

STEALTH VIRUSES: *The Hidden Epidemic*

By: Steve Haltiwanger MD, John Martin MD PhD and James Kholos ND

Forward: *I have written this booklet on stealth viruses in order to make available to the general public the groundbreaking work of Dr. John Martin. Dr. Martin has discovered the existence of an atypical group of viruses that are implicated in the pathogenesis of many psychiatric and neurological diseases. Dr. Martin has coined the name stealth viruses to describe a group of atypical viruses that can infect tissue, while at the same time being all but invisible to the cellular components of the immune system.*

Steve Haltiwanger M.D. 7/15/2001

What Are Stealth Viruses?

Stealth viruses are a molecularly heterogeneous group of atypically structured, cytopathic viruses that can induce multi-system illnesses without evoking an anti-viral inflammatory reaction (1,2). These viruses appear to be mainly derived from human and animal herpes viruses and to lack antigenic components normally responsible for evoking an effective cellular inflammatory antiviral response.

Stealth viruses typically have fragmented, genetically unstable genomes, this means their genetic structures can easily undergo alterations (3,4). Dr. Martin has shown in his research that stealth viruses can incorporate genetic material from animal cells, human cells, other viruses and even bacteria (5,6).

The occurrence of genetic exchanges between cellular and viral genomes is a well-documented phenomenon (7). It is a general scientific assumption, however, that both viral and cellular genomes are relatively stable. Stealth viruses appear to be an evolutionary exception with fragmented genetically unstable genomes and marked heterogeneity existing in their genetic structures (1,3,4). By incorporating cellular sequences into a genetically unstable replication process, stealth viruses have a potent mechanism to alter cellular functions in the tissues they infect.

Because of the unstable nature of stealth viral genomes, foreign genes can be incorporated into replicating stealth viruses through genetic recombination. The propensity of stealth viruses to incorporate the genetic material of other organisms makes stealth viruses the true chimaeras of nature.

The unstable genomes of stealth viruses also allow for the incorporation and expression of cellular oncogenes (8-10). Oncogenes are cellular genes that can cause the conversion of normal cells into cancer cells. Research currently performed by Dr. Martin and others is groundbreaking in the understanding of the role of viruses in the etiology of certain cancers (9,11).

The term "stealth viruses" has been applied to the vacuolating cytopathic viral agents cultured from blood, cerebrospinal fluid, and tissue biopsies of patients with various non-inflammatory neuropsychiatric and multi-system illnesses (1,2,12-15).

Dr. Martin's lab has cultured stealth viruses from a large number of patients with both CFS and with various neurological and neuropsychiatric illnesses (12, 15-16). The culture findings have been confirmed in patients with severe neurological diseases who have undergone brain biopsy. The spectrum of clinical illnesses seen in stealth virus positive patients has included: i) Newborns with enlarged livers, low platelet counts and brain hemorrhages, born to virally infected mothers; ii) children with autism, attention deficit, anorexia nervosa, and aggressive behavioral disorders; iii) young adults with schizophrenic, manic-depressive psychosis and drug addiction; iv) patients with various neurological disorders ranging from localized impairment of sensory, motor or autonomic functions, to otherwise unexplained coma, and v) elderly individuals with dementia, including patients labeled as having Alzheimer's disease. Many of the patients Dr. Martin has tested have had concomitant disease involving various other organ system including the gut, salivary glands, liver, pancreas, thyroid, adrenal, heart, and genital organs.

Viteria, Chimaera and Chimaerteria

Viteria is a term that has been coined to define eukaryotic viruses that have incorporated genetic sequences of bacterial and/or bacterial plasmid origin (17). Chimaera is the name of a fearful fire-breathing two-headed monster from Greek mythology that had the heads of a lion and a goat and the body of a dragon. Chimaerteria is a term that refers to the incorporation of genetic material in stealth viruses not only from bacteria and other viruses, but also animal and human cells. The acquisition of genetic sequences from multiple sources into viral genomes extends the potential role of stealth viruses as natural vectors in the transfer of genetic information.

Viteria is a description of the capacity of stealth viruses to assimilate bacterial genes. The sources of the bacteria sequences include eubacteria, archaebacteria and both cell wall containing and cell wall deficient bacteria.

Normally, viruses that are infectious in eukaryotic cells (human and animal cells) will not infect prokaryotic cells (bacterial cells), however stealth viruses appear to have the capacity to overcome this phylogenetic barrier. Stealth viruses are a transitional form of life that incorporates genetic aspects of viruses, bacteria, animal cells and human cells making them one of the most dangerous forms of microorganisms in existence. It is likely that stealth viral infections are involved in many degenerative and cancerous diseases that plague mankind.

Many of the matching bacterial sequences in stealth viruses correspond to genes involved in energy generating and metabolic conversion reactions. Dr. Martin has identified genetic sequences that participate in the transport, activation and synthesis of uncommon metabolites. He believes that by incorporating such a wide array of metabolic functions, that it is conceivable that viteria and chimaerteria

could maintain a limited capacity to metabolize, and possibly even to replicate, outside the confines of a cell. If this finding holds up under further investigation it will invalidate the precept that viruses can only grow and replicate inside of living cells.

Viruses that do not absolutely require cells for replication would have a pleomorphic character. Pleomorphic atypical stealth viruses could possibly possess several different life cycles and differing degrees of pathogenicity depending on which stage of their life cycle they are in. Pleomorphic chimaeria also could possess the ability to enter a dormant spore like stage where they could remain inactive for years only to reemerge. If such spores are formed they could be transmissible, virtually unrecognizable and extremely resilient.

The Pathogenicity of Stealth Viruses May Also Be:

- A. Partially mediated by the toxic byproducts of the various metabolic pathways encoded by the assimilated bacterial genes and
- B. Enhanced by the presence of atypical bacteria within stealth virus infected patients (18-21). The infections caused by these bacteria agents can cause cytopathic effects in affected individuals.

According to Dr. Martin the presence of bacterial-related gene sequences in stealth viruses and atypical pathogenic bacteria in affected patients may have relevance in chronic fatigue syndrome, Gulf war syndrome, chronic Lyme's disease, Alzheimer's disease, multiple sclerosis, arteriosclerosis and other diseases (18,19,22-24).

Stealth Adaptation

Stealth-adaptation refers to the mutation and/or deletion of viral genes coding the major immunogenic components required for effective cellular immunity (1,4). The process of reducing the number and amounts of antigenic material enable stealth viruses to bypass cellular immune defenses and establish persistent active non-inflammatory infections (25). Stealth adaptation is a mechanism that facilitates persistent infection because stealth viruses have lost the structural components of conventional viruses that evoke anti-viral cellular inflammatory responses.

Dr. Martin believes that stealth adaptation can occur with all of the presently known human herpes viruses and many of the herpes viruses' known to infect animals. Viral sources other than herpes viruses have been suggested in various studies to undergo stealth adaptation. As viruses downsize and simplify their common pathogenic characteristic is that they overtax the metabolic resources of the cell.

Stealth virus-1 the prototype stealth virus was isolated from the blood of a patient diagnosed in 1991 with chronic fatigue syndrome. The cellular response to the virus was a foamy vacuolated degeneration in human and in animal cell lines (1). The electron microscopy studies of the infected cultures showed

herpesvirus-like particles (1). The genetic sequences of the virus extracted from the infected cell cultures showed some relationship to human cytomegalovirus (HCMV), however the genetic sequences were subsequently shown to be more closely related to African green monkey simian cytomegalovirus (SCMV) (1,3,4). Stealth virus-1 the prototype stealth virus, while it is derived from SCMV, is missing sequences that correspond to the known major viral antigens targeted by anti-cytomegalovirus cytotoxic T lymphocytes (25).

However other sequences contained in the fragmented virus genome, were identified as cellular in origin (5).

The presence of mammalian cellular genes in the viral genome answered the question of how a virus with such a fragmented viral genome and lacking certain viral genes could retain its ability to be cytopathic for cells. Dr. Martin has also identified genes with potential oncogenic (cancer causing) activity in the stealth viruses he has studied. (10,26). Stealth adapted viruses have been repeatedly detected in both children and adults with various cancers (11).

I think Dr. Martin should tell the story of these outbreaks

The Story of the Mohave and Tennessee Outbreaks

Widespread illnesses involving a diverse group of clinical symptoms, multiple family members and whole communities can be attributed to the spread of stealth viral infections (14,27). The same infection in one person may manifest as chronic fatigue, yet other patients may have different symptoms such as headaches, liver enzyme elevations, muscle aches, attention deficit, cognitive dysfunctions etc. The diversity of symptoms in different organ systems makes stealth viral outbreaks in communities very difficult to identify making stealth viral outbreaks the true Trojan horses of disease.

How Do Stealth Viruses Damage Cells?

- A. Virally infected cell undergo metabolic cellular changes. Viruses alter the metabolic balance of the cell over utilizing the cell's energy resources causing disruption of normal cellular functions eventually leading to cell death.
- B. Viruses can damage cellular components especially the energy producing mitochondria.
- C. Viruses can damage genetic information.

How Can Stealth Viruses be Detected?

- A. Tissue culture methods provide a broad screening method for the detection of stealth viruses.
- B. Stealth virus detection can be done by using either the patient's own serum, or serum collected from various individuals exposed to a stealth or to a related conventional virus.
- C. Specific antibodies can also be used to distinguish stealth viruses from common conventional viruses.
- D. Electron microscopy studies have been helpful in evaluating viral structures.
- E. Animal transmission studies have also proven useful for stealth virus detection.

Clinical Manifestations of Stealth Viruses

"The clinical manifestations of stealth virus infections have been primarily neuropsychological. This is presumably due to the inability of the brain to readily compensate for localized damage causing a disruption in specific functions. The development of cancer provides another example where limited damage, even occurring in a single cell, can have devastating consequences (28)."

What are the Properties of Stealth Viruses?

The prototype stealth virus identified by Dr. Martin was an African green monkey simian cytomegalovirus (SCMV) that had lost the major antigenic targets for recognition by cytotoxic T lymphocytes (25). His research has discovered that this virus had captured, amplified and mutated both cellular and bacterial genetic sequences.

Dr. Martin has found that the most useful defining characteristic of a stealth virus infection is the distinctive foamy cell CPE inducible in cultures of cells from multiple species.

As a group, stealth viruses appear to have been derived from herpes and other viruses by an evolutionary process of major gene deletions and mutations (28). Electron microscopy, serology and molecular-based assays demonstrate structural and biological differences between stealth-adapted viruses from conventional cytopathic viruses including herpes viruses, enteroviruses, and adenoviruses (28).

The genetic changes in the viruses are the reason for the lack of an appreciable inflammatory response in chronic stealth viral infections.

How Can Stealth Viral Infections Be Treated?

A number of approaches have been suggested for therapy of stealth viruses. Nutritional supplements help offset the metabolic imbalances and free radical produced caused by the viruses. Viral inhibitors can be found in a number of plant extracts from *Dionaea muscipula*, Saint John's Wort and olive leaf and in insect extracts like Iridodial. A potential therapeutic viral inhibitor termed Epione named after the wife of the Greek god of medicine Asclepius has also been identified by Dr. Martin in stealth virus cultures.

In What Conditions Can Stealth Viruses Be Found?

Stealth virus infection was initially described in association with disorders of brain function. Based on cell cultures and PCR based findings, Dr. Martin has proposed that stealth virus infection could potentially account for a wide diversity of neuropsychiatric illnesses, including schizophrenia and manic-depression.

A number of conditions and neurological illnesses with by positive culture findings have been potentially connected to stealth viruses, including patients labeled as having Alzheimer's disease, autism, attention deficit disorder, multiple sclerosis, ALS, post infectious encephalopathy, fibromyalgia and chronic fatigue syndrome (CFS).

The clinical overlap between CFS, fibromyalgia, depression, anxiety disorders, psychosis, neurological diseases, etc., suggests a spectrum of illnesses involving the brain possibly with a common underlying viral pathogenesis (28). The finding of positive viral cultures highlights the possibility that a proportion of each of these syndromes could simply be different manifestations of an underlying stealth virus encephalopathy.

The hallmark of stealth viral infections is the diversity of symptom manifestations. Neurological infections, liver, thyroid, muscle, dermatological, salivary gland, gastrointestinal and genitourinary diseases have been seen in culture positive patients, their pets and some of their family members.

Without technological advances stealth viruses would never have been identified. It took the development of sensitive PCR procedures, molecular testing and specialized viral culture techniques before virologists began to understand that stealth viruses existed and how they were different from conventional viruses.

Chronic Fatigue Syndrome

Chronic fatigue syndrome (CFS) is an illness characterized by severe prolonged fatigue often accompanied by a diverse group of neurocognitive symptoms (29).

Many patients diagnosed with chronic fatigue have accompanying mood, cognitive, and neurosomatic symptoms indicative of brain dysfunction. A number of research studies have suggested that viral infections may cause CFS (14,28,30-36).

In fact CFS may be part of a spectrum of dysfunctional brain syndromes caused by stealth virus infections (37). Some of the possible pathogens include Epstein-Barr virus, human herpesvirus-6 (HHV-6), enteroviruses, and human T lymphotropic virus-II (HTLV-II)-related retrovirus (30-33). Dr. Martin and colleagues in 1991 used a combination of tissue culture and molecular techniques to identify a persistent atypical (stealth) viral infection in a chronic fatigue patient who was negative for conventional viruses. In this patient repeat cultures over a three-year period were positive for the same virus. The same virus was isolated from the patient's CSF, but there was an absence of an accompanying inflammatory response suggesting that the virus was present in the nervous system and yet did not cause the typical inflammatory response of other neurotropic viruses (1,37).

"Ongoing studies indicated that atypical viruses can be isolated from patients with a variety of neurological, psychiatric, and autoimmune diseases, as well as some asymptomatic individuals. The viruses are cytopathic for fibroblasts and other cell types of multiple species and do not give typical reactions in immunological and molecular probe assays for known human herpes viruses. Because of the absence of overt clinical signs of an inflammatory reaction in many of these patients, we have tentatively termed these agents stealth viruses (1)."

Dr. Martin has hypothesized that CFS is but one of the many differing manifestations of persistent stealth viral infections that affect the brain and other organs. Other investigators believe that the disordered brain function in CFS results from the overproduction of neuromodulatory cytokines from an activated immune system. Immune system over activity may be due to a variety of microorganisms, such as Epstein Barr virus, human herpesvirus-6, *Candida albicans*, *Mycoplasma fermentans*, *Chlamydia pneumoniae*, etc. Other investigators have focused attention on brain damage resulting from exposure to environmental neurotoxins as well as the release into the circulation of neurotoxic bacterial products from a damaged gastrointestinal tract.

Dr. Martin argues that the failure to identify primary infectious processes within the brain in CFS outbreaks results from the technological limitations and the failure to identify stealth viral infections using conventional viral detection methodologies.

Stealth virus-1 is related to a cytopathic virus cultured in early 1991 from the CSF of a comatose patient who had been previously diagnosed as having a manic-depressive illness (1).

Myalgic Encephalopathy/ Chronic Fatigue Syndrome includes clinical syndromes characterized by neurological, gastrointestinal, cardiovascular and musculoskeletal features (38). Severe forms of ME/CFS can lead to paralysis, seizures, chronic headaches, cardiac palpitations, gastrointestinal malfunction and a variety of neuropsychiatric and behavioral conditions. When the psychiatric and

behavioral symptoms are the prominent manifestation, the unlucky patient is relegated into the care of psychiatrists, who invariably treats the condition with a variety of psychotropic drugs. When this occurs it is like dealing with a smoke filled room by opening windows and bringing in fans instead and putting out the source of the fire.

Stealth viral infections with encephalopathy can present clinically as a spectrum of neuropsychiatric disorders, including autism, attention deficit and behavioral problems in children, depression, bipolar disorders and schizophrenia. When multiple organ systems are involved chronic fatigue and fibromyalgia are prominent manifestations along with the cognitive dysfunction (37).

Stealth Viral Infections and the Brain

While working as a virologist at the University of Southern California Dr. Martin developed tissue culture methods that clearly identified the presence of atypical viruses in patients with complex neurological diseases (1,13,30,37,38). These viruses were unusual in that they failed to evoke inflammatory reactions instead these viruses caused cellular destruction by destroying the metabolic machinery of the cells they infected. They were termed stealth viruses on the basis that they seemingly they lacked the target antigens needed for recognition by the body's cellular immune system (4,25). The lack or low density of expressed antigens, make these viruses nearly invisible to the body's immune system.

The anatomical fact that the brain spatially distributes its various functions renders the brain uniquely susceptible to localized viral-induced cellular damage.

Moreover, the brain exerts important controls on the functions of other organs through neural and hormonal regulation, therefore a viral brain infection can readily explain several of the non-organ disorders that have been associated with chronic fatigue syndrome, such as neurally mediated hypotension, adrenal deficiency, irritable bowel syndrome, etc.

In 1999 Dr. Martin described a stealth virus infected child whose illness, when it began in 1997, was thought to be a behavioral problem (27). Magnetic resonance imaging (MRI) when performed found extensive sub-cortical brain damage. A brain biopsy subsequently showed marked vacuolating/spongiform changes, which were caused by a stealth viral infection.

Young children with stealth viral infections have presented with autism, attention deficit and hyperactivity, learning and other behavioral disorders (13).

Positive cultures of stealth viruses have been found in patients in psychiatric hospitals, cancer patients, including essentially 100% of patients diagnosed with multiple myeloma, in patients with autoimmune illnesses, including systemic lupus erythematosus, rheumatoid arthritis and multiple sclerosis.

Viral infections have been identified in patients with schizophrenia, manic-depressive illness, multiple sclerosis, ALS and other neurological and psychiatric disorders, however since presence alone does not mean causation more work needs to be done in clarifying the role of viruses in these conditions (39-41).

Other Organ Systems Besides the Brain are Also Affected by Stealth Viral Infections

Liver and gastrointestinal tract: Slight elevations in liver function enzymes frequently occur in viral infections of the liver. If liver dysfunction occurs it can reduce the liver's detoxification capacity and account for the enhanced susceptibility to various noxious environmental chemicals that is a characteristic of many stealth viral infected patients, and a hallmark of multiple chemical sensitivity.

When subclinical viral infections occur in the gastrointestinal tract they can add to the demands of liver detoxification by helping to breach the normal barrier function of the gut bacterial and fungal toxins and allow entry into the blood stream of pathogens such as Candida and mycoplasma. Pancreatic dysfunction, and intestinal malabsorption of required nutrients can cause a wasting syndrome that has been observed in several patients.

Endocrine glands: Hypothalamic and pituitary dysfunction can occur as a result of encephalopathic infections resulting in secondary effects on menstruation, water balance, thyroid and adrenal function, etc. In addition primary thyroid and adrenal dysfunction can occur in some stealth viral infected patients. Direct viral infection of the endocrine glands can also evoke secondary autoimmune reactions further compounding endocrine disease.

Joints and renal involvement: Even though anti-viral cellular immune responses may be impaired, stealth viral infections can evoke circulating antibodies. An overproduction of antibodies reactive with a range of viral and auto-antigens and subsequent antigen antibody complexes can cause arthralgia and can also lead to long-term kidney disease. These complexes can also cause secondary vasculitis with widespread and at times disastrous manifestations.

Immune system: Persistent systemic stealth viral infections can induce immunological changes. Enhanced allergic reactions have been seen in various patients.

The Potential Dangers of Vaccines

The use of African green monkey-derived cell lines in live virus vaccine production may potentially introduce pathogenic viral variants into humans.

Evidence for stealth viruses in blood and CSF samples from a CFS patient was originally based on weakly positive polymerase chain reaction assays (14). From his research Dr. Martin has determined that the CFS of this patient was caused by a simian-related CMV (a monkey cytomegalic virus) with the most likely source being contaminated polio vaccine (25).

Immune System

In conventional viral infections the immune system has good and bad roles in that it can both decrease and increase the extent of viral damage. First circulating antibodies can prevent viruses from gaining entry into cells. Protective antibodies can be created by immunization with any materials containing viral antigens. The component of the immune system mediated by T-lymphocytes and macrophages is referred to as cellular immunity. These cellular components can reduce viral loads by destroying virally infected cells prior to the release of infectious virus particles. Viral antigens and altered subcellular components on the surface of infected cells can trigger immune responses against the expressed viral and self-antigens leading to autoimmune mediated tissue damage. Unfortunately collateral damage also occurs in nearby noninfected cells by the immune initiated inflammatory responses.

Stealth viruses simply bypass the immune system by: a) Deleting and/or mutating critical genes reducing the expression of viral antigens and in turn this reduces the cellular immune recognition of virally infected cells or b) Combining gene sequences of two different viruses forming an atypically structured cytopathic virus or c) Combining gene sequences from bacteria, other viruses, animal or human cells **creating a chimaerteric chameleon virus** that is unrecognized by cellular elements of the immune system.

Although stealth viruses may lack the antigens required for cellular immunity, some still retain antigens able to evoke circulating antibodies. The presence of stealth virus reactive antibodies may, in fact, act as a barrier to the blood borne spread of infection into the brain. The molecular heterogeneity of stealth viruses, however, poses a limitation with using a single antigen for possible immunization.

Cancer

Dr. Martin believes that stealth viruses can apparently "capture, amplify and mutate" various cellular sequences leading to cancer. Dr. Martin has repeatedly identified stealth virus infections in patients with multiple myeloma (28). Multiple myeloma is a malignancy in which differentiated B lymphocytes, with the appearance of plasma cells, accumulate throughout the bone marrow, and other body tissues, less well differentiated lymphocyte malignancies appear as lymphomas. In a study of 20 patients with multiple myeloma, peripheral blood mononuclear cells were added to human MRC-5 fibroblasts cultures; all cultures showed unequivocal cellular damage typical of stealth virus infections (28). Other examples of positive stealth virus cultures include adults with glioblastomas and several patients with salivary gland tumors. (11).

Stealth viruses have the capacity to capture, amplify, and mutate genes with potential oncogenic activity. Dr. Martin has found genes that stimulate growth of melanoma in some stealth virus samples (9,10,26).

Stealth virus replication can lead to varying re-combinations of mutated viral and cellular genetic sequences. When a virus assimilates and expresses genes coding growth factors for myeloma, melanoma or cellular growth factors of other cancers the virus could promote the development of myeloma, melanoma and other cancers.

Since many cancer patients report that they were aware that something was wrong with their body often experiencing unusual fatigue, sleep disturbance well before they are diagnosed with cancer. Testing for stealth viruses may be very beneficial in seeing whether such cancer patients are infected and whether they might benefit from anti-viral treatments.

Future Research Goals

1. Improving methods for detecting and characterizing stealth viral infections using tissue cultures, molecular, and serological techniques. This is critically important since stealth viruses have different genetic structures than conventional viruses and will not be detected by conventional viral screens. In a sense our current technology limits what we can see and for most people if it is not seen it does not exist.

2. To sequence stealth virus isolates from positive cultures of ill patients.

3. To Identify stealth viral infections with specific neurological and other multi-

system diseases. It is possible that many mental and neurological illnesses are the symptomatic manifestations of previously unrecognized non-inflammatory stealth virus infections of the brain. Because stealth viruses can capture, amplify, and mutate critical cellular genes, leading to a disruption in normal cell function, the effects are especially apparent in the brain.

4. To identify and develop therapeutic agents that inhibit stealth viruses.

5. To identify what is causing the viral inhibitory activity in cell cultures in material released from infected cells. An early observation made in the study of stealth viruses was that the intensity of the cell damaging effects could be enhanced by frequently feeding the cultures. This anomaly led to the detection that a virus inhibitory factor accumulated in the fluids of infrequently fed cultures.

6. To test various patient and control groups of individuals, to determine the prevalence of stealth virus infections.

Animal Studies

A stealth virus isolated from a CFS patient induced an acute encephalopathic illness in cats with prominent neurobehavioral changes (42). The virus was identified as a simian cytomegalic virus. While the symptoms were mainly attributed to the brain involvement, the illness was systemic with non-inflammatory, cellular damage evident in the brain and throughout the tissues of multiple organs.

It is likely that the brain symptoms are the most prominent, since brain function is more sensitive to low-level viral induced damage than most other organs.

Cellular damage was also created in the offspring of a virus inoculated pregnant cat, indicating fetal transmission of the virus. When cats were given heat inactivated viral material they did not develop the illness.

Electron microscopy studies confirmed the presence of herpes like viral particles

in the brain of inoculated animals. The viral cell cultures, animal transmission and electron micrograph findings support the role of stealth viruses in the pathogenesis of human neurological diseases.

The experimental use of cats to study disease transmission of stealth viruses was prompted by the anecdotal observations of various illnesses in the domestic pets of CFS patients. Positive stealth virus cultures have been obtained from several of these animals and reported to Public Health authorities. As with the experimentally inoculated cats, systemic changes were found to occur throughout many organs including the brain. Illness has also been induced using blood transferred from a symptomatic to an asymptomatic animal.

Because most stealth viruses will grow in a variety of animal cell cultures mice were chosen as test animals. Although, mice have only subtle behavioral changes, histological changes including cytoplasmic vacuolization, nuclear envelope irregularities and evidence of cellular destruction, were clearly identifiable in the tissues examined. The mouse model is currently being used in the evaluation of crude preparations of Epione.

Molecular Studies on Stealth Viruses

Dr. Martin identified portions of the prototype stealth virus as unequivocally derived from an African green monkey simian cytomegalovirus (3,25). Because he found genetic sequences in the stealth virus that were clearly of cellular origin he believed that an exchange of genetic material can take place between cells and viruses. His sequencing studies of other stealth viruses have revealed sequences that are homologous to various other viruses, including adenoviruses, papovaviruses and probably enteroviruses indicating that an exchange of genetic material can also take place between different viruses.

References

1. Martin W.J, Zeng LC, Ahmed K, Roy M: Cytomegalovirus-related sequences in an atypical cytopathic virus repeatedly isolated from a patient with the chronic fatigue syndrome. *Am. J. Path* 1994; 145: 441-452.
2. Martin W.J: Severe stealth virus encephalopathy following chronic fatigue syndrome-like illness: Clinical and histopathological features. *Pathobiology* 1996; 64: 1-8.
3. Martin W.J, Ahmed KN, Zeng LC: African green monkey origin of the atypical cytopathic 'stealth virus' isolated from a patient with chronic fatigue syndrome. *Clin. Diag. Virol* 1995; 4: 93-103.
4. Martin W.J: Genetic instability and fragmentation of a stealth viral genome. *Pathobiology* 1996; 64: 9-17.
5. Martin W.J: Cellular sequences in stealth viruses. *Pathobiology* 1998; 66: 53-58.
6. Martin WJ. Bacteria-related sequences in a simian cytomegalovirus-derived stealth virus culture. *Exp Mol Pathol.* 1999; 66:8-14.
7. Ewald PW: *Evolution of Infectious Disease*, Oxford, Oxford University Press, 1994.
8. Haskill S, Peace A, Morris J, Sporn SA: Identification of three related human GRO genes encoding cytokine functions. *Proc Natl Acad Sci USA* 1990; 87: 7732-6
9. Luan J, Shattuck-Brandt R, Haghnegahdar H, Owen JD: Mechanism and biological significance of constitutive expression of MGSA/GRO chemokines in malignant melanoma tumor progression. *J Leukoc Biol* 1997; 62: 588-97.
10. Owen JD, Strieter R, Burdick M, Haghnegahdar H: Enhanced tumor-forming capacity for immortalized melanocytes expressing melanoma growth stimulatory activity/growth-regulated cytokine beta and gamma proteins. *Int J Cancer* 26 1997; 73: 94-103
11. Gollard RP, Mayr A, Rice DA, Martin WJ: Herpesvirus-related sequences in salivary gland tumors. *J Exp Clin Cancer Res* 1996; 15:1-4.
12. Martin WJ, Anderson D: Stealth virus epidemic in the Mohave Valley. I. Initial report of virus isolation. *Pathobiology* 1997; 65: 51-56.
13. Martin WJ: Stealth virus isolated from an autistic child. *J Autism Dev Disord* 1995;25:223-224.
14. Martin WJ: Detection of RNA sequences in cultures of a stealth virus isolated from the cerebrospinal fluid of a health care worker with chronic fatigue syndrome. *Pathobiology* 1997; 65: 57-60.
15. Martin WJ. Simian cytomegalovirus-related stealth virus isolated from the cerebrospinal fluid of a patient with bipolar psychosis and acute encephalopathy. *Pathobiology.* 1996;64:64-6.
16. Martin WJ. Stealth viral encephalopathy: report of a fatal case complicated by cerebral vasculitis. *Pathobiology.* 1996;64:59-63.
17. Martin WJ. Viteria: Bacterial sequences in animal and human viruses. *J Degenerative Diseases* 1999;1:7-10.

18. Balin BJ, Gerard HC, Arking EJ, Appelt DM, Braningan PJ, Abrams JT, Whittum-Hudson JA, Hudson AP: Identification and localization of Chlamydia pneumoniae in the Alzheimer's brain. *Med Microbiol Immunol* 1998;187:23-42
19. Sriram S, Mitchell W, Stratton C: Multiple sclerosis associated with Chlamydia pneumoniae infection of the CNS. *Neurology* 1998;50:571-572
20. Vojdani A, Choppa PC, Tagle C, Andrin R, Samimi B, Lapp CW. Detection of Mycoplasma genus and Mycoplasma fermentans by PCR in patients with Chronic Fatigue Syndrome. *FEMS Immunol Med Microbiol* 1998;22:355-65.
21. Chia JK, Chia LY. Chronic Chlamydia pneumoniae infection: a treatable cause of chronic fatigue syndrome. *Clin Infect Dis* 1999;29:452-3.
22. Nicolson GL, Nicolson NL: Chronic fatigue illness and Operation Desert Storm. *J. Occup Environ. Med.* 1995;38: 14-17.
23. Kaiser R: Neuroborreliosis. *J Neurol* 1998; 245:247-55.
24. Cassell GH: Infectious causes of chronic inflammatory diseases and cancer. *Emerg Infect Dis.* 1998;4: 475-487.
25. Martin WJ. Stealth adaptation of an African green monkey simian cytomegalovirus. *Exp Mol Pathol.* 1999;66:3-7.
26. Martin WJ. Melanoma growth stimulatory activity (MGSA/GRO-alpha) chemokine genes incorporated into an African green monkey simian cytomegalovirus-derived stealth virus. *Exp Mol Pathol.* 1999; 66:15-8.
27. Martin WJ, Anderson D. Stealth virus epidemic in the Mohave Valley: Severe vacuolating encephalopathy in a child presenting with a behavioral disorder. *Exp Mol Pathol.* 1999; 66:19-30.
28. World Wide Web URL: <http://www.ccid.org>
29. Holmes GP: Defining the chronic fatigue syndrome. *Rev Infect Dis* 1991, 13 (Suppl. I):S53-55
30. Schooley RT: Chronic fatigue syndrome: a manifestation of Epstein-Barr virus infection. *Curr Topic Infect Dis* 1988, 9:126-146.
31. Buchwald D, Cheney PR, Peterson DL, Henry B, Wormsley SB, Geiger A, Ablashi DV, Salahuddin SZ, Saxinger C, Biddle R, Kikinis R, Jolesz FA, Folks T, Balachandran N, Peter JB, Gallo Rc, Komaroff AL: A chronic illness characterized by fatigue, neurologic and immunologic disorders, and active human herpesvirus type-6 infection. *Ann Intern Med* 1992, 116:103-113.
32. Archard LC, Bowles NE, Behan PO, Bell EJ, Doyle D: Postviral fatigue syndrome: persistence of enterovirus RNA in muscle and elevated creatine kinase. *J Roy Soc Med* 1988, 81:326-329.
33. De Freitas E, Hilliard b, Cheney PR, Bell DS, Kiggundu E, Sankey D, Wroblewska Z, Pallandio M, Woodward Jp, Koprowski H: Retroviral sequences related to human T lymphocytotropic virus type II in patients with chronic fatigue immune dysfunction syndrome. *Proc Natl Acad Sci USA* 1991, 88:2922-2926.

34. Jones JF Epstein-Barr virus and the chronic fatigue syndrome: a short review. *Microbiol Sci* 1988;5:366-9.
35. Di Luca D, Zorzenon M, Mirandola P, Colle R, Botta GA, Cassai E. Human herpesvirus 6 and human herpesvirus 7 in chronic fatigue syndrome. *J Clin Microbiol* 1995;33:1660-61.
36. Behan PO, Behan WM, Gow JW, Cavanagh H, Gillespie S. Enteroviruses and postviral fatigue syndrome. *Ciba Found Symp* 1993;173:146-54.
37. Martin WJ. Stealth viruses as neuropathogens. *CAP Today*. 1994;8:67-70.
38. Martin W.J. Viral infection in CFS patients. In: "The Clinical and Scientific Basis of Myalgic Encephalomyelitis Chronic Fatigue Syndrome." Byron M. Hyde Editor. Nightingale Research Foundation Press. Ottawa Canada pp 325-327, 1992.
39. Tyrrell DAJ, Parry RP, Crow TJ, Johnstone E, Ferrier In: Possible virus in schizophrenia and some neurological disorders. *Lancet* 1979;i:839-41.
40. Mitchell DN, Porterfield JS, Micheletti R, Lange LS, Goswami KKA, Taylor P, Jacobs JP, Hockley DJ, Salsbury AJ. Isolation of an infectious agent from bone-marrow's of patients with multiple sclerosis. *Lancet* 1978;ii:387-391.
41. Melnick JL, Seidel E, Inoue YK, Nishibe Y. Isolation of virus from the spinal fluid of three patients with multiple sclerosis and one with amyotrophic lateral sclerosis. *Lancet* 1982;i:830-3.
42. Martin WJ, Glass RT. Acute encephalopathy induced in cats with a stealth virus isolated from a patient with chronic fatigue syndrome. *Pathobiology*. 1995;63:115-8.

ALL INFORMATION, DATA, AND MATERIAL CONTAINED, PRESENTED, OR PROVIDED HERE IS FOR GENERAL INFORMATION PURPOSES ONLY AND IS NOT TO BE CONSTRUED AS REFLECTING THE KNOWLEDGE OR OPINIONS OF THE PUBLISHER, AND IS NOT TO BE CONSTRUED OR INTENDED AS PROVIDING MEDICAL OR LEGAL ADVICE. THE DECISION WHETHER OR NOT TO VACCINATE IS AN IMPORTANT AND COMPLEX ISSUE AND SHOULD BE MADE BY YOU, AND YOU ALONE, IN CONSULTATION WITH YOUR HEALTH CARE PROVIDER.