Chapter 13
Litigations for HIV Related Complications

13.1 Case 1: I Have HIV Infection

In 1992, a 27-year-old male with same sex exposure requested human immunodeficiency virus (HIV) testing anonymously at a walk-in clinic. He was advised that the test (HIV serology) was positive and he requested a repeat test (anonymously) 1 month later, which was also reported as being positive. About 2 years later, he was assessed by a general practitioner for symptoms of depression and continued medical care. At that time, investigations revealed a CD4 T-cell count of about 700 cells/uL. Sometime in 1996 a repeat blood test revealed a CD4 cell count just <500 cells/uL. No consultation to an infectious diseases specialist or HIV clinic was made. The GP(general practitioner) then initiated a regimen consisting of didanosine, lamivudine, and saquinavir for HIV infection. At that time, testing for HIV viral load was not generally available to the medical community, but became procurable in 1997. Initially, the patient tolerated the regimen well and over the next 3 years his CD4 cell count was maintained above 600–700 cells/uL and the HIV viral load remained undetectable (<50 copies). However, the patient started to show morphologic changes of moderate facial and peripheral lipoatrophy, developed mild sensory peripheral neuropathy, and increased liver enzymes attributable to fatty liver, and elevations of the fasting serum glucose. In the summer of 2000, although the CD4 cell count remained stable, the HIV viral load was reported as being over 7,000 copies/uL. At this time, the patient was referred to a university hospital HIV clinic.

At the HIV clinic, the HIV viral load and serology were repeated (as the GP never had a documented test result). The test results revealed undetectable (<50 copies) HIV-RNA and both the HIV antibody screen (ELISA) and Western blot for HIV-1 and HIV-2 were reported negative by the reference laboratory. The anti-HIV medications were discontinued and the tests repeated a month later with similar results. A special PCR (polymerase chain reaction) was performed for HIV-1 proviral DNA that was undetectable. It was finally concluded that the patient did not suffer from HIV infection, and although there was some improvement in his drug-related complications, after 6–12 months he was left with some residual abnormalities. Further investigation by the laboratory that reported an HIV viral

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load of >7,000 copies/uL came to the conclusion that there was either a mix-up in the blood specimen samples or error in the labeling or reporting. Efforts to verify or clarify the initial HIV serology were unsuccessful as no permanent records were kept for anonymous HIV serology results.

13.1.1 Medico-legal Issues

The patient (plaintiff) initiated litigation against the GP (defendant) for medical malpractice. Specific charges were: (1) the GP should have repeated the HIV serology to confirm that the plaintiff was HIV infected, (2) the defendant was negligent in starting treatment for HIV infection without proof of disease, (3) the physician lacked knowledge of HIV infection and should have referred the patient to a specialist or HIV clinic, (4) treatment of toxic medications were given for several years without any clear indication, and (5) the GP did not adequately inform the patient on the pros and cons of therapy, nor explain the potential toxicities and side-effects.

Financial compensation by the plaintiff was sought for psychological suffering over the years with the false impression that he was HIV infected, and physical suffering from the side effects of the medications and the need to take unnecessary large amounts of pills for several years. The side effects had affected his social life and left a permanent physical stigma, and also adversely affected his performance at work (due to absenteeism from adverse events). The latter had resulted in his inability to perform at a high level and thus retarded his progress in his career path. All these effects have indirectly affected his earning ability over 3–4 years, and also future earning capacity.

13.1.2 Medical Aspects

The present AIDS pandemic is caused by the HIV-1 strain and HIV-2 is predominantly found in West and Central Africa but is rare in developed nations. Seroconversion after exposure usually occurs within 2 weeks to 3 months, but occasionally may take 12 months or longer.[1] Delayed or protracted time for seroconversion may be seen especially in immunosuppressed subjects.[2] Usually by 6 months after exposure, seroconversion should occur in 95% or more of cases.[3] A period of viremia and antigenemia without detectable antibodies occurs within 4–6 weeks of initial HIV infection. At this phase, high levels of plasma p24 antigen or viral RNA can be detected, and the viremia and antigenemia decline to very low levels coinciding with seroconversion.

Detection of antibodies to HIV remains the most cost-effective and commonly used method to prove HIV infection. Enzyme-linked immunoassay (ELISA) is the most commonly used assay to test for HIV-1 and HIV-2 because of its low cost, standardized procedure, reliability, and rapid turnaround.[1] For experienced

laboratories under optimal conditions (commonly licensed kits) the sensitivity and specificity of the ELISA are both 99%.[1] False negative reactions can occur in infected persons early in the course before seroconversion and in immunosuppressed patients. False positive ELISA results can occur for various reasons, including human error, variability in the test kits, hemodialysis, auto-immune disease, multiple myeloma, hemophilia, alcohol hepatitis, positive rapid plasma regain (RPR) test, and for unknown reasons (idiopathic).[1] The ELISA uses HIV antigen to bind IgG HIV antibodies in the test sample.

The Western Blot test (WB) is the most commonly used confirmatory test for the presence of HIV specific antibodies. Compared to ELISA, the WB is more expensive, time-consuming and requires more technical expertise to interpret. False negative WB can also occur in the very early phase of HIV infection before development of antibodies. False positive reactions can occur in auto-immune disorders, polyclonal gammopathies, hyperbilirubinemia, subjects with human leukocyte antigen (HLA) antibodies, and healthy individuals. In low risk populations, the chance of false-positive reaction of ELISA and WB combined is extremely low – 1 in 135,000.[4] The probability of another test being false positive in the same person tested at another time for both tests would be 1:135,000 × 135,000 or 1 in 18 billion chance.

Although the polymerase chain reaction (PCR) can be used to detect the HIV genome before antibody production, the PCR is highly prone to contamination with nucleic acids, which causes many false-positive reactions and therefore has not been recommended for diagnostic purposes. These PCR tests are thus mainly used for serial measurements of plasma HIV-1 RNA for quantitation over the range of 75–500,000 RNA copies/mL to monitor progress and response to therapy. In high risk populations, detection of HIV-DNA by PCR has been found to have false-positive rates of 2–3.4%.[5,6] Data from Bayer on the versant HIV-1 RNA 3.0 assay (bDNA) found that all 22 of 912 false-positive samples quantitated were 1,000 copies/mL or less (personal communication with Dr. R. Ziermann from Bayer).

13.1.3 Medico-legal Discussion

The main issue in this case is related to acceptance of a patient's history of a serious disease (from a test performed elsewhere) without verifying the results. Although physicians commonly accept the history of a patient's underlying illness as valid, treatment for a disorder with potentially toxic agents should always require verification of the diagnosis. It could therefore be argued that the GP was remiss in instituting a cocktail of medications without having a confirmed copy of the test result for HIV infection. This is particularly damaging for an asymptomatic subject with no history of opportunistic infection or clinical evidence of AIDS complication. Moreover, a CD4 count cannot be used as a surrogate marker for the diagnosis of HIV infection.

Although the $CD4^+$ T lymphocyte quantitative count is a very useful and standard test to monitor patients for progression of HIV disease or response to

therapy, it can be low in many conditions. The normal $CD4^+$ T lymphocyte count usually averages 8.0–10.5 $\times$ 10^8 cells/L (800–1,050/mm^3), but the range of normality (2 standard deviations of the mean) is quite wide (500–1,400 cells/mm^3).[7] About 80% of the normal blood lymphocytes are T lymphocytes and nearly two-thirds of blood T lymphocytes are $CD4^+$ (helper) lymphocytes and most patients with lymphocytopenia have reduction in absolute number of $CD4^+$ T lymphocytes.[8] There are many conditions that can be associated with lymphocytopenia and lower than normal $CD4^+$ lymphocyte count. Although HIV infection is the most common viral infection associated with $CD4^+$ lymphocytopenia, other viral infections can transiently decrease $CD4^+$ cell counts (including measles, corona viruses and others).[8] The list of conditions associated with $CD4^+$ lymphocytopenia (besides viral infections) include bacterial and fungal sepsis (including tuberculosis), major surgery, recent trauma or hemorrhage, malignancy, glucocorticoid use, cytotoxic chemotherapy, radiotherapy, auto-immune diseases, nutritional deficiencies, organ transplantation, acquired common variable immunodeficiency, and idiopathic $CD4^+$ lymphocytopenia.[8] Furthermore, it is common to observe biologic variations in the absolute $CD4^+$ cell count even in HIV infected subjects without any other factors. A healthy adult may have, at some time, transient decrease in $CD4^+$ cell count below 500. Whether the plaintiff's $CD4^+$ cell count decline was due to viral upper respiratory tract infection or other causes was not clear. In HIV-infected patients, the T lymphocytes decline by 4% per year for every $\log_{10}$ HIV RNA copies/mL in the plasma.[7]

Currently, the optimal time to start antiretroviral therapy (ART) for asymptomatic HIV patients is not clear. There is consensus that patients with AIDS complications or symptomatic disease should be started on ART. There is still controversy as to the optimal time to initiate ART in asymptomatic patients. Some guidelines recommend considering starting ART below 350 cells/mm^3 and others recently $<$500 cells/mm^3, but there are no randomized controlled trials to provide a clear answer.

How can we resolve the issue of two HIV serology tests taken at separate times in the same subject being false positive? There are several possibilities, none of which can be proven in or out of court. It is possible, that since blood samples taken in the clinic were labeled with a code number to provide anonymity, that the samples were mislabeled and originated from a truly HIV infected subject. However, the chance of that occurring twice in a row would be extremely low or unlucky. It is also possible that the plaintiff suffered from a mental disorder or delusion (such as Munchausen's syndrome) and imagined that he had a positive HIV serology. There was no indication of a psychiatric disorder from the GPs office records. Rare false claims of a medical disease (including HIV infection) may be encountered under unusual conditions where the person can expect some form of material gain, i.e., financial, improved living conditions, sympathetic reduction in sentences for criminal offenses, etc. None of these appeared evident from review of the records.

Feigned HIV infection has been reported in malingering patients[9–11] and in young women with psychosocial disorders with history of prolonged sexual,

physical and emotional abuse.[12] A retrospective study from an HIV clinic in a municipal hospital identified seven patients with fictitious HIV infections, six of whom had a history of illicit narcotic abuse.[13] A survey of ten other local hospitals found that known cases of alleged (fictitious) HIV infection occurred at eight of the hospitals but only one of the ten hospitals routinely documented HIV infections before initiating care.[13] In a specialist HIV unit in Central London over a 5-year period, 12 patients (1.7% of admissions) with feigned HIV/AIDS were identified.[14]

13.2 Case 2: Missed Opportunities

A young man, aged 36 years, presented to a new family physician (FP) in 1994 with symptoms of 15 lb weight loss, chronic diarrhea for 3 weeks and night sweats. He was found to be unwell, with evidence of significant weight loss from wasting, oral thrush, and oral hairy leukoplakia. An HIV serology performed was positive (screen and confirmatory), and his CD4$^+$ lymphocyte count was 80 cells/mm^3. He was started on antiretrovirals and prophylaxis for pneumocystic pneumonia.

The patient was a practicing homosexual with multiple partners (none of whom were known HIV infected) and he used condoms sometimes, but inconsistently for sexual encounters. He had no known past medical illness and claimed to have previously tested negative for HIV infection in 1988. He claimed to have requested an HIV test in 1990 but there was no record of this in his previous FP records. An HIV serology was performed in the summer of 1993 (which was positive), but the patient was never informed of the results and apparently was lost to follow-up.

The records subsequently in 2000 indicated that the young man was attending an HIV clinic regularly with no opportunistic infection and was clinically stable on a combination of ART with a stable CD4$^+$ lymphocyte count of 160 cells/mm^3 and undetectable HIV (<50 copies).

13.2.1 Medico-legal Issues

The patient in 2000 initiated lawsuit against his original FP for medical malpractice. The charges against the physician were that he failed to perform an HIV test in 1990 despite the plaintiff's request and he was negligent in failing to notify the plaintiff of the result of the HIV serology in 1993. These acts of negligence by the defendant resulted in delay in the diagnosis and treatment, thus allowing his HIV infection to progress to AIDS. Furthermore, failure on the part of the defendant had resulted in missed opportunities to start earlier treatment, and the delay in initiation of ART resulted in a decrease in his expected life span and affected the quality of his life.

The defendant countered that there was no record of the plaintiff ever requesting an HIV test in 1990. Furthermore, the plaintiff never kept the appointment after the positive HIV serology in 1993 to be notified of the result. Moreover, since the

plaintiff was subsequently lost to follow-up, he never had a chance to counsel him on HIV disease or institute treatment.

13.2.2 Medical Aspect

Following acute HIV infection, about 50–70% of subjects develop clinical symptoms of variable severity, from mild flu-like illness to aseptic meningitis.[15] There is also evidence that severity and duration of clinical acute illness of a primary infection is of prognostic importance. The risk of developing AIDS within 3 years of seroconversion in subjects who were asymptomatic or had mild illness was only 10% versus 78% (eight times greater) in those with seroconversion illness of at least 14 days.[16] Peak viral replication soon after infection occurs in 2–4 weeks and levels of virus can exceed $>10^7$ copies/mL in plasma. This is associated with a dramatic drop in circulating $CD4^+$ lymphocytes, then a slowing of T-cell loss, and rebound by 9–12 weeks. This rebound of $CD4^+$ cells corresponds to a decline in viral load, which reaches a steady state (set point), which is variable by 9–12 weeks. Clinical progression of HIV disease has been tied to a set point level with lower levels associated with better prognosis.[17] At 1 year after seroconversion, patients demonstrate a fall of about 349 $CD4^+$ cells/mm^3 (mean baseline 999 cells/mm^3), followed by a more gradual decline in $CD4^+$ cells in the later period of infection.[18] There is usually a variable period of 8–10 years span before patients develop AIDS (about 50%). The typical HIV-infected person shows a progressive decline of $CD4^+$ lymphocytes (50–100 cells/year) over time.

Long-term non-progression or elite controllers represent <5% of HIV-infected subjects who maintain relatively normal $CD4^+$ cell count and very low or immeasurable viral load for 8 years to decades without therapy.[19] This is a heterogenous group of elite controllers whose benign course may result from robust immune responses against HIV, or defective poorly replicative virus secondary to deletion of the nef gene.[20,21] There is evidence that host factors that influence the course of HIV disease are correlated to polymorphisms dominating the HLA region, with class I polymorphism dominating the HLA associations.[22] There is also evidence from studies in the United States and Europe that HLA-B57 and HLA B-27 are strongly associated with long term survival or non-progression.[22] Not all long-term non-progressors are "elite or viremic controllers" (patients with undetectable HIV or plasma HIV RNA levels of 50–2,000 copies/mL). These patients with $CD4^+$ cell counts of >500 cells/mm^3 for at least 10 years most often had HIV RNA levels of >2,000 copies/mL, but had significantly lower HIV RNA than subjects with typical progression. Thus plasma set point HIV RNA levels explain <50% of the variability in rates of clinical progression.[24]

The chemokine receptor 5 (CCR5) protein serves as a co-receptor on $CD4^+$ lymphocytes for certain strains of HIV-1. Homozygosity for a 32-base pair deletion allele (CCR5Δ32) protects against HIV infection (1% of Caucasians) and heterozygosity (individuals with one allele) show a decreased progression to AIDS.[25] There

is also evidence that co-infection with GB virus (GBV-C), a flavivirus not known to cause disease (in subjects with GBV-C viremia), have slower progression and slower decrease in $CD4^+$ cell counts than those without GBV-C infection.[23] Although the reasons for this protective effect are unclear, there is evidence that GBV-C inhibits HIV replication in peripheral blood mononuclear cells in vitro, and since GBV-C infects $CD4^+$ cells, this may compete with the HIV for target cells for infection.[23]

A minority of patients with HIV infection can rapidly progress to AIDS within 1–3 years of their infection. This may be related to host genetic factors and age at the time of infection and other extrinsic conditions. Older age at the time of infection (>25 years) has been associated with faster progression of the disease in hemophiliacs and older homosexuals.[23] Concomitant co-infection with cytomegalovirus (CMV) has been associated with rapid progression to AIDS in hemophiliacs and others.[26,27] Co-infection with HTLV-I may increase the risk for development of AIDS while HTLV-2 can delay the progression of disease.[23,28,29] Active tuberculosis can also enhance HIV replication and cause rapid progression to AIDS.[30] However, although treatment of active tuberculosis for 6 months is associated with increased $CD4^+$ cell count, it does not markedly affect the HIV viral loads.[31] The role of hepatitis C-virus (HCV) co-infection on the progression of HIV disease has been conflicting, with some studies showing more rapid progression, but others have found no effect on the development of AIDS.[23]

The clade or strain of HIV-1 may play a role in the course of the disease. Clade D of HIV-1 is associated with faster progression to death in Africa than Clade-A and B.[32] Women in Senegal infected with C, D or G HIV Clade were eight times more likely to develop AIDS than those infected with Clade A subtype (the predominant sub-type).[33] Infection with multiple strains of HIV-1 (more common in women) have also been associated with faster disease progression.[34]

Socio-economic factors such as poverty, homelessness, drug and alcohol abuse, and black race play indirect roles in the prognosis and disease progression of HIV infection, primarily through lower access to medical management, delay in instituting antiretrovirals and poorer compliance with medications. Although a previous study found that alcohol and psychoactive drugs did not accelerate HIV disease,[35] there is in vitro evidence that alcohol, cocaine and narcotics can impair the immune response to HIV-1 and allow enhanced replication in peripheral blood mononuclear cells.[23] A case report of rapid progression to AIDS within a year of infection has also been attributed to alcoholism.[36]

13.2.3 Medico-legal Discussions

It would appear that the plaintiff became infected with HIV sometime between 1988 (reported HIV-negative) and 1993 (first noted HIV-positive). However, by 1994 he had progressed to symptomatic AIDS. Thus, his course was more rapid than usual HIV infected individuals were, and especially as no other conditions or factors were recognized that could accelerate his course of disease. However, the

failure of the FP to notify the patient of his HIV-positive status before recognition of his condition was only 1 year. Would an earlier diagnosis by 1 year and assuming institution of ART then, affected the outcome as to lifespan and quality of life? Appropriate treatment a year earlier with ART would likely have aborted or ameliorated his symptomatic disease, of weight loss, diarrhea, and malaise. However, it is less clear whether his expected lifespan would be any greater. If we assume that over the preceding year his $CD4^+$ cell count probably declined by 50–100 cells/mm^3, then even at that time he would have already progressed to AIDS ($CD4^+$ cell count <200 cells/mm^3). There is reasonable good cumulated evidence that starting therapy when the $CD4^+$ cell count is very low (<200 cells/mm^3) is associated with less chance of immune reconstitution and greater risk of opportunistic complications than those started on ART when the $CD4^+$ cell count was >200 cells/mm^3. The optimum $CD4^+$ cell count for initiating ART has not been well established although recent large observational cohort studies (retrospective and prospective) and suggests better outcomes for HIV infected patients receiving earlier ART with $CD4^+$ cell count ≥ 350 cells/mm^3 or >500 cells/mm^3; the data however is flawed and controversial.[37,38] Lack of randomization in these studies could result in significant biases as motivated, health-conscious individuals would likely do better that those less motivated. It is not clear in these studies as to the cause of excess mortality in those not accepting treatment. For instance, it would be expected and predictable to find excess mortality (from any disease) in marginalized people (homeless, alcoholics, drug abusers), who are less likely to start ART, which may be unrelated to HIV complications, such as suicides, homicide, accidents, drug overdose, liver failure or other diseases more prevalent in these groups (diabetes mellitus, cardiovascular disease, chronic lung disease and cancer).

The defendant denied the plaintiffs claim that earlier HIV test (in 1990) was requested. It could be argued, however, that the FP should have been doing regular HIV serology in an individual that belongs to a high-risk group (with the patient's consent). The Center for Disease Control and Prevention (CDC) estimate that nearly 50% of men who have sex with men (MSM) with HIV infection are unaware of their status. The CDC National Behavior Surveillance System of high-risk venue-based recruitment found 25% of MSM tested to be infected with HIV, and nearly 50% of the HIV infected individuals were unaware of their infection.[39] In New York City, the HIV incidence rate among MSM was 2.3%, with 52% of those infected being unaware of their HIV seropositivity.[39] It is estimated that 21% of HIV-infected people in the US who are unaware of their infection may account for up to 52% of new infections. CDC HIV testing guidelines recommend annual testing for high-risk populations (including MSM), and since 2006 have recommended universal opt-out HIV screening in all health care settings.[40] Thus, the plaintiff could argue that the defendant fell below the standard of care by not recommending and performing annual HIV tests. Furthermore, if he were found to be HIV seropositive earlier, (by 1990 or before) with careful monitoring and institution of ART before his $CD4^+$ cell count fell <350 cells/mm^3, his quality of life and life expectancy would be greater.[41]

What is the effect of life expectancy with late treatment initiation for HIV disease? In a recent study using a state-transition model of HIV disease, the

projected life expectancy of HIV uninfected and HIV infected persons with similar risk profiles were compared.[41] Those with HIV infection lost 11.92 years of life if they received care concordant with guidelines and late treatment initiation resulted in 2.60 additional years of life lost (greatest for Hispanics [3.90 years]).[41]

13.3 Case 3: Visual Impairment in HIV

An infectious disease (ID) specialist/internist was consulted to assess a 41-year-old male with mild pancytopenia and a past history of bilateral pneumonia the year before. The patient had a history of multiple sexual contacts with prostitutes 5 years prior and had refused HIV testing the year before when he developed pneumonia (which was suspected to be pneumocystic pneumonia [PCP]). At this office visit, he agreed to an HIV test and a $CD4^+$ cell count. The patient was called for a return appointment to discuss the results of the test a month later, but this appointment was cancelled by the patient for personal reasons. The blood test revealed the patient was HIV seropositive with a very low $CD4^+$ cell count of 5 cells/mm^3, but the results were not given over the phone or by mail. Thus, the subject remained unaware of his HIV status and severe immune deficiency.

About 3 months later, the patient attended an optician for blurred vision and he was referred to a hospital ER for an ophthalmologist consultation. He was briefly assessed by the attending ER physician, but due to the long waiting period pending full eye assessment, he left prematurely. The patient arranged an appointment with the ID specialist in the ER of the suburban community hospital. The subject was told of his HIV status and a brief retinal examination (without pupillary dilatation) by the ID physician revealed no abnormality. An appointment was arranged for another office visit to the ID specialist to discuss HIV therapy in 2 weeks. One week later the subject returned to the ER with respiratory symptoms and poor vision. He was admitted as possible PCP under the care of the ID physician, but no eye examination was performed. A week after his admission to hospital, a neurologist who was consulted found very poor vision with light perception only in the right eye and finger counting on the left eye. Fundoscopy revealed bilateral chorioretinitis and ophthalmology consultation was requested, but treatment of CMV retinitis was only instituted 2 days later. His course was complicated by retinal detachment secondary to CMV retinitis with almost complete blindness in the right eye and severe visual impairment of the left eye – legally blind.

13.3.1 Medico-legal Issues

Malpractice litigation was brought by the patient against the ID physician and the admitting ER physician of the hospital. The charges against the ID consultant were: (1) failure to notify the plaintiff of his HIV status and seriousness of his condition,

(2) failure to do a proper eye examination or refer him to an ophthalmologist when he was first seen in the ER a week before his admission, (3) failure to do a fundoscopy or arrange urgent ophthalmology consultation on admission to the hospital, (4) delay in starting appropriate treatment for CMV retinitis even after the neurologist findings were consistent with the diagnosis.

The claim filed against the ER physician was for neglect in performing an eye examination, despite the patient's symptoms of poor vision and failure to require an urgent ophthalmology consultation. That prompt recognition of CMV retinitis and immediate institution of antiviral therapy could have resulted in better visual result. Failure of the ID physician to inform the plaintiff of the seriousness of his condition, even by phone, could have resulted in prevention of visual loss and admission to hospital if treatment with ART and PCP prophylaxis were started 3 months before his hospital admission.

The defendant (ID specialist) countered that it was the plaintiff who canceled the follow-up appointment for counseling on his condition, and it was neither his policy nor the recommended standard to discuss these issues on the phone. Therefore, failure to initiate earlier ART before the AIDS complications was due to the fault of the plaintiff. Furthermore, his eye examination performed at the first ER visit revealed no abnormalities.

13.3.2 Medical Aspects

Visual complaints in HIV infected persons can be unrelated (as in normal people) or related directly to complications of AIDS or indirectly due to medications. Ocular manifestations are common in people with AIDS, and before the advent of highly active ART (HAART), the majority of patients with AIDS developed some ocular involvement at some time.[42] The most frequent ocular abnormality was usually silent or asymptomatic and occurred in nearly 50% of AIDS patients before the era of HAART – HIV microangiopathy, consisting of cotton wool exudates, and less frequently hemorrhages.[42] Occasionally HIV retinopathy could present with visual impairment from larger branch vein or central retinal vein occlusion.

The most dreaded ocular complications of AIDS were from opportunistic ocular infections (CMV retinitis, herpes zoster (VZV) retinitis, or herpes zoster ophthalmicus, toxoplasma retinitis and ocular syphilis), or neoplasm (Kaposi sarcoma of the lids and conjunctivae, and orbital or intraorbital lymphoma).[42]

CMV retinitis is the most frequent sight threatening ocular complication of AIDS, occurring in the late stages when the $CD4^+$ lymphocyte counts <50 cells/μL. In the pre-HAART era CMV retinitis occurred in 30% of patients with AIDS, and the number of new cases has dramatically fallen since widespread use of HAART by 55–95% (average 80%).[42] The incidence of CMV retinitis among patients with $CD4^+$ cell count <100 cells/μL was 10% per year and for many patients with $CD4^+$ cell count <50 cells/μL, it was 20% per year. Symptoms of CMV retinitis include

floaters, flashing lights, loss of visual field, or visual loss. In the early stages with small peripheral retinal lesions patients can be asymptomatic and 13–15% of persons with $CD4^+$ cell count $\leq$50 cells/μL have asymptomatic CMV retinitis.[43] Lesions adjacent to the optic nerve or fovea (posterior pole of the retina or macula) are immediately vision threatening. The retina has been divided into three zones for clinical assessment of risk to vision. Zone 1 lies within 1,500 μm from the edge of the optic nerve, zone 2 extends from the edge of zone 1 to the equator of the eye, and zone 3 extends from the equator to the pars plana (pigmented posterior zone of the ciliary body). See Fig. 13.1 for the schematic diagram of the zones of the retina. Lesions of zone 1 are immediately sight-threatening and require urgent treatment, whereas lesions of zones 2–3 may be observed for short periods of time without risk of loss of visual acuity.[42] The mean time for progression of peripheral lesions without treatment was found to be 22 days (enlargement to uninvolved retina by $\geq$750 μm in width).[44] The complications of untreated or delayed treatment of CMV retinitis include impaired vision to blindness, secondary to progressive retinitis with hemorrhages, scarring and retinal detachment. In the pre-HAART era, retinal detachment in CMV retinitis occurred in 25% at 6 months and in 50–60% at 1 year.[42]

The diagnosis of CMV retinitis can be made reliably by an experienced ophthalmologist by dilated direct or indirect ophthalmoscopy. Examination of the fundus through an undilated pupil is inadequate to diagnose or exclude CMV retinitis as only 10% of the retina can be evaluated.[42] The aim of treatment with anti-CMV drugs (ganciclovir intravenously or oral valganciclovir) is to arrest progression of the disease, prevent further spread, and preserve vision. Treatment with anti-CMV agents does not eradicate the virus but delays progression and relapse, until

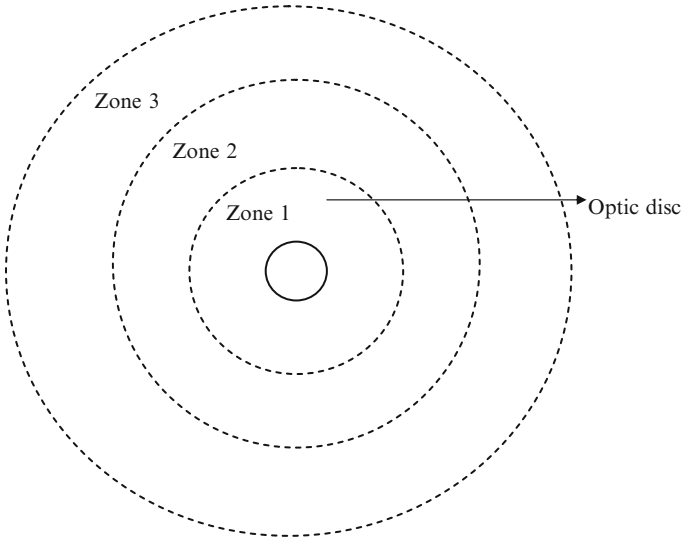

Fig. 13.1 Diagram of the zones of the retina

immunity can be restored by HAART. Anti-CMV therapy, half the dose after induction for 3 weeks, can be discontinued once the $CD4^+$ cell count is >100–150 cells/μL for 6 months. Some experts advocate intravitreal injection or ganciclovir implant in addition to systemic therapy for zone 1 CMV retinitis to avoid loss of vision.[42]

13.3.3 Medico-legal Discussion

For persons recently discovered to be HIV-seropositive, it is ideal to give the results in person confidentially, and at the same time counsel the patient on the disease. However, there are several options available if the individual were reluctant to return for follow-up appointment (or cancels the appointment). The results could be forwarded to the FP and notify him or her of the patient's cancelation plus need for counseling, close monitoring, and for initiating ART or PCP prophylaxis depending on the $CD4^+$ cell count. If the subject has no FP, then the person can be notified of the results by letter or phone, or through the public health department. Although some physicians are reluctant to discuss confidential issues on the phone, there is no edict against this practice. However, confidentiality needs to be maintained and the identification of the person on the phone should be verified. This has become a common practice with financial institutions and even lawyers who discuss medico-legal cases with medical experts on the phone. Since the defendant knew the plaintiff had advanced HIV disease (AIDS) as indicated by the very low $CD4^+$ cell count, it was mandatory that the patient be made aware of the seriousness of his condition as soon as possible by one of the above mechanisms. His failure to impart this information to the plaintiff directly or indirectly could be considered negligence by the court.

Failure of the defendant to perform a dilated ophthalmoscopy or arrange for urgent ophthalmology consultation when the plaintiff initially presented with impaired vision also falls below the standard of practice in an HIV infected individual with a $CD4^+$ cell count of <50 cells/ μL. The physician ought to have known that CMV retinitis was a main concern, and could be sight threatening and that examination by un-dilated fundoscopy would be insensitive and inaccurate. Based on the evidence presented, it could be argued by the plaintiff's lawyer that had the patient been notified earlier of the seriousness of his condition and accepted treatment with HAART 3 months before his hospital admission, it is likely that he would have had a better quality of life and preservation of his vision.

Although counsel for the defendant may counter that the plaintiff should be responsible for his own health (as he canceled the follow-up appointment), there were several avenues available to the defendant to ensure that the patient became aware of his serious illness, and he failed to utilize any of them. Whether or not a court may consider these failures as human errors from oversight in a busy medical practice and not medical malpractice would be difficult to predict.

13.4 General Discussion

What lessons can we learn from these cases?

- All patients with self-reported HIV-seropositive status should be verified by repeating the test.
- Request documentation of HIV serology from the FP or referring physician for documentation.
- Never institute ART without confirmation of HIV-seropositivity.
- Baseline $CD4^+$ cell count and HIV viral load with genotype testing for resistant mutations should be performed.
- High-risk people should have annual HIV serology and all health care contacts should be offered the tests.
- A standard practice for reporting HIV-seropositivity should be adopted, and alternative methods for notification of remissive individuals should be a part of the standard protocol.
- HIV infected patients with $CD4^+$ cell count <200 cells/μL should be immediately alerted to the seriousness of their condition and the need to start ART and prophylaxis.
- Visual disturbance in AIDS warrants urgent attention. A detailed examination after pupillary dilatation by direct ophthalmoscopy can be done by any physician to determine the presence of any abnormality. However, an urgent ophthalmology consultation is desirable.
- Any evidence of CMV retinitis in zone 1 of the retina should be considered an ophthalmologic emergency, and requires immediate attention.
- Remember, the lack of communication directly or indirectly to our patients is one of the main roots of medico-legal malpractice litigation.
- Physicians should pay more careful attention to patients' symptoms and complaints and act with reasonable promptness.
- Deal with patients' complaints as you would want to be done to yourself or relatives.

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