe that cuffing is one of the principal pathologies seen in M.E. brain vasculitis injuries.



The above microscopic photograph illustrates *cuffing*, the second basic vascular pathology occurring in both polio and M.E. The round cell cuffing necklace are the small dark reddish black speckles ringing the blood vessel. This cuffing may also be the pointer for affective treatment. If the spasm caused by cuffing can be alleviated, one may be able to treat M.E. effectively.

If the individual suffers arteriole cuffing two things can happen. But first I have to explain a bit of normal vascular physiology. If you go to a medical lab to have blood taken, a small needle is inserted into a vein in the patient's arm to draw off blood. It may not be pleasant but done properly it doesn't hurt. It doesn't generally hurt since veins have a relative absence of nerve cells and accordingly very little associated pain. Sometime a doctor has to take arterial blood. This is infrequent but it is necessary at times and it can hurt a great deal if the area is not anaesthetized or "frozen". The reason is that arteries and arterioles have a significant complement of sensory nerves. Nerve pain is a survival mechanism genetically built into mammals to prevent them endangering themselves and injuring the life sustaining arteries.

- (a) Accordingly, arteriole cuffing is associated with pain. The round cells place a stranglehold on the pain sensitive arteriole, preventing the relaxation and expansion of the artery. This in theory can cause muscle pain and muscle fatigue since inadequate perfusion exists. This is just one of the reasons some M.E. patients can have significant pain on activity. However, in the brain such cuffing would limit circulation to the memory and administrative CNS nuclei. Over time this muscle and head pain usually decreases substantially. In adults, the cognitive abilities also tend to improve in some people over the first two years and return to near normal, but those who have not improved cognitively within two years, tend to remain permanently CNS disabled.
- (b) The analogy with paralytic polio is obvious. In polio, if the patient has not recovered significantly in two or three weeks, they remain paralyzed for life in the same way that most M.E. patients remained disabled.
- (c) Vascular cuffing acts as a stopcock valve regulating blood flow to the muscles, the brain's operating functions and possibly to organs and glands. In engineering terms, cuffing operates like a valve or carburetor regulating the flow of liquid or gas to an engine.

- (d) I have mentioned one of the causes of M.E. pain. Perhaps it is more readily understood when you consider the body's most important muscle: the heart. The body has several built-in protective mechanisms, one of which is pain. If the coronary arteries supplying blood to the heart muscle are damaged and further activity does more than the heart can tolerate, severe chest pain can result due to the nerves pain in the coronary arteries (*i.e. angina*). This pain can stop the individual in their tracks and hopefully prevent sudden death due to cardiac muscle injury. Muscle pain in the (i) legs (ii) arm and (iii) intercostal muscles, necessary for breathing, cause the individual to slow down or stop, preventing permanent injury to these muscles.

Cuffing is probably only one of the several pain-generating actions that occur in some Myalgic Encephalomyelitis patients. When physicians studying M.E. talk about autoimmune injury in these patients, it is probably mediated through the cuffing around the arterioles. Cuffing in the brain arterioles may be one of the causes of severe pain early in the disease in some people, which tends to prevent any significant activity and thus prevents permanent brain injury. Certainly, cuffing in the brain arterioles is one of the causes of subsequent memory and cognitive disability in the chronic illness. Van Wart, who I mentioned earlier, also found injuries in the posterior horn cells of the spine in M.E. patients. If they exist in the lower CNS, there is no reason to believe these do not also exist in the upper CNS arterioles, in the brain.

Due to the extreme cost of testing, I have not been able to seriously investigate the role of oxygen and nutrient lack to mitochondrial ATP production and mitochondrial death. This is surely another cause of pain and exhaustion. Mitochondria, the multiple small energy factories in all cells, are the body's energy source. Many years ago, at the University of Miami, mitochondrial death was noted on electron microscope investigation of M.E. tissue.

What is the difference if both vascular obstruction and cuffing of arterioles can occur in both M.E. and Poliomyelitis?

I believe the major difference between paralytic poliomyelitis and myalgic encephalomyelitis injury is the location where the two similar enteroviral groups attack the central nervous system (CNS). I so strongly believe this, that it is a wonder someone hasn't referred to M.E. as **The Forgotten Polio**.

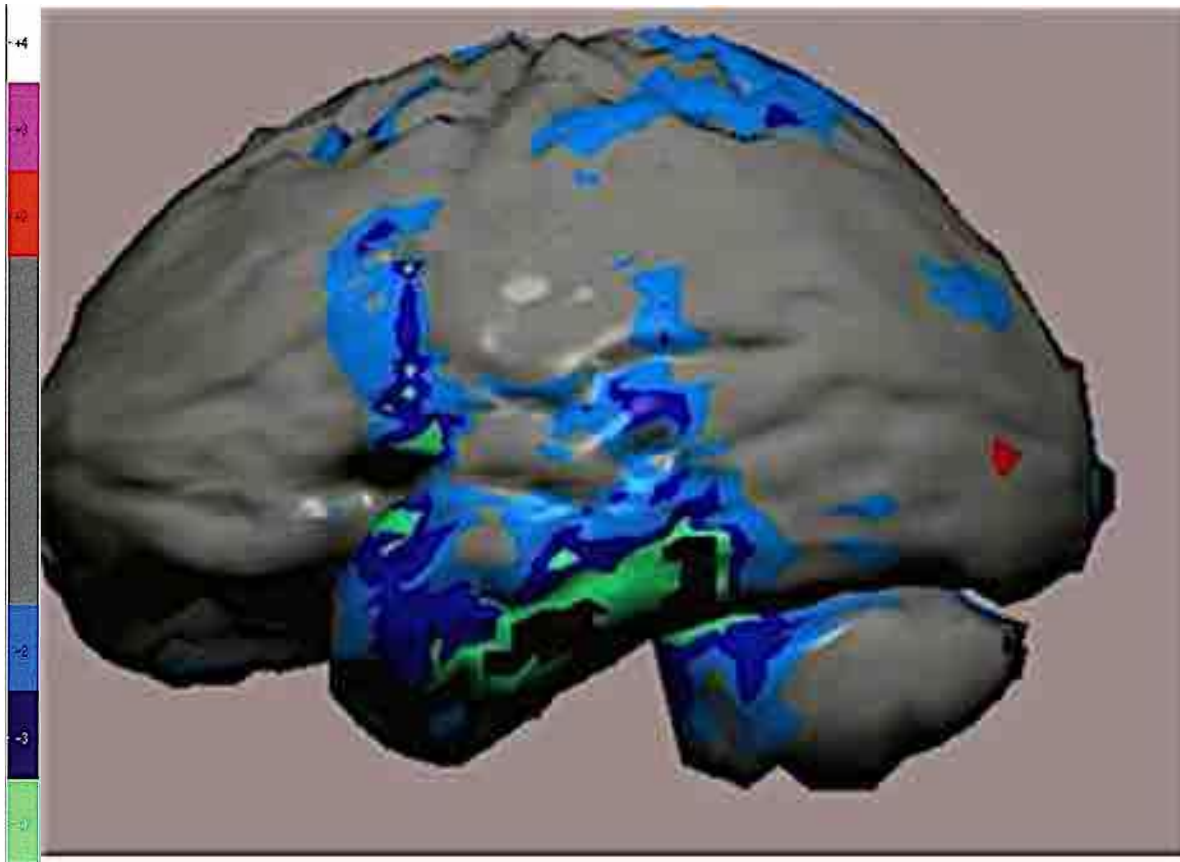
Initially, both polio and M.E. causing enteroviruses enter the body through the mouth and to a lesser extent through the respiratory system descending to the gastric system where they may cause chronic infections. From the stomach and vagus nerve different enteroviruses migrate to various target organs. The enteroviruses causing polio and M.E. injure the vascular system of the central nervous system: (*The central nervous system or CNS includes both the brain and spinal cord.*) Some enteroviruses have a predilection for the heart causing congestive heart failure and others to the pancreas causing diabetes. The more we know about enteroviruses the more we realize how dangerous there are. Depending upon the age of the infected individual, the attack site may differ. In a young child, enteroviruses may cause polio or dermatitis (hand food and mouth disease). But the same virus family can also cause M.E. or encephalitis or even pneumonia in an adult. Both age and organ sensitivity may be associated with different diseases caused by the same family of rapidly mutating enteroviruses.

The Major Difference between Polio and M.E. causing enteroviruses.

Poliomyelitis strikes the entire central nervous vascular system, but the **primary** attack site is from the brain stem down through though the spinal cord. This causes the well known associated polio related paralysis and death.

Myalgic Encephalomyelitis (M.E.) also strikes the entire central nervous system vasculature, but **primarily** above the brain stem in the upper central nervous system vasculature of the brain. This injury is what causes the well known cognitive, sensory, motor and administrative brain dysfunctions. It is assumed the injury is the cuffing injury already mentioned and this cuffing effect is illustrated in the brain map of an actual M.E. patient seen immediately below.

This vascular injury in the brain can be demonstrated in the live patient with HMPAO SPECT Segami Oasis brain scan software. The severity of M.E. can be assessed by (a) the degree of bilateralism (left and right hemisphere injury), (b) by the cortical locations of the perfusion injuries and (c) the degree of standard deviations perfusion injury below normal in any given cortical area dictate the degree and type of disability.



This brain map was developed using Segami Oasis Neurogram software.

The above brain map of my Quebec patient, SM, is just one of my typical severe M.E. injured patients.
The different colour codes represent the **standard deviations below normal**:

- a. Light blue: 2 standard deviations below normal
- b. Dark blue: 3 standard deviations
- c. Green: 3 standard deviations
- d. Black: 4 standard deviations
- e. the gray area represents normal blood perfusion areas.
- f. red and white areas represent increased blood flow.

The areas most affected in this patient are:

1. The severe, entire **anterior temporal lobe** (causing memory & administrative dysfunction),
2. The motor cortex at the posterior frontal lobe (causing injury to muscle strength and coordination),
3. The anterior superior cerebellum (balance and coordination mechanisms)
4. The insular cortex, which is a principal area regulating cardio-vascular homeostasis, function, timing and regularity.

By definition employing SEGAMI Oasis software: all M.E. patients have a perfusion damaged anterior temporal lobe and damaged cingulate gyrus.

Following enteroviral infection this 30-year-old health care worker first developed Myalgic Encephalomyelitis. This was a classical M.E. injury in which the entire anterior temporal lobe was injured along with the anterior and posterior cingulate gyrus of the limbic system. (Limbic injury in M.E. was first described by Dr. Jay Goldstein in 1989.) The SPECT perfusion injury in this patient is extensive and includes the **Insular Cortex**. She then developed both M.E. and a severe associated

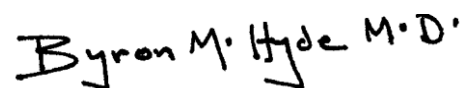
cardiac regulatory disease that required an implanted cardiac pace maker. She developed not only dysautonomia and POTS (Postural Orthostatic Tachycardia Syndrome) but a most irregular cardiac function. A pacemaker was installed to help control the irregular cardiac function. Autonomic cardiac dysfunction is so consistent with insular injury a patient with cardiovascular dysautonomia can be diagnosed by observing the decreased insular lobe perfusion.

This SPECT map of the brain seen above, particularly of the anterior temporal lobe and cingulate gyrus of the limbic system is where the negative aspect of enteroviral induced vascular cuffing plays its dramatic role. When this or any similar patient has to employ their intellectual or administrative or physical brain capacities, these vascular areas tend to go into spasm and shut down and the patient becomes rapidly cognitively and physically exhausted. Depending upon the degree of injury, it may take days or longer to return to the already injured capacities. If the injury extends to the Insular cortex, cardiovascular irregularity always occurs.

This publication was developed in association with Dr. Sonia Neubauer Grunberg, Clinica Los Condes, Santiago Chile.

The information gathered in this publication would not have been possible were it not for the Federal and Provincial health care systems in Canada which funded all of the brain SPECT examinations, and the historical, and technical examination of countless M.E. patients. I wish also to extend my sincere appreciation of the technical assistance of the brain imaging departments of (a) the University of Laval, Quebec, (b) Dr. Jean Leveillé, Sorel Hospital, Quebec, (c) Dr. Marc Freeman, Credit Valley Hospital and Mount Sinai Hospital, Toronto Ontario, (d) the Ottawa Hospital, Civic Campus, and (2) Dr. Sonia Neubauer Grunberg Clinica Las Condes, Santiago, Chile. I wish also to thank Dr. Peter Rowe, Johns Hopkins University School of Medicine for his kind and considerate advice over the many years. The brain mapping would not be so obvious were it not for the brilliant work of Philippe Briandet who along with Dr. Ismael Mena from UCLA and the University of Santiago, Chile developed the Segami Oasis Neurogram brain mapping software. The enteroviral investigations were made possible by Drs. Carron Nairn, Daniel Galbraith and CG Clements, then at Ruchill Hospital, Glasgow during the period 1984-1992. The pathological findings of cuffing and arterial obstruction of the anterior horn cells were demonstrated to me by the late Dr. Alberto Marinacci and Dr. Van Wart at the Los Angeles County Hospital. Dr. Jay Goldstein and the late Dr. Ismael Mena introduced me to the utility of SPECT brain mapping and the injuries to the temporal lobe and limbic system as a primary basis of understanding M.E. brain dysfunction. Injury to the brain's limbic system and anterior temporal lobe so clearly defined the essential CNS pathology in this chronic post-infectious enteroviral disease.

Sincerely,

A handwritten signature in black ink that reads "Byron M. Hyde M.D." The signature is written in a cursive, slightly slanted style.

Byron M. Hyde MD