A consultant pharmacist reflects on the changes in HIV as a specialism: from the early days when those with HIV had few treatment options to the current management of the infection as a chronic condition

“The role of the HIV pharmacist in managing complex polypharmacy has never been more important”

By Leonie Swaden, MSc, MRPharmS

Over the past two decades I have been fortunate to work in one of the most diverse, controversial and continually challenging areas of healthcare.

HIV infection was once considered a death sentence but, through some of the most remarkable advances in clinical care seen in any area of medicine, it has been transformed into a long-term condition. In less than 30 years over 25 antiretroviral medicines (ARVs) have been licensed, but it is the way we use and combine these to produce efficacious, tolerable and convenient regimens that is continuously changing. The role of the HIV specialist pharmacist in supporting this complex patient group cannot be underestimated — forming an integral part of a truly multidisciplinary team.

In November 1989 I was appointed as a staff pharmacist for HIV medicine at the Royal Free Hospital, London. Working with the first HIV consultant to be appointed in the UK, Margaret Johnson, and haemophilia consultant Christine Lee, we looked after a group of 225 patients, including 111 HIV-positive haemophiliacs. In the first few years of my job we had only one antiretroviral medicine, the nucleoside reverse transcriptase inhibitor (NRTI) zidovudine — also known as AZT. Although patients’ symptoms and immune systems would initially improve with AZT, they would soon fail. We now know that this was due to the development of viral resistance. These observations were confirmed by the Concorde study in which the Royal Free participated.

**Fighting infections**

During this period much of our time was spent advising on the treatment of the many opportunistic infections associated with low CD4 counts (impaired immunity). Cytomegalovirus (CMV), one of the herpes group of virus, would often present with sight-threatening retinitis. Ganciclovir was used to treat CMV disease, but myelotoxicity, especially when given with AZT, could lead to severe neutropenia; this required a careful balancing of efficacy versus toxicity. Kaposis’s sarcoma, a virally driven cancer, could be treated with chemotherapy but would often relapse, spreading throughout the body and in many cases proving fatal.

It was frequently a case of treating one opportunistic infection and sending the patient home — only for him or her to return a few weeks later with relapse or a different infection. In addition, many patients had to take prophylactic medicines at home, eg, for CMV, and the pharmacist would have an important role in ensuring patients were dispensed home intravenous therapies and given support with administration (valganciclovir, the oral form of ganciclovir was not available).

At that time we had no intervention to prevent mother-to-child transmission (MTCT) of HIV, which occurred in around one quarter of pregnant HIV-positive women. Published in 1994, the ACTG 076 study showed this could be reduced by 67% by giving AZT to the mother during pregnancy and to the neonate after delivery as post-exposure prophylaxis. Developing this strategy, together with advances in ARV treatment over the next decade, would reduce MTCT to less than 1% in the UK.

**New options**

During the early 1990s other NRTIs were licensed although, individually, none showed significant advantage over AZT. The Delta study was instrumental in paving the way for the future of combination ARV therapy by showing that dual NRTI therapy delayed disease progression significantly compared with monotherapy, particularly when used first line. This quickly became standard care.

During 1995 and 1996 two new classes of ARV were licensed by the US Food and Drug Administration. The protease inhibitors (PIs) had a substantially higher barrier to resistance than other ARVs and quite literally rescued AIDS patients from their deathbeds. However, it was the use of nevirapine, a non-nucleoside reverse transcriptase inhibitor (NNRTI), for treatment-naive patients in combination with two NRTIs that truly changed HIV therapy. The combination of three ARVs — now referred to as highly active antiretroviral therapy (HAART) — has allowed HIV to be managed as a chronic disease. If treated appropriately, people with HIV can have an almost normal lifespan.
The advances in treatment of HIV meant that large numbers of patients were started on triple therapy, consisting of two NRTIs plus either a PI or an NNRTI. The improvement in people’s health was remarkable, enabling many who had been sick for years to become well enough to return to work.

Living with HAART

Although HAART was lifesaving, the reality in the late 1990s was that people’s lives often revolved around taking it. A combination of the NRTIs AZT and didanosine (DDI) with the PI indinavir required the AZT to be taken with or soon after food twice a day, while the didanosine and indinavir needed to be taken on an empty stomach twice and four times daily, respectively, and apart from each other. Specialist pharmacists would be central to helping people manage their medication. The early drugs also had some unpleasant side effects: severe diarrhoea in the case of the PI ritonavir, lipodystrophy from some early NRTIs and lactic acidosis associated with stavudine (D4T) and DDI were common. Nevertheless, people coped with these issues knowing the lifesaving effects of the drugs.

Over the past 10 years HAART has evolved dramatically. The use of ritonavir as a pharmacokinetic booster for other PIs such as atazanavir has reduced pill burden and dosing frequency. Once-daily HAART regimens are now routine. The development of further drug classes (integrase and fusion antagonists, along with more potent inhibitors, and CCR5-receptor antagonists), along with more potent PIs and NNRTIs, has transformed the way we treat drug-resistant HIV. Tolerability has also improved substantially, although toxicity is still the leading cause for changes in people’s regimens.

We are now using genetic tests to determine the likelihood of drug hypersensitivity reactions (eg, HLA-B*5701 testing for abacavir), drug resistance testing is now routine in guiding drug selection both before starting therapy and after viral failure, and therapeutic drug monitoring is used to tailor drug dosing to individual patients. Specialist pharmacists like myself have to interpret this information and select appropriate antiviral regimens. The PIs, in particular ritonavir, are potent inhibitors of cytochrome P450 isoenzymes and have complex interactions with other drugs, which require careful management.

As our patient cohort ages and increasingly develops comorbidities, the HIV pharmacist also has to manage complex medicines regimens. The management of cardiac complications of HIV, ARVs and age are further influenced by the drug interactions of statins and antiarrhythmics with ARVs. HIV can directly affect the kidneys, particularly in black populations, leading to renal failure; it can also accelerate liver damage in patients with hepatitis C co-infection. Solid organ transplantation is increasingly becoming the standard of care to manage these in the long term, with HIV pharmacists liaising with renal and hepatology colleagues to manage drug interactions between ARVs and immunosuppressants post-transplant.

Unimaginable

My career as a HIV pharmacist has changed unimaginably over the past 20 years. The number of patients we look after has increased more than tenfold but, unlike in the early years, the outlook for the vast majority is good. My role has expanded beyond just treating opportunistic infections and suppressing the virus. Providing specialist pharmacy advice to the consultants who conduct HIV-specific clinics for cardiology, lipid management, renal and bone disease, lymphoma, pregnancy and ageing is becoming increasingly routine.

Although arguably among the most cost-effective treatments, ARVs and associated treatments are expensive, so a major part of my work involves financial monitoring and development of clinical guidelines to ensure their appropriate use.

Greater involvement of primary care clinicians in managing long-term conditions unrelated to HIV disease means HIV specialist pharmacists will need frequently to liaise with GPs, community pharmacists and patients themselves to ensure medicines are prescribed safely. As prescribers, specialist pharmacists can lead clinics to help manage the large numbers of patients who are stabilised on therapy. Consultations can be carried out face to face, over the telephone or via email, with prescriptions being provided for home delivery of medicines, thus reducing costs and increasing patient convenience. These conversations provide opportunities to deal with medicines management issues and offer adherence support to patients who are on lifelong therapy.

We now rarely see deaths due to AIDS, but better drugs, more patients and greater life expectancy bring with them new challenges for the HIV pharmacy specialist.

References