



# Test them all; an easily diagnosed and readily treatable cause of dementia with life-threatening consequences if missed

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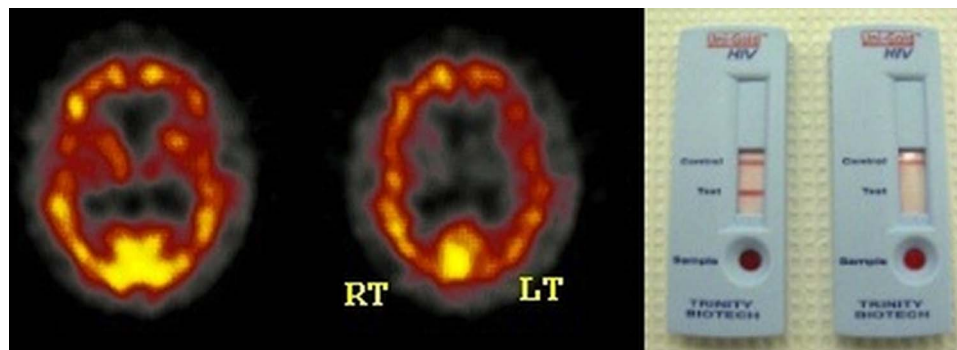
Over 90 000 people in the UK are infected with HIV, a quarter of whom are unaware of their diagnosis, and the number continues to rise.<sup>1</sup> The prognosis of HIV infection for patients on treatment is now excellent, and life expectancy approaches normal in areas with access to combination antiretroviral treatment.<sup>2</sup> As HIV frequently leads to neurological manifestations, it is crucially important that neurologists know the indications for HIV testing, and address the barriers to testing.

We were recently involved in the care of a patient with no apparent risk factors for HIV. Multiple clinicians at several sites had made extensive investigations for isolated cognitive decline; at no point was HIV tested. A technetium-99m-HMPAO SPECT scan (figure 1) provided beautiful images but failed to identify the underlying cause. Two weeks after this scan the patient was admitted to intensive care with a fatal *Pneumocystis jirovecii* pneumonia associated with advanced HIV infection.

HIV enters the brain early in infection and establishes productive infection in perivascular macrophages, microglia and to some extent astrocytes.<sup>3</sup> HIV-associated dementia occurs in advanced HIV disease due to several mechanisms, including neuronal damage from pro-inflammatory cytokines and toxic viral products, and loss of the homeostatic function of glia.<sup>4</sup> It usually develops with CD4 T-cell counts below 200/ $\mu$ L, and is an AIDS-defining condition. HIV-associated dementia is typically subcortical: there is cognitive impairment alongside prominent apathy, social withdrawal, depression and motor features, such as pyramidal slowness of fine movements, spasticity and frontal release

signs. However, not all patients have these typical subcortical features, particularly early on. Before the widespread use of combination antiretroviral therapy, HIV-associated dementia was common, affecting up to 40% of HIV-infected individuals before death.<sup>5</sup> Since treatment became available, it has become one of the few potentially reversible causes of dementia; many patients with previously marked cognitive impairment may return to independent functioning.<sup>6</sup> Without treatment, however, life-threatening complications of AIDS usually follow 3–6 months after the dementia diagnosis.<sup>7</sup>

At present, many clinicians restrict HIV testing to those with risk factors. Clearly, they should have increased suspicion in patients from HIV-endemic regions, men who have sex with men, intravenous drug users and sex workers. However, restricting testing to these will miss cases. The HIV antibody–antigen test is a quick, cheap, non-invasive and highly reliable test that should, in our opinion, be performed in all patients presenting to neurologists with cognitive impairment. This practice is supported by the British HIV Association guidelines for HIV testing, listing dementia as a neurological indicator disease (table 1).<sup>8</sup> Additionally, the Association of British Neurologists and British Infection Association National Encephalitis Guidelines recommend HIV testing for all patients with suspected encephalitis, regardless of perceived risk factors.<sup>9</sup> By contrast, the UK National Institute of Health and Care Excellence (NICE) dementia guidelines currently state that the initial investigation of dementia (usually in primary care) should not include testing for HIV or syphilis,



**Figure 1** Left: technetium-99m-HMPAO SPECT scan showing multifocal subcortical uptake in a patient with dementia due to undiagnosed HIV infection. This sophisticated technique failed to identify the underlying cause. Right: Cheap and reliable: HIV rapid antibody finger-prick card tests (2 bands=positive, 1 band=negative). Most UK clinics use a laboratory-based test combining HIV antibody and the p24 antigen, costing as little as £8.

unless there are risk factors or the clinical picture dictates.<sup>10</sup> However, the classical clinical picture is not always present. As the HIV population ages, the spectrum of disease is changing; furthermore, HIV may promote other neurodegenerative disorders, such as Alzheimer's and Parkinson's diseases.<sup>11</sup> Also, performing HIV testing on the basis of risk factors assumes that a detailed sexual history is routinely taken, and that the answers are reliable in a person with cognitive impairment. For these reasons, we feel that HIV testing should be a routine investigation for patients with dementia presenting to neurologists.

What about an elderly woman, happily married for 50 years, who has become forgetful? We admit it has not been our practice to test routinely for HIV in this situation. However, it could be argued that HIV testing should not be restricted by age, or by our perception of the likelihood of HIV risk factors, without having explicitly asked. Although HIV is unlikely, it is not impossible. Patients do present for the first time with HIV in this age group, even without apparent risk factors.<sup>12</sup> In the UK in 2012, 4.4% of new HIV diagnoses were aged over 60 years,<sup>1</sup> and HIV-associated dementia is more

common in older than in younger patients.<sup>13</sup> In an apparently low-risk patient, HIV can be quickly and easily ruled out alongside other potentially treatable causes of cognitive impairment, such as vitamin B12/folate deficiency and hypothyroidism. Indeed, serological testing for syphilis is still frequently performed in this situation, despite neurosyphilis being an uncommon cause of cognitive impairment at this age.<sup>14</sup> The oldest person we have diagnosed with HIV was aged 76 years: she had no obvious risk factors and had been in an apparently monogamous marriage since her early twenties. Only on closer questioning did it emerge that her husband had died of an unusual, undiagnosed infection a few years before. His death may have been HIV-related although he was not tested—perhaps because of assumptions made about risk factors in someone of his age.

Clinicians' reluctance to offer HIV testing partly reflects the misconception that lengthy pretest counselling is needed; however, HIV testing is no different to testing for any other serious medical condition.<sup>8</sup> If the pretest probability is low then the test needs only a brief mention; we do not counsel all smokers on the prognosis of lung cancer each time we do a chest X-ray. Rather than entering complicated and potentially embarrassing discussions about risk behaviours, our practice is simply to inform patients that we routinely test for HIV in this situation because, although very unlikely, it is an important treatable cause. In our experience, the vast majority of patients are happy to have the test when presented in this way. This practice is consistent with guidelines from the British HIV Association, and is supported by the Royal College of Physicians.<sup>8 15</sup>

Unlike other conditions, there is a stigma around HIV infection. Some feel that to offer a HIV test is to accuse the patient of infidelity, homosexuality or intravenous drug use. However, clinicians' embarrassment is no reason to deny a patient a potentially life-saving investigation. Considering a HIV test as a routine investigation for dementia can remove the stigma of

**Table 1** Neurological indicator diseases for HIV testing in adults, from the British HIV Association UK national guidelines for HIV testing 2008.<sup>8</sup>

AIDS-defining conditions	Other conditions where HIV testing should be offered
Cerebral toxoplasmosis	Aseptic meningitis/encephalitis
Primary cerebral lymphoma	Cerebral abscess
Cryptococcal meningitis	Space-occupying lesion of unknown cause
Progressive multifocal leucoencephalopathy	Guillain-Barré syndrome
	Transverse myelitis
	Peripheral neuropathy
	Dementia
	Leucoencephalopathy

the test and, moreover, avoids the need to take a detailed sexual history in all patients.

Of course, dementia is not the only neurological indication for an HIV test; table 1 gives neurological indicator diseases from the British HIV Association guidance on HIV testing.<sup>8</sup> We believe there is growing evidence that young stroke should be added to this list.<sup>16–17</sup> Some go further and advocate routine screening for HIV in all hospital admissions, regardless of clinical presentation or risk group.<sup>18–20</sup> Many parts of the USA have an opt-out strategy following recognition from the Centers for Disease Control and Prevention that targeted testing on the basis of risk behaviours was failing.<sup>18</sup> Routine HIV testing has reduced the stigma of the test and made it more acceptable to patients.<sup>18</sup> In the UK, several pilot studies have found this strategy acceptable and cost effective.<sup>1–19–20</sup> The Health Protection Agency (now Public Health England) recommends routine HIV testing for all general medical admissions in high-prevalence areas. High prevalence is defined as >2 cases per 1000, a threshold exceeded by 58 local authorities in England, including Manchester, Oxford, Coventry, Brighton and Hove, Reading, Birmingham, Leeds, Leicester, Blackpool, Nottingham and 30 of the 33 local authorities in London. Indeed, in some areas of England, HIV prevalence now exceeds 1%.<sup>20</sup>

To our knowledge, there are no data on how often HIV is missed as a cause of dementia. There are estimated to be 26 000 people in the UK with undiagnosed HIV infection, at risk of presenting in this way.<sup>1</sup> The annual incidence of HIV-associated dementia in untreated cohorts from the preantiretroviral era was around 4%,<sup>5</sup> however, these days, many present for another reason and receive treatment before developing dementia. This requires formal study and we hope that reports such as this will focus attention and promote studies into this area. What is clear is that HIV is an easily diagnosed and readily treatable cause of dementia, but with life-threatening consequences if missed. When investigating patients with cognitive impairment, even if HIV may seem unlikely, common sense (as well as national guidance<sup>8</sup>) suggests that we should test them all.

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