A comprehensive guide to AIDS and the optometrist, including a study investigating ocular involvement in the AIDS virus

Senior Project

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April 14, 1989

Abstract

Acquired immunodeficiency syndrome, (AIDS) was first diagnosed in the United States in June 1981. Since this initial case, the number of AIDS reported infections has escalated to 55,000 as of May 1988. No effective cure has been found, with over half of those infected now deceased. Common systemic conditions include generalized lymphadenopathy, Pneumocystis carinii pneumonia, Karposi's sarcoma, Cryptococcal meningitis, chronic Herpes Simplex and Toxoplasmosis gondii. Ocular manifestations of the human immuno-deficiency virus are cotton wool spots, retinal hemorrhages, Cytomegalovirus retinopathy, ocular Herpes Simplex and Herpes Zoster. Current treatments employed include azidothymidine, (AZT), ribavirin, acyclovir, dextran sulfate, and diethyldithiocarbamate have been effective only in hampering the progression of the virus.

A study of 19 HIV infected subjects were followed over a nine month course. Ocular effects of the HIV infection were investigated in all 19 subjects. The majority of the subjects in the study were asymptomatic with no ocular signs. Our investigation showed that only subjects late in the disease process had ocular signs characteristic of AIDS. Topics also covered include statistics and demographics of AIDS, general background on the course of AIDS infections, precautionary measures to take in the office and what an optometrist can do if he/she suspects a patient may be infected with the virus.

A new syndrome was first recognized in June 1981, when investigators in Los Angeles reported a highly unusual incidence of pneumocystis carinii pneumonia in young homosexual men. This condition was previously thought to occur almost exclusively in elderly immunocompromised individuals. Soon after, physicians in New York City reported unusual cases of the skin cancer Kaposi's Sarcoma in young homosexual men which had been thought to occursolely in elderly men of Mediterranean and African descent. By May 1988 more than 55,000 cases of opportunistic infections and unusual malignancies had been reported in previously healthy individuals (1). The common link in all of these cases is a similar pattern of acquired failure of cell-mediated immunity, hence the term "Acquired Immunodeficiency Syndrome" or AIDS. This syndrome is described as an assemblage of opportunistic infections, Kaposi's sarcoma, and unusual malignancies in previously young healthy individuals.

It has been a very long time since man was challenged with a disease that presented as great a threat as AIDS. Other infectious diseases such as small pox, poliomyelitis, and tuberculosis have been brought under our control. The pandemic of AIDS continues to spread. As of January 30, 1988 the World Health Organization (WHO) recieved reports from 132 countries with cumulative cases estimated as high as 150,000 worldwide; another 150,000 cases are estimated to occur in 1988 bringing the worldwide total to 300,000. The WHO estimates that between 5 and 10 million people are already infected with the virus and between 500,000 and 3 million will progress to AIDS within the next five years (34).

All fifty states and Puerto Rico have reported the presence of the AIDS virus with the majority of reports coming from New York,

California, Florida and New Jersey. Aids patients are most commonly between the ages of 20 and 49 (90 percent), white (58 percent white, 28 percent black, 14 percent hispanic) and male (93 percent) (11). Homosexual or bisexual men represent 72 per cent of the AIDS population followed by IV drug users at 17.4 per cent, haitians (4 percent), children (1.3 percent), hemophiliacs (1 percent), and heterosexual partners of persons with or at high risk of developing AIDS (1 percent) (11).

The ultimate mortality rate of persons contracting AIDS nears 100 percent (12). The mean number of months from diagnosis to death is less than 24, and of all AIDS patients in the United States carrying the disease for at least 3 years, over 80 percent have died (13).

Systemic manifestations

The range of manifestations of HIV infections is broad and can follow many different courses. The three main classifications are initial infection, progressive generalized lymphadenopathy (PGL) also known as AIDS-related complex (ARC), and full blown AIDS.

Infection with HTLV III will result in seroposivity although the patient may remain asymptomatic. Some experts believe more than 1,750,000 individuals may be infected the virus in this country (1). These individuals may or may not progress to PGL. The question still remains as to what percentage of patients with antibodies to HTLV III will develop the disease and how long the latency period is. Although not known for sure at this time, the incubation period for AIDS following initial exposure to the virus has been estimated to be as short as a few weeks or extend to several years. It is unknown why most seropositive individuals do not manifest the disease, but it is important to note that these individuals are capable of transmitting the disease.

Progressive generalized lymphadenopathy includes patients with altered immune status and lymphadenopathy but without life-threatening infections or malignancies. The Centers for Disease Control (CDC) has defined the chronic lymphadenopathy as a lymphadenopathy of at least 3 months' duration involving two or more extralingual sites; absence of any current illness or drug use known to cause lymphadenopathy; and presence of reactive hyperplasia in a lymph node, if a biopsy is done. It has beenestimated in the literature that anywhere from 5 to 17 percent of these individuals will develop AIDS within 30 months (2,3). Twenty nine percent of PGL patients will progress to AIDS within 54 months (5,6).

It is possible in patients that do not go on to develop AIDS that their condition represents the complete manifestations of a mild or more effectively controlled infection with HTLV III.

Symptoms of patients with PGL are similar to those of AIDS patients but less severe. These patients do not show any opportunistic infections or malignancies. Patients may otherwise be asymptomatic or may suffer from a variety of longitudinal symptoms such as a persistent low grade fever, anorexia, malaise, night sweats, diarrhea, a thick white coating of the tongue or throat, pallor of skin or mucous membranes, and unexplained tender lymph nodes (4).

A diagnosis of AIDS is made when any one of a variety of opportunistic infections or malignancies presents itself. Pneumocystis carinii pneumonia (PCP) is the commonest non-ocular condition confirming the AIDS diagnosis (66 percent), folowed by a highly aggressive form of Kaposi's sarcoma (KS) (24 percent), and a variety of other opportunistic infections (17 percent) including:

Protozoal

Toxoplasmosis gondii (3 percent)
Chronic Cryptosporidium enteritis (longer than one month)

Viral
- Chronic mucocutaneous Herpes simplex (4 percent)
- Cytomegalovirus infection
- Progressive multifocal leukoencephalitis
- Hepatitis B

Fungal
- Disseminated Cryptococcal meningitis (7 percent)
- Candida esophagitis
- Histoplasmosis

Bacterial
- Mycobacterium tuberculosis

Cancerous
- Non-Hodgkin's lymphomas (7,8,9)

P. carinii pneumonia

Aids is the only immunodeficiency syndrome in which PCP is the most common infection (10). There may be two different presentations of the disease the commonest exhibiting subacute symptoms of greater than 2 weeks duration including a gradual reduction of exercise tolerance and a dry, nonproductive cough. The presentation may be fulminant, with rapid onset of hypoxia and respiratory failure. The definitive diagnosis is the same in both groups; first by bronchoscopy, followed by open lung biopsy if bronchoscopy is unsuccessful (7).

Dermatologic manifestations

Many of the dermatologic manifestations found in HIV infected individuals are found in the normal population but are of sudden explosive onset and increased severity in AIDS patients. It has been stated that most cutaneous manifestations of AIDS become manifest when the T-helper lymphocyte count drops below 100 cells/ cubic mm (14).

Kaposi's sarcoma

Kaposi's sarcoma is the most common dermatologic manifestation of AIDS. Prior to the emergence of AIDS, KS in the United States was

only exhibited in various immunocompromised patients, mainly renal transplants. KS in this population of patients is similar to KS in AIDS patients in that the course is very aggressive (17). Most patients present with classic red-purple nodular skin lesions which range from several millimeters to several centimeters across depending on the time and course of the disease process. Although the lesions may appear in different forms or occur anywhere, the typical locations are the outer third of the eyelid, the tip of the nose, and the hard palate (9,15,16). When no skin lesions exist, the two most common locations for KS are in the lymph nodes and all segments of the gastrointestinal tract from mouth to anus. Although GI involvement is frequent, it is usually asymptomatic unless extensive (8,11). Other possible areas of involvement include the spleen, gallbladder, pancreas, kidney, adrenal, testis, palpebral conjunctiva, adventitia of aorta and large vessels, perineural connective tissue, and the lungs. Pulmonary involvement has been seen in only a small portion of patients and is usually associated with a rapidly progressive course and a poor prognosis (8,12).

Other dermatologic conditions affecting AIDS patients can occur anywhere on the body and include severe seborrheic dermatitis, telangiectasias, psoriasis, atopic dermatitis, itchy folliculitis, anogenital warts or ulcers, reactivation of secondary syphilis causing extensive skin lesions, herpes zoster infection, and severe wasting of musculature. These signs are commonly found in normal individual who are not HIV positive, but it is the unusual location or exaggerated expression of these common disorders that points to AIDS (14).

Nondermatologic manifestations

Toxoplasmosis

Infection with Toxoplasmosis gondii is not uncommon within the general population of the United States. Its various manifestations include an asymptomatic form, regional or generalized lymphadenopathy, and a mononucleosis-like illness. Toxoplasmosis in immunocompromised hosts (organ transplant patients) behaves quite differently exhibiting a fever and a central nervous system infection; either encephalitis or a brain mass lesion. Toxoplasmosis in AIDS patients has the same clinical presentation seen in other immunocompromised individuals and is the most common cause of CNS disturbance in AIDS patients.

It is often misdiagnosed as a bacterial brain abcess or viral encephalitis. The key to making the correct diagnosis lies in suspecting the possibility of AIDS by determining if the patient is in an increased risk group or by subtle early systemic AIDS signs and symptoms. A computed tomograph (CT) scan of the brain should be performed on all suspect patients, though a definitive diagnosis can be made only by brain biopsy. A quick diagnosis is crucial in that therapy has been found to be more successful if initiated early in the disease course (7,8,18).

Cytomegalovirus

The cytomegalovirus (CMV) belongs to the herpesvirus group and is the causitive agent in cytomegalic inclusion disease (CID). CID can be either congenital or acquired. In the congenital form, the virus is contracted through placental transfer and the severely affected infant may suffer from a whole range of abnormalities including low birth weight, hepatosplenomegaly with jaundice, purpura, thrombocytopenia, and pneumonitis. CNS involvement includes microcephaly, cerebral calcification, deafness, psychomotor retardation, and seizures.

Acquired CID has a strong predilection for the immunocompromised host (previously mainly organ transplant patients) and a persistent form of the disease occurs in AIDS patients. It is a major cause of dysfunction in a variety of organs. CMV infection of the lung results in focal and diffuse pneumonitis. Gastrointestinal involvement is characterized by ulceration in sites ranging from the esophagus to the rectum, and these ulcers may provide a portal of entry into the bloodstream for a variety of enteric organisms. In the central nervous system, CMV may cause a destructive meningoencephalitis. Ocular features include cataract, uveitis, optic nerve hypoplasia, and a multifocal chorioretinitis that will discussed later. Although several antiviral drugs are under evaluation, there is no specific treatment for the infection (8,9,19,20).

Cryptococcosis

Cryptococcus neoformans is a common cause of meningitis and disseminated disease in patients with AIDS. Cryptococcal meningitis occurs in the "general immunocompetent population" usually in an insidious manner but can have an acute aggresive course in immunocompromised individuals (21). The most common signs and symptoms associated with the disease are headache, vomiting, mental status changes (confusion, irritability, impaired memory, behavioral changes, psychosis), and neck stiffness. Cryptococcus neoformans can also cause pneumonitis, lymphadenitis, thyroiditis, and chorioretinitis (8,9,21).

AIDS dementia complex

New manifestations of AIDS related illness are still being recognized, but the most recent and disturbing discovery is that the virus may damage the brain long before signs of disease surface

elsewhere in the body (22,23). AIDS dementia complex has recently been described as the combination of neurologic and neuropsychiatric symptoms that occur in AIDS patients.

AIDS dementia results primarily from damage to the deep central white matter of the brain, particularly the basal ganglia and thalamus. CT scan of the brain shows no focal lesions, but the lateral ventricles and sulci on the surface of the brain seem to be enlarged. Results of brain biopsy show nonspecific inflammation with demyelination and cerebral atrophy (2,23).

Researchers are beginning to formulate theories on the pathogenesis of AIDS dementia. Several researchers have shown that the virus enters the brain in macrophages, perhaps in response to an infection such as cytomegalovirus. Once there, these cells harbor the virus (22). To date, there are only hypotheses to explain how the virus does its damage to nerve and glial cells once inside the brain.

A variety of symptoms have been well documented. First, affected individuals present with cognitive changes such as impaired concentration, memory loss, and confusion. Patients may become apathetic, depressed, and withdrawn. Motor ability is also impaired resulting in clumsiness, weakness, and ataxia. In the end stage, patients may become mute and sit with a vacant stare (14,23).

It is difficult to separate those symptoms caused solely from the psychological effects that occur in a patient knowing that he has the AIDS virus. Tests of memory, concentration, and psychomotor ability will need refinement to pick up early and subtle changes that are solely caused by HIV infection in the brain so that, when it becomes available, antiviral treatmant can be given before irreversible damage occurs. The number of HIV seropositive

individuals exceeds the number with AIDS by a factor of 50 or more (24), and it is these individuals who are at risk of developing HIV related neurologic disease.

Ocular Signs and Symptoms

Ocular lesions were identified in the first patients reported to have AIDS.(35) Studies have shown that 40-100 percent of those with AIDS demonstrate ocular manifestations of HIV disease. The onset of these ocular problems has not been established.(47) Human Immunodeficiency Virus has been recovered from multiple ocular tissues in a study of three AIDS patients.(39) The virus was consistently found in the conjunctiva, cornea, iris, and retina despite treatment with the oral anti-viral agent, zidovudine.(39) The following table is a grouping of AIDS Ocular Manifestations:(35)

I. **Noninfectious Vascular Disorders**
   - A. Cotton wool spots
   - B. Retinal hemorrhages
   - C. Microaneurysms
   - D. Ischemic maculopathy

II. **Opportunistic Ocular Infectious Diseases**
   - A. **Pathogens of the retina and choroid**
     1. Cytomegalovirus
     2. Mycobacterium avium-intracellulare
     3. Cryptococcus neoforans
     4. Toxoplasma gondii
     5. Herpes simplex virus
     6. Candida albicans
     7. Histoplasma capsulatum
   - B. **Pathogens of the cornea and ocular adnexa**
     1. Cytomegalovirus
     2. Herpes simplex virus
     3. Herpes Zoster virus

The most common ocular disorder seen in patients with AIDS is a form of retinopathy consisting of cotton wool spots, hemorrhages, and capillary abnormalities seen in virtually all patients with AIDS during the course of their illness.(47) Cotton wool spots are the most common ocular lesions in AIDS patients, but cannot be considered diagnostic for AIDS because of these infarcts are present in other conditions including diabetic retinopathy, hypertensive retinopathy, severe anemia, collagen vascular disease, and scleroderma.(35)

The etiology of cotton wool spot (CWS) formation in AIDS patients is from circulating immune complex deposition. HIV infected individuals have increased levels of circulating immune complexes and these immunoglobulins have been isolated adjacent to cotton wool spots.(35, 42) It is still unclear as to whether these immune complexes are present because of vascular leakage or whether they are deposits.(35) The microvasculopathy responsible for cotton wool spot formation is characterized by swollen endothelial cells, thickening of the basal laminae, narrowing of capillary lumens, degeneration and loss of pericytes.(35) These microvascular changes are similar to those seen in diabetic retinopathy.(35) One study compared the appearance of cotton wool spots in AIDS patients to those present in diabetes mellitus, hypertensive retinopathy, and central retinal vein occlusion. This study found that CWS had a predilection for the temporal quadrants in the four catagories and were smaller in patients with AIDS than in other groups.(43) Patients with central retinal vein occlusion had more CWS than the other groups. No other definite differences were detected. To differeniate cytomegalovirus retinopathy from CWS in AIDS patients, CMV retinopathy the borders of the lesions are more fluffy, the lesions lie deeper in the retina and lesions associated with CMV retinopathy tend to increase in size on follow up examination. Cotton wool spots tend to be well demarcated and are located in the nerve fiber layer of the retina.(43) Cotton wool spots will have a more transitory existence with serial observations, where CMV retinopathy will leave a permanent scar in the retina.(40) Despite many studies, CWS cannot be considered to represent

early CMV retinopathy. There have no reports of virus particles being detected in CWS.(40)

Cotton wool spots occuring independently of systemic disease must be assumed to carry a prognosis for preceeding opportunistic infections in both ARC and AIDS groups.(40) CWS can occur anywhere along the HIV infection process. Eight of twenty-eight patients studied developed severe AIDS complications within a few months after the occurance of CWS.(42) Another source reported a higher mortality rate in AIDS patients with CWS than without these lesions.(35)

Another vascular abnormality, retinal hemorrhages, are seen in 15-40 percent of AID patients. These hemorrhages appear as either blot or flame shaped. Microaneurysms are seen in 20 percent of AIDS cases.(35) Although retinal hemorrhages show a predisposition for the posterior pole, CWS are found in the midperiphery as well. Ischemic maculopathy leads to a drop in visual acuity and is the only sequela of the retinal microvasculopathy of AIDS with visual symptoms. The factors that cause ischemic maculopathy are not known.

Cytomegalovirus (CMV) retinopathy is the most frequent ophthalmic opportunistic infection in patients with AIDS, occuring in 12-46 percent of this population.(36) The incidence maybe higher in homosexual or bisexual males than AIDS patients from other risk groups.(35) CMV retinopathy is clearly a disease of immune deficiency. Prior to AIDS, CMV retinopathy was a rare disorder,occuring in 5 percent of organ transplant patients on immunosuppressive medications.(35) The usual appearance of CMV retinopathy can be described as a necrotizing tissue mixed with blood and gives the resemblance of "ketchup on cottage cheese".(45)

CMV retinopathy may be multifocal and is bilateral in 50 percent of patients. Usually infection begins in the posterior pole adjacent to the vascular arcades but the virus may begin in the retinal periphery as well. Once established, CMV retinopathy is relentlessly progressive without treatment. Lesions expand and coalesce eventually destroying the entire retina within a six month period.(35) The retina is replaced by a thin gliotic membrane Patients will usually die before this stage is reached. If the infection spreads to the optic nerve from foci of peripapillary retinopathy, early total loss of vision occurs.(35) Rhegmatogenous retinal detachment is a late complication of CMV retinopathy. Large shaggy tears develop in areas of necrotic retina, making repair difficult. CMV retinopathy elicits relatively little inflammation. The vitreous usually contains little inflammatory response, with affected eyes remaining white and painless. Infection does not usually spread across the ora serrata and the virus does not infect the choroid underlying foci of CMV retinopathy. Although the virus has been located in the cilary processes, uveal tissues appear to be relatively resistent to infection with CMV.(35) Cytomegalovirus has been conclusively found in the conjunctiva.(38)

The prognosis of patients with CMV retinopathy in the first reported series of cases was that no patient survived longer than six to eight weeks.(35) More recent studies have described patients who survive up to four months from the onset of CMV retinopathy. CMV retinopathy is the major cause of vision loss in AIDS patients.(40)

Other opportunistic infections associated with the HIV infection include Toxoplasma gondii, Candida albicans, Herpes

zoster virus, and an altered form of syphilis. Ocular toxoplasmosis accounts for less than three percent of ocular infections in AIDS patients, however, intracranial toxoplasmosis is the most common opportunistic infection of the central nervous system, accounting for 64 percent of non-viral infections.(35)

Despite high incidence of mucocutaneous candidiasis in AIDS patients, intraocular candida infections are rare.(35) The ocular appearance of candida is described as whitish colored lesions with an overlying vitreal haze of inflammatory cells. These lesions will progress in size on serial examination.(35)

Herpes zoster ophthalmicus is a manifestation of AIDS, ARC, and HIV positive patients. Ophthalmic signs include the presence of vesicles on the eyelids, conjunctivitis, dendritic keratitis, and a uveitis.(35) Herpes zoster ophthalmicus is usually seen in elderly patients. In a study by Sander and associates, Herpes zoster ophthalmicus when present in individuals under 44 year of age, 91 percent had reversals of the normal T4/T8 ratio (greater than 1.0), 21 percent went on to develop AIDS during a two year follow up.(35) Management of HZO at a relatively young age should include a referral for HIV antibody blood tests.

In a patient with syphilis with a concomitant HIV infection, the diagnosis may become obscured and impair the response of syphilis to therapy.(37) Ocular syphilis, which typically presents with a uveitis, optic neuritis and retinitis when coupled with the human immunodeficiency virus accelerates the syphilis involvement frequently attacking the central nervous system and often does not respond to standard therapy for primary and secondary syphilis.(37)

Other ocular manifestations of the HIV infection would

include Karposi's sarcoma, a neoplasm that could involve the eyelids, eyelid margins, conjunctiva, rarely within the orbit, or on any surface of the body. Karposi's sarcoma occurs in approximately 24 percent of AIDS patients, and has been found to be more prevalent in the homosexual/bisexual risk groups.(35) Although KS is considered to be a late manifestation of the HIV infection, the ocular adnexa and conjunctiva are potential sites for early development because these tissues have abundant vascular supplies.(47)

The appearance of Karposi's sarcoma on the conjunctiva appear as a bright red subconjunctival lesion easily mistaken for a subconjunctival hemorrhage. KS may regress some but never completely without treatment. Tumors typically spread slowly when invading the conjunctiva, and they rarely interfere with vision. KS of the conjunctiva most frequently involves the inferior cul-de-sac.(35) Eyelid tumors appear as purple-red nodules that can result in eyelid edema, entropian formation and trichiasis. In one study of 38 subjects who were HIV positive, there were no reported cases of conjunctival KS with seven cases of KS found elsewhere on the body.(42) If KS is detected, a referral to an internist is in order.

Cranial nerve palsies as a sequelae to an intercranial infection have been sited in patients affecting the third and fourth cranial nerves secondary to a cryptococcus infection of the central nervous system. Toxoplasmosis has also been sited to cause a rare cranial nerve palsy also affecting the third and fourth cranial nerves.(35) The frequency with which intercranial disease in AIDS patients causes cranial nerve dysfunction is not known. Papilloedema was found in 14 percent of AIDS patients

in an autopsy study by Pepose and associates.(35) A rare case of internuclear ophthalmoplegia was found in an AIDS patient thought to be secondary to CMV encephalitis.(40) Another rare case in the literature of bilateral acute retinal necrosis, (BARN) as a presenting sign of AIDS in a previously healthy man.(46) The clinical characteristics include initial anterior uveitis followed by retinal and choroidal vasculitis, vitritis, and papillitis. Visual prognosis is poor, however, intravenous acyclovir and laser photocoagulation have improved visual outcome in some reports.(46)

Available Treatments in HIV Infection

There has been a lot of research and research money dedicated to find a cure for AIDS and a vaccine for the HIV infection. Currently there is no vaccine, but there is some merit to the presently available treatments in arresting the progression of the disease and prolonging life. The following will involve a discussion of eight medications used in the fight against the AIDS virus.

Azidothymidine, (AZT) with the trade name retrovir formerly known as zidovudine is the only drug which has been approved by the FDA as a treatment for the HIV infection. AZT was discovered in the 1960's as a cancer treatment which it was found to be ineffective. In 1984, the Centers for Disease Control identified AZT as one of the first substances found to act against HIV in vitro. Presently AZT is commonly used by persons with AIDS, ARC with low T4 counts, and increasingly by people without symptoms who are HIV positive. AZT works by inhibiting reverse transcriptase, an enzyme which is critical to the reproduction of a virus. AZT does this by providing a substitute

of the disease, especially by subjects in early stages of the disease.(49) The most common side effect with ribavirin is some degree of anemia, but this is often a problem in AIDS patients with or without the drug. Like anemia produced by AZT, this is treated with dose reduction and is reversible.(49) Although ribavirin remains is the second best documented drug in HIV therapy, it has not been shown to be effective against cytomegalovirus.(36)

Acyclovir, tradename Zorivax, has received a lot of recent attention for its effectiveness against a number of infections common with HIV which include herpes simplex, herpes zoster, hairy leukoplakia (HLP), mild CMV, and Epstein-Barr virus (EBV).(49) Other support for acyclovir as a viable treatment against HIV comes from the 1988 Stockholm AIDS Conference, where it was reported that acyclovir with half the standard dose of AZT produced equivalent results to those using a full dose of AZT. Acyclovir even at higher dosage levels is usually well tolerated and is considered to be a low toxicity drug. Even with Acyclovir's effectiveness against many HIV cofactor infections, this anti-viral agent has not been found clinically beneficial against cytomegalovirus at standard doses. (36)

Another useful drug in the arsenal against the AIDS virus is Dextran Sulfate. Dextran Sulfate was first introduced in the 1950's as an anti-coagulant and to lower blood cholesterol levels.(49) Dextran Sulfate will act against HIV in two ways, first, it inhibits production of reverse transcriptase similar to the mechanism in AZT therapy.(49) Secondly Dextran Sulfate will prevent infected T cells from linking up with and attacking other T cells, which is exclusive to Dextran Sulfate. It is postulated

for one of the proteins of the virus during its reproductive cycle. When the virus is fooled by AZT, the chain of reproduction is broken, which will slow and prevent production of new virus but has no affect on existing virus. Results of placebo studies show that AZT appears to increase life expectancy of AIDS patients and slows the progression of ARC to AIDS. The main side effects with AZT are due to the damage in reproduction of red blood cells and white blood cells producing anemia and neutropenia. Doctors in Vancouver, British Columbia, claim that AZT induced anemia can be controlled by monthly injections of vitamin B12. AZT induced anemia may also be reversed by reducing the dosage of this toxic anti-viral agent. Another disadvantage to AZT is that AZT has been shown to have no preventive affect against Karposi's Sarcoma. AZT is not to be used in combination with ribavirin, another anti-viral used to fight HIV, and acetominaphen because they enhance the side effects of AZT. Other concerns are the high cost of AZT and the diminishing benefit of the drug in long term therapy.

A second anti-viral used to combat HIV is ribavirin, trade name Vilona. Ribavirin was developed in 1973 and has since been identified by the Centers for Disease Control as having activity against HIV. From 1984 through 1987, ribavirin was the most widely used treatment for HIV infection, although it has never been approved for this use.(49) Research at Harvard Medical School in 1986 shows the ability of ribavirin to cross the blood-brain barrier making this anti-viral drug capable of suppressing the virus in the brain and spinal fluids. Additional support for the drug comes from a survey of 130 HIV infected subjects who indicated the drug was helping to slow the progress

that this drug may interfere with the attachment of HIV to T4 cells.(49) These results have all been gathered in vitro and as of August, 1988 no human studies have been done to measure the effects against HIV and there is some question as to whether Dextran Sulfate is capable of crossing the blood-brain barrier.(49) The most likely side effects are problems associated with anti-coagulants. The synergistic effects with AZT are currently being studied with surveys from patients using a quarter to a half of the standard 1200 mg per day dose of AZT with Dextran Sulfate being favorable.(49)

Naltrexone, tradename Trexan, is used in the treatment of herion addiction and may play a role in regulating the immune system. Naltrexone works by stimulating the production of natural endorphins and in high doses, blocks the reception of opiates.(49) In several studies performed by the same researcher, a study group was compared against a control group on placebo. These studies showed changes which indicate improved immune response including improved helper/suppressor cell T cell ratios.(49) The dosage used is too low to work as addiction therapy and there have been no side effects reported at these low concentrations.(49)

Diethyldithiocarbamate (DTC), tradename imuthiol is a metal chelating agent which like other drugs in its class, is believed to have anti-viral properities. DTC is thought to work by stimulating the liver to produce a hormone-like activity called hepatosin. Hepatosin is reported to speed the maturation of T4 cells, thus increasing their numbers and improving the T4/T8 ratio. In addition hepatosin improve the natural killer response and will slow the reproduction of the AIDS virus.(49)

DTC is the first drug to improve T4 cell counts and is especially beneficial to patients with higher T4 counts to begin with. DTC is not easily available, but is very similar in chemical structure to Antabuse, the prescription drug used to treat alcoholism. Antabuse breaks down into DTC in the bloodstream and when used properly may produce the same benefits as DTC.(49)

Another treatment that has shown promise against the ocular manifestations of AIDS is Dihydroxypropoxymethyl Guanine tradename, Ganciclovir. Ganciclovir showed early signs of regression of CMV retinopathy with non-advancement of the edges, decreased satellite lesions, with signs of healing beginning as early as two weeks and usually complete by ten weeks.(36) Ganciclovir has also been effective against cotton wool spots showing resolution with treatment and reappearance of these nerve fiber infarcts with cessation of ganciclovir therapy.(42) In treatment of CMV retinopathy, 200 mg weekly intravitreal injections provide the best effect with rare side effects such as the potential of leukopenia, colitis, renal toxicity, and teticular atrophy.(42)

Steroid treatment in CMV retinopathy may actually exacerbate the retinal necrosis and is contraindicated in patients with CMV retinopathy.(35) In non-AIDS patients, particularly immunosuppressed transplant recipients, restoration of immune function has been shown to cause regression and healing of CMV retinopathy.(36) Vidarabine has proven to control CMV retinopathy in non-AIDS patients.(35)

Because there is no present cure for this terminal illness and because of the rapid increases in those being afflicted with the disease, education plays a crucial role in prevention.

Implications for Optometry

The optometric examination could become the primary point of preliminary diagnosis and referral for some people infected with HIV.(47) As more individuals become infected with HIV, the likihood of optometrists examining patients with known or occult HIV related diseases and its subsequent ocular manifestations will increase.(47) Herpes Zoster Ophthalmicus in patients under 50 years of age with a more chronic condition, Karposi's sarcoma of the conjunctiva or adnexa, and non-infectious AIDS related retinopathy (peripheral perivasculitis with cotton wool spots and hemorrhages) are three important ocular changes that the optometrist may diagnose in the early stages of HIV infection or in an undiagnosed case of AIDS. (47) Patients presenting with any one of these signs or symptoms discussed earlier, should be considered as potentially infected with HIV and immediately referred to a physician, where blood tests can be ordered for the presense of HIV antibodies.(47) Patients infected with the HIV virus may have as long as a six month latency period before the body produces HIV antibodies. These patients would be asymptomatic and produce a negative HIV blood test. However, patients with symptoms and manifesting ocular signs definitive of HIV infection will all test positive for HIV antibodies because HIV related symptoms as well as ocular signs are characteristics of ARC indicating the patient has been infected for some time.

The blood tests ordered by the physician for HIV antibodies are the Western Blot technique, and the ELISA, linked immunosorbent assay, smear.(41) One test verifies the accuracy of the other making the combined tests highly accurate. ELISA becomes positive three to 12 weeks after infection, but officials report as long as six months for a latentcy period.

In addition to referring the patient for diagnostic blood tests, the optometrist could provide sources for additional information on AIDS, counseling availabilities and a phone number for the latest treatments once a diagnosis has been established. These resources are all listed on the enclosed sheet entitled, "Additional Information on AIDS".

Since AIDS is both a systemic and ocular disease, it is essential that the eye care practitioner be aware of the high risk groups for contracting the disease, as well as the systemic signs and symptoms that may be a warning signal to an underlying problem. A thorough case history for all patients cannot be overemphasized.

Patients at risk for HIV infection include:

1. Persons, male or female, who have been sexually active since the mid-to-late 1970s, with multiple male or female partners;
2. Persons who have shared paraphernalia for the injection of drugs by puncture of skin or mucous membranes;
3. Persons having intimate sexual contact with an AIDS patient or someone in a high risk category;
4. Recipients of donor organs, tissue, or sperm from persons with AIDS or at risk for contracting AIDS;
5. Hemophiliacs, or others who require large quantities of blood or blood products;
6. Infants born to or breast fed by mothers who have AIDS or are at risk for AIDS (25).

Patients, especially those in high risk groups, presenting with any of the following signs and symptoms, when not easily or otherwise explained, should be referred to a health care practitioner familiar with AIDS:

1. Enlarged, hardened, or painful lymph nodes involving 2 or more extralingual sites for more than 3 months duration;
2. Reddish-purple nodular skin lumps or growths of sudden onset or slow growth;
3. Weight loss of more than 10 lbs (or 10 percent of body weight) in less than 2 months and not attributable to an obvious cause;
4. Chronic fevers or night sweats;
5. Persistent diarrhea;

Educating the public about high risk groups and the ways that HIV is contracted are the only ways to slow the spread of this fatal disease. Optometrists, as primary care providers, need to be a part of the education network. Not only is it important for our patients to thoroughly understand the ways that the disease is passed, but also to ease anxieties by assuring patients of the unlikelihood of getting infected if in the non-risk group catagory.

6. An unexplained dry, nonproductive cough with hypoxia not attributable to smoking and too chronic to be from a common cold;
7. Loss of memory, impaired concentration, impaired motor ability, mood and personality changes, or recurrent neurologic or psychiatric symptoms;
8. Herpes zoster infections in at risk populations not attributable to stress;
9. Recurrent unexplained pain;
10. Persistent unexplained fatigue, malaise, and light headedness;
11. Easy brusability or unexplained bleeding from any orifice. (2,3,4,7,23,25)

These symptoms by themselves would not allow an AIDS diagnosis to be made but they should alert the eye care practitioner to a possible more severe underlying cause.

Precautions

The human immunodeficiency virus has been isolated in tears, saliva, and the conjunctival epithelium (13,26). It should be noted, however, that very low levels of the virus exist from these sources.In the absence of accidental parenteral injection of infected blood, optometrists are at an extremely low risk for HIV infection (28,29). HIV is not a casually transmitted or air borne agent.

To date, the disease is known to have been transmitted only by sexual contact, by sharing contaminated neddles, by infected blood or blood products, by infected organ or tissue transplants, or from mother to neonate across the placenta (13,27). There are no epidemiologic data to support tears as a mode of transmission and there have been no cases of seroconversion to HIV positive antibody status attributed to tears or to contact with contaminated ophthalmic instruments (30,35).

If optometrists adhere to well-established, standardized guidelines of infection control with every patient in exactly the same manner, the risk of accidental infection to the optometrist and to his patients can be considered non-existent. This is a composite of recommendations from the CDC and other sources (30,31,32,33):

1. Handwashing should be performed routinely before, between, and after every patient. Latex gloves are only indicated if the patient has an open or oozing lesion, or if the provider has a break in the skin of the hands;

2. Instruments should be disinfected for 5 to 10 minutes with any one of the following freshly prepared (daily) solutions, irrigated with saline and dried:
   I. 1 to 10 dilution of common household bleach
   II. 3 percent hydrogen peroxide
   III. 70 percent ethanol
   IV. 70 percent isopropyl alcohol

The literature favors the use of household bleach due to its

availibility, price, broad spectrum antiviral and antibacterial properties, and it has exhibited no damage totonometer tips.

3. Contact lenses should be disinfected with a heat system (78 to 80C for 30 min) or a hydrogen peroxide system (10 min), whichever is compatible with individual lens material. Patients who are HIV positive should not be discouraged from wearing contact lenses unless ocular conditions contraindicate their use.

4. Masks are usually not indicated unless the patient has an active, easily communicable disease, e.g.,tuberculosis.

Directory of AIDS Resources

Telephone Hotlines

PHS AIDS Hotline
Phone: 1-800-342-AIDS
Phone: 1-800-342-2437

National Gay Task Force
AIDS Information Hotline
Phone: 1-800-221-7044
(212) 807-6016 (NY State)

National Sexually Transmitted Diseases
Hotline/American Social Health Association
Phone: 1-800-227-8922

Latest Treatments

Project Inform
Phone: 1-800-822-7422

Information Sources

U.S. Public Health Service
Public Affairs Office
Hubert H. Humphrey
Building, Room 725-H
200 Independence Avenue, S.W.
Washington, D.C. 20201
Phone: (202) 245-6867

Local Red Cross or
American Red Cross
AIDS Education Office
1730 D Street, N.W.
Washington, D.C. 20006
Phone: (202) 737-8300

Michigan Department of
Public Health
P.O. Box 30035
Lansing, MI 48909

Michigan Association for
for Local Public Health
P.O. Box 14065
Lansing, MI 48901
Phone: (517) 485-0660

Other Sources

American Association of
Physicians for Human Rights
P.O. Box 14366
San Francisco, CA 94114
Phone: (415) 558-9353

Hispanic AIDS Forum
c/o APRED
853 Broadway, Suite 2007
New York, NY 10003
Phone: (212) 870-1902
or (212) 870-1864

AIDS Action Council
729 Eighth Street, S.E.
Suite 200
Washington, D.C. 20003
Phone: (202) 547-3101

Los Angeles AIDS Project
7362 Santa Monica Blvd.
Los Angeles, CA 90046
Phone: (213) 876-AIDS

Gay Men's Health Crisis
P.O. Box 274
132 West 24th Street
New York, NY 10011
Phone: (212) 807-6655

National Council of
Churches/AIDS Task Force
475 Riverside Drive, Room 572
New York, NY 10115
Phone: (212) 780-2421

San Francisco AIDS Foundation
333 Valencia Street, 4th Floor
San Francisco, CA 94103
Phone: (415) 863-2437

National Association of People
with AIDS
P.O. Box 65472
Washington, D.C. 20035
Phone: (202) 483-7979

Minority Task Force
on AIDS
c/o New York City Council
of Churches
475 Riverside Drive,
Room 456
New York, NY 10115
Phone: (212) 749-1214

Mothers of AIDS Patients
(MAP)
c/o Barbara Peabody
3403 E Street
San Diego, CA 92102
Phone: (619) 234-3432

National AIDS Network
729 Eighth Street, S.E.
Suite 300
Washington, D.C. 20003
Phone: (203) 546-2424

National Coalition of Gay
Sexually Transmitted
Disease Services
c/o Mark Behar
P.O. Box 239
Milwaukee, WI 53201
Phone: (414) 277-7671

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