There are numerous possible causes of stroke in advanced HIV infection (Box 1). Opportunistic infections, intracranial malignancies, marantic endocarditis, cachexia and dehydration, and coagulation abnormalities can substantially contribute to the increased risk of stroke in AIDS [1]. These have been commonly reported etiologies of stroke in young HIV and AIDS patients.

However, the landscape of cerebrovascular disease in the setting of HIV and AIDS is changing. First, in developed countries, the prevalence of HIV infection among individuals aged over 50 years has increased substantially since the inception of the AIDS pandemic [2]. In Australia, for instance, the average age of HIV-infected homosexual or bisexual men with AIDS has increased by 1 year of age for every calendar year since the mid-1980s [3]. Currently, approximately 25% of HIV infections in the USA occur in individuals aged over 50 years [4]. To a large extent, this aging HIV-infected population is the consequence of the efficacy of highly active antiretroviral therapy (HAART) in controlling the infection and preserving immune function. Owing to longer survival, HIV/AIDS patients are more likely to experience diseases of middle and old age, such as atherosclerotic vascular disorders. Additionally, HAART itself has a potential adverse effect on the vascular system. It is known that HAART affects metabolic profiles, resulting in dyslipidemia, fat redistribution and insulin resistance, which may predispose to accelerated atherosclerosis and vascular events [5–7]. Some evidence suggests that HAART-treated patients are at an elevated risk for ischemic stroke from accelerated atherosclerosis [7–9]. Incidence rates for both ischemic and hemorrhagic stroke increased twofold after the introduction of HAART in a study from northern Thailand [10]. Mechanisms underlying this increased risk were uncertain. A similar increase in stroke was also observed between the years 1992 and 2000 in a South African HIV-infected population [11].

**Stroke risk & HIV/AIDS**

Studies addressing the risk of stroke in the HIV-infected population have been performed in several fashions. One approach has been to survey the frequency of stroke in a large HIV-infected population. For instance, Pinto and colleagues reviewed the literature available on HIV infection and stroke through December 1994 [12]. They found a total of six clinical series and 11 autopsy series with 1885 HIV-infected people. While 40% had a neurological complication, only 1.3% had cerebrovascular disease. Alternative approaches have focused on sampling the frequency of HIV infection among the stroke population.

A case-control study at a large, university-affiliated county hospital in south Florida, USA, in the late 1980s compared the prevalence of cerebrovascular disease in autopsied
patients between the ages of 20 and 50 years old, with and without AIDS [1]. Cerebrovascular disease was present, as determined by neuropathological criteria, in 13 (8%) out of 154 patients with AIDS—a large proportion for a young adult population. However, there was no statistically significant difference in the prevalence of stroke in dying patients with AIDS from dying patients matched for age and sex who did not have AIDS [1]. Another retrospective case–control study from a similar, large, inner-city public hospital revealed that, after adjusting for cerebrovascular risk factors, the prevalence of stroke among HIV-infected young persons (aged 19–44 years) was 2.3-times higher and cerebral infarction 3.4-times that of the control group [13]. The increased frequency of stroke in this group was chiefly attributed to meningitis and protein S deficiency [13].

In a cohort study, 772 consecutive HIV-infected persons were evaluated for the rate of transient ischemic attacks and completed stroke [14]. The prevalence of transient ischemic attack was 1.9% and for stroke 1.2%, with an annual incidence rate of 216 out of 100,000 people [14]. More advanced disease was associated with a greater risk of cerebrovascular disease. These investigators attributed the increased risk of stroke to HIV-associated vasculitis or vasculopathy [14].

In a population-based study of AIDS-associated stroke by Cole and colleagues, the estimated incidence of both ischemic stroke and intracerebral hemorrhage in individuals with AIDS was 0.2% per year [15]. This study used the 1987 Centers for Disease Control (CDC) definition of AIDS, rather than HIV seropositivity, to define the study population. When identifiable causes for either disorder were excluded, the incidence of ischemic stroke and intracerebral hemorrhage in individuals with AIDS was 0.14% and 0.11% per year, respectively. HIV-seropositive subjects who did not meet the criteria for the definition of AIDS were included as part of the non-AIDS control population. The authors speculated that had all HIV seropositive patients been incorporated in the study population, their inclusion would have decreased the observed association between stroke and AIDS. After the exclusion of cases with identifiable causes, AIDS conferred an adjusted relative risk of 9.1 (95% CI: 3.4–24.6) for ischemic stroke and an adjusted relative risk of 12.7 (95% CI: 4.0–40.0) for intracerebral hemorrhage [15].

A South African study that included a control population and analyzed the risk of stroke in people with HIV infection used data accumulated from a stroke registry from the KwaZulu Natal province [16]. The results showed a prevalence of HIV in a young (<50 years of age) stroke population of 16%. The prevalence of HIV in the young, black population in general was identical, which suggests that there was no significant increase in the risk of stroke associated with HIV infection. However, large-vessel cryptogenic stroke was more common among the HIV-infected cohort. Furthermore, patients with AIDS were excluded from this study, possibly biasing it to a lower rate of stroke in the HIV-infected group.

Conversely, 67 (6%) out of 1087 stroke patients in a large prospective stroke registry from Cape Town, South Africa, were HIV positive [17]. This percentage may have been an underestimate of the real incidence, as HIV serological screening was not performed routinely and there was no control population for comparative purposes [18]. The majority of patients were younger than 46 years old and had suffered ischemic stroke. The typical risk factors for ischemic stroke (i.e., hypertension, diabetes, hyperlipidemia and smoking) were not significant for this population [17]. The chief etiologies included infectious meningitis and vasculitis (28%), coagulopathy (19%) and cardioembolism (14%), with multiple etiologies present in 11% [17]. A fifth of this population was diagnosed with HIV-associated vasculopathy, either extracranial large-vessel or intracranial medium-vessel occlusion.

**Demographics of stroke in HIV/AIDS**

The demographics of the HIV-infected population with stroke parallel that of HIV infection in general, although they generally have advanced immunosuppression. For instance, between

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**Box 1. Etiologies of stroke in HIV/AIDS.**

**Ischemic stroke**

**Embolic**
- Cardiac disease
  - Marantic endocarditis
  - Bacterial endocarditis
  - HIV-associated cardiomyopathy

**Thrombotic**
- HIV vasculitis and vasculopathy
- Amphetamine and cocaine vasculopathy
- Infectious diseases affecting cerebral vessels
  - Varicella zoster virus
  - Treponema pallidum
  - Other
- Hypercoaguable states
  - Protein S deficiency
  - Antiphospholipid antibody syndrome
  - Other
- Hyperviscosity syndrome

**Hemorrhagic stroke**
- Factor VIII deficiency of hemophilia
- Thrombocytopenia
  - Autoimmune
  - Drug-induced
  - Hypersplenism
  - Disseminated intravascular coagulation
  - Other
- Intracranial malignancy
  - Primary CNS lymphoma
- Intracranial infections
  - Toxoplasmosis
  - TB
  - Other
- Amphetamine and cocaine vasculopathy
- Ruptured mycotic aneurysm

Data from [1].
1996 and 2004, Ortiz and colleagues identified 77 HIV-infected persons with ischemic stroke and five with intracerebral hemorrhage [19]. The mean age of this group was 42 years and 89% were African–American, a demographic reflective of their AIDS population. A total of 91% were known to be HIV-infected and 80% had AIDS. The mean CD4 count was 113 and 85% had fewer than 200 CD4 cells/mm³ [19]. Strokes were severe or disabling in 35% of patients [19]. Stroke risk in HIV infection is not limited to adults. In a longitudinal study of 68 HIV-infected children, stroke incidence was 1.3% per year [20].

**Stroke type**

**Ischemic stroke**

Traditionally, most major risk factors for atherothrombotic stroke are more commonly seen in middle to old age (e.g., hypertension, diabetes, hyperlipidemia and atrial fibrillation). Not unexpectedly, these have not been demonstrated to be significant risk factors for stroke in the young (<46 years old) HIV-infected population [17]. The identified risk factors for ischemic stroke in this population include infectious meningitides and vasculitides [14,17,19], coagulopathy [16,17,19] and HIV-associated vasculopathy [14,17]. Not infrequently, the stroke is the consequence of multiple factors [21]. Control of opportunistic infections with effective HAART, the progressive aging of the HIV-infected population, and the hyperlipidemia observed with protease inhibitors is likely to result in a shift of the underlying risk factors to those that are typically observed in the population at large.

**Hemorrhagic stroke**

The risk factors for hemorrhagic stroke in HIV/AIDS are diverse. Before the availability and adoption of HIV-antibody screening, hemophiliacs were at high risk for the development of HIV from contaminated cryoprecipitate; a group in whom intracranial hemorrhage is a feared complication [22], being observed in 2.2–7.5% [23]. However, other disorders of coagulation may increase the risk of intracranial bleeding with HIV, in particular, immune thrombocytopenia, which is the most common cause of intracerebral hemorrhage in HIV-infected children [20]. Intracerebral hemorrhage may also occur as a complication of AIDS-associated vasculopathy [24], cocaine and amphetamine abuse, and, on rare occasions, with AIDS-associated tumors or infections, such as primary CNS lymphoma [25], CNS toxoplasmosis [26,27] and TB [27].

**Specific stroke risk factors in HIV/AIDS**

**Thrombotic states with HIV infection**

Various disorders that predispose to a hypercoagulable state have been reported in HIV infection, including antiphospholipid antibodies and the lupus anticoagulant, deficiencies of protein C, protein S, heparin cofactor II and antithrombin, increased concentrations of von Willebrand factor and d-dimers, with resultant increased platelet activation [28,29].

With respect to antiphospholipid antibodies, antibodies (aCL) have been observed in nearly 50% of HIV-infected persons; however, as with other viral infections associated with aCL, it is rarely associated with anti-β₂ glycoprotein I antibodies and generally does not increase the risk of thrombosis [30]. The disparity between the frequency of aCL and anti-β₂ glycoprotein I antibodies and lupus anticoagulant was evident in one study of 342 HIV-infected patients in which the latter two were found in only 4 and 1% of the patients, respectively [31]. While overwhelming bacterial infections, particularly staphylococcal and gram-negative bacteria, may cause antiphospholipid antibody syndrome (APS), HIV remains one of the viral infections with which APS is most frequently associated [32]. Nonetheless, HIV-induced APS rarely leads to stroke or, for that matter, other thrombotic complications. A review of the literature revealed the rarity of the association of HIV-induced APS with symptomatic ischemic cerebrovascular disease. Nonetheless, Rubbert and colleagues found an association between significantly elevated anticardiolipin antibody titers and focal cerebral perfusion defects detected by Tc-hexamethylpropyleneamine oxime (HMPAO) SPECT [33]. Keeling and colleagues reported one patient with multiple transient ischemic attacks and mild thrombotic stroke with HIV-induced APS [34]. Brew and Miller found that 70% of 27 HIV-infected persons with transient neurological dysfunction had IgG anticardiolipin antibodies [35], but did not convincingly demonstrate a cause–effect relationship. Among the other thrombotic complications associated with HIV-induced APS are arterial thrombosis [36], deep vein thrombosis and pulmonary embolism [37,38], skin necrosis [39] and osteonecrosis [40].

Free protein S deficiency may be seen in approximately 20% of patients with stroke, but seems to be equally frequent in hospitalized control subjects [41–43]. However, protein S deficiency may be more common in the HIV-infected population with stroke. Ortiz and colleagues found that 45% of HIV-infected persons with acute stroke admitted to a large public hospital in Miami had protein S deficiency [19]. Other studies have reported that protein S deficiency is among the most common causes of stroke in HIV-infected persons [44] and that its occurrence is not an epiphenomenon [45]. Protein S deficiency was seen in 11 out of 35 (31%) stroke patients [44], and in 14 out of 27 (53%) patients with transient neurological dysfunction [35]. Cerebral venous thrombosis, and possibly arterial stroke, can occur from dehydration [1,6]. Disseminated intravascular coagulation can also cause stroke in severely ill patients [1]. Trans-sexual men taking estrogen may have an increased risk of thrombosis and stroke [47], although it is thought that venous thrombolism in trans-sexual men taking estrogen is rare [48]. Additionally, the hyperviscosity syndrome has been observed with AIDS [49–51]. Hypermotility may increase the risk of thrombotic stroke [52].

**Cardioembolism**

Cardiac emboli have historically been reported as a frequent cause of cerebral infarction in young people. It is estimated that 25–30% of cases of ischemic stroke in young adults are from cardiac sources [53]. Berger et al. found several potentially cardioembolic conditions in their series of stroke patients with AIDS [1]. These included marantic endocarditis, myxoid valvular degeneration, dilated cardiomyopathy, myocardial infarction, interstitial
myocarditis and mural thrombi. In a study by Roldan et al., pathologic changes in the heart were found in 55% of patients who died of AIDS [54]. Lesions included marantic endocarditis, toxoplasmodic endocarditis, bacterial endocarditis and lymphocytic myocarditis. Other studies have also found marantic and bacterial causes of endocarditis as causes of stroke in HIV-infected patients [55–58].

An emerging source of paradoxical emboli from the peripheral venous circulation via the heart is through a patent foramen ovale, which is estimated to be present in 27% of the general population, based on autopsy studies [59]. If HIV and AIDS patients have a prothrombotic state, it would stand to reason that those with a patent foramen ovale may be at an even higher risk of cerebral ischemia. This has been reported in two young AIDS patients with pulmonary hypertension and patent foramen ovale [60].

**Vasculitis**

Central nervous system vasculitis can be associated with various opportunistic diseases seen in AIDS, including TB [1,57], cytomegalovirus [1,61], varicella-zoster virus (VZV) [57,62], herpes simplex virus [57], syphilis [63,64], cryptococcosis [57], candidiasis [61] and lymphoma [61]. Other possible opportunistic infections causing vasculitis include toxoplasmosis [1,35,57], mucormycosis [1] and aspergillosis [1]. Syphilis causes small-vessel vasculitis (Nissl–Alzheimer arteritis), characterized by intimal proliferation without inflammation, or a larger-vessel arteritis (Heubner’s arteritis), in which a round cell infiltration of the vessel walls is accompanied by subintimal and perivascular fibrous tissue proliferation [65,66].

Varicella zoster virus infection is very common in the setting of HIV infection and may actually herald the disorder. Vasculopathy is a well-recognized complication of VZV and may affect either small or large vessels. This vasculopathy is the direct consequence of viral invasion of the vessel wall [67] and results in large and small ischemic or hemorrhagic infarcts, often both, of cortex and subcortical gray and white matter [68]. Traditionally, small-vessel disease has been thought to be more common in immunosuppressed individuals and large-vessel disease in the immunocompetent [69]; however, in the largest review to date, 50% of individuals had both small- and large-vessel involvement concomitantly. Although a preceding rash (63%) and cerebrospinal fluid pleocytosis (67%) were often observed, neither was required for diagnosis [67]. VZV vasculopathy with ischemic cerebral lesions is well reported in HIV-infected adults [70] and children [71]. Three cases of VZV meningitis-associated vasculitis with aneurysms responded to acyclovir intravenous treatment (30 mg/kg per day), although optimal antiviral and concurrent corticosteroid administration remains to be established [67].

The typical presentation of primary cerebral angiitis is progressive headache and the development of altered mental status. Pathologically, there is a mixed or granulomatous inflammation of the small arteries and veins of the brain surface and their associated leptomeninges. In non-HIV-infected individuals, the disease has high mortality (>50%) despite treatment with prednisone or other immunosuppressants. The optimal treatment in HIV infection is undetermined. A case report and literature review of isolated CNS angiitis in a HIV-infected patient summarized all cases of HIV-infected patients with cerebral vasculitis not associated with infectious or tumoral processes published in the literature as of 2002. All cases reviewed in this study were in the pre-HAART era. It was postulated that HAART could confer protection against these forms of vasculitis [72].

In a case series of four HIV-1-infected patients diagnosed with primary cerebral vasculitis, two of these patients were HAART-naïve and two had started HAART less than 4 months prior to diagnosis of angiitis [73]. The diagnoses in the four cases were all made by MRI/magnetic resonance angiography. All were treated with HAART, and three out of four were treated with corticosteroids, including one patient who was also treated with cyclophosphamide. Two of the patients treated with immunosuppressive agents showed improvement; the other two died. In all cases, the CD4+ count was low.

Antineutrophil cytoplasmic antibodies are seen in some small-sized vessel vasculitides, such as Wegener’s granulomatosis and Churg-Strauss syndrome, and can be found in HIV infection not in association with vasculitis [74]. The presence of antineutrophil cytoplasmic antibodies in an HIV-infected patient should, therefore, be considered warily prior to diagnosing vasculitis [75].

**Stroke associated with drug abuse**

Cerebral infarction, intracerebral and subarachnoid hemorrhage occur with cocaine and amphetamine, drugs commonly abused in certain AIDS groups [76]. A number of mechanisms have been proposed to explain cerebral infarction with these substances, including enhanced thrombogenesis and vasospasm [77] and vasculitis [78]; however, occasionally, no apparent explanation is forthcoming, either angiographically or at postmortem examination [79,80]. Furthermore, the cerebrovascular event may occur months after the last time the drug was used [81,82]. In one study of MRI in AIDS, 13 out of 71 patients had one or more infarctions, predominantly in the basal ganglia, and six of these 13 were cocaine or intravenous drug abusers [21].

**HIV-associated vasculopathy**

There is an emerging body of literature on vasculopathy that may be related to primary HIV infection. Vasculopathy associated with HIV infection has been reported to affect small, medium and large vessels of the CNS. Cerebral hemodynamics are also altered.

Small-vessel vasculopathy

In ten cases (5.5%), asymptomatic CNS vasculopathy was found at autopsy in the Edinburgh HIV cohort. This was pathologically characterized by small-vessel-wall thickening, perivascular space dilatation, rarefaction and pigment deposition with vessel-wall mineralization, and occasional perivascular inflammatory cell infiltrates without definitive evidence of vasculitis. These findings were identified in all patients with hypoxic and/or ischemic pathologic lesions who had no coexisting CNS opportunistic diseases or sources of embolism [83].

The
vasculopathy was similar to those found in small-vessel (lacunar) disease in non-HIV patients with longstanding hypertension and diabetes. The Edinburgh cohort, however, was young (age: 22–47 years). It is noteworthy that 48% of the cohort were intravenous drug users, and this included five out of the ten vasculopathic patients. None of these patients had been treated with HAART or protease inhibitors. No case showed evidence of vasculitis. Small-vessel occlusion was possibly observed in one case—a possible intravascular thrombus in a small, basal, ganglia-penetrating artery. Mizusawa et al. noted multiple subclinical cerebral infarcts involving cortex, striatum and brainstem in 29% of the cases reviewed. Mural thickening of small vessels was common [84].

Medium- & large-vessel vasculopathy
In the cohort of Tipping et al., which compared HIV-positive stroke patients with non-HIV-infected controls on a large South African stroke unit [87], 20% of the cohort was found to have evidence of HIV-associated vasculopathy. In that cohort, of the 1087 patients admitted to the stroke unit during the specified time period, 67 (6.2%) were found to be HIV infected. The mean age of the HIV-infected stroke patients was 33.4 years (range: 19–76) compared with a mean age of 64 years for patients not determined to be HIV infected (range: 17–96). Seven HIV-infected patients (11%) had an extracranial, nonaneurysmal vasculopathy manifesting clinically as either a total occlusion or significant stenosis of the extracranial carotid artery/carotid bifurcation. No clear cause could be found for these patients’ vasculopathy.

In their cohort, patients with extracranial vasculopathy (all nonaneurysmal) had preserved CD4 counts, interpreted as suggesting that this could be an immunocompetent vasculitis. Six patients (9%) had radiological evidence of an intracranial vasculopathy, for which no reason could be found. In the control group, matched for age, a similar vasculopathy was not identified on angiography. The intracranial vasculopathy showed medium-vessel occlusion with or without fusiform aneurysms, stenosis and vessel diameter variation by angiography (Figure 1). Vessels commonly involved were the circle of Willis and the proximal divisions of the anterior, middle and posterior cerebral arteries. Autopsy of one patient with this vasculopathy demonstrated extensive intracranial vascular degenerative ectasia with thrombosis [85]. The intracranial vasculopathy (including both aneurysmal and nonaneurysmal disease) occurred in the immunocompromised with low CD4 counts (mean: 112 cells/ml). Patients with extracranial vasculopathy had a higher CD4 count (>200 cells/ml) when compared with intracranial vasculopathy patients (p = 0.0033).

Some data suggest that cerebrovascular hemodynamic function may be impaired in HIV-infected patients with vasculopathy [86]. Cerebral perfusion problems have been documented in asymptomatic HIV-infected patients, including diminished cerebrovascular reserve capacity measured by transcranial Doppler with acetazolamide challenge [87].

HIV- & HAART-associated atherosclerosis
In general, HIV-infected patients tend to have higher rates of atherosclerosis [88,89]. Its progression may be faster than in noninfected individuals [90]. Limited evidence suggests that HIV infection alone, even early infection, contributes to vascular remodeling consistent with atherosclerosis. Increased carotid intima–media thickness and brachial endothelial-dependent and endothelial-independent vasodilation were found in 38 naive, untreated HIV-infected patients compared with 41 healthy controls [91]. The patients were young and largely free of vascular risk factors. Endothelial-dependent vasodilation was significantly more impaired in the patients with viral load values above the median (p < 0.001).

A study by Franceschi et al. suggested that chronic HIV infection itself, and not its pharmacologic treatment, increases an increase of soluble markers of endothelial dysfunction [92]. Markers such as soluble P-selectin, soluble VCAM-1, MCP-1 and von Willebrand Factor were significantly higher in HIV-infected patients than in healthy controls, whereas soluble CD40 ligand and tissue-type plasminogen activator were within normal range. The study also suggested that short-term treatment with HAART reduces some parameters of endothelial dysfunction with no observed differences between protease inhibitors and non-nucleoside reverse-transcriptase inhibitors.
Highly active antiretroviral therapy has been routinely available since the late 1990s. Its effects in reducing opportunistic infections in AIDS patients are well known. It has also been associated with an increased risk for vascular events [7]. Physicians need to be aware of the potential risk of accelerated atherosclerosis that may accompany the dyslipidemia and insulin resistance associated with HAART [7]; another possible risk factor for stroke in the AIDS population. The Data Collection on Adverse Events of Anti-HIV Drugs (DAD) study group found that increased exposure to protease inhibitors was associated with an increased risk of myocardial infarction, which was partly explained by dyslipidemia [7]. The study found no evidence of a similar association for non-nucleoside reverse-transcriptase inhibitors.

A study of HIV-infected patients who were undergoing combination antiretroviral therapy compared the risk of subclinical carotid atherosclerosis between patients at low and higher coronary risk. Measurement of carotid intimal–medial thickness with B-mode, high-resolution ultrasound was used to assess for carotid atherosclerosis. The investigators found that in patients at low coronary risk, the risk of subclinical carotid atherosclerosis was independently increased with combination antiretroviral therapy exposure [9].

A retrospective review of 506 AIDS patients treated with HAART in Thailand between May 2002 and April 2004 compared the incidence rates of various events, including stroke, in the study population with incidence rates before the HAART era [10]. During the study period, six patients presented with cerebrovascular events. There was one subarachnoid hemorrhage, one case of intracerebral hemorrhage with cerebral toxoplasmosis, and four ischemic events (three instances of large-vessel disease and one of lacunar infarction).

### Conclusion

The treating physician should always consider cerebrovascular disease in the differential diagnosis of neurological disease that occurs in association with HIV and AIDS. An underlying, potentially treatable cause of cerebrovascular disease should be sought.

The HIV patient who experiences ischemic stroke presents a challenging clinical management problem. What has always been a complex differential diagnosis to work through has now been expanded beyond opportunistic syndromes and traditional manifestations of cerebrovascular disease to include vasculopathies that may be associated with primary HIV infection or treatment with HAART.

There is little information available to guide the clinician in managing the patient with symptomatic, HIV-associated vasculopathy, but it is probably ill-advised to consider discontinuing effective antiretroviral treatments in the setting of vasculopathy. The role of secondary stroke prevention with HMG-CoA-reductase inhibitors (statins), blood pressure-lowering drugs, and antiplatelet or anticoagulant agents in HIV-infected stroke patients without usual vascular risk factors is in doubt.

Limited conclusions can be drawn on HIV/AIDS and stroke risk. Many of the studies on the subject have been population-based studies, and therefore, certain shortcomings are unavoidable. Under-reporting of AIDS in the study populations is a potential confounding factor. There is also possible under-reporting of stroke in the AIDS population, as patients in this group may have had multiple diagnoses during hospitalization that may have obscured the diagnosis of stroke or relegated it to a minor role.

A major unanswered question is whether HIV-infected patients have an increased cardiovascular and cerebrovascular risk compared with uninfected controls owing to virus-associated endothelial vascular changes or because antiretroviral agents cause a shift of metabolic profiles to a proatherogenic pattern. Future studies will need to address whether HIV in the absence of profound immunosuppression and other potential causes of cerebrovascular disease predisposes to ischemic stroke. We should also continue to study the impact of HIV therapy (HAART) on stroke and stroke management and prevention with prospective clinical trials.

### Expert commentary

No specific therapy currently exists for stroke in the HIV-infected population. The underlying etiology, when one is identified, must be promptly identified and treated. There is no series of cases or larger prospective studies that would support the use of tissue plasminogen activator in ischemic stroke with HIV; however, provided that the treating physician adheres to the guidelines for its administration, therapy with the compound is probably warranted. Prospective evaluation of the stroke risk and its predisposing causes is clearly indicated, especially with the aging HIV-infected population and the metabolic abnormalities that attend the use of newer antiretroviral medications.

### Five-year view

The incidence of cerebrovascular disease occurring in association with HIV/AIDS will probably continue to decline with aggressive management of HIV infection with effective antiretroviral therapies. However, with the advancing age of the HIV-infected population in the developed world, coupled with the atherosclerotic risk factors of protease inhibitors, it is not unlikely that an increased frequency of more traditional stroke risk factors will ensue in this population. Aggressive prophylactic management of these risk factors will be important to address this potential problem.

### Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.
Key issues

- HIV infection increases the risk of both ischemic and hemorrhagic stroke.
- Stroke typically occurs in the setting of advanced AIDS when CD4 lymphocyte counts are less than 200 cells/mm³.
- The most common underlying causes of ischemic stroke in the HIV/AIDS population are infectious meningitis and infectious vasculitis, hypercoagulability and HIV vasculopathy.
- Hemorrhagic stroke is the consequence of coagulation disturbances, thrombocytopenia, intracerebral tumors or CNS infection.
- Stroke may be the heralding manifestation of some of these underlying disorders, such as neurosyphilis and basilar meningitis.
- The widespread adoption of highly active antiretroviral regimens has resulted in a decrease in the frequency of many of the neurological complications of HIV, including stroke. However, the aging HIV population, coupled with the pernicious effects of protease inhibitors on blood lipids, suggests that the decline in stroke since the introduction of highly active antiretroviral therapy will be counterbalanced by this latter group.

References


Stroke in HIV infection & AIDS

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