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A Critical Review of the Human Immunodeficiency Virus (HIV) Infection and the Most Common Clinical Manifestations of Acquired Immune Deficiency Syndrome (AIDS)

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A CRITICAL REVIEW OF THE HUMAN IMMUNODEFICIENCY VIRUS (HIV)

INFECTION AND THE MOST COMMON CLINICAL MANIFESTATIONS OF

ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

by

Randy Willman
Bachelor of Science in Physical Therapy
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An Independent Study

Submitted to the Graduate Faculty of the

Department of Physical Therapy

School of Medicine

in partial fulfillment of the requirements
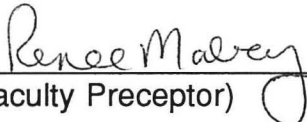
for the degree of

Master of Physical Therapy

Grand Forks, North Dakota
May
1994

This Independent Study, submitted by Randy Willman in partial fulfillment of the requirements for the Degree of Master of Physical Therapy from the University of North Dakota has been read by the Faculty Preceptor, Advisor, and Chairperson of Physical Therapy under whom the work has been done and is hereby approved.

_____
(Faculty Preceptor)

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(Graduate School Advisor)

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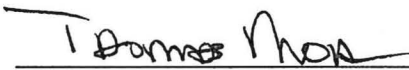

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ABSTRACT

The purpose of this independent study is to review the viral and immunologic factors in human immunodeficiency virus (HIV) infection and present the clinical manifestations most commonly associated with acquired immune deficiency syndrome (AIDS). As physical therapists, we will thus increase our knowledge base of this complex disease and understand the many opportunistic infections associated with HIV infection and the various aspects of AIDS. In addition, by having a better understanding of the disease, we may overcome our fears, improve our personal attitudes toward patients with HIV/AIDS, and improve and prolong the quality of life of individuals with the disease.

CHAPTER I

INTRODUCTION AND METHODOLOGY

No disease in modern time has had quite the impact on the civilized world as had acquired immunodeficiency syndrome (AIDS). In January 1992, the Centers for Disease Control (CDC) reported over one million Americans infected with the human immunodeficiency syndrome (HIV), 206,392 diagnosed with AIDS, and 133,232 having died from the disease.[1] AIDS is already a leading killer of men and women 15 to 44 years old in our country.[2] The scope of the HIV/AIDS pandemic is even more dramatic world wide. The World Health Organization (WHO) has estimated cumulative global total of HIV-infected adults and children as of 30 June 1993 is about 13 million, which means that, for the world population, one in every 250 adults has been infected with HIV.[3] WHO estimates that over 2.5 million cumulative AIDS cases have occurred to date, whereas over 50% of reported AIDS cases are from developed countries, about 80% of all estimated AIDS cases are from the developing world.[4] Although the outlook in the near future is promising for curative treatment or effective vaccine, the National Commission of AIDS states "even if a cure were found tomorrow the sequelae of the disease would still affect our communities for 10 to 15 more years."[5]

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Amid the social and political upheaval precipitated by the HIV/AIDS pandemic, a critical problem has silently but steadily emerged: Who is to provide care for the increasing numbers of afflicted individuals? There is a demanding need for more professionals to become active in both prevention and treatment of the HIV disease. Although few practitioners have denied their responsibility to provide care, there is a reluctance on the part of some to actively participate. Caring for those with HIV infection entails a risk. There is little doubt that the consequences of contracting AIDS are very grave, and it understandable that health care workers, physical therapist among them, may experience intense anxiety and fear.

The purpose of this independent study is to review the biology and epidemiology of HIV infection and the most common clinical manifestations of the virus. The study will allow the physical therapist an opportunity to understand the disease process and make an important contribution to people with HIV in all disease stages--acute, chronic, and terminal.

The methodology employed a review of existing literature, beginning with a Med-lin computer search. Other sources reviewed included textbook materials, government reports, and a personal interview with an HIV/AIDS individual.

CHAPTER II

HISTORY AND EPIDEMIOLOGY

Although misunderstanding, fear, and discrimination still surround HIV and AIDS, much has been learned. The earliest known case of death from AIDS occurred in 1959.[6] A paper published in Lancet, 1990, states the human immunodeficiency virus was found in the tissues of a 25-year-old seaman from northwestern part of Manchester, England who died of pneumonia in 1959.[6] The seaman's wife and three youngest daughters appear to also have been infected, as they died of similar symptoms some years later. Other early cases of HIV infection were in three members of a Norwegian family who developed AIDS in the 1960s and died in 1976.[6] Antibodies to the virus were found in the blood of an individual from Zaire, Africa also in 1959, but it is not known if the patient died from AIDS.[6] From analysis of the infection rates in Africa, it is thought that HIV has existed in Africa for 30 to 40 years.[6]

The most prominent theory of how the virus started follows. In the 1950s American doctors were testing a vaccine intended to wipe out the polio virus; the vaccine was contaminated by the simian immunodeficiency virus (SIV).[7] The contaminated polio vaccine was administered to at least 325,000 Central Africans; it is hypothesized that after a series of mutations in humans, the virus

established itself into its present deadly form.[7] The SIV is from a family of relatively harmless primate retroviruses that is endemic in green monkeys of equatorial Africa and closely related to the AIDS virus.[8]

The epidemiology of HIV has become clearer and has been discussed by a number of authorities in the United States. The Center for Disease Control (CDC) has led the epidemiological investigation of AIDS. The disease that became known as acquired immunodeficiency syndrome (AIDS) was first reported in a 1981 Morbidity and Mortality Weekly Report, published by the CDC.[9] In 1983, scientists working at the Pasteur Institute, Paris, isolated a retrovirus from the lymph node of person with AIDS-related symptoms.[10] In 1985, epidemiologic and virologic studies confirmed a ribonucleicacid (RNA) retrovirus as human immunodeficiency virus (HIV) and confirmed HIV as the causal agent associated with the development of AIDS.[10] HIV-1, a retrovirus, is related to a family of lentiviruses that generally cause chronic, indolent infections characterized by a long clinical latency period, nervous system involvement, and persistent viremia.[11]

CHAPTER III

BIOLOGY

Pathogenesis

The cellular events and reactions of HIV infection have become clearer and have been discussed by a number of authorities in the United States.[12-14] The causative agent of HIV is now known to be one of the human retrovirus that selectively infects CD4 lymphocytes and monocyte/macrophages.[15] The structure, genetic composition, and major proteins of HIV have been identified, and its basic pathophysiology defined. This chapter will cover the more important features of the pathologic mechanisms occurring in the development of the HIV disease.

Viruses are packets of infectious nucleic acid surrounded by protective coats. In a virion, the viral nucleic acid is covered by a protein capsid, which protects it from enzymatic attack and mechanical breakage and delivers it to a susceptible host.[16] The capsid itself is surrounded by an envelope containing membrane lipids and glycoproteins. The HIV virion (Figure 1) is enveloped by a lipid bilayer membrane containing two glycoproteins: gp41 and gp120.[16-18] The external envelope protein (gp120) is associated with small protrusions or spikes on the outer surface of the virion and is attached to the viral capsid via
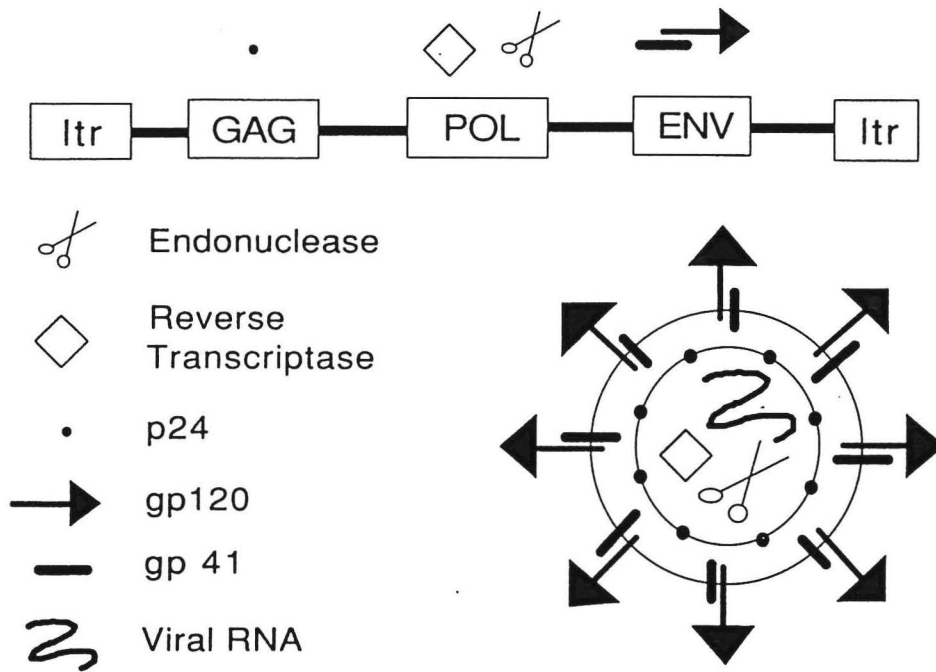
Figure 1. Structure and genetic composition of HIV. (Courtesy of Jon Fuller, MD, Boston City Hospital)

the transmembrane protein, gp41.[19] The glycoprotein gp41 spans the membrane and is disulfide-bonded to gp120, which is located on the external face.[16-19]

Retroviruses are enveloped and possess a single strand of ribonucleic acid (RNA).[20] All are characterized by their ability to serve as a template for production of deoxyribonucleic acid (DNA) in host target cells.[16,18,19] This reverse transcription is accomplished through possession of an enzyme. Reverse transcriptase, a DNA polymerase, translates a single strand of RNA into a double-stranded DNA copy.[16,18-20] An additional viral enzyme, an endonuclease, incorporates this DNA copy into the chromosomal structure of the target cell as a provirus.[21]

HIV Structure and Genetic Composition

HIV is composed of a central cylindrical core of diploid (two chromosomes) RNA surrounded by a spherical lipid envelope.[22] The viral genome (DNA and RNA) consists of three structural components: pol, gag, and env (Figure 1) which are essential for productive infection.[18,23,24] The gag gene (proteins) make up the core and the phosphoproteins that are found inside the nucleoid. The protein gag codes for p24, which is found in the core and surrounds the viral RNA. Gag or p24 also codes for other proteins, including p17, p9, and p7.[16,19,21] p24 is measurable in the serum and serves as a marker for viral replication.[16,19,21] Pol codes for the reverse transcriptase (RNA-directed DNA polymerase), which is responsible for the production of both the DNA

polymerase and endonuclease located in the viral core.[16,21] The env gene products include two glycoproteins that are part of the viral envelope: gp120 and gp41. Both proteins appear to be important for the recognition and attachment of HIV to its CD4 lymphocyte target cell.[24,25] These genes are located between long terminal repeat (ltr) segments. LTRs carry multiple signals--enhancers, promoters, and polyadenlylation sites--for the expression of retroviral genes.[16]

HIV also possesses genes that code for proteins having important regulatory functions.[24,26] The tat (transactivator) gene is responsible for production of a protein that enhances viral replication through its interaction with long terminal repeats at either end of the genome. Rev (regulator of expression) of virion proteins codes for the mechanism that results in the discontinuation of regulatory protein production and increased production of structural proteins. Vif (virion infectivity factor) codes for a protein that appears important for the budding of viral progeny from the surface of the host cells and their subsequent infectivity.

Pathophysiology of HIV Infection

The pathophysiology of HIV relates to its ability to infect human cells that possess CD4 membrane receptors. The host cell for HIV is the T4 lymphocyte, a vital contributor to the immune response; this lymphocyte was named for an antigen present on its surface. Major target cells include monocytes, macrophages, and their hematologic precursors.[27] Other cell types, including

Langerhan's cells of the skin, epithelial gut cells, and uterine cervical cells, have also been identified as harboring HIV infection.[21]

CD4 receptors have a binding site capable of interacting with two envelope proteins that are a part of the viral envelope. These include gp41, the transmembrane protein, and gp120 which protrudes from the envelope (Figure 2) and is closely associated with but not covalently linked to gp41.[18,22] Through this proposed mechanism for HIV infection of a cell, the outside viral envelope protein, gp120, attaches to a cell surface receptor, most likely the CD4 antigen. The external portion of the transmembrane protein, gp41, attaches to a proposed specific fusion receptor on the cell surface. Either receptor may permit viral entry into the cell, but both together would make this event more efficient.[16,21] Once the virus is within the cytoplasm of the host cell, the envelope of the virus is shed, and its contents are released.[16,21] It is then that reverse transcription occurs: a double-stranded DNA is made from the viral RNA template. Newly created viral DNA can exist in either free form or it can be integrated through the action of an endonuclease and go into the cellular DNA as a provirus.[21,28]

Infected cells remain in a dormant state for a variable period of time and thus elude the host immune system possibly for years, a potential reason for long incubation periods.[27,28] When activations occur, the proviral DNA transcribes genomic and messenger RNA, leading to release of infectious progeny.[21,29] After viral proteins are synthesized, new virions are assembled
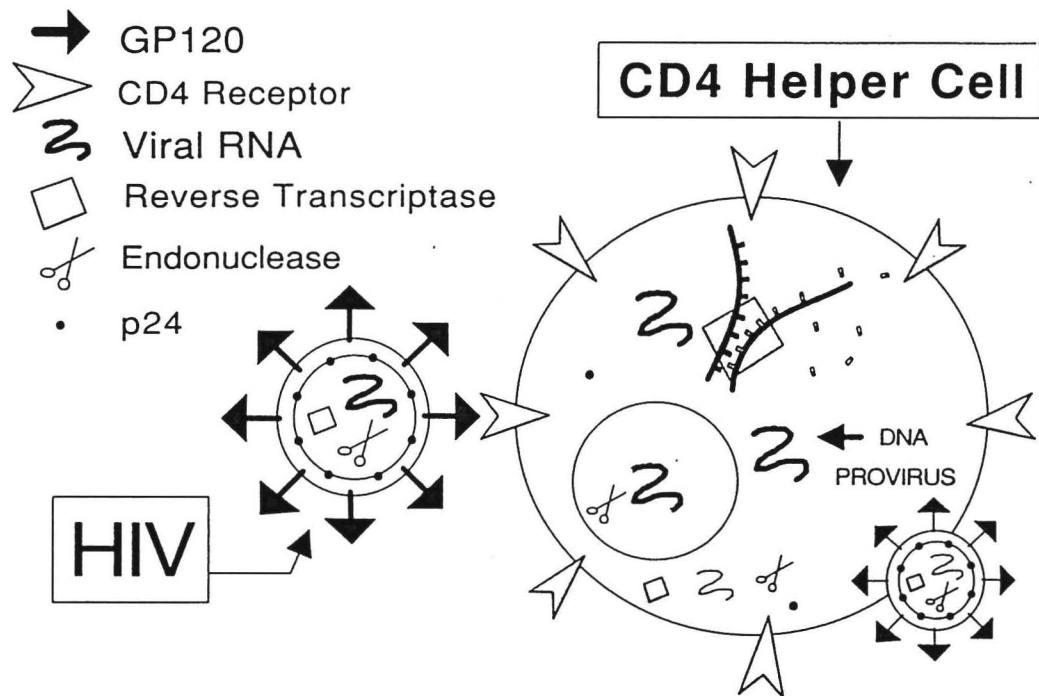
Figure 2. HIV/CD4 lymphocyte interaction. (Courtesy of Jon Fuller, MD, Boston City Hospital)

that bud from the infected cell and circulate until they identify new target cells.[21,29] These infected cells can then spread the virus through production of infectious progeny or by fusion with uninfected cells.[30] This latter cell-to-cell interaction is important because it permits the transfer of viral information into an uninfected cell and avoids exposure of the newly formed viruses to neutralizing antibodies.[21,28,29]

The initial studies of the AIDS virus revealed its presence in peripheral blood cells, particularly T-helper lymphocytes.[31-33] Subsequently, HIV was recovered from macrophages and was shown to infect a variety of other human cells, including B lymphocytes, promyelocytes, fibroblast, and epidermal Langerhans cells.[34-37] Therefore, the presence of the CD4 receptor appears to explain the susceptibility of many cells to HIV. Monocytes and macrophages serve an important role in the pathogenesis of HIV infection.[38] Once infected, they appear to be tolerant of viral replication, surviving to disseminate virus to a variety of body sites. Thus, these cells serve as an important source of immunologically protected new virus.[21] It is generally accepted that monocyte and macrophage function appears to be compromised to some degree by HIV infection, contributing further to immunosuppression.

HIV affects the central nervous system (CNS) in a complex and incompletely understood manner. It is thought that the HIV infected macrophages probably carry the virus into the CNS across the blood-brain barrier (Figure 3) by means of a "Trojan Horse" mechanism.[18,21,39] Once the
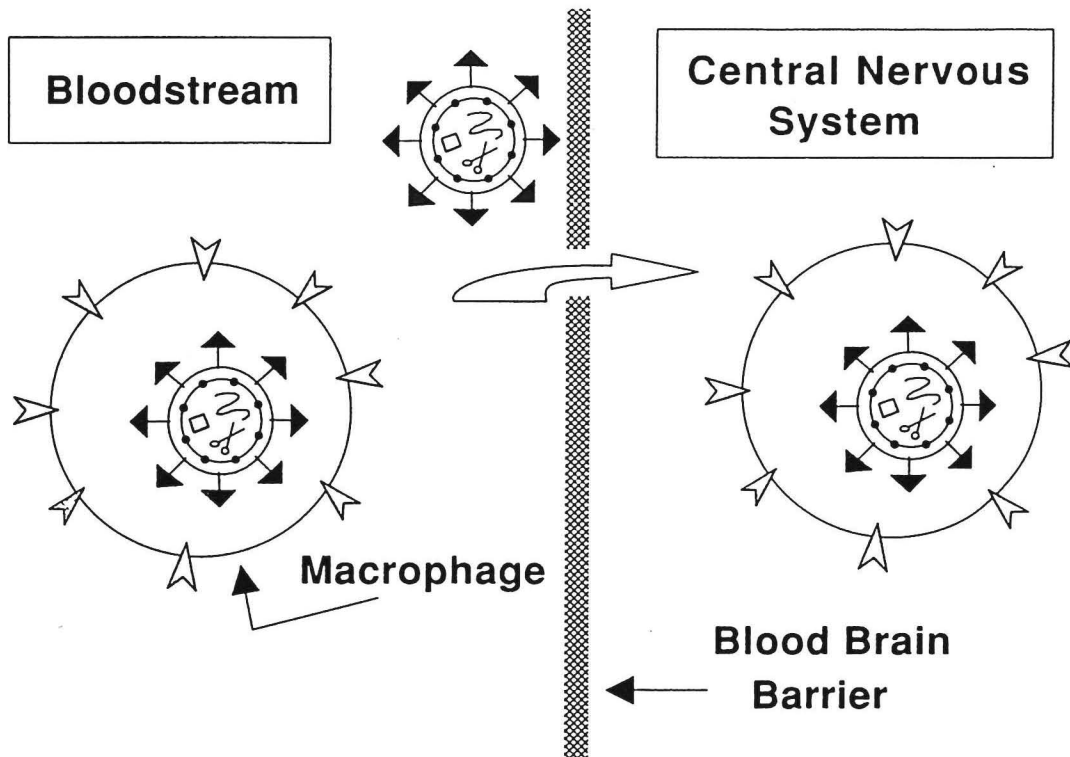
Figure 3. "Trojan horse" mechanism of central nervous system infection. (Courtesy of Jon Fuller, MD, Boston City Hospital)

virus gains access to the CNS, neurologic damage is likely to occur through several different mechanisms.[21] Although HIV does not directly infect neurons (Figure 4), infected macrophages may release toxic cytokines that are injurious to neurons "innocent bystander mechanism."[18,21,40] In addition, freely circulating gp120 may result in neuronal damage by affecting the integrity of the blood vessels supplying the nutrition or by interfering with normal calcium channel function.[18,21,28,38,39]

Response to HIV Infection and Stages of Infection

HIV infection elicits both cell-mediated and humoral immune responses from the host.[41] Soon after infection with HIV, there is a brief period of intense viral replication. During this time the patient is asymptomatic, but serologic testing reveals a rise in titer of p24 antigen during the humoral response.[21] The majority of individuals notice very few, if any, symptoms associated with seroconversion. An estimated 40% to 60% of individuals will develop symptoms of an acute mononucleosis-like syndrome, consisting of sore throat, headache, fever, myalgias, lymphadenopathy, and skin rash.[42-44]

The cellular immune response involves a decrease in absolute numbers of CD4 lymphocytes with increase duration of infection.[45] This drop is usually gradual for a prolonged period (clinical latency phase), with a more rapid decline associated with the onset of symptoms later in the course of the disease. The CD8 lymphocyte count generally increases early in HIV infection, and together with macrophages may act in concert to interfere with viral
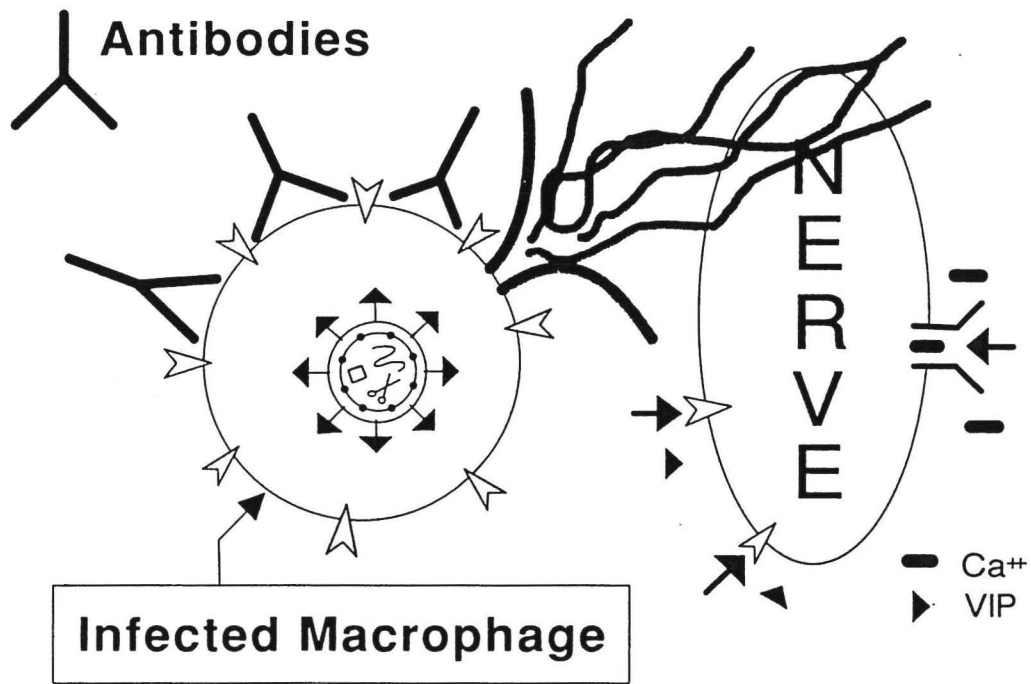
Figure 4. "Innocent bystander" mechanism of central nervous system infection. (Courtesy of Jon Fuller, MD, Boston City Hospital)

replication by production of a diffusible factor or by directly killing infected cells.[18,21,39,40] However, HIV infection is a chronic disease and in the end-stage both CD4 and CD8 cell lines become depleted. The loss of CD4 lymphocyte cells are associated with the development of the characteristic opportunistic infections and malignancies of AIDS. Thus the measurement of CD4-positive lymphocytes is one of the most important determinants for clinically staging the disease status of HIV-infected patients. The absolute CD4 count cannot be measured directly but is calculated by the following formula:[28]

```
Absolute    Total         Percent       Percent
CD4       = White Blood X Lymphocytes X CD4
Count       Count                       Cells
```

Normal values for CD4 counts are generally 800 to 1200 cells/mm^3 in adults, with fluctuations of as much as a 150 to 300 cell/mm^3 difference between morning and evening values in normal adult hosts.[28,46] Asymptomatic-lymphadenopathy may occur when the CD4 count drops below 800 cells/mm^3. When the CD4 cell count drops below 500 cells/mm^3, prophylaxis therapy is recommended in response to immune dysfunction and/or to secondary infections caused by opportunistic infections.[46]

HIV is characterized by evolving clinical and serological manifestations identified as predictors of HIV disease progression and the rate at which AIDS develops. The clinical manifestations usually depend on the stage of infection. Whether it is early infection with little immune dysfunction, or whether the infection has been present long enough to cause moderate or severe immune

impairment, HIV is a slowly progressive disease. A classification system for

these stages has been developed by the Center for Disease Control (Table 1).[47]

Table 1. CDC Classification of HIV Infection.

Group 1. Initial infection.
Group 2. Asymptomatic carriers.
Group 3. Persistent generalized adenopathy.
Group 4. AIDS and AIDS-related complex
Subgroup 4A.
     Constitutional symptoms
Subgroup 4B.
     Neurologic disease
Subgroup 4C.
     Secondary infectious disease
     Category 1 and 2
     Various opportunistic infections
Subgroup 4D.
     Secondary malignancies
Subgroup 4E.
     Other AIDS-related conditions

National Institute of Mental Health, 1991.

CHAPTER IV

FUNCTIONAL AND CLINICAL MANIFESTATIONS

The immune system is complex, with many types of defenses against infections. Understanding the effects of the HIV virus on the human immune system is the key to understanding the clinical problems of HIV patients. HIV infection is a highly lethal condition, with an average length of time from initial infection to development of AIDS of approximately 10 years and a survival time from the diagnosis of AIDS to death of approximately two to five years.[48,49] HIV is also known as a chronic disease with a fairly predictable pattern of evolution and clinical manifestations. A physical therapist may treat a person with HIV/AIDS who has several related conditions or opportunistic diseases. When the person with AIDS develops secondary neurologic, musculoskeletal, or cardiopulmonary complications the therapist provides physical therapy evaluation and treatment. It is important that the physical therapist obtains baseline data about the patient's state of being, state of fitness, and general strength. Table 2 is a summary of the common HIV signs and symptoms, and their possible causes of the HIV disease are presented.[21,28,46]

Table 2. Common Manifestations of HIV Disease

Signs and Symptoms	Possible Causes
SYSTEMIC	
Weight loss	AIDS-related wasting syndrome, enteropathy, depression
Tiredness	Wasting syndrome, anemia, opportunistic infection
Fever and night sweats	Primary HIV infection, TB, MAI, lymphoma
DERMATOLOGIC	
Discoloration	Kaposi's sarcoma, tinea corporis, basal cell carcinoma
Rash	Herpes zoster or simplex, psoriasis, molluscum contagiosum, pustular folliculitis, seborrhea, impetigo, drug reaction
ORAL	
White patches	Oral candidiasis, hairy leukoplakia, Herpes simplex, cytomegalovirus, Kaposi' sarcoma, aphthous ulcers
VISUAL	
Visual field optic	CMV or toxoplasma retinitis, syphilitic defects neuritis, progress multifocal leukoencephalopathy (PML)
FUNDOSCOPIC	
Retinal hemorrhage	CMV retinitis
Retinal infiltrates	Benign HIV disease, CMV, toxoplasma retinitis

Table 2 (cont.) Common Manifestations of HIV Disease

Signs and Symptoms	Possible Causes
LYMPH NODES	
Lymphadenopathy	AIDS-related lymphadenopathy, TB, KS syphilis, lymphoma, bacterial or viral infection
CARDIOPULMONARY	
Cough, dyspnea, SOB, tachypnea	Pneumocystis pneumonia, TB, bacterial fungal, or viral pneumonia, myocarditis, cardiomyopathy
HEMATOLOGIC	
Easy bruising, bleeding	Idiopathic thrombocytopenic purura, drug reaction, Kaposi's sarcoma
GASTROINTESTINAL	
Diarrhea	Bacterial or parasitic infection, CMV, KS, HIV-related enteropathy, food intolerance
Organomegaly	Lymphoma, TB, tumor, fungal infection (histoplasmosis), MAI
Anal pain or ulcer	HSV, sarcoma, CMV, Abscess
GENITOURINARY	
Genital lesions	Primary syphilis, HSV, chancroid, psoriasis, papillomavirus
NEUROLOGIC	
Headache	CNS toxoplasmosis, lymphoma, TB meningitis or cryptococcal, PML

Table 2 (cont.) Common Manifestations of HIV Disease

Signs and Symptoms	Possible Causes
Memory or thought deficits	AIDS encephalopathy, meningitis, PML, metabolic abnormalities, other organic disorders
Numbness/dysesthesia	Herpes Zoster, neuropathy, myelopathy
Ataxia	CNS toxoplasmosis, lymphoma, PML, syphilis, neuropathy, visual defect
Seizures	CNS toxoplasmosis, PML, CNS lymphoma, meningitis, encephalitis

Indicators of HIV Infection

In response to a growing awareness of the many manifestations of HIV infection, the CDC has changed the definition of AIDS to include encephalopathy, wasting syndrome, a CD4 count <200 cells/mm^3, invasive cervical cancer, recurrent pneumonia, and pulmonary tuberculosis.[46,50]

Neuropsychiatric Aspects of HIV Infection

The neuropsychiatric aspects of HIV infection present challenges for all health-care workers. HIV infects the body and brain, and it always affects the mind. Physical therapists will be increasingly faced with interpreting and integrating the impact of HIV on a person's central nervous system function. This section presents the neuropsychiatric manifestations of HIV-related disorders that are relevant to physical therapy treatment concerns. Many of the functional and organically based CNS disorders often affect the mental capacity, the quality of life, and the maintenance of autonomous function and independent living.

Many HIV-infected patients will have "mental symptoms" before they develop the better known opportunistic infections. Patients may complain early on of forgetfulness, mental slowing, social withdrawal, avoidance of complex tasks, and personality changes.[51] Inattentiveness, inability to concentrate, distractibility, and apathy may be subtle, and HIV patients may have accommodated slowly to changes without realizing it.[51]

Dementia (subacute encephalitis, neurocognitive syndrome) is defined as a complex of cognitive, motor, behavioral and affective abnormalities. Impairment in some or all of these four categories of function may be present at any time during the course of HIV disease.[52,53] People with HIV-infection may continue to have these mild deficits, which are differentially disabling depending on the patient's work or living situation, for long periods, without necessarily progressing to further impairment.[54] Others progress fairly rapidly from these signs to more disabling motor brain dysfunctions such as dysgraphia, dysarthria, hyperreflexia, spasticity, incontinence, ataxia, mutism, aphasia, myoclonus and seizures.[54] What is especially alarming to patients with HIV-related neurocognitive decline is that unlike the patient with Alzheimer's disease, the HIV person will retain intellectual function and consciousness of the self until quite late in the disease process.[54]

Delirium is reported as one of the most common psychiatric diagnoses among hospitalized, severely ill AIDS patients.[55] Delirium in the HIV-infected patient may result from secondary opportunistic infections and neoplasms.[54] Delirium is defined by DSM-IIIR with the general criteria as rambling, irrelevant, or incoherent speech; illusions, hallucinations, disorientation to time, place, or person; and reduced ability to maintain attention to external stimuli.[56]

Organic mood disorders are expressed commonly as grandiose ideation, delusions, mood swings, irritability, and personality changes. These symptoms are pathologic changes in the limbic system that may be caused by HIV

infection.[57,58] Adjustment disorders in HIV patients most common are anxiety and depression. Studies suggest that a depressive syndrome may be the precursor for the onset of a CNS infection and considered a reaction to HIV illness.[59,60]

Fatigue may be the presenting complaint of an underlying depression early in the course of HIV infection. In later stages of HIV infection, fatigue may be the result of chronic disease and is often perceived as untreatable.[54,57] As physical therapists, helping patients to learn about their energy levels and proportioning their energy according to tasks is essential.

Because the HIV epidemic is still relatively new, only a few related disability studies exist in the literature. Common problems among patients who were referred consecutively to a rehabilitation service included generalized deconditioning (27%) and neurologic dysfunction (45%).[61] Functional problems included impaired mobility (76%), difficulty with self-care (57%), impaired cognition (29%), and uncontrolled pain (37%).[61]

A more specific study documented the types and degrees of disability found in persons with AIDS at discharge from acute care hospitalization, based on the Functional Independence Measure (FIM).[62] The FIM was developed by the State University of New York, that covers 18 functional areas in self care, mobility, communication, and social cognition; eating; grooming; bathing; dressing (upper body); dressing (lower body); toileting, bladder management; bowel management; bed, chair, and wheelchair transfer; toilet transfer; tub or

shower transfer or both; walking or wheelchair locomotion; stair climbing;

comprehension; expression; social interaction; problem solving; and memory.[63]

Of the sample population, at least 60% required human assistance in one of the

18 functional areas; 32% in five or more areas.[63] Approximately 51% required

human assistance in stair climbing; 38% in ambulation; 33% in eating and

bathing; and 25% in transferring to the bathtub or shower.[63] These daily living

skills were further compounded by the loss of self-esteem, loss of community,

and often differentiation pain resulting from partial or complete damage to

afferent nerve pathways toward the central nervous system.[63,64]

<center>Neurological Complications of HIV Infection</center>

Although the loss of active daily living skills, psychiatric disorders, loss of

physical independence, and other problems are experienced, the most

significant disability faced by patients with HIV may be pain. The type of pain

depends on the disease process that is secondary to the HIV infection.

Potential etiologies of pain among patients with HIV include a wide variety of

rheumatologic, dermatologic, and musculoskeletal changes resulting from HIV-

related myopathy and muscle wasting syndrome.[63,65]

The etiologies of pain consists of chest pain related to pneumocystis

carinii pneumonia (PCP); abdominal pain from (HIV-related lymphadenopathy,

Kaposi's sarcoma, infectious diarrhea, organomegaly, ileus, and nonspecific

gastritis); headache pain due to toxoplasmosis, CNS lymphoma, cryptococcus

meningitis; midsternal burning or dysphagia from herpes simplex,

cytomegalovirus, candidiasis, infection; and low back pain may result from malignant lymphomas.[63,65-67] These neurologic complications may evolve acutely, during the asymptomatic phase, or during late nervous system involvement by the HIV infection.

Additional neurological complications in the 200 to 500 CD4 cell/mm^3 count may result in meningitis, ataxia, myelopathy, cranial neuropathy (CN V, VII, VIII), and brachial plexopathy.[68] During the latent phase of HIV infection a demyelinating neuropathy that resembles Guillain-Barre' syndrome and a multiple sclerosis-like illness have been reported.[69-71]

It has been estimated that up to 80% of all persons with HIV will have some type of CNS or peripheral nervous system (PNS) involvement prior to death.[72] PNS dysfunction among patients with HIV may have multiple etiologies in addition to the HIV infection itself, including malnutrition, immobility, opportunistic infections, wasting syndrome, and drug toxicities.

Distal symmetric polyneuropathy (DSPN) is one of the most common forms of neuropathy in patients with AIDS. DSPN may be described as a progressive, painful neuropathy with prominent dysesthesia and areflexia with or without mild muscle weakness.[73] Dysesthesias may be burning and constant. The patient may report numbness or tingling in the toes that spread proximally; later there may be finger and upper extremity involvement.[54,57,66,73] Tropic changes may occur in distal areas of the skin, and muscle weakness varies; generally it is mild, affecting the intrinsic foot muscles.[54,57,64,73] Distal reflexes

are hypoactive or absent but may be present at the knees or in the upper extremities.[54,64,73] Sensory dysfunction is usually moderately impaired.[54,64,73] Pathological studies suggest a retrograde process within the dorsal root ganglia neurons and a degeneration of gracile tracts of spinal cord (mostly upper thoracic or cervical cord segments).[64]

Chronic inflammatory demyelinating polyneuropathy (CIPD) is also a consequence of HIV infection in the peripheral nervous system. This syndrome is characterized by weakness in both proximal and distal muscles of the upper and lower extremities. Reflexes may be sluggish or absent.[54,68] Finally, the above symptoms of disease must be differentiated from medication side effects.

Zidovudine (formerly called azidothymidine, or AZT), and dideoxyinosine (DDI or ddi) are commonly used antiviral drugs that inhibit the replication of retroviruses, including HIV.[72] The most common candidates for drug therapy are patients with asymptomatic and symptomatic HIV infection who have a CD4 cell count <500 cells/mm^3.[74,75] Side effects from AZT may include: headaches, insomnia, nausea, vomiting, abdominal discomfort, diarrhea, malaise, myalgia, rash, fever, and severe anemia.[54,65,75] DDI, typically prescribed for patients who cannot tolerate AZT, has some of the same side effects; it may also cause sensory peripheral neuropathy in the feet and pancreatitis symptoms.[54,65,75]

CHAPTER V

SUBJECTIVE AND OBJECTIVE FINDINGS

Despite a decade of progress in understanding the molecular virology and pathophysiology of the human immunodeficiency virus, the disease caused by infection with this retrovirus remains incurable. As increasing numbers of individuals have taken heed and have determined that they are, in fact, infected with the retrovirus, they remain baffled by the lack of effective therapies.[76]

The physical therapist faces multiple challenges when providing care to this population. Of particular concern to physical therapists are the neurological, psychological, musculoskeletal, cardiovascular, cardiopulmonary, and nutritional effects of the disease. It is, at times, difficult to correlate specific clinical signs of the disease with specific pathology because HIV has an impact on all systems at variable rates of progression. This places the physical therapist squarely in the health arena and PTs may be the first care provider to see indications of HIV infection.

Good patient care requires that the diagnosis of HIV infection be made at the earliest possible time. As with any patient, treatment should be based on an accurate and appropriate assessment of the symptoms and on the patient's

past and present medical history. The choice of treatment rests in the HIV knowledge base and in the manifestation and interpretation of symptoms.

Even without evidence of gross clinical neurological symptoms or signs, a physical therapist should have a basic understanding of the immune system to recognize manifestations of the HIV disease. Pertinent information may be gathered during the *SUBJECTIVE and OBJECTIVE* phases of the evaluation.

During the subjective information gathering client history may reveal symptoms of unexplained weight loss, persistent diarrhea, night sweats, recurrent fever, swollen glands, decreasing vision with eye pain, bleeding gums, mouth sores, pain on swallowing, recent onset of headaches, easy tiring, and irritability. There may be a loss of interest in friends and unusual activity.[77-80]

Physical signs that may be directly observed by the therapist doing an objective evaluation include severe dandruff and acne, skin rashes, purplish spots, facial warts, ill-fitting clothes from weight loss, increased tone, unsteady gait. Manifestations of infections that may coexist with HIV infections are herpes (weeping skin lesions), hepatitis B (nausea and yellow eyes), tuberculosis (productive cough, night sweats, and weight loss), and shingles (angry painful rash).[77-80]

Effects on the musculoskeletal system not previously stated in this paper may include an array of pain syndromes, postural deficits, and decreases in work function capacity related to progressive weight loss and resultant fatigue.[81] Even when symptoms are lacking, motor abnormalities can almost always be

detected early in the course of the disease. Motor abnormalities include slowing of rapid successive and alternating movements of the extremities, impaired ocular smooth pursuits, and saccadic eye movements.[68] Abnormal reflexes may also be present, with generalized hyperreflexia and the development of release signs such as snout, glabellar, and grasp responses.[68,80,82,83] As the disease evolves, ataxia and, subsequently, leg weakness limits walking. Bladder and bowel incontinence is common in the late stages of the disease.[68,77,78,80,82,83]

In addition to obtaining musculoskeletal and neurological subjective and objective data, a physical therapist must also be concerned with the cardiovascular, pulmonary, and nutritional systems and the psychological implications for patients with HIV. These systems have ever changing variables that depend on the type of opportunistic infection(s) involved, the adequacy of nutrition, the level of pain, and the level of cognitive functioning.[84] Further discussion of these systems concerning medical aspects of HIV infection is beyond the scope of this independent study.

CHAPTER VI

CONCLUSION

Acquired Immunodeficiency Syndrome is now an epidemic in the United States, and all sectors of society are being affected. The care of HIV/AIDS infected patients is demanding. Thus, raising concerns among health care workers about safety, competence, and care requires both high-quantity and high-quality of time to treat this special population. As physical therapists we are in key positions to identify and intervene in the changes and losses commonly experienced by this unique disease.

The physical therapist is an important contributor at all stages of the disease. When the person with HIV develops neurologic, musculoskeletal, or cardiopulmonary complications as a result of AIDS, The PT provides baseline data about the patient's state of fitness and function through evaluations and treatments. Therefore, physical therapists have the opportunity to apply their therapeutic skills to improve function, mobility, endurance, and safety. They can also communicate the importance of healthy living and physical fitness and identify potential problems before they erode the patient's confidence and independence. Physical therapy can be an effective method to help meet the needs of this complex population.

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HIV has altered forever the ways in which we think about and act on life and living. Therefore, a solid understanding of HIV pathogenesis and a general working knowledge of signs and symptoms of HIV/AIDS are indispensable. As physical therapists we face multiple challenges when providing care to patients with HIV disease. There is a clearly articulated responsibility to take action to strengthen our personal and professional character, values, and integrity. Furthermore, we need to become role models in health care and participate in the forming of the future -- namely to "influence our professional evolution through our own awareness." The final and most obvious reason for physical therapists to become more involved in HIV/AIDS health care is the clear need of all patients for expert, comprehensive, and efficient care.

REFERENCES

1.   In: Morbidity and Morality Weekly Report. 1992;41(2):28-29.

2.   Centers for Disease Control and Prevention. Surgeon General's Report to the American Public on HIV Infection and AIDS. Health Resources and Services Administration National Institutes of Health; 1993:1-25.

3.   Global Programme On AIDS. Current and Future Dimensions of the HIV/AIDS Pandemic. WHO. January 1992:1-15.

4.   Global Programme On AIDS. The Current Global Situation of the HIV/AIDS Pandemic. WHO. July 1993:1.

5.   Coyne C. It need not be this way. Clinical Management in Physical Therapy. 1992;12(6):51-53.

6.   Concar D. How did it begin? (acquired immunodeficiency syndrome). Nature. 1990;346:92.

7.   World Health Organization. The AIDS Situation-1993. Grand Forks Herald. Oct 23, 1993.

8.   Raven PH, Johnson GB. Biology. St. Louis, Mo: Times Mirror/Mosby College Publishing; 1986:332.

9.   Goldsmith MF. AIDS activities: from day 1 to "something big" AIDS. JAMA. 1990;263:2584-2586.

10.   Henry WK. Essential HIV/AIDS facts: what you need to know in 1992. Post Grad Med. 1992;91(8):84-92.

11.   Barre-Sinoussi F, Chermann JC, Rey F, et al. Isolation of a T-lymphotropic retrovirus form a patient at risk for acquired immune deficiency syndrome (AIDS). Science. 1983;220:868.

12.   Cheng-Mayer C, Seto D, Tateno M, et al. Biology features of HIV-1 that correlate with virulence in the host. Science. 1988;240:80.

13.   Cooper DA, Imrie AA, Penny R. Antibody response to human immunodeficiency virus after primary infection. J Infect Dis. 1987;155:1113.

14.   Fahey JL, Taylor JMG, Detels R, et al. The prognostic value of cellular and serologic markers in infection with human immunodeficiency virus type 1. N Engl J Med. 1990;322:166.

15.   O'Brain TR, Shaffer N, Jaffe JW. Acquisition and transmission of HIV: AIDS and HIV infection in office practice. Primary Care. 1992;95:1-5.

16.   Stryer L. Biochemistry. 3rd ed. Stanford University: W.H.Freeman and Company, New York; 1988:851-879.

17.   Yarchoan R, Mitsuya H, Broder S. Clinical and basic advances in the antiretroviral therapy of human immunodeficiency virus infection. Am J Med. 1989;87:191.

18.   Fuller J. Pathophysiology of infection. Primary Care. 1992;19(1):2-6.

19.   Levy JA. The multifaceted retrovirus. Cancer Res. 1986;46:5457.

20.   Varmus H. Retrovirus. Science. 1988;240:1427.

21.   Libman H. Pathogenesis, natural history, and classification of HIV infection. Primary Care. 1992;19(1):1-9.

22.   Greene WC. Mechanisms of disease: the molecular biology of human immunodeficiency virus type 1 infection. N Engl J Med. 1991;324:308.

23.   Essex M, Allan J, Kanki P, et al. Antigens of human T-lymphotropic virus type III/lymphadenopathy-associated virus. Ann Intern Med. 1985;103:700.

24.   Kieny MP. Structure and regulation of the human AIDS virus. J AIDS. 1990;3:395.

24.   Dalgleish AG, Beverley PCL, Clapham PR, et al. The CD4 (T4) antigen is an essential component of the receptor of the AIDS retrovirus. Nature. 1984;312:763.

25.   Klatzmann D, Champagen E, Chamaret S, et al. T-lymphocyte T4 molecule behaves as the receptor for human retrovirus LAV. Nature. 1984;312:767.

26.	Cullen BR, Greene WC. Regulatory pathways governing HIV-1 replication. Cell. 1989;58:423.

27.	Ho DD, Pomerantz RJ, Kaplan JC. Pathogenesis of infection with human immunodeficiency virus. N Engl J Med. 1987;5:278.

28.	Sande MA, Volbending PA. The Medical Management of AIDS. 3rd ed. San Francisco, Calif: Burroughs Wellcome Company; 1992:33-44.

29.	Gelderblom HR, Hausmann EHS, Ozel M, et al. Fine structure of human immunodeficiency virus (HIV) and immunolocalization of structural proteins. Virology. 1987;156:171.

30.	Lifson JD, Feinberg MB, Reyes GR, et al. Induction of CD4-dependent cell fusion by the HTLV-III/LAV envelope glycoprotein. Nature. 1986;323:725.

31.	Barre-Sinoussi F, Nugeyre M, Dauguet C, et al. Isolation of a T-lymphotropic retrovirus from a patient at risk for AIDS. Science. 1986;220:868.

32.	Levy JA, Hoffman AD, Krammer SM, et al. Isolation of lymphocytopathic retroviruses from San Francisco patients with AIDS. Science. 1984;225;840.

33.	Gallo RC, Salahuddin SZ, Popovic M, et al. Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS. Science. 1984;224:500.

34.	Levy JA, Kaminsky LS, Morrow WJ, et al. Infection by the retrovirus associated with AIDS. Ann Intern Med. 1985;103:694.

35.	Levy JA, Shimabukuro J, McHugh T, et al. AIDS-associated retroviruses (ARV) can productively infect other cells besides human T helper cells. Virology. 1985;147:441.

36.	Tateno M, Gonzalez-Scarano F, Levy JA. The human immunodeficiency virus can infect CD4-negative human fibroblastoid cells. Proc Natl Acad Sci USA. 1989;86:4287.

37.	Tschachler E, Groh V, Popovic M, et al. Epidermal Langerhans cells: a target for HTLV-III/LAV infection. J Invest Dermatol. 1987;88:233.

38. Ho DD, Rota RT, Hirsch MS. Infection of monocyte/macrophages by human T lymphotropic virus type III. J Clin Invest. 1986;77:1712.

39. Gendelman HE, Leanord HE, Dutko FJ, et al. Immunopathogenesis of human immunodeficiency virus infection in the central nervous system. Ann Neurol. 1988;23(suppl):78.

40. Levy RM, Bredesen DE. Central nervous system dysfunction in acquired immunodeficiency syndrome. J Acquir Immune Defic Syndr. 1988;1:41.

41. Fauci AS, Schnittman SM, Poli G, et al. Immunopathogenic mechanisms in human immunodeficiency virus infection. Ann Intern Med. 1991;114:678.

42. Henderson DK, Saah AJ, Zak BJ, et al. Risk of nosocomial infection with human T-cell lymphotropic virus type III/lymphadenopathy-associated virus in a large cohort of intensively exposed health care providers. Ann Intern Med. 1986;104:644-647.

43. Joline C, Wormser GP. Update on a prospective study of health care providers exposed to blood and body fluids of acquired immunodeficiency syndrome patients. Am J Infect Control. 1987;15:86.

44. Ruprecht RM, O'Brien LG, Rossoni LD, Nusinoff-Lehrman S. Suppression of mouse viraemia and retroviral disease by 3'-azido-3'-deoxythymidine. Nature. 1986;323:467-469.

45. Lane HC, Masur H, Gelmann EP, et al. Correlation between immunologic function and clinical subpopulations of patients with the acquired immune deficiency syndrome. Am J Med. 1985;78:417.

46. AIDS NEWSLINK. Mountain-Plains Regional AIDS ETC. University of Colorado Health Sciences Center, Denver, Colo. Winter 1993.

47. TABLE 1. National Institute of Mental Health Grant No. NIMH 5427-0425. Washington, D.C.; 1992.

48. Moss AR, Bacchetti P. Natural history of HIV infection. AIDS. 1989;3:55-61.

49. Wenger JD, Whalen CC, Lederman MM, et al. Prognostic factors in AIDS. J General Intern Med. 1988;3:464-470.

50. Centers of Disease Control. Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. MMWR. 1987;36(1S):3S-15S.

51. Knox MD, Charles FC. Early HIV detection: a community mental health role. J Mental Health Adm. 1991;18(1):21-26.

52. Blumm OF. Subcortical dementia: a clinical approach. In: Mayeux R, Rosen WG (eds). The Dementias. New York, NY: Raven Press; 1983.

53. Cummings JL, Benson DF. Subcortical dementia: a review of an emerging concept. Arch Neurol. 1984;41:874-879.

54. Forstein M. The neuropsychiatric aspects of HIV infection: AIDS and HIV in office practice. Primary Care. 1992;;19(1):97-117.

55. Perry SW, Tross S. Psychiatric problems of AIDS inpatients at the New York Hospital: preliminary report. Public Health Report. 1984;99:200-205.

56. Diagnostic and Statistical Manual of Mental Disorders, ed IIIR. American Psychiatric Association, Washington, DC; 1987.

57. Forstein M, Baer J. HIV infection. In: Sederer L (ed). Inpatient Psychiatric-Diagnostic and Treatment. Baltimore, Md: Williams & Wilkins. 1991;19-211.

58. Kerman E, Drab S, Alpert M. Organic brain syndrome in three cases of AIDS. Compr Psychiatry. 1984;25:294-297.

59. Dilley JW, Macks J. Secondary depression in patients with AIDS. In: International Conference on AIDS. Paris, France; 1986; abstract.

60. Holland JC, Tross S. The psychosocial and neuropsychiatric sequelae of the acquired immunodeficiency syndrome. Ann Intern Med. 1985;103:760-764.

61. O'Connell PG, Levinson SF. Experience with rehabilitation in acquired immunodeficiency syndrome. Am J Phys Med Rehabil. 1991;70:91-95.

62. O'Dell MW, Bohi ES, Bonner SJ. Disability in persons hospitalized with AIDS. Am J Phys Med Rehabil. 1991;70:191-195.

63. Galantino ML, McReynolds M. The ever-changing challenge of HIV. Clinical Management. 1992;12(6):29-33.

64. Vinter H, Anders K. Neuropathology of AIDS. Boca Raton, Fla: CRC Press Inc.; 1990:23-26.

65. Galantino ML, McCormack G. Pain management. In: Galantino ML, ed. Clinical Assessment and Treatment in HIV: Rehabilitation of a Chronic Illness. Thorofare, NJ: SLACK,Inc; 1992:101-104.

66. Brew BJ. Medical management of AIDS patients: central and peripheral nervous system abnormalities. Med Clin North Am. 1992;76(1):63-81.

67. Fox R, Eldred LJ, Fuchs EJ, et al. Clinical manifestation of acute infection with HIV in a cohort of gay men. AIDS. 1987;1:35-38.

68. Worley JM, Price RW. Management of neurologic complications of HIV-1 infection and AIDS. In: The Medical Management of AIDS. 3rd ed. San Francisco, Calif: Burroughs Wellcome Company; 1992:193-215.

69. Cornblath DR, McArthur JC, Kennedy PGE, et al. Inflammatory demyelinating peripheral neuropathies associated with human T-cell lymphotropic virus type III infection. Ann Neurol. 1986;21:32-40.

70. Berger JR, Sheremah WA, Resnick L, et al. Multiple sclerosis-like illness occurring with HIV infection. Neurology. 1989;39:324-329.

71. Gray F, Chimelli L, Mohr M, et al. Fulminating multiple sclerosis-like leukoencephalopathy revealing HIV infection. Neurology. 1991;41:105-109.

72. Scherer P. How HIV attacks the peripheral nervous system. Am J Nurs. 1990;5:66-70.

73. Cornblath DR. Treatment of the neuromuscular complications of human immunodeficiency virus infection. Ann Neurol. 1988;23:588-591.

74. Fischl MA, Richman DD, Hansen N, et al. The safety and efficacy of zidovudine (AZT) in the treatment of subjects with mildly symptomatic human immunodeficiency virus type 1 (HIV) infection: a double-blind, placebo-controlled trial. Ann Intern Med. 1990;112:727-737.

75. Meng TC, Fischl MA, Boota AM, et al. Combination therapy with zidovudine and dideoxycytidine in patients with advanced HIV infection: a phase I/II study. Ann Intern Med. 1991;116:13-20.

76. Personal Interview: AIDS patient. November 14, 1993.

77. Redfield RR, Burke DS. HIV infection: the clinical picture. Sci Amer. 1988;259:90-98.

78. Horwath E, Kramer M, Cournos F, et al. Clinical presentation of AIDS and HIV infection in state psychiatric facilities. Hospital Community Psych. 1989;40:502-506.

79. Redfield RR, Wright DC, James WD, et al. Disseminated vaccinia in a military recruit with HIV disease. N Engl J Med. 1989;316:673-676.

80. Navia BA, Jordan BD, Price RW. The AIDS dementia complex I: clinical features. Ann Neurol. 1986;19:517-524.

81. Nath A, Jankovic J, Pettigrew LC. Movement disorders and AIDS. Neurology. 1987;37:37-41.

82. Simpson DM, Wolfe DE. Neuromuscular complications of HIV infection and its treatment. AIDS. 1991;5:917-926.

83. Snider WD, Simpson DM, Nielsen S, et al. Neurological complications of acquired immunodeficiency syndrome. Analysis of 50 patients. Ann Neurol. 1983;14:403-418.

84. Galantino MA, Harris MH. HIV comparing children and adults. Clinical Management. 1992;12(6):78-83.