

# The interplay of HIV and NTM-PD

**Maddy Crabbe — Medical Writer, Remedica Communications**

World AIDS Day is annually marked on December 1st. This global health awareness day was established in 1988 to support HIV-infected people and remember the estimated 40 million people who have died of AIDS-related illnesses since the beginning of the pandemic.<sup>1-4</sup> The advent of the COVID-19 pandemic brought with it increased concern about HIV and AIDS as health issues of global significance. The vulnerability of immunocompromised individuals, the psychosocial impacts of isolation, and reduced access to healthcare facilities in some countries created challenging circumstances for people living with HIV.<sup>5</sup> The COVID-19 pandemic highlighted the potential for respiratory tract infections to be a significant cause of morbidity and mortality in immunocompromised people.<sup>6</sup> For people living with HIV, the increased likelihood of treatment interruption because of social isolation and reduced access to healthcare facilities during the COVID-19 pandemic may lead to immune system compromise and loss of virologic suppression.<sup>7</sup>

Aside from COVID-19, well-characterised respiratory infections that have high mortality rates in people living with HIV include fungal, viral, or parasitic pneumonias and bacterial bronchitis.<sup>8,9</sup> A lesser known sign of advanced HIV infection is disseminated disease caused by non-tuberculous mycobacteria (NTM).<sup>10</sup> Non-tuberculous mycobacteria (NTM) are mycobacterial species other than those that cause tuberculosis (TB) or leprosy.<sup>11,12</sup> Disseminated NTM infections can affect the lungs, sinuses, lymph nodes, joints and muscles, and the central nervous system.<sup>11</sup> Non-tuberculous mycobacteria-associated pulmonary disease (NTM-PD) is the most common clinical manifestation of NTM infection.<sup>13</sup> Symptoms of NTM-PD include a persistent cough, fatigue, unintended weight loss, dyspnoea, haemoptysis, increased mucous production, and night sweats.<sup>14,15</sup>

The non-specific symptoms of NTM-PD make diagnosis challenging and this may lead to delays in receiving treatment. Survival rates of HIV-infected patients with NTM-PD are higher when appropriate antimicrobial therapy is administered.<sup>10</sup> NTM species are highly prevalent in environmental sources such as water and soil and can infect humans through inhalation of aerosolised droplets or inoculation due to mechanical trauma.<sup>16,17</sup>

NTM-PD can lead to extensive pulmonary damage and respiratory failure.<sup>14</sup> Species such as *M. avium* can cross bronchial mucosa and evade host immune responses, which may already be weak in a person living with HIV. The formation of biofilms contributes to the chronic character of NTM-PD, because this allows the bacteria to persist within the phagosome. Glycopeptidolipid molecules in the cell wall of NTM confer immunogenic properties by interacting with toll-like receptors (TLRs) that promote inflammatory responses.<sup>13,18,19</sup> Chronic inflammation in HIV is thought to be linked to gut microbiota dysbiosis, and is associated with increased risk of cardiovascular disease, osteoporosis, anaemia, and physical frailty.<sup>20</sup>

It is therefore important to diagnose and treat NTM-PD within HIV-positive populations who are vulnerable to severe pulmonary and systemic injury. An individual must satisfy specific clinical, radiographical, and microbiological criteria to be diagnosed with NTM-PD.<sup>15</sup>

HIV testing is recommended for all patients who are diagnosed with NTM-PD.<sup>21</sup> This allows physicians with experience of treating NTM-PD to collaborate with HIV specialists and devise the optimal treatment strategy for the patient. The clinically burdensome nature of managing NTM-PD with pharmacotherapy is associated with the need for at least 12 months of treatment.<sup>13,15</sup> Complicated multidrug regimens and treatment-related adverse events are key challenges for healthcare professionals in this therapy area.<sup>13</sup> With the incidence of NTM-PD infection increasing in places where tuberculosis (TB) is highly prevalent, it remains of paramount importance to investigate the interplay of NTM-PD and HIV, due to the similarities between radiographic and clinical features of NTM-PD and TB.<sup>16</sup> Misdiagnosis of TB (which is a leading cause of mortality in patients living with HIV)<sup>22</sup> has led to NTM-PD patients being inappropriately treated with anti-TB therapeutics which increase the risk of antibiotic resistance.<sup>12,23,24</sup>

World AIDS Day is an opportunity to evaluate society's progress in addressing one of the most critical health crises of a generation. Caring for people living with HIV requires knowledge of opportunistic infections that

may be caused by organisms such as NTM. Screening for NTM in people living with HIV will play a vital part in determining the most effective treatment strategy for each patient. Maintaining immune system function and achieving virologic suppression may be a more realistic prospect in the management of comorbid NTM-PD and HIV when appropriate information and training is made available to healthcare professionals who have a critical role in improving the standard of care for some of society's most clinically vulnerable individuals.

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