AIDS: Ocular and Systemic Manifestations

Gary S. Yee
and
Anthony D. Spitler

April 9, 1993

Adjunct Faculty
Douglas L. Totten, O.D.
Ferris State University
College of Optometry

To this date, only five human retroviruses have been isolated. Only Human immunodeficiency virus I (HIV-1) and Human immunodeficiency virus II (HIV-2) are known to cause Acquired Immunodeficiency Syndrome (AIDS). Human T cell leukemia virus I (HTLV -I) is associated with T cell leukemia/lymphoma and tropical spastic paraparesis. HTLV-II was first isolated from a individual with hairy cell leukemia. HTLV-IV was first isolated from a patient with lymphoma. HTLV-II and HTLV-IV has not been associated with any known human disease.

The first case of human immunodeficiency was reported in 1959 involving a British seaman (1,2). There have been many reported cases of HIV seropositive individuals from Africa dating back to the 1960's and 1970's (2). In June of 1981, the Center for Disease Control (CDC) reported a cluster of immunodeficient men around the Los Angeles area. In 1983, a French scientist isolated the HIV-1, two years after the first case of immunodeficiency syndrome appeared in medical literature. In 1984, an American team linked that virus to the AIDS (2, 4, 5). The DNA sequence was first identified in 1985. Human immunodeficiency virus II was first isolated in 1985 from a Portuguese man living in Cape Verde Island (2, 4, 5). That individual had symptoms of HIV-1 (immune suppression and lymphadenopathy), without the HIV-1 infection. Antibodies to HIV-2 has been isolated from individuals from Europe, South America, and the United States. HIV-2 is most prominently found in individuals who live/traveled in West Africa, had sexual relation with people in West Africa, and people who received blood transfusion/blood products from West African donors. HIV-2 was first identified through diagnostic screening for HIV-1 with definite similarities and differences.

The outer envelope of HIV consist of the outer envelope protein (gp120) and transmembrane protein (gp41). The outer envelope surrounds the internal envelope or matrix protein (p17/p18), which in turns surrounds the core shell (p25/p24). The core shell surrounds the RNA, p9, p7, RT, & p66. The viral envelope contains information that is necessary to infect different cells. The regulation regions of the virus (i.e. tat and rev) contain information necessary to control intracellular replication of the virus. The HIV-1 contains many regulatory genes. These include the tat, rev, nef, vif, vpu, and vpr. The tat (transactivator) consists of a positive feedback regulator that increase synthesis of all viral protein. The rev (regulator expression of virion) regulates expression of virion protein with negative expression of regulatory genes. The vir (virion infectivity factor) increases the infectivity of the virus. The vpu (viral protein U) facilitates the assembly and budding of viral particles. The vpr (viral protein R) accelerates the rate of viral reproduction. The differences between HIV-1 and HIV-2 are gag (p17/p18, p9, p7/p6, & p24/p25), pol (protease, reverse transcriptase, RNH, & integrase), and the presence of vpu in HIV-1 and the presents of vpx in HIV-2. HIV-1 and HIV-2 can differ from each other in the envelop region by as much as 55 %.

HIV-1 can evade recognition by changing its surface antigen (i.e. primary glycoprotein) thereby evading the memory immune system cells primed to detect a specific HIV antigen. HIV proceeds to attack the immune system by choosing to attack those cells that are design to defend the body from disease, the immune system. The HIV preferentially infects and destroy the CD 4 T-cells (i.e. helper/inducer), monocytes and macrophages. Whether the natural killers (NK) cells are infected or not is unclear at this time. With the destruction of the CD 4 cells, the rest of the immune system remains dormant and fails to respond to

opportunistic diseases. Without the CD 4 cells functioning, the B cells, suppressor T-cells, NK cells, cytotoxic T cells (CD 8), and macrophages/monocytes all remain non-functional. These cells require the CD 4 cells to release cytokines (interleukin and gamma-interferon) to trigger the necessary immune response. The CD 4 marker is found primarily on B lymphocytes, macrophages, and some brain cells.

The two immune systems responsible for defense against infections are the cellular immune system and the humoral immune system. The cellular immune system is generally responsible for viruses, parasites and fungi infections. The humoral immune system is generally responsible for defense against bacteria, some viruses, and other soluble antigens. The cellular immune response is the most important of the two immune systems. The cellular immune system is mediated primarily by T-lymphocytes (CD 4 and CD 8), macrophages, and NK cells. The humoral immune system (i.e. IgG, IgA, IgD, IgE, and IgM) remains significantly impaired without the necessary response from the CD4 helper cells. With the progression of AIDS, the number of CD4 cells continue to decrease (while the number of CD8 cells remaining constant), and with it, the strength of the humoral immune system is greatly decreased.

HIV heterogeneity refers to the ability of the HIV to vary its surface antigen. This is the key to the survival of the HIV. Not only are there slight variations between individual HIV strains, but also in strains isolated from the same individual, at different times. The variability in the HIV strains determine the type of cells that can be infected, the extent of the infection, the efficiency of the infection, and the amount of cells that can be destroyed by the infection.

Infection to cells can be achieved by one of two methods, through production of infectious progeny or by fusion of unaffected cells with infected cells. In order for the HIV to infect unaffected cells, it must first bind to the cell membrane. This is primarily via the CD4 antigen complex. A direct interaction between the viral gp 120 (glycoprotein 120) and CD 4 molecule demonstrates potential for infection. Evidence from other laboratories has shown that the gp 41 (transmembrane protein of HIV) could bind to a separate cellular receptor that would facility the binding process. Antibodies to the gp 41 have been shown to prevent viral infection Infected cells that lack the CD 4 marker have a galactosyl ceramide receptor, which when blocked with an antibody, blocks the HIV infection. However, not all infected cells that lack the CD 4 marker have the galactosyl ceramide receptor. Cells susceptible to HIV include hematopoietic, brain and cerebrospinal fluid (CSF), skin cells, colon cells, bowel cells, and renal cells. The HIV cells have been isolated from many body fluids. These include plasma, tears, ear secretions, saliva, urine, vaginal/cervical secretions, semen, milk, and cerebrospinal fluid. Tears, saliva, and ear secretions contain 0.1% to 0.01 % of the amount of virus in blood and plasma.

Worldwide, the World Health Organization (WHO) estimates that a total of 8 to 10 million individuals are infected with HIV (13). They estimate that North America is infected with approximately one million, Latin America and the Caribbean are infected with one million, Europe and the USSR are infected with 520,000, Africa is infected with over six million, Asia is infected with 500,000, and Australia is infected with 30,000. In the United States, as of December 31, 1991, there are a total of 206,392 AIDS cases that have been reported to the CDC, with 133,232 reported deaths associated with AIDS (T914). Table 1 list the category and percentages of Aids cases from 1981 to 1990 (6). Homosexuals and bisexual

males accounted for 59 % and intravenous (IV) drug users accounted for 22 % of all reported AIDS cases. Between 1990 and 1991, the number of heterosexual contacts without IV drug use, have increased 21.0 % (15). The number of blacks and Hispanic increased 10.2 % and 11.5 %, respectively (15). The number of female infected increased by 15 % (15). These numbers indicates an increase proportion of heterosexual individuals contracting HIV, while a decrease proportion of homosexual/bisexual individuals contracting HIV. It is estimated that by the end of 1993, 390,000 to 480,000 cases of AIDS will be reported, with 285,000 to 340,000 deaths (16). By the end of 1994, it is estimated that 415,000 to 535,000 individuals are expected to be diagnosed with AIDS and 330,000 to 385,000 are expected to die (23).

The HIV has been isolated from many body fluids. Evidence of HIV transmission has only be documented in blood, semen, vaginal fluid, and breast milk (7). The CDC recommends that universal precautions be used when dealing with any blood, semen, vaginal fluid, spinal fluid, pleural fluid, peritoneal, pericardial fluid, and amniotic fluids (8).

The route of transmission of HIV can be divided into four categories: sexual, parenteral, maternal, and cutaneous. Sexual transmission includes heterosexual, homosexual, and bisexual contact. Parenteral includes intravenous drug use, needle sticks, invasive medical and dental procedures, and transfusion of blood or blood products. Maternal transmission includes transmission from mother to child via perinatal, delivery, or breast feeding. Cutaneous involves skin and mucous membrane. The risk of transmission of HIV is summarized in Table 2 (7). The risk of transmission assumes that the HIV state is not known.

Sexual transmission of HIV can occur from male to male, male to female, and female to male. The risk of transmission from male to female is 1:500 to 1:1,000 and the risk from female to male is 1:1,000 to 1: 1,500. The risk is greatest with anal intercourse, lower with vaginal intercourse, and lowest with oral sex. The risk increases as the number of partners increase. With the presence of other vernal diseases, the likelihood of transmission is increased (7,9).

With parenteral transmission, IV drug users have the highest risk of transmission. This is due to the sharing of needles and a practice known as "booting" (drawing blood back into the syringe before injecting). The risk increases as the number of partners increase and the number of times the same needle is used.

The rate of transmission of HIV to transfusion recipient and hemophiliacs has decreased dramatically with the screening of HIV antibodies form donated blood. The risk of receiving HIV infected blood for transfusion is estimated at 1:36,000 (0.0028 %) (10). The risk of receiving HIV from clotting factors is zero. This is due to the screening of HIV antibodies from donors and the heating process which destroys the HIV.

The risk of infection from needle sticks is estimated to be 0.03 % among nurses who work on AIDS wards (12). This is clearly on the high end of the spectrum for transmission. The risk of transmission increases when HIV infected cells are present, the needle size is increased, and if the object is hollow as opposed to being a sharp object.

To this date, only one case of salivary transmission has been reported in the world, and that was in the USSR (11). This case involved a HIV infected infant who was being breast feed by the mother. The infant had oral lesions and the mother had a cracked or bleeding nipples. The transmission was from child to mother. The risk of perinatal transmission of HIV is considered to be low. But with children that are HIV positive, 82% of them have HIV positive mothers (7).

The CDC has recommended universal precautions when dealing with blood and body fluids (semen, vaginal secretions, CSF, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, and amniotic fluid), body secretions that contain blood (feces, nasal secretions, sputum, sweat, tears, urine, and vomitus), breast milk (banks), and saliva (dental settings) with all patients. Exposure is defined as contact with blood or body fluid through a percutaneous inoculation or contact with an open wound. Hand and skin washing should be done thoroughly after contamination with blood or body fluid. Use of protective barriers such as mask, protective eye wear, face shields, gloves, and gowns should be used. Instruments or devices that enter tissue or contact blood or body fluids should be sterilized or disinfected to manufactures' recommendation. Disinfection can be achieved with 500 to 5,000 ppm of sodium hypochlorite. Contact lens should be disinfected by use of hydrogen peroxide systems or heat at 78 to 80 degrees centigrade for thirty minutes.

The first "AIDS test" was developed by using a tissue culture to try and isolate the HIV-1 infection. There are five major groups which the HIV test can be divided into: virus culture techniques (e.g. Peripheral Blood Mononuclear Cells Coculture for HIV-1), antibody detection tests (e.g. ELISA and Western blot), antigen detection tests (e.g. HIV p 24 Antigen test and Acidified p 24 Antigen

test), viral genome amplification (e.g. Polymerase Chain Reaction Technique), and immune function tests (e.g. CD 4 and CD8 counts). At the present time, the most commonly used test to test for HIV-1 are the ELISA and the Western blot. This is because these test are faster, easier, less hazardous, and less expensive than some of the other test methods available. Antigen detecting tests are currently used to screen blood donors.

ELISA was first introduced in April of 1985 for the Screening of donated blood. This test is extremely sensitive, inexpensive and easy to perform. The ELISA test determines the presents of the HIV antibodies and determines the quantitative amount of antibodies present. This is accomplished by using spectrophotometry. By spectrophotometrically comparing the optical density of the individual serum to that of a known control, the amount of the HIV-1 antibody can be quantitatively determined.

Western blot test determines the presence of anti HIV-1 antibodies and the specific antigen which the antibody is directed. This is accomplished by using electrophoresus procedures. This test is highly sensitive and highly specific. The CDC/ASTHPHLD criteria requires the presence of two of the three p24, p41, or gp160/120 for positive result, no matching bands for negative result, and the presence of any HIV-1 related region for an indeterminate result.

CD4 and CD8 cells are measured by specific monoclonal antibodies directed against specific glycoproteins. These immune function tests are used to monitor the progression of the disease, as opposed to the diagnosis of the presents of the HIV.

Most antibody tests are based on the detection of IgG even though IgM and IgA appear sooner than IgG (IgG are present in much higher quantities than either IgM or IgA). The accuracy of the HIV testing can not be reliably assessed until the age of 15 months (due to the maternal antibodies present).

One significant problem associated with HIV testing is the seroconversion window. It is estimated to be 2 to 14 months, with an average of 6 to 12 weeks. Seroconversion has been documented to be as long as 28 months.

The CDC has continued to monitor the progression of AIDS and has been revising the definition of AIDS. As of August of 1987, the diagnosis of AIDS can be made if: 1) laboratory diagnosis of HIV infection is positive and a diagnosis of one of the following in Table 3; 2) laboratory diagnosis of HIV infection is positive and a diagnosis of one of the following in Table 4 is presumed; 3) laboratory diagnosis of HIV infection is inconclusive and a diagnosis of one of the following in Table 5 is presumed; or 4) laboratory diagnosis of HIV infection is negative and all other causes of immunodeficiency are excluded, a definitive diagnosis of any disease in Table 3, and a CD4 count of below 400 cells/mm^3. The CDC has classified stages for HIV infections. Stage I is defined as having an acute infection (i.e. fever, malaise, rash, or lymphadenopathy). Stage II is defined as asymptomatic infection. Stage III is defined as a persistent generalized lymphadenopathy. And Stage IV consist of having an opportunistic disease. As or January 1, 1993, the diagnosis of AIDS can be made if the CD4 cell count is below 200 cells/mm^3, a positive HIV infection, or if one of the following conditions listed in Table 6 is present. Table 7 list the revised classification system for HIV infection and AIDS definition for adults and adolescents. Category A consist of one or more of the following condition: 1) Asymptomatic

HIV infection, 2) persistent generalized lymphadenopathy (PGL), or 3) HIV infection with illness. Category B consist of: 1) HIV infection or indication of a defect in cell-mediated immunity or 2) a condition in which requires medical management due to complication of HIV infection. Category C consist of those conditions listed in Table 6.

The ultimate goal of medical research is to eliminate or suppress HIV-1, prevent transmission to non-infected individuals, and restore depressed immune function. The ultimate goal of treatment is to delay progression and improved immune deficiency, prevention of opportunistic infection, and recognition of and treatment of complication of immune deficiency.

Infection with HIV begins with the binding of envelope protein to the cellular receptor. Agents that block the initial phases of viral replication should prevent infections of new cells, but will not affect cells already infected. Agents that block the later phases of viral replication should block the infected cells, but will not prevent non-infected cells from becoming infected.

Currently the compounds under evaluation for treatment of HIV-1 include zidovudine, zalcitabine, didanosine, didehydrodideoxythymidine, and phosphonoformate.

Zidovudine (Azidothymidine or AZT) is a thymidine analog that inhibits the replication of HIV by inhibiting reverse transcripase, an essential enzyme in reproducing the HIV.. The serum half-life of zidovudine is one hour. Current recommended dose is 100 mg every four hours for a total of 600 mg per day for symptomatic patients. For asymptomatic patients with HIV infections, the

recommended dose is 100 mg every four hours for a total of 500 mg per day. The National Institute of Health AIDS Clinical Trial Group has documented that the current recommended dose is as effective as the initial dose tested, without the level of toxicity (17). The initial dose tested was 250 mg every four hours for a total of 1500 mg daily. Patients that have been treated with zidovudine have an average survival rate of 18 months longer (18). The median survival time for patients with AIDS on zidovudine is approximately 124 weeks, a 2 to 3 fold longer survival time, indicating that AZT has beneficial short term effects (18). Zidovudine does not eradicate the HIV infection or result in a sustained immunological improvement. Progression of the HIV infection and increased frequency of opportunistic infections, mortality, and wasting are likely. Benefits of AZT treatment includes prolonged survival time, increased CD4 cell counts, and increased CD8 counts, decreased p24 antigen levels in serum and CSF, improved cognitive functions, delayed progression of AIDS, and decreased frequency and severity of opportunistic infections.

The most common short-term adverse reaction to zidovudine include headaches, nausea, and malaise (20). Also present are insomnia, vomiting, diarrhea, fever, rash, myalgia, and abdominal pains (20). These symptoms generally subside with ongoing therapy. Rarely has the patient been removed from treatment. Myopathy (e.g. myalgias, proximal muscle weakness, wasting, and elevated serum creatine kinase) has been associated with long-term treatment of zidovudine. When this occurs, treatment is usually discontinued and anti-inflammatory agents used. Other long-term adverse reactions include bone marrow toxicity, anemia, neutropenia, thrombocytopenis, and macrocytosis (17, 18). Other side effects include disease progression and the development of resistance strains to drug treatment.

Didanosine (i.e. Dieoxyinosine, ddI) has a serum half-life of 1.6 hours. ddI is available in either chewable tablets or a buffered powder, with the tablets having greater bioavailability. ddI was first introduced into clinical trials in 1989. To this date, the FDA has approved its use for patients with advanced HIV infections who are unable to tolerate zidovudine treatment. Patient with advance HIV infections (i.e. recurrent opportunistic infections, wasting, or deterioration in immune function) should also be considered for ddI treatment. ddI treatment has resulted in decrease p 24 antigen levels as well as decrease HIV RNA (18,20). However, ddI is less effective than either AZT or ddC, as reported in vitro studies by Dr. Raphael Dolin (20). ddI is less cytotoxic then either AZT or ddC. Current recommended dose is a single chewable tablet twice a day on an empty stomach. Adverse reactions include peripheral neuropathy (tingling, burning, aching in lower extremities), pancreatitis, hyperamylasemia, elevated serum urate levels, diarrhea, hepatic toxicity, and cardiac arrhythmia (18). Signs and symptoms that warrant discontinuation of ddI are peripheral neuropathy and pancreatitis. ddI has no hematological toxicity like AZT and only mild peripheral neuropathy.

Zalcitabine (i.e. Dideoxycytidine, ddC) has a serum half-life of 1 hour. ddC is capable of entering the central nervous system (leads to high neurotoxicity). When ddC was compared to zidovudine as a mode of treatment alone, ddC had a significantly greater mortality rate than zidovudine (18). Phase I studies of ddC included doses of .03 to .06 mg/ kg every eight hours. This resulted in a decrease p 24 antigen level and increase CD 4 level. Adverse reactions include maculovesicular cutaneous eruptions, aphthous oral ulceration, and fever(18). The major dose limiting toxicity of ddC is painful sensorimotor peripheral

neuropathy involving the lower extremities. Treatment involves discontinuation of ddC. Rarely will pancreatitis occur. Almost no hematological toxicity is associated with ddC (i.e. neutropenia, thrombocytopenia, and anemia).

There are many drugs that are under evaluation for the treatment of HIV-1, some of them are foscarnet, sulphated polysaccharides, ribavarin, castanospermine, and avarol (74). Foscarnet is a non-competitive inhibitor of RT, with a short half-life. Sulphated polysaccharides posses anticoagulant activity that protects the CD4 cells from being infected, in vitro. The sulphated polysaccharides drugs have been less promising in clinical trials. Ribavarin is a guanosine analogue that has activity against many RNA and DNA viruses. Castanospermine interferes with the post-translation glycosylation. It inhibits the cleavage of the gp 160 to gp 120. Avarol is a quinone which inhibits HIV replication by unknown mechanism. It is estimated that the mean survival time is 7 to 24 months after AIDS is diagnosed, with a prolonged survival time with treatment (19).

Skin disorders are commonly associated with HIV infections. The skin may be the first organ affected by the virus. Individuals with HIV and skin disorders may show an increase in severity of the skin disorder. Many common skin diseases may not respond to the normal route of treatment and may require higher doses for a prolong period. The treatment maybe indefinite. Table 8 summarizes the viral, bacterial, fungal, and some non-infectious skin disorders, along with the treatments of choice (17, 21).

The most common cutaneous bacterial pathogen is staphylococcus aureus. Associated with the staphylococcal infections are folliculitis, bullous, impetigo, ecthyma, abscesses, hictradenitis, suppurative plaques, and cellulitis. Bacillary

angiomatosis is an uncommon skin disorder that is found most commonly in immunal suppressed individuals. The skin lesions present as friable vascular papules, subcutaneous nodules, or cellulitic plaques, most commonly found in the respiratory track and conjunctiva. The most common visceral disease associated with bacillary angiomatosis is liver disease. Also present are spleen disease, osteolytic bone lesion, lymphadenopathy, and bacteremia. Herpes simplex (HSV) and varicella zoster virus are the most common disease associated with cutaneous viral pathogen. HSV usually effects the genital, digital, or orofacial areas. Secondary infections may occur over the HSV lesion. Any chronic lesion should be cultured with fluorescent antibodies. HZV occurs most often during the asymptomatic stage of HIV. Molluicum contagiosum are seen most commonly during symptomatic stages of HIV. Lesion are generally seen on the face, genital, or trunk area, with the most common on eye lids. Hypersensitivity disorders are commonly seen with antibiotics (PCN and sulfa drugs). Trimethoprin-sulfamethoxazole commonly results in maculopapular eruption. Other reaction also include urticasia and erythema multiform.

Oral opportunistic infections occur in a variety of systemic conditions such as HIV and leukemia, radiation therapy, chemotherapy, bone marrow suppression and diabetes. Some of the oral lesion that are associated with HIV infections are listed in Table 9 (17). The most common form of candidiasis is pseudomembranous, which presents with a removable white plaque. Hyperkeratosis is another form of candidiasis that presents as a white plaque that is not removable. Erythematous is another form of candidiasis that presents as a smooth red patch. Angular cheilitis is the last form that presents as erythema, cracks and fissures at the corner of the mouth. Periodontitis occurs in approximately 30 % to 50% of AIDS patients. Gingivitis presents as a fiering red

marginal line. Gingivitis and periodontitis does not present in its usual form. Periodontal disorders is often severe and progresses rapidly. Herpes simplex virus is a common oral lesion of HIV patients. Herpes zoster and cytomegalovirus occasionally occur. Hair leukoplakic appears as a white thickening of the oral mucosa, occasionally with vertical folds. Hairy leukoplakic is almost always associated with HIV patients. Human papillovirus presents as papilliferous warts with multiple white and spike projections as pink cauliflower-like masses. Kaposi's Sarcoma present as red or purple macules, papules, or nodules. They may be asymptomatic or inflamed and painful.

Gastrointestinal tracts disorders are common amount HIV patients. Almost all patients will present with weight loss, dysphagia, anorexia, diarrhea, odynophagia, hemorrhage, jaundice, and/or abdominal pains. CMV does not only have occular affects, but also can affect the GI tract and the lungs. It has been found in 60 % of AIDS patients (22). Treatment depends on location, but generally involves acyclovir or ganciclovir.

Pneumocystic carinis pneumonia (PCP) affects approximately 80 % of AIDS patients (22). Diagnosis can be made with chest x-rays and arterial blood gases. This organism is normally found in the lungs, but in immunodeficient patients, it is a life threatening disease. This disease normally does not present its self until the patient is severely immuno-compromised (i.e. CD4 below 200). Typical symptoms are dyspnea, fever, and persistent coughs and may be proceeded by fatigue and weight loss. Treatment normally involves aerosolized pentamidine isethionate or oral trimethoprim-sulfamethoxazole (TMP/SMZ), with oral TMP/SMZ being more effective. The median survival rate is twelve months (22). The guidelines for prophylactic treatment against PCP, according to the CDC is

monitoring CD4 cell counts every 3 to 6 months above 500 cells/mm^3. With cell counts between 200 and 500, treatment with antiretroviral agents should be initiated. With cell counts below 200, prophylactic treatment for pneumocystis pneumonia should be initiated. As with any treatment with antiretroviral agents, it is necessary to monitor for drug toxicity and disease progression.

Cerebral toxoplasmosis is usually diagnosed with the help of CT scans/MRI, as well as monitoring the progression of the pathogen. The treatment of choice involves the use of pyrimethamine and sulfadiazine with levcouorin calcium (to treat the toxicity). Maintance dosage must be maintained for life. Corticosteroids can be used to treat the cerebral edema associated with toxoplasmosis. The extent of the toxoplasmosis infection is directly proportional to the degree of immunodeficiency.

Mycobacterium avium-intracellulare is usually diagnosed with blood cultures and chest radiographs. It has been isolated in up to 20% of autopsy individuals (22). Treatment involves the use of four of the five combinations: rifabutin, rifampin, clarithromycin, ciprofloxacin, and clofazimine.

Cryptococcal infections can be diagnosis by fungal cultures of blood and urine specimen. Generally, patients present with unexplainable fevers. Treatment usually begins with IV amphotericin B and later it is changed to oral fluconazole, once the infection is under control.

It is well known that HIV causes an immune deficiency by attacking the body's natural defense mechanism, less is said about its neurotropic ability allowing the nervous system to be invaded. The primary infection may involve the brain,

meninges, spinal cord, peripheral nerves and cerebral vessels (25). At least 40 percent of patients with AIDS will manifest neurological symptoms (32). Autopsy examination exhibits CNS abnormalities in 70 to 80 % and peripheral nervous system abnormalities in 35 (60).

How does HIV infect the CNS? One possible mechanism is that HIV is carried passively into the nervous tissue by infected lymphocytes and monocytes. Another theory is that HIV can directly infect endothelial cells. Once the virus is in the CNS it would attack monocytes and lymphocytes as these cells are "fighting-off" an opportunistic infection (25).

Neurological manifestations can occur at any stage of HIV infection. Though primary infections of the CNS have been reported in patients whom developed acute aseptic meningitis and complained of headaches (HA), fever, and a stiff neck (34). The majority of neurological disorders do not become evident until an opportunistic infection occurs (28). The disease can be classified into three categories: primary disease due to HIV, opportunistic infections due to HIV, and disease of unknown etiology, which may be immunologically related (26).

Dementia is the most common syndrome demonstrated by HIV individuals. Though the word dementia means many different things to a lot of people, here we will define it broadly as an impairment of cognitive, motor and behavior function. This dementia is called AIDS Dementia Complex (ADC), and 70 % of AIDS patients will develop a moderate to severe dementia during the course of the disease (25). John Hopkins University had noted that 25 % of HIV patients presented with ADC before any other symptoms (25). Table 10 shows the many signs and symptoms of ADC. These signs and symptoms are a continuum, and

may progress over weeks and months. ADC may be difficult to diagnose through specific testing, though one can look at anatomy and by knowing the function, can get a feeling of why the pathological manifestions occur. CT scans show some degree of cerebral atrophy in 80 to 90 % of these patients, which show up as hypodense spots within the white matter (25). MRI is more sensitive and may show more subtle changes. In ADC patient s there is an elevated IgG total proteins in the CSF. These individuals may also have progressive slowing of basal activity (7-9 Hz) in the electro-encephalogram (EEG) (25, 26).

The most common form of meningitis is an acute aseptic meningitis, which presents as a febrile illness in the first weeks of HIV infection (27). It is believed to be an reactivity to the seroconversion. In this meningitis, there exists an elevated T8 cell count, in contrast to elevated levels of T4 cell count which are usually found in meningeal viral infections. This type of aseptic meningitis is usual self-limiting, but it is important to exclude other forms of treatable meningitis (26).

Vacuolar myelopathy is another CNS disease. It is characterized by vacuolization of white matter of the spinal cord and is apparent in the posterior and lateral columns at the thoracic level. As this disease process takes place it clinically manifests itself with a progressive paraparesis with spasticity, ataxia, and urinary incontinence. This type of myelopathy has s similar degeneration associated with vitamin B12 deficiency and must be ruled out in the differential diagnosis.

Yanker et al also described a case of cerebral granalomatous angitis of unknown origin, although it is thought to be very rare (26).

There also are three types of peripheral neuropathy caused by HIV. One of them being is a very painful sensory neuropathy, thought to be caused by an infection of the dorsal root ganglion. Poly neuropathy is the second form, and is also at the sensory level with damage at both axonal and myelin levels. The third form is a peripheral inflammatory demyelination neuropathy (26, 28).

Other neuropathies in AIDS patients involving the eye may be caused by opportunistic infections. The most common CNS lesions include cerebral toxoplasmosis in 10 to 15 % of AIDS patients, cryptococcal meningitis in 10 %, and cytomegalovirus (CMV) involvement in one third of all AIDS patients at time of autopsy. Other opportunistic infections are included on Table 13. Neuro-ophthalmic findings were present in approximately 8 % of patients with AIDS and 73% of autopsied bodies revealed neuropathological changes (28). These findings were many, as highlighted in Table 12. Important ones to ophthalmologists and optometrists include eye movements disorders, optic nerve palsies, optic neuropathy and visual field defects (24 , 29, 24, 35).
Ocular motility appeared to be the most commonly reported dysfunction when measured by instrumentation. This can be seen early in the HIV infection. Peak saccadic velocities were abnormal, which seen to be associated with neurological changes in the subcortical structures.

Ocular nerve palsy may be the presenting CNS complaint in AIDS patients. Palsy of the third, fourth, and sixth cranial nerve have occurred in AIDS individuals, and may be bilateral or a combination of cranial nerves. Most of these cranial nerve palsies were due to focal brainstem toxoplasmotic lesions around the cranial nerve nuclei. On CT scan, the lesion has showed up as a

hypodense or isodense area. Gaze paresis of the nuclear supranuclear lesions of the parmedian pontine reticular formation and medial longitudinal fasiculus were also noted (25, 26).

Papilledema and papillitis are also common in HIV infected individuals. Papilledema occurs approximately 1 % of these patients (28). This can be caused by cryptococcal meningitis, cerebral toxoplasmosis, and CNS lymphoma. Optic neuritis was detected on approximately one third of patients with CMV retinitis (31). Papillitis can also be caused by syphilis, VZ, toxoplasmosis, and hepatitis B virus. Retrobulbar optic neuritis may be caused by syphilis, crytococcal, and CMV. Anterior ischemic optic neuropathy (AION) may also occur, and any of these infections can cause optic atrophy secondary to the disease. Visual fields are also listed in Table 12 and will correspond to where in the afferent visual system the lesion is located. There is also a miscellaneous category which lists other signs and symptoms (28).

Differential diagnosis of the opportunistic infections are very difficult, because all of them have the potential affinity for any part of the CNS including the optic nerve and optic tract. Though CT and MRI's are helpful in locating the lesion they do nothing for identifying the causative organism (26, 28).

Cerebral toxoplasmosis is made by brain biopsy since serological tests for toxoplasmosis are unreliable in AIDS patients (25). Most internists "play a hunch" along with other clinical findings before the biopsy and initiate treatment in which we will describe later (28).

Cryptococcal meningitis may be distinguished by lumbar puncture and the cryptococcal antigen test is positive 95 % of cases (28, 32).

Syphilis must also be ruled out for any CNS infections. CSF is obtained through lumbar puncture for diagnosis, though non-reactive serum and CSF have been found (26).

Another cause of CNS complications is tumors. Primary and metastatic CNS lymphomas occur in 9 % of AIDS patients (26), and my be indistinguishable from cerebral toxoplasmosis. It is generally diagnosed by exclusion. Other tumors include astrocytomas, and metastatic Kaposi sarcoma (rare). Other implications include intracerebral hemorrhage (2 % of AIDS patients), and cerebrovascular accidents (26,28).

Recognizing neurological manifestations associated with HIV is important. They are the most frequent and serious complications of the disease. The primary care optometrist can be a great asset in recognizing or being suspicious of HIV infected patients by history and exam. Early diagnosis for any HIV -neurological related disorders provides the most favorable outcome.

Though CNS complications are of a serious nature, some other uncommon opportunistic infections can also effect the anterior segment of the eye, including the eyelids, with better resolution. Kaposi sarcoma is rare in the CNS, but it is the most common disease of the ocular adnexa, occurring in approximately 20% of all patients with AIDS and systemic Kaposi sarcoma (36).

Clinically Kaposi sarcoma takes on many different shapes and sizes. The early signs of Kaposi sarcoma may be confused with subconjunctival hemorrhage, granuloma, pyogenicum, conjunctival cyst, inflamed pinguecula, foreign body, granuloma, blepharitis, and eyelid edema. The more advanced type appear as raised, discrete, solid, vascular lesions, often with surrounding angiogenesis, and tend to be less than 3 mm in height and of less than four months duration. This type of sarcoma can be found on the fornix, caruncle, lid margin, bulbar or palpebral conjunctiva, usually inferior conjunctival (93%) (37). This is an important diagnosis for several reasons. First, and the most obvious, is to stop the progression by initiating treatment as soon as possible. Second, by having an irregular surface on the conjunctiva, close to the cornea, it will cause the cornea to thin and dry making it susceptible to infection. If the lesion is located on the lid causing an ectropian, the corneal epithelium may dessiacte and again will be susceptible to infection (37).

There is also non-Hodgkin's lymphoma of the orbit in AIDS patients, but is very uncommon. The typical clinical manifestation is that of a rapidly enlarging nodal or extra nodal mass with the histological pattern of large-cell lymphoma. Conjunctival sqaumous cell carcinoma, causing necrotizing scleritis has also been documented (39).

The anterior segment can also be involved with AIDS patients. The infectious organisms are HZV, candida albicans, N. gonorrhea, P. aeruginosa, Encephalitozoo caniculi, and Mycobacterium avium.

Herpes zoster ophthalmicus is usually a disease of the elderly, and can also occur in children. It has been also reported in young AIDS patients, manifesting itself

as a keratoconjunctivits with an anterior uveitis. A diminuation in the proportion of T4/T8 cell has been found.

Gonococcal ophthalmic infections should always be considered in a purulent conjunctivitis, since genital symptoms may be absent, or patients may not readily connect their ocular complaint with a genital infection. N. gonorrhea can cause corneal perforation with in 24 hours (40).

Pseudomonas aeruginosa is another bacteria that may manifest itself in HIV patients. This organism is the most common gram negative bacteria in the United States, and is often responsive to antibiotic treatment (41).

Microsporida are small obligate intracellular parasites. The protozoa have been reported in humans with HIV. The appearance of the keratitis is similar in all cases, with the disease confined to the superficial corneal epithelium and minimal involvement of the conjunctiva. Symptoms include photophobia, foreign body sensation, blurred vision, and dryness. Visual acuity can range from 20/20 to light perception, and may be variable throughout the disease. The conjunctiva when involved is largely confined to the inferior fornix where a fusiform swelling is present. There also may be a slight anterior chamber reaction (42, 43).

In patients with AIDS, M. avium-intracellular is the most common disseminated bacterial infection (44). This bacteria can cause an endophthalmitis. The symptoms of endophthalmitis are pain accompanied by conjunctival injection, photophobia, tearing, and foreign body sensation. Signs include lid edema with marked conjunctival injection. The cornea will have marked diffuse punctate

epithelium defects. The anterior chamber will have cell and flare; a hypopyn may be present (45).

We have only listed a few organisms that may be present in AIDS patient, with an affinity for the anterior segment of the eye. Any organism has potential of causing infection, especially one who's immune system is compromised. The optometrist or ophthalmologist should treat the specific infection and it is imperative to culture all keratoconjunctivitis in HIV infected person, though a proper treatment regimen is always initiated first. When dealing with a resistant organism of unknown origin, cultures of the blood, sputum, urine, and stool should be taken, along with a TB test. Note: If the signs appear of a microsporidial keratoconjunctivitis, do not culture the cornea, but the conjunctiva. You further the risk of either secondary infection or penetration into deep stroma. Though anterior infections alone are rare in AIDS patients, the choroid and retina are not.

There seems to be a correlation between ocular pathology and CD4+ lymphocyte counts. Almost all of the patients with ocular anomalies also have a CD4+ count of less than 200 cells/ml, suggestive that ocular lesions have a negative prognostic significance. Table 11 shows a breakdown of patients corresponding to the percentage of ocular pathology. Note Groups A and B are indicated by total CD4+ lymphocyte count over 200 cells/ml and under 200 cells/ml, respectively (45).

The most common lesions are cotton-wool patches, found in the retina, affecting 40 to 75 % of all AIDS patients. These are focal areas of hypoxia in the nerve fiber layer, associated with diffuse retinal microvasculopathy. These are usually seen

along the major vessels and may resolve. A variety of causes have been hypothesized, including damage caused by HIV infection of endothelial cells (48), and alteration in blood flow (47). Cotton wool spots may lead to diffuse retinal dysfunction, with subtle visual changes. It may be a contributing factor of axonal loss in optic nerves of patients with AIDS and associated defects in color vision and contrast sensitivity (48). Other pathological conditions include vascular congestion, hemorrhages, and chorioretinitis (46).

The opportunistic infections that cause chorioretinitis are growing. To date, there have been documented cases of syphilitic chorioretinitis, cryptococcal choroiditis, ocular histoplasmosis, toxoplasma godii retinochoroiditis, pneumocystis carinii chorioditis, varicella zoster virus retinitis, acute retinal necrosis of unknown etiology, and the most common of the chorioretinitis, CMV.

Acute syphilitic posterior placoid chorioretinitis (ASPPC) is the thought to be caused from Treponema pallidum. Patients will present with vitritis associated with bilateral large, solitary, placoid, pale-yellowish subretinal lesions, usually showing evidence of central fading and a pattern of coarsely stippled hyperpigmentation of the retinal pigmented epithelium (RPE). Early phase fluorescein angiography shows hypofluorescence in the area of opacification, and a stippled pattern of nonfluorescence in the faded portion of the lesions. Late phase angiograms show staining at the level of the RPE that is more intense in the areas of opacification changes. There may also be evidence of a serous detachment, mild perivasculitis, and an iritis. This type of chorioretinitis must be differentiated from the other types of gray-white of yellow placoid lesions involving primarily the outer retina and RPE. ASPPC shares much in common with acute posterior multifocal placoid pigment epithelopathy (APMPPE).

Although most APMPPE lesions are multiple and .5 to 1.5 disc diameters in size, large solitary macular lesions occasionally occur. The lesions of both disorders tend to fade centrally, and may resolve in a couple of weeks. When partly faded, the APMPPE lesions, unlike ASPPC lesions, tend to hypofluorescence more, and after fading, they leave more prominent and discretely outlined areas of pigment derangement. Retinitis caused by viruses and the protozoan toxoplasma godii may cause one or many gray-white areas of acute retinitis anywhere. Unlike ASPPC, the full thickness of the retina is opacified. In older patients, large cell non-Hodgkin's lymphoma should be considered in the differential diagnosis. These patients usually present with vitritis and develop mound-like elevations of the RPE, usually in the extramacular area. The histopathology and pathogenesis of ASPPC are unknown. Angiographic findings suggest that an active inflammatory reaction is present at the level of choriocapillaris/pigment epithelial/retinal complex. This reaction causes the very slightly elevated opacitication of the retinal dysfunction. This abnormality may be largely reversible, leaving only a course pattern of clumping and near normal visual function. VDRL & FTA-ABS serologic testing should always be performed, but have been shown to be falsely negative in many cases. Meanwhile, the biomicroscopic and angiographic findings appear to be the most specific of the fundus changes described in secondary syphilis (49).

Cryptococcal choroiditis is a rare ocular infection caused by the fungus, Cryptococcus neoformans. Ocular complications have included papilledema, diplopia, nystagmus, ophthalmoplegia, ptosis, optic atrophy and chorioretinitis. Hiles and Fort (51) documented that 50% of the cases caused by intraocular cryptococcosis presented with chorioretinitis, 25 % presented with endophthalmitis, 17% presented with chorioditis and 8% presented with

neuroretinitis. Carney, Combs, and Weschler (52) documented two cases of choroiditis secondary to cryptococcal meningitis. Many authors suggest a possible progression of cryptococcal eye involvement. The initial stage includes cryptococcal choroiditis and/or optic nerve involvement. The second stage includes cryptococcal chorioretinitis. And the last stage includes cryptococcal uveitis/vitritis/endophthalmitis. This type of choroiditis is described as deep, hypopigmented, slightly elevated, and can occur with optic disc edema. This has been demonstrated to block choroidal fluorescence, in fluorescein angiograms. In the final stage, no vitritis is present. Later stages of this fungal chorioretinitis are harder to differentiate. A diagnosis of cryptococcal meningitis can be made by a lumbar puncture (i.e. an elevated cryptococcal antigens) (52).

Disseminated histoplasmosis is one of the life-threatening opportunistic infections associated with AIDS. Histoplasma capulatum is a common fungus which is found in central eastern United States. These fungi can disseminate to affect the lungs, liver, spleen, and the eye. Its ophthalmic signs are often a creamy-white intraretinal -subretinal infiltrates surrounded by hemorrhage. Retinal infiltrates may have distinct borders. Lesions can be localized in the macular region, and a neovascular membrane may form. A chest X-ray may help the diagnosis of histoplasmosis. If in fact it has disseminated to the pulmonary system, hilar adenopathy will show up. There is also a histoplasmosis skin test (53). (This test is not recommended with ocular signs because it can trigger an inactive lesion in the eye).

Toxoplasma gondii is the most common cause of posterior uveitis in adults, however, there are only a few reported cases of ocular toxoplasmosis in patients with AIDS. Toxoplasma retinochoroiditis can spread to the CNS, unlike the

reactivated congenital lesions in many non-immuno-compromised hosts. This type of retinochoroiditis can clinically mimic CMV. This toxoplasma organism can also cause an optic neuritis in patients with AIDS. An increase in the toxoplasma antigen may be increased during a post or active infection (54).

Pneumocystis carinii pneumonia (PCP) is the most common systemic infection in patients with AIDS, and it occurs in approximately 60 % of AIDS patients (55). Treatment of this pneumonia can be treated with aerosolized pentamidine therapy with good success (Gupta and associates of the 1990 ARVO annual meeting). Even though pneumonia symptoms had decreased with treatment, patients complained of blurred vision. Ophthalmoscopy revealed round yellow-white flat or slightly raised choroidal lesions, with no anterior or posterior chamber reactions. This choroiditis has only developed with patients receiving aerosolized pentamidine. Several authors have describe extrapulmonary P. carnii in patients receiving prophylactic aerosolized pentamidine therapy. Concern has been expressed over the possible disadvantage of poor systemic absorption (56, 57, 58).

Mycobacterium avium intracellular choroiditis may accompany PC choroiditis. Little local tissue destruction and inflammation are associated with M. avium infection, with normal acuity despite subfoveal lesions. In the absence of reliable systemic testing or antibiotic agents, the diagnosis of M. avium choroiditis can be made only by biopsy (58).

Varicella-zoster (VZ) can present clinically with patchy and deep retinal lesions, succeeded by diffuse thickening of the retina. The retinitis usually begins in the posterior pole, with little or no clinical evidence of vasculitis. Other signs include

optic nerve involvement, cherry red spot appearance at the macula, and early clearing of retinal whitening in a perivascular distribution. Patients are usually left with atrophic and necrotic retinal, and narrowed vasculature. There is scarce or no vitritis. Eruption of dermatomal zoster will either succeed or coincide with the retinitis. This disease process must be differentially diagnosed from acute retinal necrosis syndrome, and many authors believe it may be a continuum with VZ retinitis (59).

Typical acute retinal necrosis (ARN) is characterized by an acute necrotizing retinitis associated with moderate to severe vitritis and anterior chamber reaction. This disease is believed to be viral in origin, with VZ and HSV being implicated. The necrosis begins as confluent areas in the periphery, which usually progresses to the posterior pole. The vitritis causes vitreal traction and secondary retinal detachment may occur (59, 60).

CMV is a member of the herpes virus family. CMV can cause symptomatic or asymptomatic disease, latent infection, or even chronic disease. The mode of transmission of CMV include prenatal exposure, perinatal events, sexual transmission, organ transplantation, blood transfusion and exposure to body fluids including semen, breast milk, amniotic fluid, blood, urine, salivia, and tears. Seroprevalence of antibodies of CMV ranges from 50 to 100 %, depending on age, geographical location and immune status. CMV in an immunosuppressed patient can cause retinitis, colitis, esophagitis, gastritis, hepatitis, adrenalitis, nephritis, and pneumonitis (61, 62, 63).

CMV is considered to be a late stage manifestation of AIDS, reflecting a profound loss of immune functions. It has been presenting sign leading to the diagnosis of

AIDS in about 1 to 10 % of cases (64, 65). CMV retinitis is the most common retinal opportunistic infection in approximately 12 to 46 % of patients with AIDS (64, 65). The proposed pathophysiology of CMV retinitis is similar to that of CWS, but CMV retinopathy is a discrete clinical entity (64). Clinical presentation of CMV retinitis is that of visual symptoms ranging from hazy vision to a visual field defect, depending on where the lesion is located. CMV retinitis is described as discrete fluffy white deep retinal patches, often having granular edges. They mostly appear along the major vascular arcades, or near the optic nerve head. All layers of the retina are involved including the RPE. Bruch's membrane prevents the virus from infecting the choroid. Advancement of the CMV is characterized by infiltration of white blood cells and subretinal fluid giving it a raised appearance. Later in the disease process, the affected area takes on a grayish white and hazy appearance, which is accompanied by a minimal vitritis, with new areas of the retinal becoming infected. Retinal necrosis occurs leaving scar tissue and RPE mottling in the atrophic areas. CMV retinitis may present in three variations. First, intraretinal hemorrhages accompanying the inflammatory lesion. This has been described as "catsup and cottage cheese" appearance and is the classical presentation. This is an active lesion. CMV can also take the form of a "brush-fire." This results in the leading edge of a yellow-white lesion indicative of advancing disease, which in the adjacent middle areas is atrophic, necrotic retina where the retinitis was previously active. There is also a granular CMV retinitis, which looks sandy and is thought to be disruption of the RPE. This type of retinitis has been observed primarily in peripheral lesions and in treated cases (64, 67).

CMV may also infect the optic nerve head causing a papillitis. Optic atrophy may also be seen, though diseases of the optic nerve head are not common.

Periphlebitis is most often observed, although retinal arteriolar sheathing also has been noted. Non-rhegmatogenous retinal detachments are typically seen in patients with active posterior pole lesions, and rhegmatogenous RD has been seen in patients with peripheral lesions (68). RD tend to occur in areas of healing and thinning (65,70). Where there is an area of thinning, it may be difficult to detect the presence of inflammation of retinal tissue (65, 70).

The diagnosis of CMV retinitis is typically made after the diagnosis of AIDS. The clinical diagnosis of CMV retinitis is better made on the basis of funduscopic appearance. Other diagnostic techniques including tissue biopsy (69), viral cultures, serological testing, and the detection of viral DNA through hybridization studies, though all of these have their short comings (62, 63, 64).

The differential diagnosis of CMV must include all of the other different types of infectious retinitis as well as neoplastic diseases. Vascular diseases that include anterior ischemic optic neuropathy, diabetic retinopathy, hypertensive retinopathy, and central retinal vein occlusion must also be ruled out. One must be careful for there have been documented cases of diabetic retinopathy associated with AIDS (71). Neovasculization of the disc has also been noted in patients with AIDS and CMV (72). Other differential diagnoses must include cotton wool spots, myelinated nerve fiber, optic neuritis, and sarcoid (64).

Treatment of all these infections is aimed at finding the specific pathogens. Table 15 lists the infectious agents, primary medications, alternative drugs, along with comments. The amount of medication depends on a range of factors which may include body weight, health status, patient preference, severity of clinical

presentation, and common adverse effects of the medications, which are listed in Table 14.

Table 16 summaries the AIDS patients that we have encountered along with their ocular signs, systemic signs, CD4 counts, CD8 counts, and the medications (if any) they are were taking at the time of patient encounter. As you can see, most of the patients we encountered, lack any signs associated with AIDS. Nine of the eighteen patients had CD4 counts below 200cells/mm^3. Only three of the eighteen patients showed ocular signs associated with AIDS (e.g. one patient had CMV and two patients had CWS). Four other patients presented with ocular signs not related to AIDS (e.g. RPE hyperplasia, non-rheg. RD, retinal hole, and retinoshiasis.

Note:

The studies of the Ocular Complications of AIDS Research Group at 12 clinical centers, compared the efficies and toxicity of ganciglovir and foscarnet. Because of patient survival differed, the study's policy and data monitoring board recommended suspending randomization of treatment. The study found that patients initially treated with foscarnet lived for a median of approximately 12.6 months with treatment, whereas patients initially treated with ganciclovir lived for a median of approximately 8.5 months (73).

Table 1
Cumulative AIDS cases by exposure category

Exposure category Adult/Adolescent	Number	Percentage
Male homosexual/bisexual	94,126	0.58
Injectable-drug use	34,398	0.21
Male homosexualbisexual contact and IDU	10,557	0.07
HemophiliaCoagulation disorder	1,386	0.01
Heterosexual contact	8,440	0.05
Receipt of blood transfusion	3,684	0.02
Other/Undetermined	5,696	0.04
Pediatric	2,786	0.02
Total	161,073	1.00

Table 2
Risk of HIV Transmission

Route of transmission	Risk of Transmission
Sexual	
Anal	High
Vaginal	Moderate
Oral	Very Low
Blood-borne (parenteral)	
IV drug user	High
Hemophilia	Currently low
Transfusion (recipent)	Currently low
Transfusion (donor)	None
Needlestick	Low
Human Bite	None
Perinatal	
During pregnancy/delivery	Low
Breast feeding	Low
Other	
Mosquitos	None
Food-borne	None
Formite	None
"Casual" familia	None
"Casual" occupational	None

Table 3
Diagnosis of AIDS requires a definitive diagnosis of one of the following

Candidiasis of the esophagus, trachea, bronchi, or lung
Coccidioidomycosis, disseminated
Cryptococcosis, extrpulmonary
Cryptosporidiosis with diarrhea persisting more than 1 month
Cytomegalovirus disease of an organ other than lever, spleen or lymph node in a patient older than 1 month
HSV infection causing a mucocutaneous ulcer that persists for more than 1 monthe; or bronchitis, pneumonitis, or esophagitis caused by HSV in a patient older than 1 month
Histplasmosis, disseminated
HIV encephalopathy; ADC
HIV wasting syndrome
Isosporiasis with diarrhea
Kaposi's sarcoma
Lymphoid interstitial pneumonitis and/or pulmonary lymphoid hyperplasia affecting a child under 13 years of age
Mycobacterial
M. tuberculosis disease
Non-Hodgkin's lymphoma
Pneumocystis carinii pneumonia
Progressive multifocal leukoencephalopathy
Salmonella septicemia, recurrent
Toxoplasmosis of the brain
Any two of the following within 2 years in a patient less than 13 years of age: septicemia, pneumonia, meningitis, bone or joint infection, or abscess of internal organ or body cavity caused by Haemophilus, Streptococcus, or other fever-inducing bacteria

Table 4
Diagnosis of AIDS can be made with the presumptive diagnosis of one of the following

Candidiasis of the esophagus
CMV retinitis with loss of vision
Kaposi's sarcoma
Lymphoid intestitia pneumonitis and /or pulmonary lymphoid hyperplasia affecting a patient less than age 13
Mycobacterial disease, disseminated
Pneumocystis carinii pneumonia
Toxoplasmosis of the brain in patient older than one month

Table 5
Diagnosis of AIDS can be made with the definitive diagnosis of one of the following

Candidiasis of the esophagus, trachea, bronchi, or lung
Cryptococcosis, extrpulmonary
Cryptosporidiosis with diarrhea persisting more than 1 month
Cytomegalovirus disease of an organ other than lever, spleen
HSV infection causing a mucocutaneous ulcer that persists for more than 1 monthe; or bronchitis, pneumonitis, or esophagitis caused by HSV in a patient older than 1 month
Kaposi's sarcoma
Lymphoma of the brain (primary) affecting a patient less than 60 years of age
Lymphoid interstitial pneumonitis and/or pulmonary lymphoid hyperplasia affecting a child under 13 years of age
Mycobacterium avium complex of M. kansasii disease, disseminated
Pneumocystis carinii pneumonia
Progressive multifocal leukoencephalopathy
Toxoplasmosis of the brain

Table 6
Diagnosis of AIDS can be made with the definitive diagnosis of one of the following

Candidiasis of the esophagus, trachea, bronchi, or lung
Cervical cancer , invasive
Coccidioidomycosis, disseminated
Cryptococcosis, extrpulmonary
Cryptosporidiosis, chronic intestinal
Cytomegalovirus disease of an organ other than lever, spleen or lymph node in a patient older than 1 month
Cytomegalovirus retinitis with loss or vision
HSV infection, chronic ulcers (> 1 month;s duration); or bronchitis, pneumonitis, or esophagitis
Histplasmosis, disseminated or extrpulmonary
Isosporiasis, chronic intestinal
Kaposi's sarcoma
Lymphoma, Burkitt;s
Lymphoma, immunoblastic
Lymphoma, primary, of brain
Mycobacterium avium complex or M. kansasii disseminated or extrpulmonary
Mycobacterium tuberculosis, any site
Pneumocystis carinii pneumonia
Pneumonia, recurrent
Progressive multifocal leukoencephalopathy
Salmonella septicemia, recurrent
Toxoplasmosis of the brain
Wasting syndrome due to HIV

Table 7
1993 Revised classification for HIV infections and AIDS

CD4 T-cells	Asymptomatic, acute HIV or PGL	Syptomatic, not (A) or (C)	AIDS-indicator Conditions
> 500/μL	A1	B1	C1*
200 to 499/ μL	A2	B2	C2*
< 200μL	A3*	B3*	C3*

*Illustrate the expanded AIDS surveillance case definition

Table 8
Diagnosis and treatement of skin condition affecting HIV infections

Condition	Morphology	Treatment
Staphylococcal folliculitis	Erythematous follicular pustules or papules	Dicloxacillin or penicillinase
Bacillary angiomatosis	Friable, vascular papules, cellulitic plaques, subcutaneous nodules	Erythromycin Doxycycline
Herpes zoster	Grouped vesicles on erythematous bases	Acyclovir
Herpes simplex	Grouped vesicles on erythematous bases, resolving into superficial mucocutaneous ulceration or fissures	Acyclovir
Molluscum Contagiosum	Pearly flesh-colored papules w/ umbilication	Cryotherapy or cantharidin or electrosurgery or curettage
Insect bite reactions	Erythematous, urticarial papules	Lindane or permethrine
Photosensitivity	Eczematous eruption	Sun protection
Eoxinophilic folliculitis	Urticarial follicular papules	Astemizole and topical steroids
Seborrheic dermatitis	White scaling w/o erythema(dandruff) to patches yellowish, greasy scale	Hydrocortisone and ketoconazole
Psoriasis and Reiter's Syndrome	Sharply marginated plaques with silvery scale	Triamcinolone acetonide

Table 9
Treatment of oarl diseases associated with HIV infections

Condition	Treatment
Fungual	
Candidiasis	Anti fungals
Histoplasmosisi	Systemic therapy
Geotrichosis	Polyeme anti fungals
Crptococcosis	Systemic therapy
Bacterial	
HIV-associated gingivitis	Plaque removal Chlorhexidine
HIV-associated periodontitis	Plaque removal, debridement povidone-iodinem, metronidazole chlorhexidine
Nexrotizing stomatitis	Debridement, povidone-iodine, metronidazole, chlorhexidine
Mycobacterium avium	Sytemic therapy
Kebsiella stomatitis	Sytemic antibiotic therapy
Viral	
Herpes simples	Acyclovir
Herpes zoster	Acyclovir
CMV ulcers	DHPG
Hairy leukoplakia	Acyclovir
Warts	Excision
Neoplastic	
Kaposi's sarcoma	Palliative surgical or laser excision
Non-Hodgkin's lymphoma	Chemotherapy
Squamous cell carcinoma	Excision or radiation therapy
Other	
Aphthous ulcers	Topical steroids
Immune thrombocytopenic purpura	None recommended
Salivary gland disorder	Salivary stimulants

Table 10
Signs and symptoms of AIDS dementia complex

	Motor	Affective
Mild	Exaggerated tremor	Decreased recent memory
	Mild unsteady gait	Mild apathy
	Slowed eye movement	Diffculty with routine tasks
Moderate	Frank weakness of extremities	Decreased concentration
	Myoclonus	Decreased problem solving
	Seizures	Decreased timed performance
		Increased apathy
Severe	Incontinence	Absolute mutism
	Parakinesis	Severe dementia

Table 11
Percentage of lesions found

Group	Subgroup	Percentage (Number)
Asymptomatic	A	0 (0/54)
	B	33 (4/12)
PGL	A	0 (0/38)
	B	100 (1)
ARC		37 (3/8)
AIDS		76 (29/38)
Overall		25 (38/153)

Table 2: *Neuro-ophthalmic findings in AIDS—literature review*

- Cranial nerve palsies
  - CNS infections [toxoplasmosis (3,39,40), cryptococcosis (3), varicella zoster (29), PML (47), CMV (42)]
  - CNS lymphoma (primary or metastatic) (44,48)
  - Orbital lymphoma (49)
  - Cavernous and orbital apex eosinophilic granuloma (10)
- Optic neuropathy
  - Papilledema [cryptococcal meningitis, CNS toxoplasmosis, CNS lymphoma (29)]
  - Optic neuritis [CMV (9,20,22,26,35), syphilitic (17,18,37), varicella zoster (2,5), hepatitis B (19), toxoplasmic (38)]
  - Retrobulbar optic neuritis [syphilitic (30,31), CMV (9), cryptococcal (2)]
  - Optic nerve perineuritis [syphilitic (2), cryptococcal (15)]
  - Anterior ischemic optic neuropathy (33)
  - Toxic optic neuropathy [e.g., ethambutol toxicity (11)]
  - Optic atrophy as a sequelae of the neuropathy
- Eye movement disorders
  - Slowed saccades and abnormal oculokinetic response [HIV encephalopathy (4,14,16,24,26), CMV encephalitis (42)]
  - Progressive convergence insufficiency (24)
  - Reverse ocular dipping [cryptococcal meningitis (25)]
  - Parinaud's syndrome [herpes encephalitis (23), HIV encephalopathy (24)]
  - Internuclear ophthalmoplegia [CMV encephalitis (6,27), cerebral mucormycosis (43)]
  - PPRF lesions [HIV encephalopathy (24)]
  - Blepharospasm [HIV encephalopathy (24)]
  - Opsiclonus (11)
  - Skew deviation (11)
- Visual field defects
  - Homonymous hemianopsia [PML (13,44,47,52), cryptococcal meningitis (25), internal carotid occlusion from meningovascular syphilis (50)]
  - Homonymous quadranopsia [CNS astrocytoma (45)]
  - Enlarged blind spot [PML (12)]
  - Pericentral scotoma [PML (12)]
- Miscellaneous
  - Cortical blindness [cryptococcal meningitis (5), CNS tuberculosis (46)]
  - Visual allesthesia (44)
  - Visual hallucination (1,8)
  - Photophobia (cryptococcal meningitis) (53)

PML, progressive multifocal leukoencephalopathy.

TABLE 3. *Central nervous system complications in AIDS—literature review (54)*

- HIV infection (56)
  - Asymptomatic encephalomeningitis (abnormal CSF)
  - Aseptic meningitis (headache)
  - HIV encephalopathy-dementia complex (subcortical dementia with disturbance in cognition, motor skills, and behavior; cerebral atrophy by CT scan and white matter pallor histopathologically) (4)
- Opportunistic infections
  - Cerebral toxoplasmosis (13% of AIDS patients) (39,44,55,57)
  - Cryptococcal meningitis (10% of AIDS patients) (44)
  - Progressive multifocal leukoencephalopathy (3% of AIDS patients) (12,44,58,59)
  - CMV encephalitis (42,60)
  - Varicella zoster and herpes simplex encephalitis or cerebral vasculitis (56,62)
  - Tuberculosis and atypical mycobacteria (2% of AIDS patients) (45)
  - Mucormycosis (43)
  - Bacterial abscess (63)
- Tumors
  - Primary and metastatic CNS lymphomas (9% of AIDS patients) (54,57)
  - Astrocytoma (45)
  - Metastatic Kaposi's sarcoma (rare)
- Other complications
  - Intracerebral hemorrhage (2% of AIDS patients) (44,63)
  - Cerebrovascular accidents (63)

CSF, cerebrospinal fluid.

TABLE 14
Medication and their common adverse effects

Therapy	Adverse Effects
Ganciclovir IV	Immune toxicity
Intravitreal ganciclovir	Retinal detachment
Foscarnet	Anemia/nephrotoxicity
Acyclovir PO or IV	Renal and GI effects
Vidarabine IV	Gastrointestinal
TMP-SMX IV/PO	Pancytopenia
Pentamidine IV or aerosolized	Dysglycemia, neutropenia, renal
Pyrimethamine PO and sulfadiazine PO	Bone marrow toxicity
Amphotericin B IV	Fever, chills, nausea, vomiting, renal
Isoniazid PO and Rifampin PO	CNS, GI, drug fever prurtis optic neuritis
Ethambutol PO	None
Procaine penicillin IV	Hypersensitivity

Table 3. Treatment of Infections Associated With AIDS

Page 15

Disease	Primary agents and techniques	Alternatives	Comments
Pneumocystis pneumonia	Trimethoprim-sulfamethoxazole Parenteral pentamidine isethionate (Pentam 300)	Trimethoprim (Poloprim, Trimpex) plus dapsone Clindamycin (Cleocin) plus primaquine phosphate BW566C80 Trimetrexate glucuronate, which must be given with leucovorin calcium (Wellcovorin)	Avoid aerosolized pentamidine isethionate (NebuPent) as sole therapy If $Pao_2 < 70$ mm Hg or $PAo_2 - Pao_2 > 35$ mm Hg, concomitant corticosteroid therapy is indicated
Toxoplasmosis	Pyrimethamine (Daraprim) plus sulfadiazine with leucovorin	Pyrimethamine plus clindamycin BW566C80	
Cryptosporidiosis, *Microsporidia* infection	Supportive therapy Octreotide acetate (Sandostatin) Hyperalimentation		No known effective antimicrobial agents Paromomycin sulfate (Humatin) and azithromycin (Zithromax) under study for cryptosporidiosis Albendazole (Zentel) under study for *Microsporidia* infection
Cytomegalovirus disease	Ganciclovir sodium (Cytovene) Foscarnet sodium (Foscavir)	Intravitreal ganciclovir (can be used in cases of retinitis if toxicity makes systemic therapy impossible)	
Herpes simplex	Acyclovir (Zovirax)	Foscarnet (useful for acyclovir-resistant virus strains)	

Disease	Primary agents and techniques	Alternatives	Comments
Cryptococcal disease	Amphotericin B (Fungizone)	Fluconazole (Diflucan) used to prevent recurrences and as primary therapy in selected cases	
Candidiasis	Clotrimazole (Mycelex) Ketoconazole (Nizoral) Fluconazole	Amphotericin B (rarely necessary)	
Histoplasmosis	Amphotericin B	Itraconazole (Sporanox) may prevent recurrence	Monitoring of *Histoplasma* antigen may be helpful
Mycobacterium avium-intracellulare infection	Combination of 4-5 of the following: ethambutol HCl (Myambutol), clofazimine (Lamprene), ciprofloxacin (Cipro), amikacin sulfate (Amikin), clarithromycin (Biaxin Filmtabs), rifampin (Rifadin, Rimactane), rifabutin (Ansamycin)		Optimal regimen not defined
Tuberculosis	Isoniazid (Nydrazid) Rifampin (with pyrazinamide for first 2 mo)		Be alert for multiple drug-resistant viral isolates; alter regimen if drug resistance suspected Drug susceptibility testing and monitoring of compliance and response essential
Syphilis	Parenteral penicillin		Optimal management unclear Consider possibility of neurosyphilis

Table 16
Summary of patients encountered

Patient Number	Age/Race/Sex	Diagnosis of HIV (+)/ Stage	Systemic History	Ocular Signs
1	24 /B/M	9-91/IV	Pneumonia	CWS
2	38/B/M	1-91/IV	Pneumonia, Lymphadenpathy	None
3	41/W/M	3-89/IV	Pneumonia Lymphadenpathy	CMV retinitis with +1 vitritis
4	35/B/M	8-90/IV	NA	CWS, vascular congestion
5	35/B/F	9-89/NA	NA	None
6	40/B/M	NA/NA	Lymphadenpathy	None
7	40/B/M	1989?/NA	NA	RPE hyperplasia
8	30/B/M	8-88/NA	NA	None
9	39/B/M	NA/III	NA	Retinal Holes
10	40/B/M	1990/NA	NA	None
11	40/B/M	1986/NA	NA	None
12	37/B/M	1989/IV	CNS-ARD	Eratic saccade, 360 PPS +1C, +4 F OU, BRAO-OD, Non-rheg RD-OS
13	28/W/M	1991/NA	URI	None
14	23/B/M	1992/NA	NA	None
15	36/B/M	NA	Lymphadenpathy	None
16	30/W/F	NA	Lymphadenpathy Fever, chills & PPD	None
17	35/B/M	NA	NA	None
18	43/B/M	11-91/NA	NA	Retinoschiasis
KEY	W= caucasian B= Afro-American	NA = not available	URI=Upper respiratory infection	C=cells, F=flare PPS= Peripheral posterior syneciae BRAO=branch retinal artery occulsion

Patient Number	Absolute CD4,CD8, Ratio of Lymphocytes	Medications
1	37, 1061, 0.04, 49	None
2	39,1027, 0.10, 1300 (abs)	AZT, Bactrim, Zovivax
3	35, 1010, 0.06, 35	zirovax ung 5%prn, AZT 100 mg 5X/day dapsone 100mg/week
4	7, 386, 0.02, 19	ZDU 100mg QID, dapsone 200mg/weekly, Tetrecyline
5	394, 995, 0.40, 49.4	None
6	250, 854, 0.30, 43.3	AZT 100mg TID &200mg hs
7	66, 1716, 0.04, 50	AZT 100mg TID & 200mg hs folic acied 1 mg/day
8	640, 1173, 0.55, 43	None
9	177, 1920, 0.10, NA	None
10	103,1161, 0.09, NA	NA
11	81,1129,<.1, NA	AZT 100mg TID &200mg hs
12	20, 1100, 0.02, 10	AZT, gancyclovir 300 mg IV 2X/day
13	450, 800, 0.8, 30	None
14	490, 915, 0.53, 33	None
15	320, 1100, 0.29, 51	None
16	210, 1012, 0.21, 43	None
17	NA	INH for PPD
18	436,812, NA,39	
KEY	Normal values 490 to 1200, 182to 785, 1 to 5, 14 to 41	

1 Crobitt, G., Bailey, A.S. and William, G. (1990) HIV infection Manchester 1959. Lancet 1, 51
2 Blattner, William A. (1991) HIV epidemiology: Past, Present, and Future. FASEB J. 5(10), 2340-8
3 Poiesz, B. J., Ruscett, F. W., Gazdar, A.F., Bunn, P.A., Minna, J.D., and Gallo, R.R. (1980) Detection and Isolation of type C retrovirus particles from fresh and cultured lymphocytes of a patient with cutaneous T cell lymphoma. Proc. Natl. Acad. Sci. USA. 77, 7415-7419
4 Barre-Sinoussi, F., Chermann, J.C. Rex, F., Nugeyre, M.T., Chamaret, S., Gruest, J., Dauget, C., Axler-Bin, C., Vexinet-Brun, F., Rouzioux, C., Rozenbaum, W., and Montagnier, L. (1983) Isolation of T-lymphotrophic retrovirus from a patient at risk for AIDS. Science 220, 868-870
5 Gallo, R.C., Salahudding, S.Z., Popovic, M., Shearer, G.M., Kaplan, M., Haynes, B.F., Palker, T.J., Redfield, R., Oleske, J., Safai, B., White, G., Foster, P., and Mankham, P.D., (1084) Frequent detection and isolation of cytopathic retroviruses (HTLV- III) from patients with AIDS and at risk for AIDS. Science 224, 500-504
6. CDC. Acquired Immunodeficiency Syndrome-Dade County Florida, 1981-1990. (1991) Morbid. Mortal. Wkly. Rep. 29, 489-493.
7. Lamm, Steven H. Epidemiology of AIDS: An overview of AIDS Epidemiology and Major Modes of Transmission, (1990) Am. Ind. Hyg> Assoc. J. 51(11), A742-A746
8. CDC. Update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other blood borne pathogen in health-care setting. MMWR. (1988), 37(24), 377-388
9. Greenblatt, R.M., Lukehart, S.L., and Plummer, F.A. Genital ulceration as a risk factor for human immunodeficiency infection in Kenya, Third International Cjonference on AIDS, Washingto D.C. June 1-5, 1987
10. Cohen, N. Munoz, A., Reitz, B.A., Ness, P.K., Frazier, O.H>, Yawn, D.H., Lee, H., Blattner, W., Donahue, J.G., Nelson, K.E., and Polk, B.F. TRansmission of retrovirus by Transfusion of Screened Blood in Patients undergoing Cardiac Surgery. (1989) N. Engl. Med. 320, 1172-1176
11. Blattner, William A. (1991) HIV epidemiology: Past, Present, and Future. FASEB J. 5(10), 2340-8
12. McCormick, RD. Maki, DG. Epidemiology of needle stick injuries in hospital personnel. Am J Med. (1981), 70(4), 928-932
13. Palca, J. (1991) The Sobering GEography of AIDS. Science. 252, 372-373
14. CDC. The Second 100,000 CAses of Acquired Immunodeficiency Syndrome-United States (1992), JAMA. 267(6), 788
15. CDC. Update: Acquired Immunodeficiency Syndrome-United States 1991 (1992), MMWR. 41(26), 463-468
16. Lifion, A.R. Current Issues Concerning the Epidemiology of Acquired Immunodeficiency Syndrome and Human Immunodeficiency Virus (1992), The Western Journal of Medicine. 156(1), 52-56

17. Sande, MA. Volberding, PA. The Medical Management of AIDS, Third Edition, (1992)
18. Fischl, M.A. Treatment of HIV Infections. (1992) The Medical Management of AIDS, Third Edition, 97-110
19. Henry, WK. Essential HIV/AIDS fact. Postgrad. Medicine. (1992), 91(8) 84-93
20. Berger, JR. et al. Aids Summary 90. (1990), 138-167
21. Berger, JR. et al. Aids Summary 90. (1990), 168-228
22 Poulton, T.B. Chest Manifestations of AIDS (1992) American Family Phyiscian. 45(1), 163-168
23. CDC. MMWR. 41(RR-18), 5-7
24. 1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults. MMWR. 41 (RR-17), 1-19
25. Dal Canto MC. AIDS and the nervous system. Mum Pathol 1989, 20: 410-16.
26. Neurological Manitestations of AIDS. J Am Optom Assoc 1990, 61: 760-67.
27. Levy RM, et al. Neurological Manifestions of the Aquired Immunodeficiency syndrome: experience of USCF and review of the literature. Neurosurg 1985, 62: 475-95.
28. Journal of Clinical Neuro-ophthalmology 1990, 10(3): 167-74.
29. AIDS and the Eye: What You Need to Know. Review of Optom Feb. 1992; 76-80.
30. Ho DD, et al. HTLV-III from cerebrospinal fluid and neural tissue of patients with neurological syndromes related to acquired immunodeficiency syndromes. N Engl J Med 1985, 313: 1493-97.
31. Schuman JS, ORellana J, Friedman AN, Teich SA. Aquired immunodeficiency syndrome (AIDS). Surv. Ophthal 1987; 31: 384-410.
32. Bredesen D, Levy R, Rosenblaum ML. The neurology of human immunodeficiency virus infection. Q J Med 68: 665-77.
33. Journal of Clinical Neuro-ophthalmology 12(1): 1-5, 1992 Bilateral Optic neuropathies with Remission in Two HIV-Positive Men.
34. Golnik, et al. Cryptococcal Optic Neuropathy in the Aquired Immune Deficiency Syndrome. Jour of Clin Neuro-Ophthal 11(2): 96-103, 1991.
35. Schanzer, et al. Primary Ocular Malignant Lymphoma Associated with the Aquired Immune Deficiency. Ophthal Jan. 1991 Vol. 98 Number 1.
36. ShulerJD, Holland GN, Miles SA, Miller BJ, and Grossman, I. Kaposi sarcoma of the conjuctiva and eyelids associated with the acquired immunodeficiency syndrome. Arch Ophth 107: 858 1989.
37. Dugel, et al. Ocular Adnexal Kaposi Sarcoma in Aquired Immunodeficiency Syndorme. Amer Jour of Ophthal 110: 500-03 Nov. 1990.
38. Goldberg, et al. Primary Eyelid Non-Hodgki8ns Lymphoma in a patient with Aquired Immunodeficiency Syndrome. Am Journ of Ophthal Vol. 113, Number 2: 216-217.

39. Kim, et al. Necrotizing Scleritis Sencondary to Conjunctival Squamous Cell Caarcinoma in Aquired mmunodeficiency Syndrome. Am Journal of Ophth Vol. 109, Number 2: 231-32.
40. RKW Lau et al. Adult gonococcal keratoconjunctivitis with AIDS. British Journ of Ophth 1990, 74: 52.
41. Nanda et al. Fulminant Pseudomonal keratitis and Sceritis in Human Immunodeficiency Virus-Infected Patients. Arch Ophth Vol. 190 April 1991: 503-05.
42. Friedberg, et al. Microsporidal Keratoconjunctivitis in Aquired Immunodeficiency Syndrome. Arch Ophthal Vol. 108 April 1990: 504-08.
43. Metcalfe, et al. Microsporidial Keratoconjunctivtis in a patient with AIDS.
44. Young LS, Inderlied CB, Berlin OG, et al. Mycobacterial infections in AIDS patients, with emphasis on the Mycobacterium avium complex. Rev Infect Dis 1986 8: 1024-1033.
45. Cohen, et al. Endophthalmitis due to Mycobacterium avium in a Patient with AIDS. Ann Ophthal 1990 22: 47-51
46. Gabrieli, et al. Ocular Manifestaions in HIV-Seropositive Patients. Ann Ophthal 1990 22: 173-76.
47. Pepose et al. Aquired immune deficiency syndrome Pathogenic mechanisms of ocular disease. Ophthal 92: 472, 1985.
48. Pemerantz RJ et al. Infectin of the retina by human immunodeficency virus type I. N Eng J Med 317: 1643, 1987.
49. Quiceno et al. Visual dysfunction without retinitis in patients with aquired immunodeficiency syndrome. Am J Ophthal 113: 8, 1992.
50. Gass et al. Acute Syphilitic Posterior Pacoid Chorioretinitis. Ophthal Oct. 1990 Vol 97 Number 10: 1288-97.
51. Hites DA, Font RL. Bilateral intraocular Cryptococcosis with unilateral spontaneous regression. Am J Opthal 1968 65: 98-108.
52. Carney, et al. Cryptococcal choroiditis. Retina. 1990 Vol. 10 Number 1 27-32.
53. Specht, et al. Ocular Histoplasmosis in a Patient with Acquired Immune Deficiency Syndrome. Ophthal Sept. 1991 Vol. 98 Number 9 1356-59.
54. Grossnidlaus, et al. Toxoplasma gondii Retinochoiditis and Optic Neuritis in Aquired Immune Deficiency Syndrome.
55.. Hughes WT. Comparisons of dosages, intervals, and drugs in the prevention of Pneumocystis carnii pneumonia. Antimicrob Agents Chemother 1988; 32: 623-5.
56. Foster, et al. Presumed Pnemocystis carnii Choroiditis. Ophth Sept. 1991 Vol. 98 Number 9 1360-65.
57. Friedberg, et al. Pneumoncystis carnii Choroiditis. Ophthal May, 1992 959-96.
58. Rosenblatt, et al. Choroidal lesions in patients with AIDS. British Jour of Ophthal May 1990 74: 610-14.
59. Margolis, et al. Varicella-Zoster Virus Retinitis in Patients with the Aquired Immunodeficiency Syndrome. Am Journ of Ophthal 112: 119-31 August 1991.

60. Forster, et al. Rapidly Outer Retinal Necrosis in the Aquired Immunodeficiency Syndrome.
61. Wilson, Cytomegalovirus retinitis in AIDS. Journ Am Opt Assc Vol. 63 Number 1 Jan 1992 49-58.
62. Gross, et al. Longitudinal Study of Cytomegalovirus Retinitis in Aquired Immune Deficiency Syndrome. Ophthal May 1990 Vol. 97 Number 5: 681-86.
63. McClusky, et al. Cytomegalovirus retinopathy and the aquired immune deficiency syndrome: Results of treatment with ganciclovir. Australian and New Zealand Journ of Ophthal 199 18(4): 385-91.
64. Henderly, et al. Cytomegalovirus retinitis and acquired immunodeficiency syndrome. Am J Ophthal 1987; 103: 316-20.
65. Jabs, et al. Cytomegalovirus retintis and aquired immunodeficiency syndrome. Arch Ophthal 1989; 107: 75-80.
66. Palestine AG, et al. Ophthalmic involvement in aquired immunodeficiency syndrome. Ophthal 1984; 91: 1092-99.
67. Holland, et al. Survival of paaatients with acquired immune deficiency syndrome after development of cytomegalovirus retinopathy. Ophthal 199; 97: 204-11.
68. Caskey PJ, et al. Posterior segment manifestions of AIDS. Ophthal Clin North America 1990; 3: 393-412.
69. Freeman, et al. Pathologic observations made by retinal biopsy. Retina 1990 Vol. 10 Number 3 19995-204.
70. Sidikaro, et al. Rhegmatogenous Retinal Detachments in Patients with AIDS and Necrotizing Retinal Infections.
71. Adan, et al. Diabetic Retinopathy Associated with Aquired Immunodeficiency Syndrome. Am J of Ophthal June, 1990 744-45.
72. Lee, Everett AI. Disc Neovascularization in Patients with AIDS and Cytomegalovirus retinitis.
73. Studies of Ocular Complications of AIDS (SOCA) Research Group in collaboration with the AIDS Clinical Trials Group (ACTG). Mortality in patients treated with either foscarnet or ganciclovir for cytomegalovirus retinitis. N Engl J Med 326: 213, 1992.
74. Wilks, David. Dalgleish, AG. Antiretroviral Therapy. Aids and the New Viruses. (1990) 55-80