The human immunodeficiency virus and ageing

Introduction

HIV, first described clinically in 1981 and identified in 1983, rapidly emerged to be a major cause of morbidity and premature mortality. Prior to the introduction of combination antiretroviral therapy (cART) in 1996, life expectancy was poor—typically <2 years after initial diagnosis—with the majority of deaths arising secondary to AIDS defining illnesses [1]. Presently, for HIV-positive individuals receiving cART in accordance with recommended guidelines, life expectancy has improved significantly, with many studies suggesting it to be near normal [2–3]. The majority of deaths now occurring in this population are secondary to non-AIDS defining illnesses [1].

The United Kingdom: a changing epidemiological picture

In 2012, the Health Protection Authority (HPA) published epidemiological estimations, predicting there were 96,000 people in United Kingdom living with HIV (95% credible interval: 90,800–102,500), of whom, 73,660 are diagnosed and in care [1]. As the number of new diagnoses per year remains at best stable, and as outcomes improve, this total figure continues to increase year on year. Largely as a result of this improved survival, the demographics of those accessing care is changing. In 2011, one in five adults (22%, 16,550) receiving HIV care in the United Kingdom was aged over 50, whereas in 2002 the comparable figure was one in nine (12%, 3,640) [1]. In the United States, it has been estimated that by the year 2015, over 50% of HIV-positive patients in care will be over the age of 50 [4].

It is important to note that the short-term mortality in those diagnosed late (with an initial CD4 count <350 cells/mm$^3$) remains high despite the availability of cART, with an observed 10-fold increase in mortality when compared with those diagnosed early (CD4 count > 350 cells/mm$^3$) [1]. Multiple data have shown that older persons are significantly more likely to be diagnosed later than younger persons and thus are at significantly higher risk of short-term mortality [5]. It is imperative therefore that geriatricians consider HIV infection within their differential diagnosis and recommend testing particularly in those with clinical indicator diseases, as recommended in national and international HIV testing guidelines (http://www.bhiva.org/documents/Guidelines/Testing/GlinesHIVTest08_Tables1-2.pdf) [6] (Figure 1).

The impact of ageing on HIV

Prior to the advent of cART, it was demonstrated that older individuals recently acquiring HIV infection had a significantly faster progression to AIDS or death [7], although this effect appears to be reduced or even lost since the advent of effective therapy. On initiation of cART, overall it appears that older patients have a similar or improved virological response—likely driven by improved adherence to therapy, although the immunological response to cART may be impaired [8, 9]. Some guidelines have recommended earlier initiation of cART amongst older individuals, defined by their considered cardiovascular risk [10].

The impact of HIV on ageing

It has been proposed that HIV infection is associated with accelerated or premature ageing. First, in the ageing and the HIV population a similar disruption to normal immune function, described as immunosenescence, is seen—this is summarised in Table 1 [11].

Second, it is postulated that, despite viral suppression by cART, there remains a persistent low grade systemic immune activation and inflammation which contributes to an accelerated ageing pattern [11]. Third, it has been proposed that this accelerated or premature ageing may be a consequence of either toxicities resulting from long-term use of antiretroviral
therapies, or from other lifestyle factors (e.g. smoking, alcohol, recreational drugs) or co-infections (e.g. CMV, HCV) that are more common in the HIV-positive population. This theoretical association of HIV with ageing has been discussed extensively due to a reported increase in co-morbidities associated with normal ageing in HIV cohorts (e.g. cardiovascular disease, renal impairment, neurocognitive impairment, reduced bone mineral density, malignancy and frailty), which may explain the continued observed increase in premature mortality. However, increasingly this traditional view is being challenged. The impact of HIV on ageing may be explained by the presence of co-infections or lifestyle factors rather than HIV per se, thus it becomes possible that in the absence of significant co-factors the association between HIV and any reduction in life expectancy may be lost. Currently enrolling are longitudinal studies in the United Kingdom and elsewhere which aim to resolve this issue [3, 12, 13].

**Implications for patient care**

Whether HIV causes accelerated ageing or not, it is clear that the HIV cohort is ageing and that non-HIV physicians—including elderly care physicians—will be increasingly involved in the care of these patients. Historically, certainly within the United Kingdom, the medical care of patients with HIV has been largely within either genitourinary medicine or infectious diseases clinics, even if the relevant clinical issue is not directly related to HIV. As this relatively new chronic illness develops HIV physicians could learn from the experience in management of other complex chronic diseases, incorporating an awareness of the need for a more comprehensive approach, that takes account of the mental, functional, and social aspects, in addition to the medical issues. It is increasingly apparent that HIV specialists are less confident and less likely to treat significant co-morbidities such as hyperlipidaemia, hypertension and diabetes [14]. These aspects of care could be enhanced by geriatricians as they are experienced in the complexities of managing multiple co-morbidities. In other specialties the adaption of the comprehensive geriatric assessment (CGA) tool has been of benefit, but continued efforts will be needed to determine the optimal model of care in this emerging field.

Conversely, when HIV patients are treated by other specialties, it is increasingly recognised that care may be suboptimal; and in particular, that major risks are associated with polypharmacy and the potential for significant drug–drug interactions. Geriatricians will therefore need to be aware of the significance of potential drug–drug interactions (example. e.g. with statins, inhaled or injected corticosteroids and proton-pump inhibitors). The risk of such interactions can be easily reduced by discussion with local HIV clinicians and pharmacists or by utilising information resources such as the Liverpool University pharmacology website (www.hiv-druginteractions.org). Some larger HIV clinics within the United Kingdom are starting to develop a shared-care approach between Care of the Elderly and HIV clinical teams to optimise the management of this evolving group of patients.

**Conclusion**

There have been dramatic developments in HIV management since the introduction of cART, but new challenges continue to emerge. There is an increasing older population of HIV-positive patients who may require the input of geriatricians who are aware of the clinical and psychosocial issues particular to this group. Furthermore, geriatricians need to enhance their diagnostic consideration of undiagnosed HIV infection and offer HIV testing to persons with clinical indicator diseases irrespective of age in order to prevent unnecessary morbidity and mortality.

**Key points**

- As a result of major improvements in antiretroviral therapy, an increasing proportion of individuals with HIV infection are living into older age.
- Management of the older HIV patient requires consideration of complex drug–drug interactions and multiple co-morbidities.
- Many older patients with HIV are diagnosed late and geriatricians need to be aware of possible clinical presentations and offer HIV testing where undiagnosed HIV infection may be present.
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Second-eye cataract surgery: valuable investment or unaffordable luxury?

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Cataract is common (affecting over half of 80 year olds), and in older people most often bilateral. Cataract surgery is one of the most commonly performed operations. Modern cataract surgery is quick (20 min), restored vision is almost immediate, and surgical complication rates are low (1%). Most operations are now performed under topical anaesthesia. Once present, cataracts usually progress over time, but a prosthetic lens will last lifelong.

It is not surprising that successful surgery is reflected in improved quality of life, although the utility value of cataract surgery varies with how it is measured. Utilities are used to adjust for quality in calculation of Quality Adjusted Life Years (QALY). Weighted preference methods (such the EQ-5D and the SF-6D) do not incorporate sensory functions, so tend to underestimate gain. Alternative methods, using the standard gamble or time-trade off, yield higher values. Using this approach, Brown et al. [1] recently calculated a QALY gain of 1.6 for first-eye surgery and 2.8 for bilateral surgery [1]. We previously showed that second-eye surgery meets usual criteria for cost-effectiveness [2].

Against this backdrop of success, Meuleners et al. [3] report a population-based record-linkage study of 28 396 older Australians who had surgery to both eyes, showing that there may be an unexpected downside. They demonstrated that the rate of injurious falls doubled between first- and second-eye surgery, and that this reduced after second-eye surgery, but remained 25% above baseline. This raises three questions. Why? Are these results compatible with previous

References