Review

The aging HIV population

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Practice Points

- HIV infection will soon be a disease of older patients, with more than half the infected population in the USA over the age of 50 years by 2015.
- Research into the interplay of aging and HIV is needed on several levels, including mechanisms of aging, biomarkers and clinical indices, multimorbidity and societal/caregiving issues.
- Identifying older patients at risk for HIV is essential to getting them into care; earlier diagnosis and treatment are linked to improved outcomes.
- Older patients are more likely to present with more advanced disease.
- Comorbidities associated with HIV and aging include higher risk for cardiovascular disease, renal insufficiency, bone loss, neurocognitive impairment, depression, malignancy and liver disease.
- Antiretroviral therapy is recommended by annually updated guidelines.
- Polypharmacy is a particular risk in older patients with HIV.
- Evaluation and management of older patients with HIV includes a routine, thorough history and physical with special attention to HIV-related medical history, ongoing risk behavior, medication interactions and adherence, and social factors such as stigma, isolation, independence and advance directives.
- Multidisciplinary care for older patients with HIV is essential.

As we move into the fourth decade of the HIV epidemic, this illness, once considered nearly always fatal, is now viewed as a chronic disease in most industrialized nations, due to advances in treatment. Patients with HIV are growing older and the number of infected patients over the age of 50 years is growing steadily. With this shift in demographics, the medical field is turning its attention toward the need to both care for older patients whose disease is long-standing, and identify newly infected older patients. It is increasingly apparent that older HIV-infected patients are vulnerable to a variety of non-AIDS-related conditions and the interplay of aging and HIV occurs in multiple ways. Identifying older patients at risk, the importance of getting patients into care and the impact of aging on the course of the infection are discussed as are common comorbidities such as cardiovascular disease, chronic kidney disease and neurocognitive decline. Recommendations for the evaluation of an older HIV-infected patient are outlined, recognizing that optimizing comprehensive, multidisciplinary care is essential.

Keywords: aging • AIDS • elder • geriatric • HIV

It is generally recognized that the first cases of HIV in the USA were described in the Morbidity and Mortality Weekly Report of June 1981, in which five young, previously healthy homosexual men in Los Angeles developed pneumocystis pneumonia, an infection

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virtually unheard of in this country at the time [1]. These were not, of course, the first actual cases. Many physicians practicing in urban areas in the late 1970s and in 1980 might remember an unexplained illness or unexpected death in a patient, usually a young man, from that time.

We are now in the fourth decade of the HIV epidemic. The disease has run a fast, dramatic course and we have witnessed a phenomenal medical success in our ability to bring what was once a virtual death sentence under relatively safe and predictable control. In many parts of the world, however, the epidemic is still raging, particularly in countries that have minimal healthcare infrastructure. Worldwide it is estimated that over 34 million people are infected with HIV and that fewer than a third of those infected have access to effective care. In some African nations there are areas where the HIV seroprevalence rates exceed 30% in the adult population. The life expectancy in these areas has declined to mid-20th century levels, erasing decades of gains that had resulted from economic growth and political stability [2,3].

In the USA, there was a dramatic drop in the death rates from HIV after the introduction of effective antiretroviral therapy (ART) in the mid-1990s. While the number of new infections fell off sharply as well, there have always been more new cases than deaths, resulting in an overall increase in the total number of people infected. Patients with HIV are living longer and as a result the average age of the HIV-positive population is rising. The CDC estimates that by the year 2015 more than half the HIV-infected patients in the USA will be over 50 years old [4]. In our own urban, hospital-based HIV clinic, the percentage of patients over the age of 50 years rose from 13% in 2001 to 40% in 2011 [Ball SC, Unpublished Data]. As the number of patients in this age group rises, the risk of transmission will also rise, not necessarily due to increased risky sexual behavior, but because of higher prevalence rates [5].

Clinicians are increasingly recognizing the importance in this shift in demographics within the USA [6–10]. Going forward, care for older patients with HIV will require attention not only to the issues of immune suppression but of the HIV-associated non-AIDS conditions that have particular relevance in an aging population. In addition, discussions of risk and prevention remain essential.

Recognizing the limits of knowledge & the need for research

A special report on HIV and aging was published in 2012 [6]. The NIH Office of AIDS Research commissioned a working group to assess both areas of knowledge and areas in need of research for older patients with HIV. HIV and geriatrics experts from around the country including clinicians, scientists and nurses participated in discussing four major areas: mechanisms and triggering of functional decline/aging in HIV infected persons; biomarkers and clinical indices as predictors/surrogate outcome markers; aging with HIV infection: multimorbidity and the clinical research agenda; and societal infrastructure, mental health/substance abuse and caregiving issues. As a result of their collaboration, The HIV and Aging Working Group identified several predominant themes:

- Multimorbidity, polypharmacy and the need to maintain function;
- Complexity of assessing HIV versus treatment effects versus aging versus concurrent disease;
- Inter-related mechanisms of immune senescence, inflammation and hypercoagulability;
- Utility of multivariable indices for predicting outcomes;
- Need to emphasize human studies to account for complexity;
- Required focus on issues of community support, caregivers and systems infrastructure.

Ultimately the working group sought to tease out and identify the multiple issues that confront the older patient with HIV and his or her physician, recognizing that the population has some unique features socially and biologically, and that differentiating the pathophysiology of aging from that of chronic HIV infection, or HIV infection in an older person, has not been adequately clarified. In addition, caregiving issues for older patients with HIV incorporate geriatric approaches as well as societal accommodations and recognition.

Identifying older patients at risk for HIV

The CDC estimates that there are approximately 1.2 million people currently infected with HIV in the USA. Of those, approximately 20% are unaware of their diagnosis [11]. HIV-infected but as yet undiagnosed individuals pose a risk to their sexual partners. While it has been shown that patients typically modify their behavior when they know that unprotected sex can transmit HIV, condom use may be less prevalent in couples unaware of the potential risk. Older individuals, divorced, widowed or otherwise embarking on new sexual relationships are among the vulnerable. Patients over the age of 50 years represented 13% of new HIV diagnoses in 2009, increased from 11% in 2007 [11]. For the general internist or family practitioner, making a new HIV diagnosis in an older patient requires

awareness and understanding of ongoing risk in this patient population. Patients over the age of 50 are less likely to be asked about their sex lives by their physician despite the fact that patients continue to be sexually active. In one large study, over half of patients aged 65–74 said that they were sexually active [12]. Studies of who have sex with men show ongoing sexual behavior outside of primary relationships and individuals with a history of drug use may continue to use and put themselves at risk through injection drugs or unprotected sex [13]. Patients often overlook or forget to discuss a recent or distant history of risky sexual behavior or intravenous drug use. At the same time, healthcare providers may be uncomfortable speaking about sex to their older patients and this discomfort can result in a failure to ask relevant questions. In asymptomatic individuals potentially risky behavior may not be brought to light.

Age and its attendant manifestations may also act as a barrier to making an HIV diagnosis. Physicians may fail to include HIV in their differential diagnosis in those with vague or nonspecific symptoms such as decreased appetite, skin or hair changes, or subtle mental status changes; such symptoms may be attributed to the aging process and not to the effects of immune deficiency. Failure to recognize their significance may result in a delayed diagnosis of HIV in older patients. In addition to these barriers in the doctor's office, older patients may have their own barriers, including avoidance of the medical system, denial of symptoms, lack of access, affordability and fear of stigma. It is incumbent upon healthcare providers at all levels and in all disciplines to consider the potential for an HIV diagnosis in their older patients, both for the patient's wellbeing and to reduce the risk of further transmission.

Effect of age on presentation

Older patients are more likely than younger patients to present late for HIV diagnosis and care. Cuzin *et al.* showed that patients aged 50 years or older were significantly more likely to have a diagnosis of AIDS within a year of their HIV diagnosis than were younger patients [13]. Cuzin's work echoes an earlier study, carried out by Ferro and Salit, that assessed HIV in the elderly [14]. In this study, from 1992, patients over age 55 years were compared with younger patients for risk factors, diagnosis of AIDS at presentation and progression to AIDS. Notably, 21% of older patients versus 3% of controls (those under the age of 55 years) had acquired their infection from blood transfusions, a reflection of the tainted blood pool prior to late 1985 and in contrast to transfusion being a negligible factor for HIV transmission in the USA today. Regardless of this risk factor (which often led to a dramatic downward course for those infected due to the massive inoculum received through infected blood), 36% of older patients versus 5% of controls had an AIDS diagnosis (using the pre-1993 definition) at the time of their HIV diagnosis, and at 40 months, 90% of older patients versus 20% of controls had developed AIDS. These authors commented that older patients have a loss of immune function as evidenced by the increased frequency of reactivation conditions such as varicella zoster or tuberculosis and the addition of HIV infection may aggravate existing immunodeficiency. Interestingly, in the pre-highly active ART (HAART) era in which they wrote their paper, cardiovascular disease (CVD) or decreased renal function were advanced as conditions of aging, which might reduce an individual's capacity to respond to an opportunistic infection, not as the common comorbidities in which they are viewed in HIV-infected older patients today. Given the high mortality rates of that time period (35% 1-year survival for the older patients), and unlike this paper, the authors were not discussing how HIV-infected patients were growing old with the disease.

Currently, more advanced immunosuppression usually speaks to a longer-standing infection; a Gay Men's Health Crisis (GMHC) study from 2010 assessing degree of illness on diagnosis indicated that over half of the patients over age 50 years with a new diagnosis of HIV already had an AIDS diagnosis. This is in contrast to younger patients, where lower percentages of patients with new HIV diagnoses have AIDS at the time of diagnoses with each age decrement. That is, 44, 38 and 24% of patients had an AIDS diagnosis on presentation in age groups 40–49, 30–39 and 20–29 years, respectively [15].

More advanced disease in older patients may be explained in part by the disease itself being more aggressive in older patients. Cellular senescence may provide a microenvironment where the virus can flourish, to the detriment of the host. Further evidence of how older patients may have more-aggressive disease is the blunted immune response in older patients when they do receive ART. This was demonstrated in the ATHENA cohort, an observational study of the effect of ART on HIV infection. Several groups of patients in The Netherlands were followed for at least 7 years after starting ART (the study went from July 1996 to June 1998). For patients over 50 years, regardless of where their CD4 cell count was upon initiation of therapy, the subsequent rise in cell count was always less than that of their younger counterparts [16].

Comorbidities of aging patients with HIV

Cardiovascular disease

Shortly after the advent of HAART, patients on these medications were noted to have increases in their

lipid levels and there were case reports of sporadic but notable cases of acute myocardial infarction (AMI) and death [17,18]. This led researchers to focus on the lipid effects of ART and the link of these effects to increased risk of heart disease. As patients lived longer on effective ART, it became apparent that there is a link between HIV and CVD, not just through its effect on lipids. This has been intensely studied in large cohorts in Europe and the USA [19–23]. Increased relative risk for AMI ranges from 20 to 100% higher in patients with HIV when compared with uninfected controls, depending on the study. For example, data from the Veterans Administration (VA) system included 28,000 patients and noted an increased risk of AMI in HIV-positive patients at an adjusted hazard ratio of 1.94 when compared with uninfected controls [24]. Triant *et al.*'s report on a data registry from Boston assessed AMI visits at two major hospital emergency rooms from 1996 to 2004 and included 1,044,589 HIV-negative patients with AMI and 3851 patients with HIV. Patients were stratified for age and across all age groups the AMI rates per 1000 person-years were higher in the HIV-infected patients, with older HIV-positive patients having sharply higher numbers of events and the overall adjusted relative risk being 1.75 (Figure 1) [21].

The relationship between HIV and CVD is likely dependent on several intertwined factors including traditional risk factors for CVD, HIV-mediated changes including heightened inflammatory markers and immunologic changes, and the effects of antiretroviral medications including their impact on lipid levels. Atherosclerosis has been assessed in patients with HIV using various parameters such as carotid intima–media thickness, endothelial dysfunction, and coronary artery calcification and plaque, supporting the concept of a multifactorial etiology for disease in these patients [19].

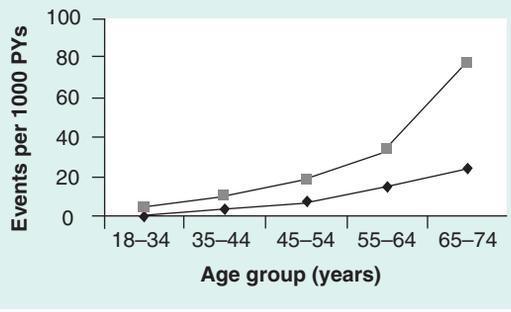

Figure 1. Myocardial infarction rates by age group.
Light line indicates patients diagnosed with HIV disease. Dark line indicates patients not diagnosed with HIV disease. Data shown include both sexes. Rates represent number of events per 1000 PYs as determined by IDC coding.
IDC: International Disease Classification; PY: Person-year.
Reproduced with permission from [19].

Smoking plays a significant role in risk for CVD and is present in a disproportionate number of patients with HIV. In the general population smoking rates average approximately 20% across ages and genders. By contrast, in some HIV study populations, over 50% of patients with HIV smoke cigarettes [25]. HIV-positive smokers have significantly higher risk of MI than nonsmokers but with smoking cessation the incidence ratio drops over time. Given smoking's contribution to cancer as well as CVD, care providers in all disciplines should stress the importance of smoking cessation with their patients.

Other traditional CVD risk factors such as diabetes, metabolic disorders and hypertension are also present in somewhat increased rates among patients infected with HIV. When adjusting for AMI rates between HIV-positive and negative patients, traditional risk factors play a role but do not solely account for the increased rates of CVD seen in HIV patients.

The D:A:D study, which began in 1999, was a large observational cohort that tried to assess the contribution of ART to the risk of heart disease among patients with HIV. Trying to distinguish the contribution of the medication separate from the increased lipid levels in patients on protease inhibitors, the study group found an adjusted relative risk of AMI of 1.16 per year taking ART [26]. Another large study from the VA, however, did not find any contribution of risk from ART toward increased risk of AMI [27]. The drug abacavir came under great scrutiny for a brief period when results indicated taking the drug transiently raised one's risk for AMI. Several exhaustive studies looking into this failed to demonstrate a conclusive risk of AMI from this medication [19].

The role of inflammation and its contribution to CVD risk have been in the spotlight in recent years. Inflammation and immune dysfunction are important factors for increased CVD risk in patients with HIV. The SMART study looked at levels of IL-6 and D-dimer in patients interrupting their HIV treatment or maintaining their viral suppression. These two biomarkers of inflammation were present in higher levels in patients with higher HIV viral loads and the rate of cardiovascular events was increased in the study arm in which patients interrupted their therapy [28,29]. Similarly, patients with CD4 cell counts that are less than 200/μl, a condition of advanced immunosuppression, also have higher rates of AMI [19].

Heart disease is a leading cause of death in adults around the world. As research has shown, there is a higher risk of CVD in patients with HIV due to several

inter-related factors, including traditional risk factors, immunologic imbalance, inflammatory factors and the virus itself. The role of ART, while contributing to diabetes, lipid abnormalities and metabolic syndrome, has not been definitively proven as an independent contributor to CVD risk. As HIV-positive patients get older, their vulnerability to the risks of CVD will increase resulting in a greater burden of morbidity and mortality from the combination of these two conditions. The WHO predicts that by 2030, HIV, AIDS and ischemic heart disease will be the major causes of morbidity in the world [30].

Chronic kidney disease

Chronic kidney disease (CKD) is defined as reduced function or evidence of renal damage of over a 3-month duration, thus distinguishable from acute kidney problems that are often reversible, such as dehydration or drug effects. Kidney disease is one of the most common findings in long-term HIV infection, worsening the natural effect of aging. Risk factors contributing to CKD attributable to HIV include low CD4 count, longer duration of HIV infection and high viral load. Reduction in the estimated glomerular filtration rate to less than 60 ml/min/1.73 m^2 occurs in up to 9.7% of HIV patients depending on the study [31]. HIV directly affects the kidney in several ways, most commonly as glomerular disease mediated by viral infection of renal epithelial cells, known as HIV-associated nephropathy (HIVAN). Deposition of antigen–antibody complexes (HIV immune globulin) and HIV-related thrombotic microangiopathy are two other forms of renal damage caused by HIV infection.

Concomitant conditions including hypertension, diabetes and hepatitis C accelerate renal decline in HIV-infected patients just as in HIV-negative individuals. African–Americans are notably prone to the glomerular disease characteristic of HIVAN; among HIV patients on dialysis, 91% are African–Americans [32].

In addition, certain HIV medications can decrease estimated glomerular filtration rate through their effects on the glomerulus or on renal tubular transport (notably tenofovir). Multiple other medications used by patients with HIV can also have deleterious renal effects, for example, amphotericin, ganciclovir, NSAIDs, metformin, aminoglycosides and pentamidine. Box 1 lists factors contributing to CKD in patients with HIV.

Chronic proteinuria is extremely common in patients with HIV and may be present in trace amounts for years in infected patients without further evidence of renal impairment. One study estimated up to 32% of patients with HIV in the USA have proteinuria [31]. Not all patients with proteinuria progress to end-stage kidney disease so proteinuria, while a common finding in HIV-positive patients, is not considered a specific marker of future renal failure.

Because HIV itself has been recognized as an important causative factor in kidney damage, for patients not yet on ART, the presence of HIVAN is an indication to start therapy even in the presence of low levels of viremia and high T-cell counts [33]. In such patients, virally mediated kidney damage is often reversed when the virus is brought under control.

Given the association of so many factors in the development of kidney disease in older patients with HIV, it may be difficult to distinguish specific root causes. For example, an elderly African–American male who has had well-controlled HIV for 15 years and a normal CD4 cell count might have hypertension and diabetes and take medications for all of these conditions. When his kidneys start to fail efforts are made to remove aggravating causes. Often this will involve adjusting various medications to try to limit any nephrotoxic

Box 1. Factors contributing to chronic kidney disease in patients with HIV.

Direct HIV infection
- HIV-associated nephropathy: infection of glomerular epithelium
- HIV immune globulin: deposition of immune complexes
- Thrombotic microangiopathy: HIV-related thrombotic microangiopathy

HIV-related factors
- Low CD4 cell count
- High HIV RNA viral load
- Duration of infection

Non-HIV-related factors
- Hypertension
- Diabetes
- Hepatitis
- Medications (e.g., aminoglycosides, NSAIDs and amphotericin)
- Increased age
- African–American heritage

agents. Close attention to control of hypertension is crucial and management of blood sugar is also important given that both hypertension and diabetes are major contributors to renal failure. Vigilance to intercurrent infection and fluid status are also important as an episode of pneumonia or transient dehydration can tip a fragile, failing renal condition into one of overt failure. Chronic renal replacement therapy in the form of dialysis or transplant is often the only remaining treatment option.

Bone disease

Bone loss increases as people age and patients with HIV have higher incidences of bone loss and fracture than do uninfected individuals of the same age. Decreased bone mineral density (BMD) is a result of a combination of factors, including traditional risks for osteoporosis such as aging, postmenopausal state, vitamin D deficiency and smoking, as well as HIV itself. Furthermore, treatment of HIV incurs bone loss. In a review by McComsey *et al.* [34], starting ART was associated with a decrease in BMD of 2–6% over 2 years, which was likened to the change in BMD in women in the first 2 years of menopause. While often considered a condition of older women, osteoporosis in HIV is present in both genders [35,36]. Lifestyle changes such as smoking cessation and increased exercise are ways to reduce decline in BMD. Treatment modalities are varied depending on the clinical setting. While vitamin D deficiency is common in patients, replacement therapy is of uncertain utility.

Neurocognitive decline & depression

The impact of HIV on the brain and brain function has been studied since the early 1980s, when HIV first appeared. Some of the opportunistic infections affecting the brain include CNS toxoplasmosis, progressive multifocal leukoencephalopathy and primary CNS lymphoma. HIV-associated dementia (HAD) was present in up to 16% of patients with HIV in the pre-HAART era [37]. Aging, however, has significant effect on the presence of dementia in patients with HIV. A 2004 study from the Hawaii Aging with HIV Cohort that showed notable rates of HAD in both comparator arms nonetheless demonstrated HAD in 25.2% of patients over the age of 50 years and in only 13.7% of younger patients [38]. Study of neurocognitive decline in patients yielded a broad spectrum of conditions ranging from the asymptomatic to the frankly demented, neurologists referring to this spectrum as HIV-associated neurocognitive disorders. In the post-HAART era there has been a significant decline in the opportunistic infections previously seen in patients with extremely low CD4 cell counts. Similarly, HAD is diagnosed much less commonly [39]. By contrast, HIV-associated neurocognitive disorder persists at rates near the pre-HAART levels, albeit in less-overt, clinically quieter ways. Pre-HAART neurocognitive impairment (NCI) presented more commonly with loss of motor skills, cognitive speed and verbal fluency whereas the NCI of the post-HAART era involves reduced memory and learning as well as decreased executive functions. The source of this damage is not fully known although a number of mechanisms have been put forward, including subtle brain damage incurred prior to initiation of ART, ongoing damage from poorly controlled virus due to poor penetrance of ART into the CSF, and the effect of low levels of viremia or its resultant inflammation in the brain [40].

Depression increases with age, with HIV positivity adding to the risk for depression. Contributing to depression in older patients with HIV is social isolation and other factors such as lack of access, lack of mobility, financial restrictions, lack of support systems and other social conditions [41]. These may contribute to depression even in the absence of NCI. Many older patients live alone; stigma and prejudice may add to older patients' sense of isolation, preventing them from finding companionship or company in places such as church, neighborhood centers and community activities. For clinicians, depression in older HIV-positive patients may present as weight loss, insomnia, moodiness, poor adherence or poor personal hygiene. Clinicians need to be alert to these changes as treatment of the depression can greatly improve a patient's quality of life. Perhaps more importantly, depression has a major adverse impact on patients' adherence to medication regimens. As adherence is the single most significant factor in the successful treatment of HIV infection, addressing depression becomes a life-saving measure [42].

Malignancy

Several infection-related malignancies are known to occur more commonly in patients with HIV, including Kaposi's sarcoma, liver cancer and non-Hodgkin's lymphoma. As AIDS-defining malignancies have decreased in the post-HAART era, non-AIDS malignancies have increased. Studies have shown that cancer of all kinds occurs in HIV-positive individuals at younger ages than their HIV-negative peers [43]. Box 2 shows possible links to tumorigenesis in patients with HIV.

Liver

Liver disease is aggravated by a number of factors including aging and HIV disease. Hepatitis C is of particular concern among aging HIV-positive patients, being prevalent in up to 80% of current or former injection drug users. Hepatitis C is the most common

cause of liver transplantation in the USA, yet nontransplant treatment of hepatitis C is rapidly evolving for both mono- and co-infected patients. Interferon has long been a toxic, variably successful treatment for hepatitis C. Exciting advances in hepatitis C treatment include regimens that are both more effective and avoid the need for interferon [44,45]. Other factors that can impact liver function and are of concern in older HIV patients include ongoing illicit drug use, alcohol, diabetes, obesity and concomitant hepatotoxic medications.

ART in older patients with HIV

Treatment guidelines in the USA have not addressed age as a condition of starting therapy. Current guidelines support initiating therapy in patients with CD4 cell counts below 500/mm^3 and in certain situations such as pregnancy or the presence of HIVAN, therapy is started notwithstanding T-cell count. There is an ongoing study (START trial) sponsored by the NIH to try to discern if in fact all patients, regardless of their CD4 cell counts, should be on ART. In Great Britain and Europe, the guidelines include age as a recommendation for treatment, advocating treating all patients who are over the age of 50 years [46].

Virtually no antiretroviral medication has been studied in an exclusively older population. In all the preapproval drug trials that have been carried out over the years, the average ages of the patients studied range from the mid-30s to the low 40s. The approval in 2012 of the most recent single-tablet regimen for the treatment of HIV specifically noted in its package insert that the drug had not been studied in patients over the age of 65 years [47]. Drugs are known for their hepatic or renal metabolism but little or nothing is known of the variability of medications' impact in older populations.

Box 2. Factors related to cancer formation in patients with HIV.

- Traditional risk factors
- Smoking
- Alcohol
- Sun
- Aging
- Oncogenic-associated viruses
- HPV
- EBV
- HHV8
- Hepatitis B and C
- Direct oncogenic effect of HIV
- Cytokine dysregulation
- Immune dysfunction
- Genomic instability

Polypharmacy

Treatment of HIV in older patients involves the vexing issue of polypharmacy. Geriatricians are faced with this problem on a daily basis so when HIV and its medications are added to this mix the problem grows even more complex. Polypharmacy becomes nearly unavoidable in older patients as incidence of hypertension, diabetes, CVD, renal dysfunction and malignancy are but a few of the conditions associated with aging that require pharmacological intervention. Adding ART introduces further issues of drug–drug interaction, side effects and drug toxicity. Older patients are

Box 3. Routine history on initial encounter.

Past medical history
- HIV-related: risk factors for HIV, previous disease course including CD4 nadir, opportunistic infections, medications and genotype (if available)
- Non-HIV-related: hospitalizations and medications
- Psychiatric history: treatment history, hospitalizations and ongoing care

Medications & allergies
- Review of prior treatment history (including genotype results, if known) and other medications taken, including over-the-counter, complementary and alternative medications

Health maintenance
- Immunizations: patients should receive flu shots, pneumovax, hepatitis screening and vaccinations, tetanus, purified protein derivative screening, meningitis vaccines in relevant risk groups and varicella zoster virus screening
- Cancer screening: routine cancer screening recommendations (e.g., mammograms and colonoscopies) are in effect with HIV-specific recommendations for cervical, anal and liver cancer
- Dental care and ophthalmology: annual dental and ophthalmologic exams are recommended

Family history
- Review of illnesses, causes of death and substance use in family history

Social history
- Review of current housing, social conditions, support networks (friends, family), cigarette, alcohol or substance use, education and work history

potentially more sensitive to medications, may have reduced hepatic or renal metabolism of drugs or may have comorbid conditions that affect either drug tolerability or efficacy. For clinicians it is important to review and reconcile patients' medication profiles on a regular basis. It is further recommended that patients deal with only one pharmacy in order to reduce the risk of duplication or redundancy in treatment, particularly if a patient is seeing different providers.

Recommendations for management of older patients with HIV

As patients live longer on effective ART and the number of HIV-positive patients aged over 50 years increases, HIV specialists and geriatricians will be working more closely together to optimize their care and treatment. The Work Group for the HIV and Aging Consensus Project [7] is another work group assembled with the intention of better understanding the issue of HIV and aging in order to make comprehensive care and treatment recommendations for patients. The experts comprising this panel began their work in 2009, bringing backgrounds equally representing HIV medicine and geriatrics. They published their summary report of treatment strategies in 2012, using a case study to illustrate their recommendations [7].

A member of the NIH Office of AIDS Research working group, Dr Amy Justice, argues for the need for a new paradigm of care for older patients with HIV, recognizing that older patients' status and progress

Box 4. Considerations in ongoing care.

Comorbidities

- Awareness and screening for cardiovascular disease, diabetes, hypertension, renal impairment and osteoporosis, as well as depression, psychiatric conditions or subtle neurocognitive decline

Risk reduction

- Risk reduction is crucial to maintaining optimal health
- Smoking cessation: of all the interventions, this carries the highest benefit for patients in reduction of cardiovascular risk, cancer risk, pulmonary health and cerebrovascular health
- Nutritional management: avoidance of excessive weight, awareness of salt, carbohydrate and saturated fat intake, reducing risk for hypertension, diabetes and hyperlipidemia and their links to increased morbidity and mortality
- Exercise: recognized for its role in improving state of mind and quality of life as well as lowering hypertension, reducing cardiovascular and diabetes risk, and maintaining bone health
- Reduction/cessation of substance use: illegal drug use should be addressed and referral to detoxification, rehabilitation or mental healthcare providers should be routinely offered as appropriate

Medications

- Drug–drug interactions and polypharmacy: regular review and reconciliation of medications, awareness of hepatic and renal metabolism, toxicities and dosage adjustments, and coordination with pharmacies to avoid overlap with generic and brand-name medications
- Adherence: an essential factor in control of HIV, adherence can be optimized with multidisciplinary assistance to ensure consistency and tolerability
- Substance abuse: providers must be attentive to patients taking or requesting medications for treatment of anxiety, pain or insomnia. Alcohol intake should be addressed regularly and, where appropriate, patients should be advised to discontinue or minimize their consumption. Referrals to counselors, treatment programs or support groups may be indicated. Clinicians should be attentive to coexisting, underlying psychiatric conditions and address these conditions with support from mental health experts

Social/aging factors

- Sexual health: providers need to remain vigilant to their patients' sexual history, behavior and risks with routine screening for high-risk behavior. Sexually active patients may benefit from hormonal therapies. Patients must continue to practice safer sex and remain adherent to their antiviral regimens
- Advance directives: patients should also consider late-life care options including delegating healthcare proxies, options for alternative living situations, decisions about invasive medical interventions, and need for last will and testament
- Addressing stigma: older patients, particularly those with a new diagnosis of HIV, may be vulnerable to rejection from family or friends due to continued prejudice and ignorance in the community. Patients benefit greatly from individual and group support around these issues
- Maintaining independence: patients should be supported in their desire and ability to remain independent in their living circumstances and activities as much as possible. Self-acceptance is an important factor as is accessing family or community support networks, acknowledging limitations and limiting potential for risks such as falls, medication errors or other adversities

rest upon much more than their viral load, CD4 cell count and AIDS-defining illnesses. She argues that a new metric needs to be devised that includes lifestyles' characteristics and comorbidity, and can additionally take into account concepts of frailty and functional status [9].

A general overview for patients aged older than 50 years who are coming into care with new or established HIV infections might include the routine history on initial encounter described in Box 3 and the considerations in ongoing care described in Box 4 [33,48].

Conclusion

Patients with HIV are living longer; the population of HIV-infected patients over the age of 50 years is growing at a rapid pace. This translates to a higher number of new cases among older patients due to the increase in the transmission pool [6], as well as to the greater need for geriatrics awareness for HIV clinicians and HIV awareness for geriatricians. As more attention is paid to these rising needs on both an individual practice level and a national resource level, providers are shifting their focus to address the multiple aspects of care required. While risk assessment and HIV testing need to be increased in order to get patients into care, the approach to the HIV-infected patient aged over 50 years includes a comprehensive assessment of demographics, medical history, comorbidities, social factors and individual needs. A multidisciplinary approach should encourage and support the patient's active engagement in his or her healthcare decisions and activities.

In a few short years, most HIV care in the USA will involve older patients. This shift affects patients, providers and society as a whole. Increased efforts in education, research, testing parameters, treatment modalities and comprehensive assessments are urgently needed and will enable us to prepare for and provide patients with optimal care in the years ahead.

Future perspective

The treatment options for patients infected with HIV have evolved in ways that few could have imagined in the late 1980s or early 1990s. Many patients take one pill once a day for complete viral suppression and retention of intact immune function. The future of HIV will see the focus on this disease in two main domains: in the industrialized world the overall prevalence of the illness is growing and the majority of those infected will soon be over the age of 50 years, raising issues of geriatric and palliative care that have yet to be fully addressed. The second domain will be the continued drain that the infection puts on sub-Saharan Africa, with tens of millions of people infected and millions of new infections and deaths each year. Some treatment success has been seen in this part of the world, but Sub-Saharan Africa will not easily or soon step out from the shadow of this epidemic where treatment options are far fewer and the overall healthcare infrastructure remains deficient in vast parts of the continent. A preventive vaccine is essential for bringing this disease under control in Africa, but the urgency to develop such a vaccine has waned as effective treatment renders HIV less menacing in industrialized nations. Philanthropy has played an enormously important role in third-world countries with high rates of HIV infection. Perhaps philanthropy will also lead to the research and development of more effective preventative therapies.

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Papers of special note have been highlighted as:

- • of interest
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