I am truly honoured to be invited to speak to you today. May I begin by thanking my gracious Swedish hosts, particularly Birgitta Björlevik and her committee in Göteborg and Lisa Forstenius and her committee in Malmo. I fully realize that these meetings take an enormous amount of work and expense both in time, hard work and funds.

I would like to discuss the following topics

1. What is M.E. (Myalgic Encephalomyelitis)?

2. The Investigation Roadmap to Understanding any Disease Process, Including M.E. and Fibromyalgia.

3. The Recent Discovery of the Retrovirus Association with M.E.

4. What you might discover when you investigate M.E. patients.

5. What you might discover when you investigate the underlying pathology of Fibromyalgia Patients.
1: What is M.E. or Myalgic Encephalomyelitis

M.E. can be either epidemic or sporadic, but always is characterized by its acute onset. M.E. was first called Benign Epidemic Myalgic Encephalomyelitis, benign simply because the epidemics were only infrequently associated with patient death. However, deaths did occur. Deaths were documented in the 1934 Los Angeles, the 1947 Iceland epidemics and the 1955 Cumberland epidemics. Over 60 M.E. epidemics have been described. Benign was soon dropped due to the severe and chronic disability associated with this illness.

One important clue as to the CNS injury occurred in the Iceland epidemics circa 1947 when three children fell ill and died of Parkinson-like illness. The three children were all younger than 10 years of age, strongly suggesting that M.E. in the Iceland Akureyri epidemic was associated with an injury of the CNS in the basal ganglia area of the brain. The Basal Ganglia are located in the base of the forebrain and closely connected to the cortex. The basal ganglia are closely associated with motor, learning and executive functions. When I went to Iceland to examine these patients in 1988 the 1947 patients were still ill although some were able to work. One who I interviewed was the mayor of Reykjavik who still had difficulties with muscle strength but whose cognitive difficulties had totally recovered.

M.E. is characterized by endemic (dispersed among the public) and epidemic (large numbers of individuals falling ill either in clusters or in hundreds or thousands). As in all true illnesses there is variable degrees of disease penetration where some individuals barely fall ill, recovering rapidly and in under unusual circumstances, some die. These extremes are not recognized as M.E. and become obvious only during epidemics. It is those patients, who to various degrees fall chronically ill, who are recognized as M.E. Those least injured often return to work, those most injured can be housebound, but most simply have severe inability to do their day to day house and home duties.

The name Myalgic Encephalomyelitis can be destructured into the following segments:

- **My**: muscle
- **-algic**: pain
- **Enceph**: brain
- **mye**: spinal cord
- **itis**: inflammation

The Question Concerning Inflammation

The problem has always been with the **-itis** or inflammation part of the term. The gold standard for inflammation is the ESR, a very simply test by taking a 100 mm glass pipette full of blood and measuring how many millimeters of Red Blood Cells form after one hour. An elevation of over 20 mm in a male or 30 mm in a female in the ESR,
(Erythrocyte Sedimentation Rate or simply Sed Rate) suggests inflammation. However the red blood cells do not settle out in many conditions, including

(a) spherocytosis,
(b) sickle cell anemia,
(c) illnesses that change the shape of the red blood cells as can occur in M.E. or
(d) decreased protein manufacture interfere with sedimentation.

Most chronic M.E. patients have 0 or low Sed Rates. This has caused some physicians to state that there is no inflammation (or –itis), in M.E.

In most acute inflammatory diseases such as in many acute rheumatoid arthritis or acute infectious diseases the ESR can rise as high as 50-70 mm. Inflammation is associated with the initial immune response to infection when the Natural Killer Cells, attack the infection that results in a production of anti-viral antibodies and an inflammatory response. It has been shown that the normal accelerated antibody response to viral or immunological invasion is blocked in M.E. with the significantly decrease in number and activity of NKC (Natural Killer Cells), the primary response to infection. This failure of the NKC system allows the viral or immunological pathogen to persist for a sufficiently long time that this infectious pathogen is recognized as self, not susceptible to the normal human antibody response. This blocking of the normal immune or inflammatory response, allows the pathogen to cause long standing disease of multiple organs, particularly the CNS (Central Nervous System = brain+ spinal cord), muscle, vascular systems of the body and to a lesser extent various other organs and systems.

Not until the 1984 North American epidemics, that continued on up until 1989 in large numbers, usually peaking during the August to Christmas periods was there physiological brain imaging in place to ascertain brain injury. It was shown that a significant majority of these epidemic, cluster and sporadic patients had persistent pathophysiological hypoperfusion brain changes that could be measured by brain SPECT and brain PET. D

**The Injury to the CNS is not a theory:** In M.E. the irregular diffuse attack upon the CNS (central nervous system) can be measured by various techniques first noted by Drs. Jay Goldstein and Ismael Mena in California in 1998. They pathological findings include abnormal persisting changes in:

(a) Brain SPECT (Single Photon Emission Computed Tomography)
(b) Quantitative EEG (QEEG Scan or BEAM Scan in the USA) or
(c) Brain PET (Positron emission tomograph) and even the inexpensive
(d) Transcranial Doppler as developed at Harbor View Hospital in Seattle.
(e) Neuropsychological Testing
2: The Investigational Roadmap:
How does a physician investigate any illness including M.E. and Fibromyalgia scientifically?

All disease can be investigated in terms of the following 5 areas:

1. **Preconditions:** What are the genetic, earlier weakening injuries, physical trauma, and social conditions such as deprivation, crowding that increase the risk of falling chronically ill with any illness including M.E. illness? This phase of investigation can only be ascertained by good epidemiological studies. This requires long term will and financing to investigate and long-term follow-up of the disabled patient. **No long-term epidemiological study has ever been done for either M.E. or Fibromyalgia patients.**

2. **Triggers:** Triggers can include, infectious injury, trauma, toxic injury, radiation injury recent or remote, injury caused by immunization usually due to an immune weakened or susceptible host or at times to defects in the construction of the immunization vehicle itself. **The patient is not always a reliable or knowledgeable witness of the trigger causing their own disease. I can find no serious investigation into the triggers of M.E. and Fibromyalgia other than what Nightingale has explored.**
The Problem With Some Patient Statements as a Basis for Assessing Illness Triggers: For instance, a University professor patient who insisted he fell ill due to an immunization but upon investigation I found that his illness was due to the presence of undiagnosed, unknown chronic syphilis eating away at his brain and also untreated unknown Hepatitis B. He had been seen by some 8 physicians who had diagnosed him as CFS and missed these causal pathologies. He conformed to the 1988 & 1994 CFS definitions.

Immunizations, largely safe, can cause M.E. like illness and even deaths: Examples: (a) the first rounds of poliomyelitis immunization in 1954 caused multiple deaths in Newfoundland and the island of Grenada and was withdrawn. (b) In 2005, reputedly the entire influenza immunizations supplied by Chiron to the UK, the USA and Canada was contaminated with Serratia marcescens bacteria causing wide spread illness. The immunization was made public in October 2005 but was only discovered in January and withdrawn leaving no
immunization available for the rest of the 2005-2006 immunization year. Chiron promptly went bankrupt and its assets sold so no legal action was taken against the company. (c) Reputed problems with encephalitis immunization in Norway.

3. Primary Organ or System Injury: In M.E. the primary injury site in most epidemics appears to be the brain and possibly the spinal cord. Both the CNS vascular system and the neurons are diffusely injured. These changes are measurable. Very little has been published concerning the CNS injuries associated with M.E.

4. Secondary Organ or System Injury: The CNS (central nervous system) injury is associated with measurable immune dysfunction and probably dysfunction of the chemical and hormonal regulatory system that allows for proper functioning of the endocrine glands, the peripheral vascular system and muscle physiology. The most traumatized and injured organs in M.E. are (a) the thyroid gland that in part regulates energy and (b) the normal homeostasis of the vascular system to respond to temperature change and changes in normal physical activity. All of these pathologies are measurable. One of the most severe forms of Secondary injury in M.E. patients are the thousands of patients, easily diagnosed and who have an associated dysautonomia, vascular incompetence where the patient is unable to maintain normal stable blood pressure with any activity. Many of these patients are bed or house bound. We know the pathology but almost no new or effective treatments have been marketed to treat these people during the past 20 years.

5. The social outcome of disease and illness: (a) Loss of ability to work or ability to attend school, (b) isolation from friends, work and community, (c) unaccustomed poverty, (d) secondary economic and social injury to spouse and children for the married patient, (e) scorn, ridicule and neglect of former physicians, friends, colleagues and loved ones. (f) personality changes in the patient due to these factors and (g) the increased risk of suicide. To my knowledge, no government in the world has taken these patients seriously and come to their assistance. Insurance companies take advantage of their severe and chronic illness in most cases by refusing to pay their disability pensions thus aggravating their social illnesses. Example: October 2009: Patient with severe M.E. is refused her private disability insurance after they send her to a University of Ottawa Professor of Medicine and he does no tests on her and states she can work. The Professor is probably paid $1,000 - $2,000 for 30 minutes work to say she is able to work. The insurance company saves $40,000 dollars a year until she is 65. She is then investigated by our clinic, which does a very complete investigation, finding significant pathologies. We send her to 4 specialists who state she is permanently unable to work. We then send her for a Canadian Federal Government Insurance, which will pay her perhaps $10,000 a year. The Federal Government refuses to issue her a Federal Disability Pension although she has paid for over the year. The Government quotes the insurance
doctor who states she can work, despite the 4 specialists and myself who state she is chronically too ill.

What we have here is the result of almost 75 years of almost no serious investigation or humane treatment of the chronically ill M.E. or CFS or Fibromyalgia patient. It is a wonder that so few ever commit suicide.

3: The Whittemore Peterson Institute CFS - Retrovirus Announcement

The Cause of CFS is a Retrovirus: In 2009, Dr Peterson, is probably one of the nicest and learned colleagues in the field of CFS, recently from the brand new, just opened, multi-million dollar Whittemore Peterson Institute in Reno Nevada, announced overwhelming evidence that the cause of M.E. or CFS, is XMRV retrovirus. The XMRV mouse retrovirus occurred in 68% of the CFS patient’s blood samples and only 4% of non-CFS patients. Pretty convincing!

This retrovirus theory comes with a history: It was first raised as a possibility by the gay community at a symposium I attended in San Francisco in 1987 and again by Florida based researcher Dr DeFreitas in the early 1990s. Dr DeFreitas discussed this retrovirus theory in our textbook, The Clinical and Scientific Basis of M.E. /CFS.

At the very least, this retrovirus discovery is great free advertising for the Whittemore Peterson Institute. It will possibly bring them in many millions of dollars from, patients willing to be separated from their assets, generous charities and governments before the retrovirus theory is once again thrown into the garbage bin. I should add that incubation period of XMRV is up to 21 days which makes it impossible to cause an epidemic illness. One theory to explain this “new” finding is that XMRV is a mouse virus and since many research institutes have tens of thousands of mice, cross contamination of specimens are inevitable.

The Cause of CFS is Human Herpes Viruses 6 & 7: In June 2008 I was paid by the Swiss pharmaceutical company, ROCHE to attend a symposium on CFS in Baltimore, Maryland. There were well over 100 “eminent” speakers from around the world, all the speakers except for a salaried researcher from the Canadian Government Viral Detection Laboratory in Winnipeg stated they found Human Herpes 6 & 7 in the 70-80% of all CFS patients but not in healthy controls. Now I am under the opinion that the technology for demonstrating HHV 6 & 7 may be under copyright to a USA laboratory. It is also possible they give cash or free travel grants to University researchers who can prove the HHV-CFS association but not to those who do not find this association. It is my belief that the US laboratory which sponsored this Symposium has the copyright of this test. Whether money is changed hands or not, if I am correct, such a symposium with over 100 research papers could ultimately bring in several million dollars or more a year of royalties to this laboratory. Also, Roche Pharmaceuticals who paid my way along with 10
of the other researchers, one from the Whittemore Peterson Institute, were offering a carrot of 30 million dollars in research grants to the ten researchers and myself who would treat CFS patients with their new Herpes Virus anti-viral. Dr Peterson, the Whittemore- Peterson researcher was one of the ten at this private meeting with me. He too stated that he found conclusive evidence that the cause of CFS was HHV 6 & 7. I was the only invitee who told the Roche representatives that they were wasting their money. If ROCHE had funded the Whittemore Peterson it might have been financial suicide, to then state that the XMRV retrovirus was the cause of CFS.

**The Cause of CFS is an Enterovirus:** In 2007, the son of California Infectious Disease specialist, Dr John Chia fell ill with M.E. He also complained of stomach pain. Dr Chia examined his son’s stomach and saw an infection that when biopsied, turned out to be a Coxsackie enterovirus. This is a virus in the same family as poliovirus. This is the same virus family associated with the Akureyri Iceland epidemics in 1947. It is the same group of viruses associated with the M.E. pandemic in Canada in 1984-1986. There is no money to be made with this virus since there is no patent on it and it is difficult to recover. In four of the sixty M.E. Epidemics an enterovirus was recovered. In over 50 other epidemics, no virus was recovered but the average incubation period of the infection in these epidemics was 3-6 days, as it is in all enterovirus infections. HHV6 has an incubation period of 10-12 days. The EBV incubation period is 40 days.

So in three consecutive years, 2007, 2008 and 2009 three absolutely certain causes of CFS were announced.

**3a: What are my opinions of the cause of M.E.?**

**A: In epidemics or Clusters:** any virus that attacks the brain that has a short incubation period of 2-6 days can provoke epidemics of **acute onset disease.** This excludes HHV6 & 7, EBV, and HMRV with 10 to 40 day incubation periods. Among common viral infections, enteroviruses & influenza viruses with a 2-6 day incubation period can fit this epidemic possibility or any milder encephalitic viruses. **In both Epidemic and Sporadic Illness the overwhelming majority are patients are in the health care and teaching professions, both in daily contact with infectious disease.**

**B: Sporadic (individual) acute onset cases of M.E.:** any infectious, traumatic, or immunization agent causing diffuse low grade diffuse brain injury or encephalopathy can cause M.E. This can be due to epidemic viruses such as enteroviruses and influenza viruses or non-epidemic viruses such as Epstein Barr Virus in Adults:

1. The enteroviruses infections Coxsackie, ECHO and numbered enteroviruses but also Varicella (chicken pox) in adults and EBV in adults. I have never had a case of chronic EBV last longer than 3 years.

2. Any number of infectious agents capable of causing an encephalopathy. (Viruses infecting children and youths tend to have a less injurious action on the brain than the same viral infection affecting adults over 25.)
3. Certain immunizations given to some adults, but particularly Recombinant Hepatitis B (RHHB) and Influenza immunizations can cause M.E., even when not contaminated as in the Chiron influenza immunization. This causal link may be due to the fact they are two of the few immunizations that adults receive frequently. Chronic illness such as M.E. can occur if the patient is travelling or in contact with minor infectious agents in the 3-week period following any immunization. The trick is never to receive any immunization immediately prior to travel, particularly to a third world country.

4: The underlying pathology of patients diagnosed with M.E. and CFS.

CLINICAL, TECHNOLOGICAL & LABORATORY DIAGNOSTIC CHARACTERISTICS OF 53 CONSECUTIVE PATIENTS DIAGNOSED AS M.E./CFS & INVESTIGATED AT THE NIGHTINGALE CLINIC

Hyde, Byron; Green, T; Neron, D; Nightingale Research Foundation, Ottawa

OBJECTIVE: This is a study of 53 consecutive patients who had been referred to the Nightingale Research Foundation for clinical investigation with a diagnosis of M.E. or CFS. The first part of the study was to review the sleep pathology. This second study was to ascertain the number and frequency of any associated major pathological anomalies in the same patients that might be contributing to the severe sleep pathology in the M.E. and CFS patients. All patients conformed to what the referring physicians and institutes believed were CFS patients under the 1994 Fukuda criteria. We further sub-categorized the M.E. patients as acute onset patients and the CFS patients as gradual onset patients. Historically all M.E. epidemic and endemic patients in the literature are acute onset. The 1984 and 1992 CDC definitions make no such distinction so that many of the CFS patients are gradual onset illnesses.

METHODS: All 53 patients were examined and an extensive personal history of their health history, education and work history since birth. A detailed genetic history to include three generations was recorded except in adopted patients. The patients were all referred to Ottawa and Montreal area hospitals for a battery of clinical studies as well as to state funded private laboratories. We did not distinguish the patients by sex, profession, race, age or geographical distribution. Since the 53 patients were the last consecutive patients investigated who had complete investigational data there was no prejudice of inclusion (cherry picking) since all patients were fully investigated and all were included in this study. Tests and examination all included brain SPECT, MRI of brain and head, MRI of cervical spine, complete cardiac assessment including 24 hr
Holter monitor, treadmill and / or Persantine stress tests, echocardiograms, X-ray of spine and chest, carotid and transcranial doppler, abdominal and pelvic ultrasound, exhaustive testing of blood, serum, stool and urine tests by up to 60 different test procedures. All patients were seen by a psychiatrist and any organ or system pathology uncovered was followed up by referral to appropriate specialists in cardiology, neurology, autonomic nervous system, gastroenterology, urology, ENT, oncology and vascular specialists as required. All anomalies and pathologies were retested and more detailed investigations and referrals were ordered. For purposes of brevity we will discuss extensively only the largest subgroup, the educational institution group.

RESULTS:

1: Normal Sleep Characteristics: 52 of 53 patients had grossly abnormal sleep patterns as noted in study (1).

2: Patients by Sex: 66% were female which is lower than the usual approximate 80% in the general public and 75% in the Belgian study from Antwerp University.

3: 53 Patients Grouped by Income: 51 patients were from middle to high-income families and two were low-income patients. Students were categorized under their parent’s level of income. The two low-income patients consisted of 1 Native American and 1 Métis who worked in low paid physical labour jobs. Since all patients have equal access to free medical care and investigation the financial basis of these patients should not have been a question of access.

4: Patients by Education: 53% of patients had post secondary school education.

5: Type of onset:
   Acute Onset: 77% were acute onset patients.
   Gradual Onset: 23% were gradual onset patients.

6: Triggers: The real or perceived triggers among acute onset patients were as follows: (Note: a few had multiple apparent triggers)

   45%: Post-infectious or post-immunization trigger in the 53 patient groups
   17%: Post-traumatic: vehicle collision, sports injuries, surgery and post concussion injury many associated with infectious or allergic diseases
   06%: Toxic or Nuclear Exposure
   06%: Iatrogenic: Myocardial infarct from indwelling catheter for treatment of a non-existing Lyme disease
   04%: No perceived trigger

7: General Occupation: 41 of the 53 patients fell into the following major groups:

   19 School Associated: Teachers and pupils: 37%
   9 Federal or Provincial Civil Servants: 17%
5 Hospital or Medical workers: 9%
4 Accountants or bookkeepers: 6%
2 Engineers: 4%
2 Physical Labour workers: 4%

8: Average Present Age: 33 years

9: Occupation of School Associated Group at Illness Onset:

32% Students: Primary School Students: 1 (5%)
  Secondary School Students: 3 (16%)
  University Students: 2 (11%)

68% Teachers: Primary School Teachers: 3 (16%)
  Secondary School Teachers: 8 (42%)
  University Professors: (11%)

10: Onset: 15 (79%) were acute and 4 (21%) were gradual onset. All gradual onset patients were teachers. It is perhaps relevant to discuss these 4 gradual onset teachers who collectively had been seen by over 30 physicians prior to being investigated by our clinic. Each had been diagnosed with depression, anxiety or neurosis.

The occupations of 2000 consecutive M.E. patients were tabulated during the epidemic period of 1984-1992. These patients came from across Canada, the USA and to a lesser extent the UK. Consequently the figures are not prejudiced by local employment. By single largest percentage by population rate was among respiratory technologists, followed by health care workers, including physicians, nurses and technicians in residential institutions for the disabled that may have an increased infectious rate.
M.E. Patient Occupation at Illness Onset

- 1 Nurses & Physicians
- 2 Teachers
- 3 Health Care Workers
- 4 Secretarial workers
- 5 Bookkeeper
- 5 Teller
### B: TABLE OF GRADUAL ONSET PATIENTS IN SCHOOL GROUP:

Please see the following table for further details on these 4 patients.

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Physician</th>
<th>Pre-Investigation Diagnoses</th>
<th>Nightingale Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 University Professor</td>
<td>5 including insurance physicians</td>
<td>CFS &amp;/or Depression</td>
<td>Illness triggered by a pneumococcal immunization on a CNS already injured by pre-existing. Missed (1) Tertiary Syphilis &amp; (2) Hepatitis B.</td>
</tr>
<tr>
<td>2 High school Teacher in Aboriginal Community</td>
<td>4 including insurance physicians</td>
<td>CFS, Depression, food addiction, metabolic syndrome</td>
<td>No trigger but (a) Missed insulin dependent type II diabetes, Missed myocardial infarct &amp; left ventricle hypertrophy, Missed severe hyperlipidemia, Missed Hashimoto’s thyroiditis, Missed brain &amp; cerebral artery atrophy.</td>
</tr>
<tr>
<td>3 Primary School Teacher</td>
<td>6 including insurance physicians</td>
<td>Whiplash following Motor Vehicle Accident (MVA), CFS + Fibromyalgia a Depression</td>
<td>Illness reputedly triggered by MVA, (1) Missed severe hypoperfusion of cerebral vascular system, (2) Missed Hashimoto’s thyroiditis, (3) Missed seronegative rheumatoid disease with highly positive Citrullinated peptide,</td>
</tr>
<tr>
<td>4 High school Teacher</td>
<td>20 + physicians including insurance physicians</td>
<td>CFS, Fibromyalgia a Anxiety Neurosis, Depression. No physical diagnosis ever made despite 20 physicians seen.</td>
<td>(1) Genetic or infection triggered thyroid failure in father &amp; 3 year old daughter. (2) Sero-negative rheumatoid arthritis &amp;/or r reflex dystrophy, (3) Oxygen saturation falling to as low as 51% when sleeping, (4) Dysautonomia</td>
</tr>
</tbody>
</table>
11: **Measurable Respiratory Dysfunction:** 10 (53%) had measurable respiratory dysfunction. Not considering pre-existing asthma or chronic or recurrent bronchitic allergy or infections 10 of the 19 subjects had measurable pulmonary dysfunction with or without associated upper airway obstruction.

12: **Measurable Brain Dysfunction:** 19 (100%) had measurable brain dysfunction. In addition to significant SPECT brain anomalies and multiple cases of subnormal oxygen saturation abnormalities, the following pathologies were identified in this group at the Nightingale Clinic. All noted examples had previously been missed by all their physicians: (a) Tertiary CNS Syphilis, (b) 2 dysautonomia and / or POTS, (c) 2 abnormal EEG, (d) Chiari Syndrome with Ventricular megaly, (e) brain atrophy, (f) middle cerebral artery atrophy or stenosis, (g) large subarachnoid cysts (these are often considered developmental & of little significance). (As mentioned earlier, one student not included in this study had a cyst that took up 2/3 of the anterior left hemisphere leaving only part of the left parietal lobe and left occipital lobe without any decrease in IQ but severe associated fatigue.) (h) Large CNS venous anomaly, (i) leukoencephalopathy with ventricular hypertrophy, (j) missed multiple frontal seizure disease occurring over 14 years. Over 30 physicians and psychiatrists dismissed this as attention seeking or maternal Munchausen-by-proxy syndrome since physicians never ordered EEG during nighttime when his seizures occurred or took the mother or son seriously.

13: **Thyroid Dysfunction:** 12 (74%) of these 19 patients had measurable thyroid dysfunction. The most common were Hashimoto’s or atrophic or burned-out-Hashimoto-like disease in the presence of normal TSH, FT3 and FT4 and only in some cases elevated thyroid antibodies. Only 1 of these 19 patients had thyroid malignancy. Unfortunately most primary care physicians simply do not do thyroid ultrasounds, thyroid antibodies nor do the do reverse T3 calculations to ascertain much of the thyroid pathology associated with these patients. When they do find thyroid disease they almost never do brain SPECT where I find CNS pathology intimately connected and congruent with thyroid disease. I believe that it is partly for these reasons that simply treating the thyroid is insufficient to assist most M.E. and CFS patients.

14: **Significant Other Disease:** 9 (47%) had or were developing significant other disease including (a) Missed Infectious Hepatitis B, (b) Missed 4 cases of Cardiovascular disease including daytime tachycardia in excess of 110 bpm, pulmonary valve disease, (c) Missed case of juvenile diabetes & 1 case of Type II diabetes, (d) Missed Ehlers-Danlos Syndrome & 2 cases of hyper-reflexia syndrome and significant Raynaud’s phenomena, (e) Missed Post-polio Syndrome, (f) several cases of obstructive ENT pathology, (g) Genetic illness (including keratosis pilaris), (h) Coagulation defects.

15: **Psychiatric Disease Diagnosis:** 6 (32%) or one third of the 19 educational institution related patients were diagnosed with Major Depressive Disease (Unipolar depression) or other psychiatric disease by psychiatrists. When we examined these patients we found
only 3 (16%) of the same patients with possible psychiatric disease. These figures need to be discussed.

DISCUSSION

Discussion 1: DEFINITION: The first question that requires an answer is “Are these 53 patients actual CFS patients?” The answer is a two-fold yes! They are CFS patients in that they correspond to the faulted Fukuda, CDC 1994 definition. However that definition also stipulates that intensive investigation is not required in this group of patients. When a good understanding of this debilitation illness is still lacking, our foundation simply thinks that is silly. Both the Holmes 1988 and the Fukuda 1994 definitions have leant to acrimonious criticism by both patient and physicians ever since their first publication. This ongoing dispute had taken up much of the time of the community of interested physicians and patients who in general remain openly hostile to these definitions. However, for what they are worse, the physicians and patient groups who referred these 53 patients believe that they do conform to the Fukuda definition.

1B: PERCEPTION OF DISEASE BY DEFINITION: There is a bigger question than the problems of defining M.E. and CFS that appears to have been totally missed by the M.E. and CFS community. That question is “What is the average physician and psychiatrist’s perception of what constitutes a CFS patient?” We all know that the majority of non-M.E./CFS physicians and many patients still believe that CFS is caused by Epstein Barr Virus although Holmes found in his 1987 paper that the 1984 Lake Tahoe definition was not caused by EBV. Many newspapers still refer to CFS as EBV disease. It is this reality that really drives M.E. and CFS. Due to the huge drops in medical income over the past three decades in the western world and the necessity to economize time, the average primary care physician and internist simply have no time to assess the very complex M.E. or CFS patient. There is simply one solution for most physicians. Send that patient to a psychiatrist. As we have shown in this document, most psychiatrists simply do not believe that M.E. and CFS patients are psychiatric patients and so dismiss them. This leaves these disabled M.E. and CFS patients in a no-mans-land where they snipe at both sides and from where the fire is returned against them.

DISCUSSION 2: SLEEP DYSFUNCTION: All physicians know that the majority of M.E. and CFS patients sleep badly and have non-restorative sleep. Few physicians or M.E. or CFS patients themselves know how poor their sleep really has become since falling ill. There are two closely knit parallels in this investigational paper and they are that for all practical purposes, (1) 100% of M.E. and CFS patients have major complex sleep dysfunction and (2) 100% have measurable brain dysfunction. These findings are welded together. Which comes first? I believe that the brain injury causes the sleep dysfunction but I have no way of proving that statement, nor to my knowledge does anyone else. It would be a good thing if I am wrong and that the sleep dysfunction causes the brain injury since we could at least look at ways of restoring type 3 & particularly type 4 deep sleep that is missing in majority of patients. It is primarily during stage 4 sleep that growth hormone is produced and growth hormone is essential for repair and synthesis of protein, for the metabolizing of fat, particularly cholesterol. It is in stage 4
Delta Sleep that the excitatory cortisone hormone spigot is turned off and the production of growth hormone that is responsible for cell restoration is turned on fully. Only then can the brain and body rest. Growth hormone restores brain and muscle tissue, decreases stress, and builds new synapse chains that are essential for the implantation of necessary information as memory. This of course is an over-simplification of a most complex system that the most knowledgeable poorly understand. However it may be a start in our understanding of how to manage the repair of brain physiology and function.

Sleep clinics tend to be of little assistance other than documenting sleep dysfunction in M.E. and CFS patients. They tend to be able to treat some cases of obstructive and central apneas and hypopneas and restless leg movement. To my knowledge these clinics have been unable to (1) sufficiently improve oxygen saturation in most patients with low levels of oxygen or even in most cases notice the importance of this variable; (2) they have not dealt with the low circulating blood volumes found in many of these patients; (3) Although there are some medications that reputedly assist the restoration of type 4 sleep, I know of no case where they have successfully restored type 4 sleep in an M.E. or CFS patient; (4) there has been no inexpensive and practical way to adequately assess these sleep modalities in a home situation; (5) I have seen no sleep clinic that has successfully restored the enormous numbers of the non-cognizant awakenings in these patients. This is not a criticism of private and hospital sleep clinics, I am simply pointing out that this is a new science that is still poorly understood.

**DISCUSSION 3: TRIGGERS:** The apparent triggers of M.E./CFS-like-disease outside of epidemics are simply not reliable indicators of cause. Even when a patient falls ill immediately after a particular immunization such as Recombinant Hepatitis B, and we have seen too many, we simply do not know what the underlying brain dysfunction might be that was responsible for this explosive action. In terms of epidemic causes we are on safer ground. Of the more than 60 reported epidemics, the only infectious cause that we have seen repeated was an enterovirus and most commonly an ECHO 21 like virus that occurred in three known epidemics or clusters. Enteroviruses are notoriously difficult to recover outside of specialty labs with well-trained enterovirologists.

**B: TRAUMA AS A TRIGGER:** We list multiple post trauma injuries. Since the 1988 and 1994 CDC definitions of CFS do not mention specific triggers there can be no definitional criteria to exclude them. As mentioned above, outside of epidemics and clusters, triggers are simply not reliable indicators of cause. For instance trauma to the upper cervical cord or brain may appear to cause no obvious testable concussion but it may injure the integrity of the CNS sufficient to allow an infection or immunization to provoke M.E./CFS onset. We simply do not know sufficient about associated injury and M.E./CFS. However I have seen significant acute onset M.E. associated with young women in University level rugby, hockey and other contact sports where there has been either repeat or significant upper neck/head trauma to be closely followed by M.E./CFS and fibromyalgia-like syndromes. In this group we also have a profession football player as well as a locomotive engineer and a large number of individuals following vehicular accidents that despite collecting insurance benefits for the injury, simply never recovered. I would not put most of these people into the M.E. group but certainly into the CFS.
group. It is obvious from our investigations that all of these patients have an overlooked or missed diffuse injury of the CNS.

**C: RECORDED TRIGGERS HAVE CHANGED:** It is possible that what we are calling M.E. and CFS in 2008 may not be the same as what we called M.E. and CFS in 1984 at the explosive beginning of the 1984-1992 M.E. epidemic period. In our study of close to 2000 of our patients seen in the period 1984 to 1992 we found the following division:

**DISCUSSION 4: OCCUPATION:** Our figures are undoubtedly skewed due to both location and the relatively low number of patients (53) in this study. Although these patients came from across Canada, due to the location of our clinic in Ottawa, the nations capital, there was an occupational bias towards civil servants and accountants. Had we increased the study to 100 or 200 last seen patients the hospital and medical workers would have placed either first or second under the general occupation list. This is important since in our 1992 study of close to 2000 across Canada and the USA and UK patients who fell ill during the epidemic period of 1984-1992 the highest incidence of disease was in health care workers and school associated patients.
School Associated Group. This was by far the largest single group: In the 53 consecutive patients there were 19 who were either teachers or students; 13 were teachers and 6 were pupils. Teachers: The 13 teachers comprised 2 university professors, 8 high school teachers and 3 primary school teachers in this group. The teachers represented 13 or 68% of the school group. Students: There were 6 students or 32% of the school group.

School Associated Patients by sex: In the school associated group of teachers and pupils, 53% were female, which is significantly lower than the usual approximate 80% in the general public and 75% in the Belgian study from Antwerp University.

DISCUSSION 5: GRADUAL ONSET CFS: At a recent symposium on the place of HHV6 as a cause of CFS at Baltimore, at a private meeting called by Hoffman-La Roche Inc, each of the leading 6 CFS North American specialists invited only referred to the obvious conditions of acute onset disease. This acute onset classification does not appear as a different category in either of the CDC definitions yet it is this acute onset that partially describes one of the many differences between M.E. and CFS. When we review the findings in the table of the 4 patients who fell ill gradually, the enormous discrepancy in findings by reputable physicians and actual patient pathology becomes obvious. We refer to all gradual onset patients as CFS since by far the majority constitutes not only missed major disease but also often life threatening and sometimes treatable disease. This distinction must me considered by any new definitional committee.

DISCUSSION 6: PSYCHIATRIC DISEASE: Primary care and referral physicians usually refer patients to psychiatrists, often after a consultant states they cannot find any physical cause of disease. Well over 100 physicians have seen this group of 19 educational institution related patients yet in no case did any of these often excellent physicians find any evidence of physical disease. In many ways most physicians are simply not equipped intellectually and financially to take on the burden of chronic illness, particularly when the patient appears to know and thinks they know more about the condition that the physician themselves. This can be humiliating to some physicians. There is another problem. When the psychiatrist consultations occurs, they usually assume that the patient has been well investigated by the primary care and consultant physicians have examined a patient and naturally enough often attributes the patient’s manifestations as psychiatric illness. Tearfulness in women is often mis-interpreted as depression. Nevertheless, since all of these patients had been seen by a psychiatrist before coming to our clinic and the psychiatrists have rejected 13 of the 19 as having no psychiatric disease despite their physicians finding no physical evidence of disease, one can only laud the psychiatrists for their good sense. When we look at the 19 patients in this group 10 were female and 9 male, roughly 50% were women. Yet the psychiatric diagnosis noted that 4 (80%) were women and only 1 (20%) were men. Even so, the women were classified as Major Depressive Disease (Monopolar) and placed on anti-depressive medications. The single male psychiatric diagnosis was “acting out, or attention seeking” and given no medication but the mother was labeled as Munchausen-by-proxy for insisting her child was having seizures that they could not find. It was this
same child that drowned due to a seizure in a swimming pool but who was fortunately
resuscitated. When our office referred these 20 patients for psychiatric evaluation we also
provided the psychiatrist with our investigation profile and only 3 of the 6 who were
previously given a psychiatric diagnosis. Yet only one of them was given an
antidepressive medication. There is an explanation for this as well. Our national disability
pension service appears to grant a disability pension for psychiatric disease for patients
who cannot work on a psychiatric diagnosis if the diagnosis is made by a psychiatrist. Yet
the same pension board often does not give a pension to a patient on the basis of a
diagnosis of complex and severe physical disease from a primary care physician or from
many internists. It is not simply the patient, but disability boards who tend to fear
psychiatrists or fear to delve into their diagnostic acumen. Is it, knowing this, that the
psychiatrists, often out of kindness give the patient a psychiatric diagnosis to enable them
to obtain a disability pension. This unfortunately is a two edged sword. Some private long
term disability pensions give only a two year pension for a psychiatric diagnosis whereas
they are obliged to place a patient on long term disability pension for as long as they can
be proven to be physically incapable of working.

EXCLUDED PATIENTS: 15 Patients were excluded from the survey due to
incomplete data. Three young adult patients were seen who were at Chernobyl as infants
when the reactor disintegrated. One died from brain malignancy and one is in a
psychiatric hospital. This third patient has one third of his left anterior brain hemisphere
missing but still was able to obtain a MA degree. Three patients who apparently died
following RHB immunization were seen but due to the severity of their illness were
excluded due to my inability to complete their investigation. We had a further patient
with M.E. with no history of depression or psychiatric disease who committed suicide.
We have subsequently found her missing investigations and she will be included in a later
study. Since our investigation is long and arduous and requires attending hospitals in
different cities, we have at least 5 patients who were too ill and house bound to complete
any significant testing. In effect, those M.E. patients who are most ill, most housebound
are also the least examined and often most apt to commit suicide. To my knowledge,
nowhere in the world has any physician, including myself systematically examined these
shut-in patients to find out whether they have treatable disease.

CONCLUSIONS: These findings suggest that what we perceive as M.E. and CFS
constitute a much more serious group of complex illnesses with greater patho-physiology
than is generally recognized by either non-M.E./CFS physicians or even M.E./CFS
physicians. It is simply not credible that any single causative agent that can cause these
patient’s diverse illnesses or that any single treatment can be widely employed to give a
successful resolution to the vast majority of M.E. and CFS patients. This study also
suggests that the over-riding finding of all patients that we have examined seen as M.E.
by both physician and patients are intimately associated with a diffuse injury of the CNS
and than this type of injury in the past has not been readily diagnosable by classical
neurologists or other internists who have been centered on the Oslerian concept of single
pathology disease. It is possible, that malignancies and thyroid disease as seen in our
earlier paper, arthritic disease, autoimmune disease, respiratory dysfunction, major sleep
dysfunction and psychiatric disease are all interconnected by a diffuse brain injury.
It is my belief that it is necessary to develop a new category of physicians with appropriate university / hospital based research support whose work is based on Neurophysiology, the Autonomic Nervous System and the Neuro-Endocrine System of Whole Body Regulation and Dysregulation if ever we want to successfully treat these complex M.E. patients.

5: The underlying pathology of patients diagnosed with Fibromyalgia.

Fibromyalgia Syndrome Patients and Other Pain Provoking Conditions

Fibromyalgia Syndrome (FS): Historically the condition was called muscular rheumatism. In 1904 Sir Edward Gowers coined the term fibrositis and in 1989 the American College of Rheumatology defined it as Fibromyalgia Syndrome (FS). By general usage the term Fibromyalgia is employed.

Fibromyalgia is defined arbitrarily by the American College of Rheumatology (39 Russell) as pain that must be present in at least 11 of 18 bilateral tender points however these points are not consistent and may vary both by number of pain sites and the degree of pain (38,39 Russell) from hour to hour and from day to day. FS varies accordingly to the physical and psychiatric stress to which the patient is subject. FS patients tend to be much stiffer and painful in the mornings and for days after excessive physical stress. Minor infections that might not trouble the non-FS patient may exacerbate the pain levels in the FS patient.

FS can be primary or secondary. Many physicians and the affected general public frequently misdiagnose multiple pain associated medical conditions as Fibromyalgia. It is essential that the psychiatrist have an understanding of the following pain conditions that can be mistaken for Fibromyalgia and for which the treatments if they exist can often be specific to the condition.

Primary generalized non-articular rheumatism disorders include:

a. Fibromyalgia Syndrome,
   b. Polymyalgia Rheumatica and
   c. Hypermobility Syndrome. (23 Russ)

Fibromyalgia Syndrome should be distinguished from regional disorders such as Myofascial Pain Syndrome.

Secondary Fibromyalgia exists in a large number of medical conditions of which the psychiatrist should be aware.

1: Fibromyalgia Syndrome can occur secondary to Rheumatic Diseases that include:
a. Systemic Lupus Erythematosus,
b. Rheumatoid Arthritis,
c. Osteoarthritis,
d. Scleroderma,
e. Polymyositis
f. Generalized Spinal Arthritis due to genetic, traumatic or infectious origin and
g. Psoriasis
h. HLAB27 positive patients despite absence of ankylosing spondylitis.

2: Fibromyalgia Syndrome can occur secondary to chronic infectious disease including:

a. Tuberculosis,
b. Tertiary Syphilis,
c. Bacterial Endocarditis and
d. Subacute and chronic viral infections.

3: Fibromyalgia Syndrome can occur secondary to malignancy and endocrine disorders such as:

a. Hypothyroidism and
b. Hyperparathyroidism
c. PMS induced or aggravated.

4: Fibromyalgia Syndrome can occur secondary to or made worse by multiple pharmacological agents including:

a. Excessive use of non-steroidal antiarthritic agents: NSAIDS
b. Analgesic and narcotic addiction, corticosteroid withdrawal

5: Fibromyalgia Syndrome can occur due to or be made worse by sleep dysfunction, stress, depression or anxiety.

**Personal experience on a principal cause of Fibromyalgia:** Almost every primary fibromyalgia patient that I have examined began his or her illness with a localized pain associated with a localized injury. Two typical examples are: (a) isolated trauma to a shoulder in a sports injury or (b) cervical spine area soft tissue injury in a motor accident. The patient is often given NSAIDS that decrease or remove the pain but after a short while the medication dosage has to be increased or the type varied to control the pain. Before long the patient has a generalized pain syndrome diagnosed as Fibromyalgia. It is difficult not to consider that NSAIDs provoke a change in pain appreciation at a central level, giving rise to an altered sensation of pain. At the same time the patients tend to have increasing sleep dysfunction. Is this sleep dysfunction related to the pain or could it be that both the pain and sleep centres are changed due to NSAIDS?

Once the physician comprehends the complexity of the above mentioned pain conditions the question arises from a mental health point of view, how best can the psychiatrist understand assist the patient? This is not an easy task.
Diagnosing the Pain Patient

I would like to remind both patient and the physician public alike, that it is very easy to do little or no testing and due to failure to test adequately or with knowledge, it is easy to find nothing. **Absence of obvious disease markers is not necessarily absence of disease.** Let me make myself very clear:

A patient presents at their physicians office with a history of chronic pain and the symptoms M.E. or Fibromyalgia or even Lupus or Rheumatoid arthritis. The patient looks fine, they are young, and they may look attractive and well. The doctor never the less does a few tests: blood count, ESR (sedimentation) and an ANA (anti-nuclear antibodies) are all, normal. Lupus or rheumatoid arthritis is discounted as a disease. Two weeks later the patient returns but once again the same tests are repeated and are still normal. The patient may be given a pain killer or anti-inflammatory but the pain and/or the rheumatoid symptoms persist or even become worse. The doctor then usually assumes that the patient is either after narcotics or is simply an anxiety neurosis. Sometimes the patient is diagnosed as Fibromyalgia, an illness that many, many physicians believe is imaginary. The physician no longer believes the patient or simply is too busy treating patients that he can help. He simply doesn’t have time nor does he wish to see you again.

**SOME TESTS THAT CAN DIAGNOSE PAIN SYNDROMES**

What if the physician ordered the following tests, which came back positive, such as?

a. **X-ray of the spine and HLA B27 or HLA B60:** They might have diagnosed ankylosing spondylitis, a missed compression fracture, genetic variations, TB of the spine, metastatic malignancy.

b. **ENA, dsDNA, Russel Viper Venom, Rheumatoid factor:** They might have diagnosed lupus, scleroderma or early rheumatoid arthritis,

c. **IgM, IgG Anti-cyclic Citrullinated Peptide, Lp (a) Lipoprotein:** They might have diagnosed seronegative rheumatoid arthritis or mixed connective tissue diseases that do not show up in regular dsDNA or anti-ENA or ANA positive patients.

d. **ELISA for anti-cardiolipin antibodies (ACA), Factor V Leiden, Prothrombin mutation VIII levels, Protein C & S, Lupus anticoagulant:** They might have diagnosed Hughes Syndrome.

e. **HsCRP or C Reactive protein:** They may have diagnosed inflammatory disease.
f. **Elevated C Reactive Protein, Sedimentation Rate, Rheumatoid Factor:** They might have diagnosed polymyalgia rheumatica if she is over 60 but under 60 the rheumatologist might say, you can’t have polymyalgia rheumatica if you are a young person even though physicians have no idea what polymyalgia rheumatica may be.

g. **Smooth Muscle Antibodies, mitochondrial antibodies:** They might have diagnosed illness affecting these organs and systems.

h. **Suspecting NSAID induced Fibromyalgia, pain syndromes & NSAID induced Lupus:** The classical patient has a traumatic injury involving one joint, example a shoulder trauma in a ski injury. The pain is only located in this one joint but it may persist for days or weeks and there is no fracture. The physician puts the patient on an NSAID and before long the patient has a generalized pain syndrome diagnosed as Fibromyalgia or Lupus. Over the years I must have seen this history repeated in 20 such patients.

-but what if all of these were normal and the patient still complained of severe chronic illness. Do we then diagnose anxiety neurosis, psychiatric disease and refer the patient to the psychiatrists or simply refuse to see them again? I have found such patients with all of the above normal tests. What do I do then? I will believe the patient.

i. **I will then do a Nuclear Bone Uptake Scan.** Often in this nuclear bone scan group, you will find significant increased inflammatory disease in the joint areas, diagnostic of a rheumatoid or interstitial disease or at times, metastatic or bone malignancy. Yet all of the other tests are normal. Why is this? Why are the tests all normal? I don’t know. I find this goes back to one simple rule of medicine: **BELIEVE THE PATIENT.**

j. **The above is not a complete list.** I have not discussed in any detail (a) muscle (b) vascular mediated, (c) genetic or (d) repetitive use and (e) generalized hand arm vibration pain syndromes that can be misdiagnosed as M.E. or Fibromyalgia.

You would now think that I have excluded all physical evidence of disease causing pain and fatigue. Wrong. We have only started. Regular physicians simply do not have the time and are simply not paid to spend so much time with the patient. In effect, physicians in most health systems, whether it is the private insurance dominated system or the aenemic public health system of the USA or UK welfare health systems are simply not paid to investigate. In fact, in many systems, physicians ordering tests may even be penalized.

**Testing this Theory that if there is pain there is a cause.**

We examined 53 consecutive patients who were referred to our clinic with M.E, with and without fibromyalgia, with and without accompanying pain syndromes using the above investigative protocol.
We have just started to check this group of patients with both M.E. and pain debilitating pain syndromes so our data is not complete. Nevertheless we have already diagnosed cause in a number of these pain patients that could be sufficient cause for their pain syndromes and fibromyalgia.

(a) The very painful spinal disease called Ankylosing Spondylitis is associated with the gene HLA B27 and HLA B60. In Ontario where most of our patients came from we do not have access to the HLA B60 test by which to correlate spinal changes.

(b) Two of our pain patients committed suicide before testing was completed.

(c) Several patients returned to their home Province or Territory where all of the above tests were not available.

Pathological conditions in M.E. patients with pain and Fibromyalgia patients include:

(a) 11 with significant spinal arthritis, but only 2 positive for HLA B27:
(b) 9 positive for Rheumatoid arthritis with serological markers:
(c) 4 with elevated ESR: 
(d) 2 with polymyalgia rheumatica
(e) 2 with Raynaud’s
(f) 1 with NSAID induced arthritis,
(g) 1 with prescription induced Lupus
(h) 1 with reflex Dystrophy
(i) 1 with elevated mitochondrial Ab.